Transforming Medicine with the Unlimited Potential of iPS Cells

T-CiRA

Takeda-CiRA Joint Research Program
for iPS Cell Applications

What is T-CiRA?

CiRA × Takeda = ∞

Combined strengths, high hopes

T-CiRA is a 10-year joint research program launched in fiscal year 2016 by the Center for iPS Cell Research and Application (CiRA) at Kyoto University and Takeda Pharmaceutical Company Limited (Takeda). In Japan, it has traditionally been challenging to rapidly translate outstanding academic research into practical applications.
T-CiRA was created to bridge this gap between academia and industry.

By working together as one integrated team—as exemplified by T-CiRA—universities and pharmaceutical companies can accelerate and streamline the transition of research findings into clinical applications.
Within T-CiRA, about 100 researchers from CiRA and Takeda have collaborated over the past 10 years on diverse projects aimed at advancing iPS cell technologies toward clinical use. Their efforts span cancer, rare and refractory diseases, gastrointestinal disorders, and neurological conditions, driving the development of innovative therapeutic approaches—from human disease-modeling technologies and next-generation drug discovery platforms to cell therapies and gene-editing treatments.

The roles of CiRA and Takeda

〈CiRA〉

- To direct the research program
- To provide iPS (induced pluripotent stem) cell technologies
- To provide drug development targets and assay systems
- To provide principal investigators, researchers and postdoctoral fellows

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〈Takeda〉

- To provide collaborative funding of 20 billion yen over a 10-year period
- To provide more than 12 billion yen worth of research support
- To provide R&D know-how
- To provide research facilities at Shonan Health Innovation Park
- To provide platforms for drug discovery
- To provide access to compound libraries
- To provide researchers

*The T-CiRA program is managed and operated by the Global Advanced Platform at Takeda.

Executive Summary

The T-CiRA (Takeda-CiRA) Joint Research Program was established in partnership between Takeda Pharmaceutical Company Limited and the Center for iPS Cell Research and Application (CiRA) at Kyoto University, with the goal of creating innovative medical solutions utilizing iPS cell technology.
This summary presents the program's achievements, challenges, and strategic transitions as of 2025. T-CiRA has continuously pursued challenges across a broad spectrum, from basic research to clinical application, marking an important step forward for the future of regenerative medicine and drug discovery.

Technology transfer to Takeda Research

Four key assets/platforms have been transferred from the T-CiRA program to Takeda laboratories, all of which represented scientific and technological breakthroughs and were important steps that opened up possibilities for next-generation healthcare.
1) CD19-iCAR-T/iCAR-T Platform: The iCAR-T platform, which demonstrated antitumor efficacy in preclinical models with CD19-targeted iPS cell-derived CAR-T cells (CD19-iCAR-T), later became a platform in the field of cell therapy. 2) iENPs (Enteric Neural Progenitors): Developed for the treatment of Hirschsprung's disease, iENPs have demonstrated the potential to restore intestinal motility in organoid models, offering a new direction for regenerative medicine. 3) LNP-CRISPR technology: As an innovative genome editing approach for Duchenne muscular dystrophy (DMD), a method to deliver CRISPR-Cas9 in lipid nanoparticles (LNPs) has been established. Local therapeutic effects were confirmed and a new foundation for gene therapy was created. 4) iPS cell phenotype screening-derived compounds: We used iPS cell models derived from ALS and ASD patients to identify drug candidates and proposed a new perspective in disease understanding and drug discovery strategies.

Establishment of new company and externalization

Orizuru Therapeutics, Inc. (Orizuru) was established on April 9, 2021, mainly by the members of the β-cell project and the cardiomyocyte project. The company inherited all the data, intellectual property and technology from these projects.
Clinical trials of β-cell therapies began in 2025 and have achieved First Patient In status. Cardiomyocyte technology is being developed as a potential radical treatment for severe chronic heart failure.
Takeda licensed the rights to the iCAR-T platform to Alloy under a collaboration and licensing agreement signed in 2024.
Alloy is leveraging a unique business model to expand access to technologies for the partners, including academia and bio-venture companies, to develop cancer treatments, including solid tumors.

Publication

The T-CiRA program has contributed significantly to the advancement of iPS cell-based therapies and drug discovery with numerous high-impact publications. Key results included:

1.Minagawa, A. et al. Enhancing T Cell Receptor Stability in Rejuvenated iPSC-Derived T Cells Improves Their Use in Cancer Immunotherapy. Cell Stem Cell 23, 850-858 e854 (2018).
2.Gee, P. et al. Extracellular nanovesicles for packaging of CRISPR-Cas9 protein and sgRNA to induce therapeutic exon skipping. Nat Commun 11, 1334 (2020).
3.Koido, M. et al. Polygenic architecture informs potential vulnerability to drug-induced liver injury. Nat Med 26, 1541-1548 (2020).
4.Iriguchi, S. et al. A clinically applicable and scalable method to regenerate T-cells from iPSCs for off-the-shelf T-cell immunotherapy. Nat Commun 12, 430 (2021).
5.Kenjo, E. et al. Low immunogenicity of LNP allows repeated administrations of CRISPR-Cas9 mRNA into skeletal muscle in mice. Nat Commun 12, 7101 (2021).
6.Miki, K. et al. ERRgamma enhances cardiac maturation with T-tubule formation in human iPSC-derived cardiomy ocytes. Nat Commun 12, 3596 (2021).
7.Yoshida, Y. et al. Loss of peptide:N-glycanase causes proteasome dysfunction mediated by a sugar-recognizing ubiquitin ligase. Proc Natl Acad Sci USA 118 (2021).
8.Taha, E. A., Lee, J. & Hotta, A. Delivery of CRISPR-Cas tools for in vivo genome editing therapy: Trends and challenges. J Control Release 342, 345-361 (2022).
9.Kawakami, E. et al. Complement factor D targeting protects endotheliopathy in organoid and monkey models of COVID-19. Cell Stem Cell 30, 1315-1330 e1310 (2023).
10.Hiyoshi, H. et al. Identification and removal of unexpected proliferative off-target cells emerging after iPSC-derived pancreatic islet cell implantation. Proc Natl Acad Sci U S A 121, e2320883121 (2024).
11.Yano, H. et al. Human iPSC-derived CD4(+) Treg-like cells engineered with chimeric antigen receptors control GvHD in a xenograft model. Cell Stem Cell 31, 795-802 e796 (2024).
12 .Saiki, N. et al. Self-organization of sinusoidal vessels in pluripotent stem cell-derived human liver bud organoids. Nat. Biomed. Eng. (2025).

Looking back on 10 years of T-CiRA

If I were to describe the 10 years of T-CiRA in a single word, it would be “an unconventional industry academia collaboration.”

From the very beginning, everything about this partnership was unconventional. About ten years ago, I met Christophe Weber, Takeda’s CEO, during his visit to CiRA. I still vividly remember being surprised by one of the first things he told me. He said, “The first thing I did after coming to Japan was to climb Mt. Fuji, carry skis to the summit, and ski down in one go.”

He then asked me, “We would like to conduct joint research between Takeda and CiRA. What scale would be best—large, medium, or small?”

I answered without hesitation, “Large, please.”

And with that, T-CiRA was launched. Normally, reaching an agreement for a large scale collaboration takes considerable time, yet under the strong leadership of the CEO, the contract was finalized within just a few months.

Afterward, Dr. Seigo Izumo, who became responsible for Takeda’s side, selected promising projects—such as cardiac and pancreatic islet regenerative medicine—from among CiRA’s young PIs. Dr. Izumo had previously been a professor at Harvard University, and I myself once applied to his lab as a postdoc candidate. Many years later, to be able to work together again on a major industry academia collaboration felt deeply meaningful to me.

