

With you CellSeed

vol.16



Let's plant the seeds of hope for regenerative medicine.

At CellSeed, we deliver cell sheet-based regenerative medicine, cell cultureware, and regenerative medicine contract services as our primary business.

In the regenerative medicine business, we have been developing allogeneic chondrocyte sheets aiming to cure knee osteoarthritis based on the results of clinical research conducted at Tokai University. With the support of the Japan Agency for Medical Research and Development (AMED), we established a master cell bank that has confirmed its efficacy and safety as a raw material for making allogeneic chondrocyte sheets. Since we submitted an investigational new drug (IND) application for Phase III clinical trials of allogeneic chondrocyte sheets (CLS2901C) to the Pharmaceuticals and Medical Devices Agency (PMDA) on September 20, 2023, development has made significant progress.

In 2023, in the cell cultureware business, we conducted active sales promotion activities to expand sales of cultureware products, and as a result, our overseas sales have significantly increased, achieving record-high sales. We will continue to focus on developing new products that meet the needs of mass cell culture technology for manufacturing a large amount of cells to be used in immunotherapy and the development of cellular foods, such as cultured meat, and strive to expand into new markets. In the regenerative medicine contract business, we achieved record sales due to contract manufacturing of autologous chondrocyte sheets used in the Advanced Medical Care B program.

As our name implies, CellSeed will make every effort to plant small seeds of cells into big hopes and bring smiles to people all over the world.

President/CEO
Setsuko Hashimoto



MISSION

We will take the initiative of contributing to global health care in the valuable and innovative field of regenerative medicine.

VISION

We will establish a cell sheet business platform and provide excellent regenerative medicine products around the world.

CellSeed will contribute to the
advancement of regenerative medicine.



History

CellSeed was founded in 2001 with the aim of realizing regenerative medicine based on “cell sheet engineering,” a unique invention that originated in Japan. It allows cells to be recovered as sheets without damaging them. Since our founding, we have been consistent in conducting research and development to deliver regenerative medicine based on cell sheet engineering to patients. We will continuously strive to serve as a bridge to deliver advanced regenerative medicine to patients as quickly as possible, contributing to health care in Japan and around the world.



●The 1st Cell Sheet Engineering Innovation Forum held

●Start of regenerative medicine contract services

●Approval to manufacture specified cell processing products acquired

●Listing on JASDAQ

●Sales of *RepCell*® and *HydroCell*® launched

●Head office relocation to the Telecom Center Building
●Cell Processing Center established
●Clinical trial on epithelial cell sheets for esophageal regeneration initiated

●Sales for *UpCell*® launched
●Clinical trial on epithelial cell sheets for corneal regeneration initiated in France

●CellSeed founded

●Sales of a new lineup of the *UpCell*® series launched
●Public symposium held

●Aomi Cell Cultureware Innovation Center newly established
●The 2nd Cell Sheet Engineering Innovation Forum held

Submission of an IND application for allogeneic chondrocyte sheets

CellSeed has been conducting development with the aim of obtaining marketing approval of allogeneic chondrocyte sheets as a regenerative medicine product for patients with knee osteoarthritis. We submitted an IND application for Phase III clinical trials to the PMDA.

The 3rd Cell Sheet Engineering Innovation Forum held

Since 2019, CellSeed has been holding Cell Sheet Engineering Innovation Forums to spread cell sheet engineering, a world's first technology originating from Japan, to as many researchers as possible. The 3rd Cell Sheet Engineering Innovation Forum was held in November 2023. It was the first time in four years that the forum was held face-to-face. Attendees not only had Q&A sessions at the lectures but also had lively discussions at the poster sessions and social gatherings.

Scan here to see the video from the day of the forum.



Allogeneic Chondrocyte Sheets

We will continue to focus our efforts on commercializing cell sheet regenerative medicine to bring these products to market.

We have been conducting development of allogeneic chondrocyte sheets as a fundamental cure of knee osteoarthritis, which causes pain when walking.

We submitted an IND application for Phase III clinical trials in September 2023.

What is Knee Osteoarthritis?

Knee osteoarthritis is a condition in which the surface of the knee joint cartilage wears out and degenerates due to aging, obesity, genetics, trauma, etc. It causes pain in the knee and makes it difficult to bend or straighten the knee. Fundamental cure to regenerate worn-out cartilage and cure knee osteoarthritis has yet to be established.

