Message from CEO

Bringing Hope for Better Health through the Infinite Power of Science

We are an R&D-driven company, focusing on the development of iPS cell-based regenerative medicine and the application of iPS cell technologies.

In 2015, the Center for iPS Cell Research and Application (CiRA), Kyoto University and Takeda Pharmaceutical Company Limited launched the joint research program T-CiRA to accelerate the research and advancement of iPS cell technologies as well as its application in regenerative medicine and drug development. In 2021, Orizuru Therapeutics Inc. was established for the purpose of transferring some of their outcomes into clinical practices as sustainable business.

Our portfolio was initially focused on two potential therapies researched under the T-CiRA program. One was with iPS cell-derived cardiomyocytes led by Project Leader Yoshinori Yoshida (Associate Professor at CiRA) and the other was iPS cell-derived pancreatic islet cells led by Project Leader Taro Toyoda (Junior Associate Professor at CiRA). We will continue to seek other potential therapy where iPS cell technology may play a critical role. Another business scope is to support any drug discovery research activities and to build an iPS cell research platform based on our advancing iPS cell technologies.

Even though we have just started, we are comprised of over 50 staff who are either best-in-class researchers or with in-depth expertise as technicians in the latest iPS cell technologies. We have a mind in young, open, and free, yet our heart is "to help society and patients per iPS cell technologies come from Japan." This is the origin of our company's name, Orizuru.

We inherit the scientific technologies of CiRA and Takeda, and will build new cultures on top of these here at Shonan iPark campus, Kanagawa, Japan. By providing regenerative medicines, we will contribute to the future for medical practice, our people, and our society.

Kenji Nonaka

M.D., Ph.D.
President, Representative Director and CEO of Orizuru Therapeutics, Inc.

Qualifications

1990: Graduate Kyorin University, School of Medicine, and obtained Medical License
2002: Doctor Degree

Business career

1990-1994: Resident, Kyorin University Hospital, Department of Thoracic Surgery
1994-1996: Chief Resident, TORANOMON Hospital, Tokyo, Japan,
1996-1999: Staff, Kyorin University Hospital, Department of Cardiovascular Surgery, Tokyo Japan,
1999-2001: Instructor, Baylor College of Medicine, Department of Surgery, Houston, TX,
2002-2008: Research Director, Research Development Center, Banyu Pharmaceutical K.K. Tokyo Japan,
2008-2011: Director, Clinical R&D Department, Abbott Laboratories, Tokyo Japan,
2011-2016: Director, Head of Japan R&D, Abbvie Inc., Tokyo Japan,
2016-2021: Vice President, Head of Japan R&D, Janssen Pharmaceutical K.K., Tokyo Japan,

Company Overview

Orizuru Therapeutics promotes the social implementation of cell therapy products and innovative iPS cell-related technologies (platform innovation).

Scope of Business	1. Development of regenerative medical products through cell transplantation. 2. Support for drug discovery research and development of regenerative medicine research infrastructure by utilizing iPS cell-related technologies.
Company Name	Orizuru Therapeutics, Inc.
Founded	April 9, 2021
Address	2-26-1 Muraoka-higashi, Fujisawa-shi, Kanagawa, 251-8555 Japan
Representative Director	Kenji Nonaka

Access

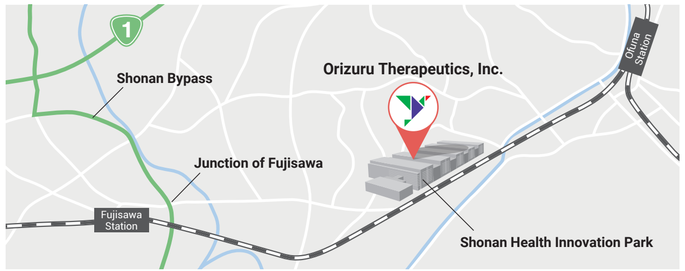
Location: Shonan Health Innovation Park, 2-26-1 Muraoka-higashi, Fujisawa-shi, Kanagawa, 251-8555 Japan