Even after T-CiRA was launched, a number of “unconventional” developments continued. Takeda implemented a major strategic shift and removed cardiovascular diseases and diabetes from its development focus areas. The Shonan Research Institute, once one of Takeda’s key research sites, transitioned to iPark, and the facilities—previously all red—turned blue. The Takeda leadership overseeing T-CiRA also changed several times.

Despite these unforeseen changes, T-CiRA members—led by Mr. Yasushi Kajii—steadily advanced the project. As research and development progressed, there was less I, as a basic researcher, could contribute directly, but I was continually excited to see the achievements being made. The projects in heart and diabetes have progressed toward social implementation through Orizuru Therapeutics Inc., a venture company originating from T-CiRA, and several other projects have continued in various forms.

Our ability to sustain this partnership for 10 years has been thanks to the unwavering support of Mr. Christophe Weber and Dr. Andy Plump, as well as the tireless dedication of all T-CiRA members, including Mr. Yasushi Kajii. For those of us in academia, having the opportunity to witness the front lines of drug development , firsthand has been a truly irreplaceable experience.

I would like to express my heartfelt gratitude to everyone involved in T-CiRA and wish continued success for all.

Shinya Yamanaka
T-CiRA Director
Honorary Director and Professor
Center for iPS Cell Research and Application,Kyoto University (CiRA)

T-CiRA, a bridge to the next generation therapeutics

iPS cell technology has a wide range of potential to realize medical innovation. Takeda ran T-CiRA, a 10-year industry-academia collaboration program, in order to apply this wonderful technology discovered by Professor Yamanaka to drug discovery. We welcomed outstanding researchers from leading research institutions in Japan, Kyoto University Center for iPS Cell Research and Application, RIKEN and Institute of Tokyo Science, to our Shonan Research Center as Principal Investigators, who worked with Takeda researchers to solve various challenges in drug discovery. The iPS cell therapy has the potential to realize off-the-shelf medical treatment that overcomes the limitations of conventional primary cells. Some outcomes from T-CiRA have been transferred to Orizuru Therapeutics, Inc. and the other one has led to a strategic partnership with Alloy Therapeutics, Inc., preparing for social implementation. We are also developing new experimental platforms that can reproduce some of the functions of the human body at a high level, such as iPS neural networks and various organoids. Such new drug evaluation systems, combined with automation technology and rapidly evolving AI technology, have laid the foundation for a next-generation drug discovery platform. T-CiRA also made some important discoveries related to diseases for which there is a high social demand for treatments, such as COVID-19 and rare diseases. Indeed, one of these has actually become the scientific basis for conducting clinical trials for an ultra-rare disease. On top of these achievements, the researchers/scientists who have participated in the T-CiRA program from both industry and academia are active in a variety of organizations, including startups, demonstrating this program has made a significant contribution to developing the excellent human resources that support the drug discovery ecosystem. Although the outcomes from T-CiRA have not yet been directly implemented in society, we are proud that we have fully played a role in building a bridge to the realization of next-generation medical treatments, and we would like to express our sincere gratitude to everyone who participated in the program.

Yasushi Kajii
R&D Japan Region Head
Takeda Pharmaceutical Company Limited

T-CiRA's Values

Vision

A world with the prospect of better health through the infinite power of science

Purpose

Transform medicine with the unlimited potential of iPS cells

Mission

Discover the seeds of treatment options and nurture them for clinical applications

Identity

INNOVATORS
Opening up new possibilities in healthcare without fear of failure

PIONEERS
Always keeping up with patients' needs using the wisdom of science

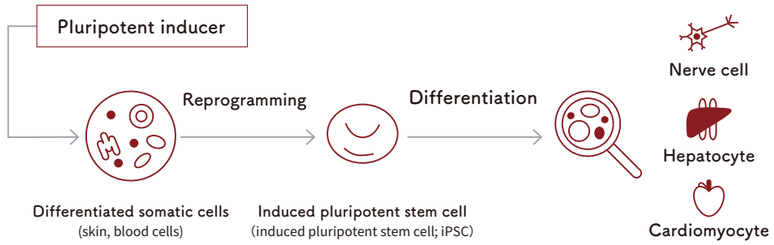
SCIENTISTS
Conducting next-generation research for drug discovery within an industry-academia collaboration

What We Do

Transform medicine with the unlimited potential of iPS cells

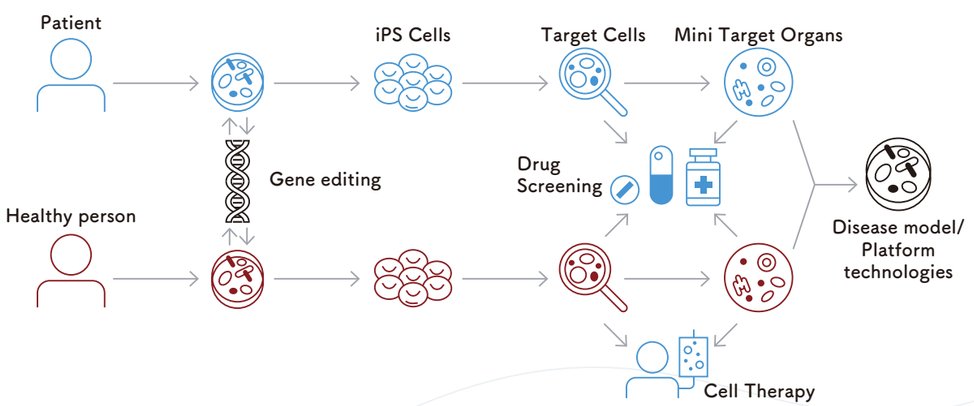
What are iPS cells?

Induced pluripotent stem cells (iPS cells) are created by introducing specific reprogramming factors into somatic cells, such as skin or blood cells. These iPS cells have the ability to differentiate into multiple cell types.



Innovative Research Conducted using iPS Cell Technologies

T-CiRA is conducting cutting-edge research into the clinical applications of iPS cells in drug discoveries,cell therapies and platform technologies. In vitro human disease models based on iPS cells and mini-organoid cells (known as "diseases in a dish") help scientists and physicians understand the pathophysiology or mechanism of various diseases. iPS cell-derived cells or mini organs are used to screen drugs in both efficacy and potential safety assessments. We also expect applications in regenerative medicine and transplanting iPS cell-derived cells, tissues or mini organs.



Key research areas

At T-CiRA, we have applied iPS cell technology to projects in diverse fields, including cancer, refractory muscle diseases, gastrointestinal diseases, and neurological disorders.