Still no fundamental cure for knee osteoarthritis

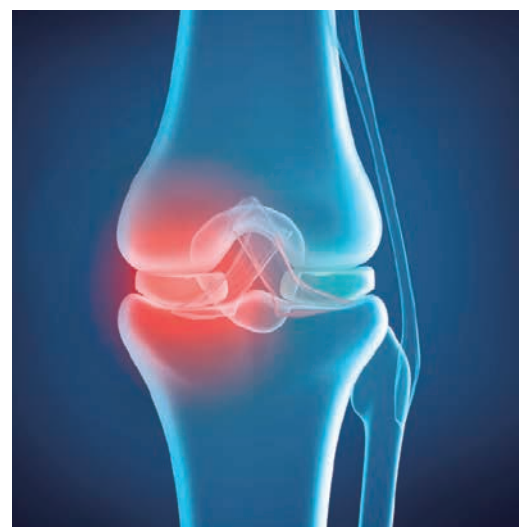


Number of potential patients
Approx. 30 million
(Japan)



Number of symptomatic patients
Approx. 10million
(Japan)

- The prevalence increases with age.
- 1.5 to 2 times more common in women than in men.
- The number of patients is expected to increase due to the aging of the population.



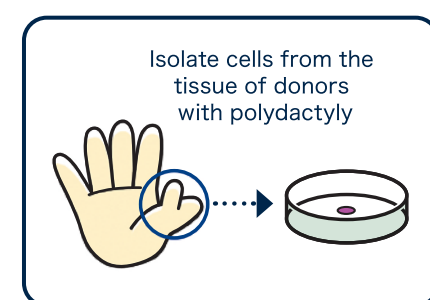
Treatment Method Using Allogeneic Chondrocyte Sheets

Allogeneic chondrocyte sheets use chondrocytes as a raw material, which are collected from surgery to remove excess fingers from donors with polydactyly. Compared to autologous chondrocyte sheets, allogeneic chondrocyte sheets do not require

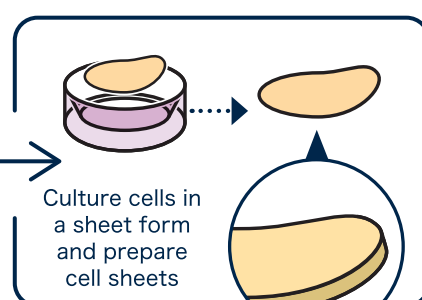
surgery to collect chondrocytes, reducing the stress on the patient. Another advantage is that preparing a cell bank of chondrocytes makes it possible to provide products of consistent quality.

Treatment method

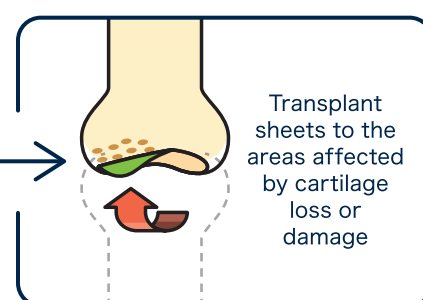
① Collect tissues from pediatric donors with polydactyly