By train

From JR Ofuna Station: Take the Enoden Bus toward Fujisawa Station Kitaguchi (bus stop No. 1 at the East Exit bus terminal south of Lumine Wing) and get off at Shonan iPark. (Approx. 15 mins)
From JR Fujisawa Station: Take the Enoden Bus toward Ofuna Station Higashiguchi Shiki-no Mori (bus stop No. 9 at the North Exit bus terminal) and get off at Shonan iPark. (Approx. 15 mins)

By car

From Tokyo: About 11 km from the Kamiyabe Interchange on the Yokohama Bypass (Yokohama Shindo) via Route 1 Harajuku
From Odawara: About 6 km from the Fujisawa Interchange on the Shin-Shonan Bypass via Fujisawa-Bashi



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https://orizuru-therapeutics.com/en/

ORIZURU THERAPEUTICS

Orizuru Therapeutics Inc.

Bringing Hope for Better Health through the Infinite Power of Science

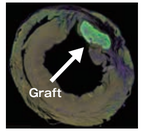
iCM Project

We are developing a definitive therapy for severe heart failure patients with limited therapeutic options.

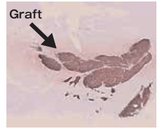
What is iCM

iCM is a human iPS cell-derived cardiomyocyte created by a T-CiRA's project led by Dr. Yoshinori Yoshida, Associate Professor at CiRA, Kyoto University. The myocardial differentiation method, which has been studied at CiRA, has been further improved toward practical use by utilizing the cardiomyocytes purification method with small molecule compounds discovered in the T-CiRA program. By transplanting iCMs, highly engraftable, pure, and safe cardiomyocytes, into the patient's heart, they are expected to replenish the cardiomyocytes lost as the disease progresses and promote remuscularization. Restoring the cardiac function of patients with severe heart failure, which has been considered difficult to treat, can be expected to improve the quality of life (QOL) and prognosis of these patients.

Engraftment of implanted cell in rat myocardial infarction model



Engraftment of implanted cell in monkey myocardial infarction model



Research and development of regenerative medical products using iCM

Cardiomyocyte therapy requires the delivery of hundreds of millions of cardiomyocytes or more to patients. To provide cell products to patients with severe heart failure who are awaiting treatment, it is necessary to develop cell manufacturing technologies that can efficiently produce large numbers of cells. One of the most important technologies is a culture technique in which cells are suspended in a medium and cultured. Since the early stage of development, we have been working on a method for cardiomyocyte differentiation using a suspension culture system, which has been considered difficult to obtain high-quality cardiomyocytes. In addition, we have discovered unique small molecule compounds that efficiently remove non-cardiomyocytes generated during cardiac differentiation. By combining these state-of-art technologies with the differentiation method for preparing highly engraftable cardiomyocytes found in CiRA, high-performance, safe iCMs can be produced with a simple differentiation process. iCMs are highly effective when administered as single cells, eliminating the need for sheet or aggregate reformation. In addition, iCM is suitable for a wide range of administration methods, including catheter administration, enabling minimally invasive treatment with less burden on the patient.

	iPS cells	iPS cell-derived cardiomyocyte	Highly convenient product	To severe chronic heart failure
Solution provided by iPS cell-derived cardiomyocyte (iCM)	Stable supply and off-the -shelf treatment with the mass production-friendly allo-iPS cells	Achievement of both high productivity and high-purity. Mass production-friendly suspension culture system. Removal of non-cardiomyocytes that could induce adverse effects, such as arrhythmia and cancer risk.	Cryopreservable and easy-to-use cell product. To be supplied to people who need it when they need it.	Highly efficient engraftable cells assist cardiac function for a long period of time. Continuous improvement of cardiac/physical functions will be achieved beyond the current drug therapy.

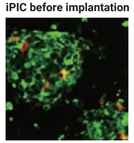
iPIC Project

We are developing a definitive therapy for brittle type 1 diabetes patients who are unable to control their blood glucose level.