Human iPS cells

Cell type	Research subjects	Category		
Immune cell T cell	• Cancer • Autoimmune disorders • Allogeneic transplant rejection	Cell therapy		Shin Kaneko CiRA
Intestinal nerve Intestinal organoid Renal fibrosis model Kidney organoid	• Hirschsprung's disease • Renal fibrosis • Renal toxicity assessment	Cell therapy Basic technology Drug discovery		Makoto Ikeya CiRA
Liver organoid	• Coagulation and complement disorders • Drug-induced liver injury	Basic technology Drug discovery		Takanori Takebe Institute of Science Tokyo
Skeletal muscle cell	• Duchenne muscular dystrophy	Gene editing therapy		Akitsu Hotta CiRA
Cardiomyocyte	• Hypertrophic and dilated cardiomyopathy	Basic technology		Yoshinori Yoshida CiRA
Motor neuron cell Cortical neuron cell Astrocyte Brain organoid	• Amyotrophic lateral sclerosis (ALS) • Autism spectrum disorder (ASD)	Basic technology		Haruhisa Inoue CiRA
Motor neuron cell Brain organoid	• NGLY1 deficiency	Basic technology		Tadashi Suzuki RIKEN

As of 2023

Driving Our Mission Forward

At T-CiRA, researchers from academia and Takeda work together as one team to accelerate research aimed at developing cell-therapy and drug-discovery platforms.
Established in fiscal year 2016 as a 10-year program, T-CiRA has since proven itself as a source of innovation in iPS cell technologies by consistently delivering achievements and meaningful outcomes.
Our mission is to discover seeds of new treatment options and nurture them into therapies that can be applied clinically.
To fulfill this mission, we are committed to overcoming challenges and transforming innovative ideas into medical discoveries and real-world applications.

T-cell therapy project

Shin Kaneko
CiRA

This project aimed to develop allogeneic, off-the-shelf immune cell therapy products by combining allogeneic iPS cell technology and autologous CAR-T cell therapy, which was beginning to show clinical efficacy at the time. Multiple processes previously developed in Professor Kaneko's laboratory at CiRA, Kyoto University, were integrated to establish a feeder-free T cell manufacturing protocol:

- Feeder-free culture of iPS cells
- Introduction of TCR genes into iPS cells derived from non-T cell sources
- Differentiation of iPS cells into hematopoietic progenitor cells
- Differentiation of hematopoietic progenitors into immature T cells
- Maturation of immature T cells
- Expansion of T cells

Through the T-CiRA collaboration, we successfully improved and optimized the entire manufacturing process, including TCR gene introduction, purification of immature T cells, T cell differentiation, and expansion.
Furthermore, we developed protocols for CAR gene introduction and established a method for producing CD19-targeted CAR-T cells. Technologies to enhance antitumor efficacy and optimize evaluation methods for efficacy, safety, and *in vivo* cellular kinetics of iCAR-T cells were also developed. As a result, CD19-targeted iPSC-derived CAR-T cells (CD19-iCAR-T) demonstrated antitumor effects in a mouse xenograft model.

Technology transfer to Takeda Research

CD19-iCAR-T cells were transferred to Takeda Oncology's portfolio, and the iCAR-T platform became one of Takeda's cell therapy platforms. Some project members joined Takeda's research division to contribute to asset and platform development, with Professor Kaneko serving as a Scientific Advisor to Takeda. However, for business reasons, development of CD19-targeted iCAR-T was discontinued, and the focus shifted to developing mesothelin-targeted iCAR-T for solid tumors. Although the manufacturing process for first-in-human studies was established and preclinical preparations were completed, a business decision was made to externalize both the assets and the platform.
The rights to the iCAR-T platform were licensed to Alloy Therapeutics based on a collaboration and licensing agreement concluded between Takeda and Alloy in 2024.

Publication

01.Minagawa, A. et al. Enhancing T Cell Receptor Stability in Rejuvenated iPSC-Derived T Cells Improves Their Use in Cancer Immunotherapy. Cell Stem Cell 23, 850-858 e854 (2018).
02.Iriguchi, S. et al. A clinically applicable and scalable method to regenerate T-cells from iPSCs for off-the-shelf T-cell immunotherapy. Nat Commun 12, 430 (2021).
03.Ishiguro, Y. et al. Lineage tracing of T cell differentiation from T-iPSC by 2D feeder-free culture and 3D organoid culture. Front Immunol 14, 1303713 (2023).
04.Kassai, Y. Current status and prospects of immune system organoids: application to immune cell therapy and disease models. Experimental Medicine 42, 744-749 (2024).

Immune tolerance project

Shin Kaneko
CiRA

This project aimed to generate immune cells capable of inducing immune tolerance and immunosuppression, with the goal of establishing next-generation immune cell therapies. After the transfer of the iCAR-T platform to Takeda, the research focus shifted toward exploring the potential of novel immune cell therapies, with particular attention given to two distinct cell types.
The first is ProT cells. ProT cells differentiate extrathymically and possess the capacity to further differentiate into lymphocytes, migrating to the thymus and maturing into functional T cells. We established a protocol for differentiating iPS cells into ProT cells and demonstrated that, upon transplantation into neonatal mice, these cells engraft in the thymus and give rise to a diverse repertoire of T cells. Furthermore, by introducing the CD19-CAR gene into ProT cells and administering them to mice, we confirmed that these cells differentiated into T cells with CD19-CAR-specific antitumor activity.
The second is Treg cells. Treg cells are CD25+ CD4+ T cells endowed with potent immunosuppressive functions. We developed a novel T cell differentiation method, enabling the generation of Treg cells from differentiated T cells. These Treg cells exhibited robust anti-GvHD activity in a GvHD mouse model. In addition, we advanced protocols for xenogeneic-free manufacturing and enhanced the stability and immunosuppressive function of these Treg cells.

Publication

01.Yano, H. et al. Human iPSC-derived CD4(+) Treg-like cells engineered with chimeric antigen receptors control GvHD in a xenograft model. Cell Stem Cell 31, 795-802 e796 (2024).

Muscular dystrophy project

Hidetoshi Sakurai
CiRA

The following important results were obtained through the joint research, which is an important step toward realizing innovative therapies for refractory muscle diseases.

• We have established a protocol to stably induce differentiation of mature skeletal muscle cells from iPS cells. This enabled the development of a drug discovery screening platform using muscle cells obtained from patient-derived iPS cells, which advanced the search for compounds as treatment candidates for refractory muscle diseases.

• Screening with this platform led to the identification of several hit compounds, as well as potential biomarkers for these diseases.

Publication

01.Kokubu, Y. et al. Phenotypic Drug Screening for Dysferlinopathy Using Patient-Derived Induced Pluripotent Stem Cells. Stem Cells Transl Med 8, 1017-1029 (2019).
02.Takada, H. et al. Identification of 2,6-Disubstituted 3H-Imidazo[4,5-b]pyridines as Therapeutic Agents for Dysferlinopathies through Phenotypic Screening on Patient-Derived Induced Pluripotent Stem Cells. J Med Chem 62, 9175-9187 (2019). https://doi.org/10.1021/acs.jmedchem.9b01100
03.Gee, P. et al. Extracellular nanovesicles for packaging of CRISPR-Cas9 protein and sgRNA to induce therapeutic exon skipping. Nat Commun 11, 1334 (2020).
04.Uchimura, T., Asano, T., Nakata, T., Hotta, A. & Sakurai, H. A muscle fatigue-like contractile decline was recapitulated using skeletal myotubes from Duchenne muscular dystrophy patient-derived iPSCs. Cell Rep Med 2, 100298 (2021).
05.Uchimura, T. & Sakurai, H. Orai1-STIM1 Regulates Increased Ca(2+) Mobilization, Leading to Contractile Duchenne Muscular Dystrophy Phenotypes in Patient-Derived Induced Pluripotent Stem Cells. Biomedicines 9 (2021).

ALS/ASD project

Haruhisa Inoue
CiRA

The aim of this project was to identify therapeutic candidates for amyotrophic lateral sclerosis (ALS) and autism spectrum disorder (ASD), both of which represent areas of significant unmet medical need. For ALS and ASD, disease models were constructed using motor neurons and cerebral cortical neurons differentiated from disease-specific iPS cells possessed by CiRA, and compound screening was conducted using Takeda's proprietary compound library.

For ALS research, we developed a high-throughput screening platform using key cellular phenotypes—including motor neuron death, splicing alterations, RNA foci, and abnormal protein aggregation—as primary indicators. Furthermore, by integrating AI-driven hit prediction models, we successfully identified multiple promising compounds that effectively suppress neuronal cell death.

For ASD research, we observed impaired neurite outgrowth and abnormal electrophysiological activity in cerebral cortical neurons differentiated from ASD patient-derived iPS cells. Screening platforms designed to improve these cellular phenotypes were subsequently established, leading to the identification of candidate compounds capable of ameliorating neurite outgrowth deficits and functional abnormalities.

Technology transfer to Takeda Research

In this project, compounds targeting cell death associated with mutant SOD1 and sporadic ALS, as well as antisense nucleic acids and small-molecule compounds directed against C9orf72 repeat expansion, were transferred to Takeda laboratories for further development. Following comprehensive safety evaluations and an integrated assessment of business strategy, the above assets—while having achieved certain milestones—were concluded at this stage rather than advanced to the next development step.

Publication

01. Hidaka, T. et al. Prediction of Compound Bioactivities Using Heat-Diffusion Equation. Patterns (N Y) 1, 100140 (2020).
02. Shibata, K., Imamura, K., Yukitake, H. & Inoue, H. A study of autism and dementia using iPS cells. Cell 53, 671-675 (2021).
03. Maezawa, M., Yukitake, H., Imamura, K. & Inoue, H. Research on neurodegenerative diseases using iPS cell data and artificial intelligence. Experimental Medicine 41, 2531-2536 (2023).
04.Munezane, H. et al. Elimination of the extra chromosome of Dup15q syndrome iPSCs for cellular and molecular investigation. Eur J Cell Biol 103, 151446 (2024).

Cardiomyocyte project

Yoshinori Yoshida
CiRA

This project used iPS cell-derived cardiomyocytes to advance the development of a new treatment strategy for heart disease.
In our cell therapy program, we have established a scalable bioreactor culture system and small molecule purification technology to stably produce cardiomyocytes that can be used in the clinic.
In our drug discovery program, we developed in vitro models of anticancer drug-induced cardiotoxicity and a scoring algorithm to quantify morphological changes. These efforts have led to the identification of compounds that improve myocardial contractility, and improved survival in mouse models. Furthermore, candidate compounds with antihypertrophic effect were identified using genome-edited iPS cell-derived cardiomyocytes that mimic hypertrophic cardiomyopathy (HCM), and their in vivo efficacy was also verified.
Basic research has also advanced to the development of reporter cell lines to monitor maturation of cardiac myocytes, and ERRγ agonists have shown promise as maturation-promoting factors. A dual-parameter assay system was also established to assess electrophysiological properties. In addition, CD151 was identified as an atrial-specific marker , and a novel gene was identified whose expression drives the maturation and engraftment of iPSC cardiomyocytes.

Establishment of NewCo (new company)

Cell purification technologies using low molecular weight compounds and manufacturing technologies for iPS cell-derived cardiomyocytes with high purity and clinical-grade safety, established in our cell therapy program, were transferred to the iCM Division of Orizuru Therapeutics, Inc. These technologies are currently being developed as potential curative treatments for severe chronic heart failure.

Publication

01.Miki, K. et al. ERRgamma enhances cardiac maturation with T-tubule formation in human iPSC-derived cardiomyocytes. Nat Commun 12, 3596 (2021).
02.Yoshida, Y. et al. Loss of peptide:N-glycanase causes proteasome dysfunction mediated by a sugar-recognizing ubiquitin ligase. Proc Natl Acad Sci U S A 118 (2021).
03.Fujiwara, Y. et al. ERRgamma agonist under mechanical stretching manifests hypertrophic cardiomyopathy phenotypes of engineered cardiac tissue through maturation. Stem Cell Reports 18, 2108-2122 (2023).
04.Fujihira, H. et al. ELISA-based highly sensitive assay system for the detection of endogenous NGLY1 activity. Biochem Biophys Res Commun 710, 149826 (2024).
05.Nakanishi-Koakutsu, M. et al. CD151 expression marks atrial- and ventricular- differentiation from human induced pluripotent stem cells. Commun Biol 7, 231 (2024).
06.Fujiwara, Y. et al. A polystyrene-film-based device for engineered cardiac tissues enables accurate analysis of drug responses on contractile properties. Lab Chip (2025).
07.Takaki, T. et al. Simultaneous optical recording of action potentials and calcium transients in cardiac single cells differentiated from type 1 CPVT-iPS cells. Front Physiol 16, 1579815 (2025).

Neural crest cell project

Makoto Ikeya
CiRA

Neural Crest Cells (NCCs) are very unique cells that exist only in the early stages of development and have the ability to differentiate into various cell types such as bone and peripheral nerves. However, their biological properties remain largely unknown. This project involved the use of a differentiation protocol developed by Associate Professor Makoto Ikeya of CiRA to induce iNCC from iPS cells and a series of studies aimed at expanding the possibilities of therapeutic applications of neural crest cells.
1.We have established a robust culture system that maintains the multiple differentiation potential of iPS cell-derived neural crest cells (iNCCs).
2.We have developed a method to produce intestinal neural progenitor cells from NCCs. These cells can be stably maintained in vitro and have been shown to differentiate into various intestinal neurons and synapse with native neurons in mice.
3.We successfully created renal stromal cells and identified several molecules involved in renal fibrosis. These molecules have shown promise as new drug discovery targets.
4.We established a differentiation protocol to mesenchymal stem cells (MSCs) and demonstrated that the obtained MSCs exhibit immunosuppressive properties.

Technology transfer to Takeda Research

The development of intestinal neural progenitor cells is a joint development with Takeda's research laboratories as a potential cell therapy for Hirschsprung's disease. Validation using iPS cell-derived intestinal organoids as a disease model showed that intestinal neural progenitor cells effectively contribute to the restoration of intestinal motor function. However, this project was eventually terminated due to a business strategic decision.

Publication

01.Kamiya, D. et al. Induction of functional xeno-free MSCs from human iPSCs via a neural crest cell lineage. NPJ Regen Med 7, 47 (2022).
02.Kamiya, D. et al. Generation of human GAPDH knock-in reporter iPSC lines for stable expression of tdTomato in pluripotent and differentiated culture conditions. Stem Cell Res 60, 102704 (2022).
03.Yamashita, T. et al. Generation of a human SOX10 knock-in reporter iPSC line for visualization of neural crest cell differentiation. Stem Cell Res 60, 102696 (2022).

In vivo genome editing treatment project for Duchenne muscular dystrophy

Akitsu Hotta
CiRA

Duchenne muscular dystrophy (DMD) is the most common and severe genetic disorder among muscular dystrophies affecting children. While therapeutic options such as small molecule compounds, antisense nucleic acids, and gene therapy are emerging, no cure currently exists. This project aimed to create novel therapies that directly target the genetic mutation causing DMD. We focused on developing methods to safely and efficiently deliver genome editing tool, which specifically modifies target sequences, into skeletal muscle.

Building upon an optimized mutation repair method using iPS cells derived from DMD patients, the T-CiRA project primarily focused on developing delivery technologies. In addition to conventional viral vector methods, we developed protein delivery using virus-like particles (VLPs), direct protein delivery, and mRNA delivery using lipid nanoparticles (LNPs). Using DMD model mice with partial replacement of the mouse target gene with patient-derived sequences, and reporter mice that luminescence upon successful gene modification, we successfully demonstrated therapeutic effects through intramuscular administration.