What is iPIC

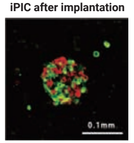
iPICs are human iPS cell-derived pancreatic islet cells expected to be suitable for cell therapy. They were discovered after a five-year optimization study through T-CiRA based on the pancreatic cell differentiation method (Stem Cell Res. 2015;14:185-97) discovered by Dr. Taro Toyoda, Junior Associate Professor at CiRA. iPIC is an aggregate of highly-purified pancreatic endocrine cells that contains both insulin and NKX6.1 positive cells, a characteristic of pancreatic β cells. After implantation in vivo, pancreatic islet-like structures containing glucagon positive cells, another important endocrine cell type, are formed, and physiological insulin-secreting capabilities can be demonstrated in response to glucose loading and hypoglycemia.

iPIC before implantation



Maturation in vivo

iPIC after implantation



Human cadaveric pancreatic islets

Development of novel cell therapy product utilizing iPIC

To provide the novel treatment option for brittle type 1 diabetes patients, we have established the original subcutaneous implantation method that supports the long-term engraftment of iPICs even in less-vascularized subcutaneous environments. We have demonstrated proof-of-concept that implanted iPICs can treat diabetic rodents and pig models. One of the most important features of iPICs is the high purity of expected endocrine cells, which is achieved by the combinatory approach of single-cell RNA sequencing-based transcriptomics and unique compound-based purification. Fruitful collaboration with expertized equipment manufacturers enables us to yield billions of cells from one batch with a cell culture system optimized for iPICs. Since iPICs are cryo-preservable, the product can be supplied as ready-to-use within a few days from the frozen iPICs, allowing flexible setting of the implantation date.

	iPS cells	iPS cell-derived islet-like cells (iPICs)	Subcutaneous implantation	To Brittle Type 1 diabetes
Solution with iPIC	Unlimited supply	・Scalable culture process ・Uniform and stable quality ・High purity	・Pancreatic islet-like morphology ・Physiological insulin secretion ・Less invasive and retrievable surgery	・Freedom from hypoglycemic events ・Independence of insulin injection ・Minimization of immunosuppressant use

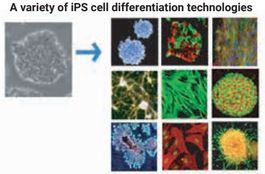
Platform Innovation

We promote innovation in drug discovery research and development of regenerative medicine by utilizing cutting-edge iPS cell technology.

Platform Innovation by Orizuru Therapeutics

A variety of iPS cell differentiation technologies and the related technologies cultivated through the Takeda-CiRA Joint Program for iPS Cell Applications (T-CiRA) and many researchers and specialists who can comprehensively utilize the technologies have been consolidated at Orizuru Therapeutics. With such unique organizational advantage, Orizuru Therapeutics will develop and improve a new drug discovery support platform to accelerate discovery of innovative pharmaceutical products (disease-specific iPS cell differentiation technology, organoid technology). Additionally, a new medical research platform for research and development and clinical application of iPS cell-derived cell therapy products (original iPS cell platform including hypoimmunogenic iPS cell line) to promote the use of iPS cell technology in society.

A variety of iPS cell differentiation technologies



Abundant analysis technologies of celluklar function

Platform Innovation of Orizuru Therapeutics

The benefits from the iPS cell technology, a cutting-edge scientific achievement originating in Japan, have not been fully offered to the industries, medical institutions, and patients who need it. Through the platform innovation, Orizuru Therapeutics will support the discovery of innovative pharmaceutical products based on the iPS cell technology by offering one-stop services to provide a variety of iPS cell- based cell differentiation/induction technologies, extensive function analysis technologies, and the original versatile iPS cell platform to be developed in the future in line with the needs of our customers.
We will promote the use of iPS cell technology in society based on the excellent human resources base and the original iPS cell platform.

Solutions provided by platform innovation	Consolidation of human resources who inherit the cutting-edge iPS cell utilization technology cultivated at T-CiRA	Production and analysis technologies for a wide variety of iPS cell-derived cells and tissue organoids	Support for drug discovery research utilizing iPS cell technology and development of regenerative medicine research platforms