Furthermore, by administering LNP to DMD model mice via limb perfusion, therapeutic effects were confirmed in a broader range of skeletal muscles. Moving forward, we aim to further develop these delivery technologies and collaborate with external partners to advance the development of genome editing therapies for DMD.

Publication

01.Ifuku, M. & Hotta, A. New development by fusion of iPS cells and genome editing. Japanese Journal of Clinical Medicine 75: 788-794 (2017).
02.Makita, Y., Hozumi, H. & Hotta, A. Feature: Frontier of Muscle Research Topics: Development trends of genome editing technology for the treatment of muscular dystrophy. CLINICAL CALCIUM 27: 391-399 (2017).
03.Ifuku, M., Iwabuchi, K. A., Tanaka, M., Lung, M. S. Y. & Hotta, A. Restoration of Dystrophin Protein Expression by Exon Skipping Utilizing CRISPR-Cas9 in Myoblasts Derived from DMD Patient iPS Cells. Methods Mol Biol 1828, 191-297 (2018).
04.Iwabuchi, K. A. & Hotta, A. Current status of genome editing technologies and their applications. Hematology Frontier 28: 343-352 (2018).
05.Iwabuchi, K.A. & Hotta, A. Genome editing as a therapeutic strategy for Duchenne muscular dystrophy. DOJIN BIOSCIENCE SERIES 29 Genome editing for medical applications - From latest trends to technical and ethical issues-, 122-136 (2018).
06.Gee, P. et al. Extracellular nanovesicles for packaging of CRISPR-Cas9 protein and sgRNA to induce therapeutic exon skipping. Nat Commun 11, 1334 (2020).
07.Kita, Y., Iwabuchi, K. A. & Hotta, A. Development of genome editing technology and its application to neuromuscular diseases. Clinical Neuroscience 38, 323-329 (2020).
08.Kenjo, E. et al. Low immunogenicity of LNP allows repeated administrations of CRISPR-Cas9 mRNA into skeletal muscle in mice. Nat Commun 12,7101(2021)
09.Taha, E. A., Lee, J. & Hotta, A. Delivery of CRISPR-Cas tools for in vivo genome editing therapy: Trends and challenges. J Control Release 342, 345-361 (2022).
10.Kitabatake, Y. & Inukai, N. Emerging Medical Applications of Genome Editing. Experimental Medicine 42, (2024).
11.Mochida, T., Fujimoto, N., Asahina, M., Asano, S., Araki, S., Inukai, N. & Hotta, A. Editing of muscle satellite cells by LNP-CRISPR-Cas9 to resist muscle injury. Cell Reports, 45, 116695 (2025).

Organoid medicine project

Takanori Takebe
Institute of Science Tokyo

Building upon the liver organoid technology using iPS cells developed by Professor Takebe's group, T-CiRA conducted studies aimed at further pharmaceutical application involving drug safety, development and therapeutic investigations. The key highlights are:

1. Prediction of Drug-Induced Liver Injury (DILI): We successfully demonstrated, for the first time, that Poly genic Risk Scores (PRS) can predict DILI susceptibility. This was achieved by combining human iPS cell-de rived organoids, human primary hepatocytes and clinical datasets. This integration of PRS with in vitro liver panels in toxicology screening paves the way for precision medicine by accurately predicting individu al disease risks in drug discovery.
2. Vascularized Liver Organoids: We developed a system to drive the differentiation of human iPS cells into CD34-positive hepatic sinusoidal progenitor cells. The newly developed Inverted Multilayered Air-Liquid Interface (IMALI) culture method allowed for the self-organization of four disntinct lineages: hepatic endo derm, mesenchyme, arterial, and sinusoidal progenitors. This led to the symbiotic generation of a organ-specific vascular network embedded in adjacent parenchymal cells, resulting in mature and vascu larized liver tissue formation upon orthotopic transplant.
3. Organoid based Therapeutic: coagulation factors derived from these sinusoidal organoids complemented the clotting capacity of plasma deficient in factors V, VIII, IX, and XI. Furthermore, they improved the bleed ing tendency in hemophilia A model mice via culture supernatant infusion or direct transplantation. This technology is expected to deepen our understanding of organ-specific vasculatures, and promote organ oid maturity and structural organization, ultimately towards therapy.

Publication

01.Koido, M. et al. Polygenic architecture informs potential vulnerability to drug-induced liver injury. Nat Med 26, 1541-1548 (2020).
02.Saiki, N. et al. Self-organization of sinusoidal vessels in pluripotent stem cell-derived human liver bud organoids. Nat. Biomed. Eng. (2025).
03.Kawamura, S. et al. Modeling antithymocyte globulin-induced microvasculopathy using human iPSC-derived vascularized liver organoids. Cell Rep. Med. 102433 (2025).
04.Kawakami, E. & Takebe, T. iPS drug discovery strategy using liver organoid technology. Cell 51, 173-177 (2019).
05.Nio, Y. & Takebe, T. Organoid Models of Development and Disease Towards Therapy. (Springer Nature eBOOK, 2019).
06.Saiki, N. & Takebe, T. Single cell analysis of liver organoids. Experimental Medicine 37, 61-67 (2019).
07.Oohori, M., Nio, Y., Kawakami, E. & Takebe, T. Feasibility and issues of organoid medicine. Experimental Medicine 38, 44-49 (2020).
08.Funata, M., Nio, Y., Erion, D. M., Thompson, W. L. & Takebe, T. The promise of human organoids in the digestive system. Cell Death Differ 28, 84-94 (2021).
09.Kawakami, E. & Takebe, T. My medicine with liver organoids. Journal of Clinical and Experimental Medicine 276, 86-92 (2021).
10.Nio, Y., Oohori, M. & Takebe, T. Frontier of liver fibrosis research using stem cells/organoids. Journal of Clinical and Experimental Medicine 279, 777-781 (2021).
11.Funata, M., Nio, Y. & Takebe, T. Frontier of human organoid research in the liver. Experimental Medicine 39: 2870-2876 (2021).
12.Saiki, N. & Takebe, T. Frontier of biliary tract disease research Frontier of liver organoid research. Gastroenterology & Hepatology 11, 1-9 (2022).

NGLY1 deficiency project

Tadashi Suzuki
RIKEN

We established NGLY1-deficient rats and mice for the first time in the world. Using these animals, the pharmacological effect of adeno-associated virus carrying the NGLY1 gene (NGLY1-AAV) was verified, and it was confirmed that NGLY1-AAV improved several symptoms. This achievement was shared with the Grace Science Foundation (GSF) in the United States and led to the initiation of a clinical trial (GS-100) by GSF.
Analysis of NGLY1-deficient mice revealed that oxytocin inhibits epileptiform symptoms. Motor neurons and organoids were produced using iPS cells derived from patients with NGLY1 deficiency, and the mechanism was analyzed at the cellular level. In addition, drug repositioning was performed to improve the observed abnormalities.
We developed multiple techniques to detect biomarkers of NGLY1 deficiency that were used to raise awareness among pediatric neurologists and search for potential patients. As a result, the first case report was made in Japan in 2023.

Publication

01.Asahina, M. et al. Ngly1 -/- rats develop neurodegenerative phenotypes and pathological abnormalities in their peripheral and central nervous systems. Hum Mol Genet 29, 1635-1647 (2020).
02.Asahina, M. et al. JF1/B6F1 Ngly1(-/-) mouse as an isogenic animal model of NGLY1 deficiency. Proc Jpn Acad Ser B Phys Biol Sci 97, 89-102 (2021).
03.Asahina, M. et al. Reversibility of motor dysfunction in the rat model of NGLY1 deficiency. Mol Brain 14, 91 (2021).
04.Yoshida, Y. et al. Loss of peptide:N-glycanase causes proteasome dysfunction mediated by a sugar-recognizing ubiquitin ligase. Proc Natl Acad Sci U S A 118 (2021).
05.Fujihira, H., Asahina, M. & Suzuki, T. Physiological importance of NGLY1, as revealed by rodent model analyses. J Biochem 171, 161-167 (2022).
06.Hirayama, H. & Suzuki, T. Assay for the peptide:N-glycanase/NGLY1 and disease-specific biomarkers for diagnosing NGLY1 deficiency. J Biochem 171, 169-176 (2022).
07.Hirayama, H., Tachida, Y., Seino, J. & Suzuki, T. A method for assaying peptide: N-glycanase/N-glycanase 1 activities in crude extracts using an N-glycosylated cyclopeptide. Glycobiology 32, 110-122 (2022).
08.Tachida, Y., Hirayama, H. & Suzuki, T. Amino acid editing of NFE2L1 by PNGase causes abnormal mobility on SDS-PAGE. Biochim Biophys Acta Gen Subj 1867, 130494 (2023).
09.Fujihira, H. et al. ELISA-based highly sensitive assay system for the detection of endogenous NGLY1 activity. Biochem Biophys Res Commun 710, 149826 (2024).
10.Hirayama, H. et al. Development of a fluorescence and quencher-based FRET assay for detection of endogenous peptide:N-glycanase/NGLY1 activity. J Biol Chem 300, 107121 (2024).
11.Makita, Y., Asahina, M., Fujinawa, R., Yukitake, H. & Suzuki, T. Intranasal oxytocin suppresses seizure-like behaviors in a mouse model of NGLY1 deficiency. Commun Biol 7, 460 (2024).
12.Yang K. et al. The STING pathway drives noninflammatory neurodegeneration in NGLY1 deficiency. J Exp Med. 222(10), e20242296. (2025). doi: 10.1084/jem.20242296.

β cell project

Taro Toyoda
CiRA

iPS cell-derived pancreatic islet cells (iPIC) for allogeneic transplantation that secrete insulin according to blood glucose levels were established based on a method for induction of pancreatic differentiation (Stem Cell Res. 2015; 14:185-97) developed by Junior Associate Professor Taro Toyoda of Kyoto University CiRA. To demonstrate the efficacy of iPIC in large animals, we developed a unique model of diabetic immunodeficiency in pigs. Furthermore, using gene expression profiling, we established a purification method that selectively removes unintended cells that are sometimes observed during the manufacturing process of iPICs, and collaborated with a manufacturer to develop a culture bag to produce large amounts of homogeneous pancreatic islet cells. These are important foundations for moving to clinical research.

Establishment of NewCo (new company)

A startup company, Orizuru Therapeutics, Inc. (Orizuru Inc.) was established on April 9, 2021, mainly by the members of the β-cell project and the cardiomyocyte project of T-CiRA. Based on the results of these projects, our goal is to develop iPSC-derived cell therapies. All data, intellectual property(IP), materials, and technology from the β-cell project were transferred to Orizuru for development to initiate a clinical trial. The clinical trial started in 2025, and enrollment has been completed.

Publication

01.Mochida, T. et al. Insulin-Deficient Diabetic Condition Upregulates the Insulin-Secreting Capacity of Human Induced Pluripotent Stem Cell-Derived Pancreatic Endocrine Progenitor Cells After Implantation in Mice. Diabetes 69, 634-646 (2020).
02.Hiyoshi, H. et al. Characterization and reduction of non-endocrine cells accompanying islet-like endocrine cells differentiated from human iPSC. Sci Rep 12, 4740 (2022).
03.Sakuma, K. et al. CDK8/19 inhibition plays an important role in pancreatic beta-cell induction from human iPSCs. Stem Cell Res Ther 14, 1 (2023).
04.Hiyoshi, H. et al. Identification and removal of unexpected proliferative off-target cells emerging after iPSC-derived pancreatic islet cell implantation. Proc Natl Acad Sci U S A 121, e2320883121 (2024).
05.Yamasaki, M. et al. Xenogenic Engraftment of Human-Induced Pluripotent Stem Cell-Derived Pancreatic Islet Cells in an Immunosuppressive Diabetic Gottingen Mini-Pig Model. Cell Transplant 33, 9636897241288932 (2024).

AKATSUKI project
-COVID-19 cross-project taskforce-

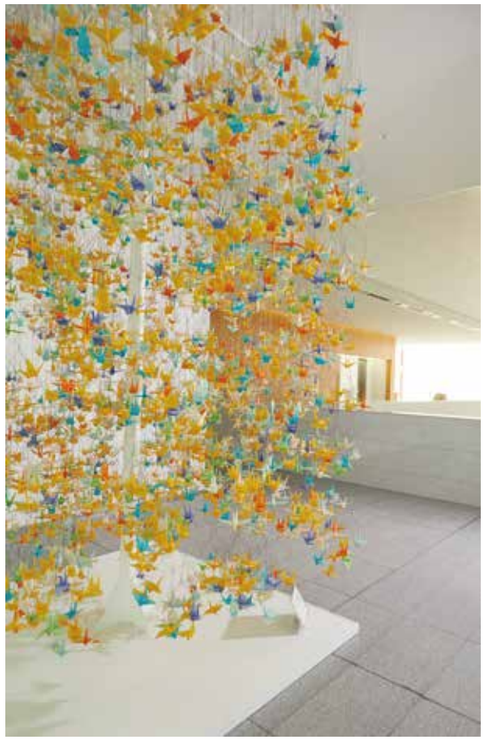
Takanori Takebe
Institute of Science Tokyo

Leveraging the vascularized organoid technology developed in the Takebe project, we established new, collaborative taskforce team in response to pandemic. This team aimed to elucidate the mechanism of COVID-19 pathogenesis and develop therapeutic interventions. Analysis of blood samples from patients with severe COVID-19 confirmed the presence of endotheliopathy associated with the activation of the alternative complement pathway. Consequently, we engineered a human vascular organoid model of COVID-19 infection. Molecular profiling of this model revealed that the alternative complement pathway drives endotheliopathy and thrombosis.
Targeting Factor D, a key amplifier of this pathway, we successfully ameliorated endotheliopathy symptoms in a SARS-CoV-2 infection model using a long-acting (half-life extending) anti-Factor D antibody in non-human primate. These results provide a foundation for future infectious disease investigations. More broadly, our taskforce demonstrated how nimble we can respond to emerging threat in a highly collaborative manner.

Publication

01.Kawakami, E. et al. Complement factor D targeting protects endotheliopathy in organoid and monkey models of COVID-19. Cell Stem Cell 30, 1315-1330 e1310 (2023).
02.Nio, Y. Ameliorative effect of anti-complement factor antibody on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected macaque. Translational and Regulatory Sciences 3, 98-101 (2021).

Inside T-CiRA



The T-CiRA laboratory is located in the Shonan Health Innovation Park (Shonan iPark) in Fujisawa City, Kanagawa Prefecture, and has served as a branch office of the Center for iPS Cell Research and Application, Kyoto University (CiRA). In the extensive research area of T-CiRA, which is 7,500 m², approximately 100 researchers from CiRA, Institute of Science Tokyo, RIKEN, and Takeda have worked side by side every day to advance iPS cell research. This research area has the world's most advanced equipment, Takeda's rich compound library, and all the necessary resources. It provides a “one stop” environment where everything from basic research to clinical application research can be conducted. In addition, iPark is home to many companies and organizations in the area of next-generation medical care, AI and venture capital. It serves as a vital ecosystem of life sciences in Japan and fertile ground for prompting technological innovation.

Optimally Advancing the Commercialization of T-CiRA's Achievements

Four programs originating from T-CiRA were strategically transferred to the most suitable partners to advance clinical development. Among them, the "iCART Program," designed for cancer immunotherapy, was transferred to Takeda in 2019, where research and development continued. In 2024, Takeda entered into a collaboration and licensing agreement with Alloy Therapeutics, entrusting Alloy with ongoing research and development of the program. Furthermore, the "iCM Program" and "iPIC Program" were transferred to Orizuru Therapeutics Inc., a company established in 2021 to drive the development of regenerative medicine products utilizing iPS cell technology. Additionally, some of the technology developed through in vivo genome editing treatment project for Duchenne muscular dystrophy were transitioned to a collaborative research initiative between CiRA and C4U corporation, ensuring continued efforts to deliver innovative therapies to patients.

"iPS cell-derived CAR-T cell (iCART) program"

Providing a CAR-T cell therapy for patients with cancer using T cells generated from iPS cells, and realizing a stable and reliable supply of this therapy to patients.

CAR-T therapy is an advanced form of immunotherapy in which a patient's T cells are collected via leukapheresis, genetically modified, expanded ex vivo, and then infused back into the patient. This approach enables the engineered T cells to recognize and eliminate malignant cells with high specificity.
While autologous CAR-T cell manufacturing is highly personalized, it is also resource-intensive and time-consuming. To address these challenges, T-CiRA initiated research to generate CAR-T cells from iPSC-derived T cells, aiming to create an "off-the-shelf" product suitable for broader clinical application. Preclinical studies demonstrated robust antitumor activity of these iPSC-derived CAR-T cells.
In 2019, the program was transferred to Takeda, which further developed the iCAR-T platform, optimizing product design, nonclinical evaluation, and manufacturing processes. The technology was expanded to target not only hematologic malignancies but also solid tumors. In 2024, under a licensing agreement, the rights to the platform were licensed to Alloy Therapeutics, which is advancing the commercialization of iCAR-T technology in collaboration with academic institutions, biotech ventures, and pharmaceutical companies.

*CAR-T　CAR is a Chimeric Antigen Receptor and T is a T lymphocyte.

"iCART Program"
Timing of transfer: July 2019
Transferred to
Takeda Pharmaceutical
Company Limited.

→

"iCART Program"
Timing of license : 2024
Licensed to
Alloy Therapeutics, Inc.

"iPS cell-derived cardiomyocyte (iCM) program"
"iPS cell-derived pancreatic islet cell (iPIC) program"

Providing a new cell therapy for patients with severe heart failure using human iPS cell-derived cardiomyocytes (iCM), and realizing a radical treatment for patients with type 2 diabetes mellitus through the transplantation of human iPS cell-derived pancreatic islet cells (iPIC).

With the evolution of the two T-CiRA programs, a new company, Orizuru Therapeutics, Inc., was established at the Shonan Health Innovation Park—an ecosystem fully equipped to support innovation—using external funding as a new framework to accelerate the timely and effective realization of iPS cell-based therapies.

The first major achievement is the "iCM Program," led by Associate Professor Yoshida at CiRA. Through a proprietary purification method, highly pure and safe cardiomyocytes named "iCM" can be efficiently generated from human iPS cells using a streamlined differentiation process, enabling myocardial regeneration upon transplantation, offering the potential to restore cardiac function in patients with severe heart failure, while also providing a less invasive therapeutic approach.
The second achievement is the "iPIC Program," led by Lecturer Toyoda at CiRA.
By developing an innovative culture device, the team succeeded in the large-scale, uniform production of human iPS cell-derived pancreatic islet cells (iPICs). iPICs are distinguished by their advanced differentiation into both insulin-secreting β cells and glucagon-secreting α cells, as well as their low tumorigenic potential. Transplantation of iPICs in patients with type 1 diabetes aims to restore physiological insulin secretion and achieve a fundamental cure.

"iCM program" and "iPIC program"
Timing of transfer:　July 2021
Transferred to　Orizuru Therapeutics, Inc.

Making Discoveries Together

At T-CiRA, which brings together members with diverse backgrounds, we organized various activities—such as retreats and monthly reporting meetings—to encourage interaction across projects and between researchers and administrative staff. We also fostered active discussions among researchers and held meaningful dialogue sessions with patients. Engaging in activities that reach beyond our organization broadens researchers' perspectives and helps drive significant innovation.

Monthly Meeting

At T-CiRA, all project members come together once a month for a debriefing session where they share their project progress.These open discussions allow participants to freely exchange ideas, gain a clear understanding of research being conducted in other projects, and acquire new perspectives—often sparking collaborations across project teams.
Members from Takeda's international R&D offices, including Boston and San Diego, also join virtually.

Publication

Numerous articles from T-CiRA have been published in leading scientific journals. To help ensure that these research findings are widely understood and utilized, we have created opportunities to provide explanations directly to members of the media. Presentations delivered by the authors themselves offer meaningful opportunities for the public to clearly understand the content and background of the research in an accessible way.

Interactions with Patients

It is very important in drug discovery research to know and understand the symptoms and needs that are different among patients with the same disease. T-CiRA invited patients and patient organizations and created opportunities for interaction where project members listened to patients and explained the status of research.

Retreat

Before the coronavirus pandemic, T-CiRA held an annual retreat that lasted 2 days and 1 night for all members. Participants had opportunities to get to know each other in various ways, such as morning jogging, poster sessions, and afternoon discussions about the future of T-CiRA. In February 2022, the retreat was held online, featuring new activities and events designed specifically for the virtual format.

" One T-CiRA"

"OneT-CiRA" is a tool that enables all T-CiRA members to smoothly share information.
It is a communication tool that all members can access from anywhere, regardless of their affiliation, hierarchy, or project framework.
It is useful to share a wide range of information, from scientific discussions to reports on events held by each project.

Featured in Major Media

T-CiRA and the CiRA / Takeda relationship

March 5, 2016	The Yomiuri Shimbun
August 25, 2016	The Mainichi
October 27, 2016	The Chemical Daily
January 2, 2017	Nikkei Biotech
February 14, 2017	Nikkan Kogyo Shimbun
March 15, 2017	Kyoto Shimbun
April 13, 2017	TV Tokyo "Cambria Palace"
September 11, 2017	NHK "Professional Work Style"
November 20, 2017	Asahi Shimbun
January 29, 2019	The Chemical Daily
August 11, 2021	Nihon Keizai Shimbun, etc.
December 21, 2021	BS TV Tokyo "Nikkei News Plus 9"
October 7, 2021	NHK "Humanience "iPS Cells and Us""

T-CiRA Researchers Working at Shonan iPark

January 1, 2020	The Yakuji Nippo
August 23, 2021	Nikkei Business Daily

T-CiRA's Research Projects

September 25, 2018	Nikkan Kogyo Shimbun, etc. [ALS/ASD Drug Discovery Project]
July 10, 2019	Nikkei Business Daily, etc. [Intractable Muscular Disease Project]
July 17, 2019	Nihon Keizai Shimbun, etc. [iCART Program]
February 19, 2020	The Chemical Daily, etc. [iPIC Program]
June 2, 2020	Nikkan Kogyo Shimbun, etc. [iCART Program]
September 8, 2020	The Chemical Daily, etc. [Organoid Medicine Project]
November 12, 2020	Nikkei Biotech, etc. [ALS/ASD Drug Discovery Project]
June 16, 2021	Q Life Pro medical news, etc. [NGLY1 Deficiency Project]
June 21, 2021	Kyoto Shimbun, etc. [iCM Program]
December 8, 2021	Nihon Keizai Shimbun, etc. [Genome Editing Therapy for Muscular Dystrophy Project]
September 15, 2022	Kyoto Shimbun, etc. [Neural Crest Cell Project]
August 4, 2024	Nihon Keizai Shimbun, etc. [Organoid Medicine Project]
June 8, 2025	NHK "NHK special "The Human Body III" Collection 4" [Organoid Medicine Project]

Research Achievements （as of March 2025）

246 Presentations at Scientific Conferences

58 New Patent Applications

8 Publicly funded programs

66 Publications (as of the end of October 2025)

The Journey of T-CiRA

December 2015	The Center for iPS Cell Research and Application, Kyoto University (CiRA) and Takeda Pharmaceutical Company Limited. (Takeda) established a 10-year joint research program toward clinical applications of iPS cell technology (Takeda-CiRA Joint Research Program for iPS Cell Applications; T-CiRA). Based at Takeda Pharmaceutical Shonan Research Institute (currently Shonan Health Innovation Park), it aims for clinical application of iPS cell technology in six disease areas, including cancer, heart failure, diabetes, neurodegenerative diseases, and refractory muscle diseases.
November 2016	Yokohama City University participated in T-CiRA. The drug discovery application research project was started based on human iPS cell-derived mini-liver technology.
March 2017	The Institute of Physical and Chemical Research (RIKEN) participated in T-CiRA. The drug discovery research project for the treatment of NGLY1 deficiency was started.
July 2019	Research results on iPS cell-derived CAR-T cell therapy (iCAR-T) created by T-CiRA were handed over to Takeda.
July 2021	Human iPS cell-derived cardiomyocytes (iCM) and human iPS cell-derived pancreatic islet cells (iPIC), which are part of the T-CiRA results research, were transferred to new company Orizuru Therapeutics Inc. (OZTx) as candidates for regenerative medicine products.
March 2024	An open-label Phase 1/2/3 study of gene therapy with NGLY1-AAV was initiated, and the first patient was treated.
November 2024	Takeda Pharmaceutical Company Limited and Alloy Therapeutics, Inc. have entered into a collaboration and licensing agreement to develop the iCAR-T platform.

Takeda-CiRA Symposium
at Takeda Global Headquarters on February 3, 2026

T-CiRA, A Bridge to the Next Generation Therapeutics

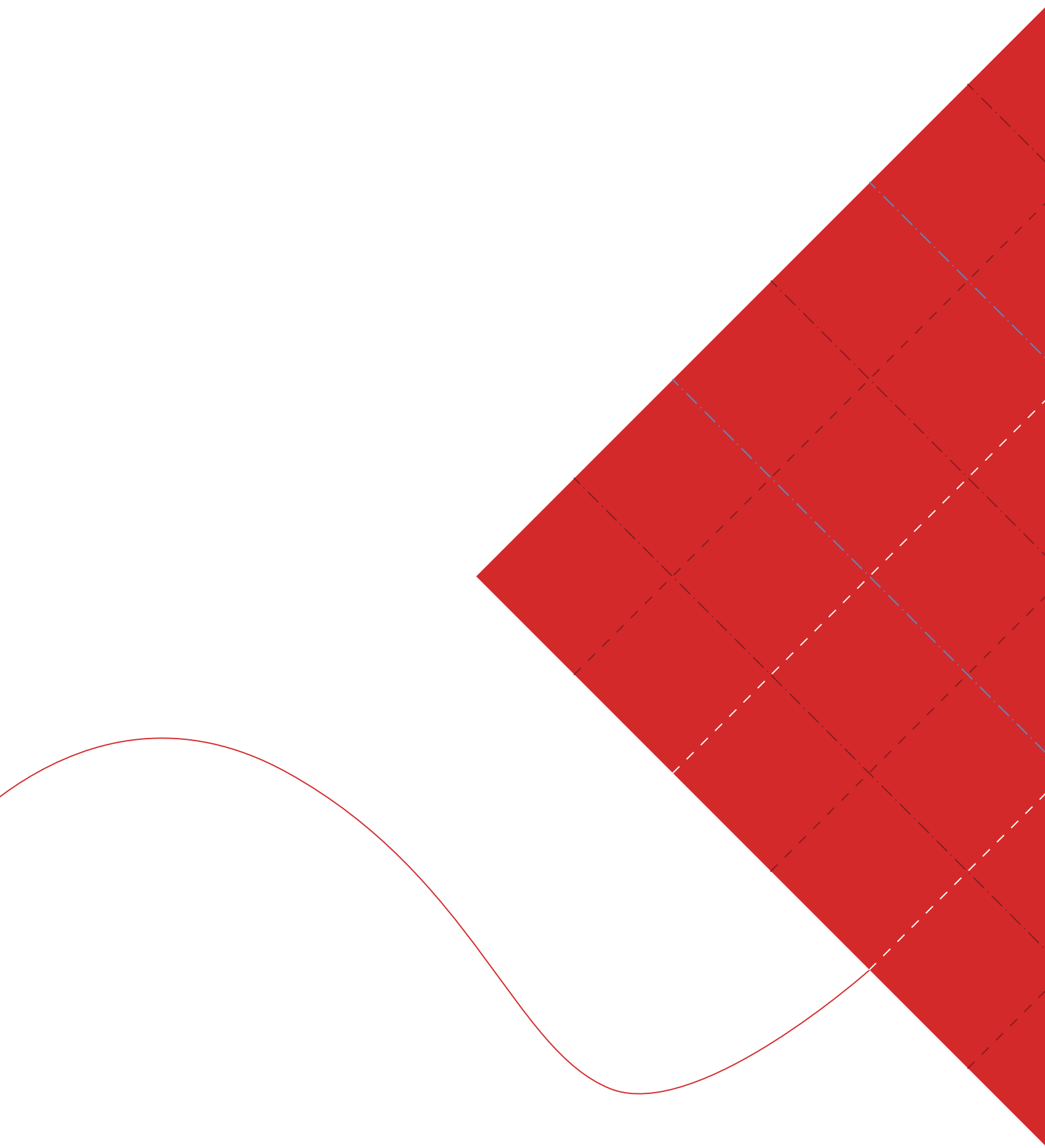
We will hold an event to sum up the research results of the T-CiRA Program, which is a 10-year industry-academia collaboration research program started in 2016 by the Center for iPS Cell Research and Application, Kyoto University and Takeda Pharmaceutical Company Limited.

Takeda-CiRA Symposium: A Bridge to the Next Generation Therapeutics

"Future Prospects for Social Implementation of T-CiRA Research Results"

Key speakers

Professor Shinya Yamanaka,	Center for iPS Cell Research and Application, Kyoto University/Gladstone Institute
Professor Shin Kaneko,	Center for iPS Cell Research and Application, Kyoto University/Institute of Medicine, University of Tsukuba
Professor Haruhisa Inoue,	Center for iPS Cell Research and Application, Kyoto University/ BioResource Research Center, RIKEN/Center for Advanced Intelligence Project, RIKEN
Professor Takanori Takebe,	Graduate School of Medicine, Osaka University/Institute of Integrated Research, Institute of Science Tokyo/Cincinnati Children's Hospital/Communication Design Center, Yokohama City University
Ryo Ito, Division Manager,	Orizuru Therapeutics, Inc.



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