② Manufacturing of cell sheets



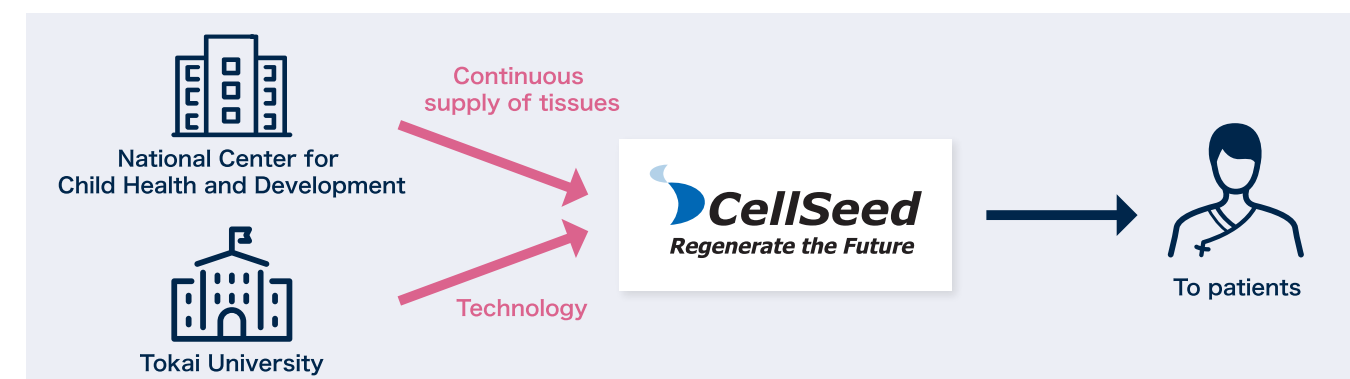
③ Transplantation into patients



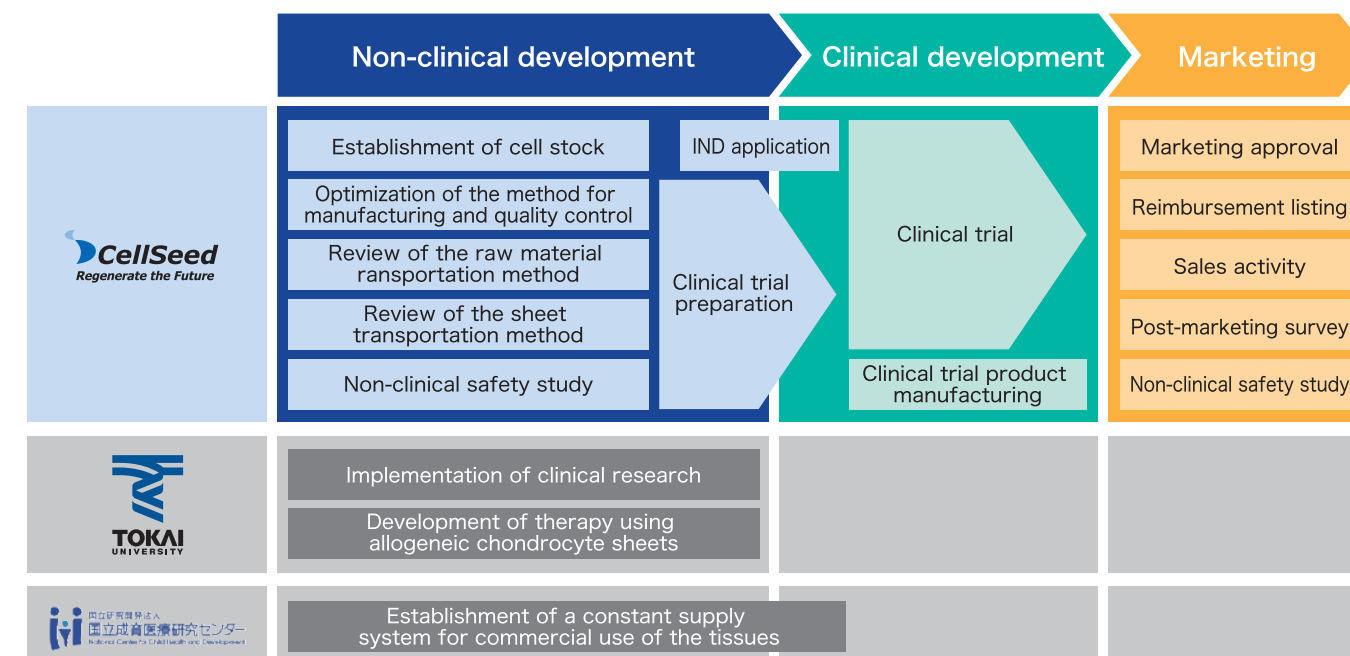
CellSeed's Solutions

A therapy using allogeneic chondrocyte sheets was originally developed at Tokai University. Based on the therapy research results from Tokai University, CellSeed has been proceeding the therapy-related development with the aim to obtain marketing approval under the *Act on Pharmaceuticals and Medical Devices* (the "PMD Act"). When we first started the therapy-related development, a system

and structure for companies to procure allogeneic cells domestically for regenerative medicine products was still under development. Through joint research with the National Center for Child Health and Development, we have built a system to provide a constant supply of tissues for commercial use and established a cell bank to be used in clinical trials.



Development process



Cell Cultureware

In CellSeed's cell cultureware business, we have been developing various cell culture related products, as well as providing a variety of products with temperature-responsive cell cultureware *UpCell*® as a key product worldwide.

In recent years, we have also been focusing on developing new products to meet the growing demand for large-scale cell recovery in order to provide products for various research fields beyond regenerative medicine.

UpCell® Series Temperature-responsive cell cultureware for “Cell Sheet” engineering . . .

This cell cultureware can harvest the adherent cells by temperature change without using trypsin or cell scrapers. It is possible to recover intact cells without damaging the cells' intrinsic physiological functions or the proteins expressed on the cell surface.

- Adhesion and detachment of cells to/from the surface of cell cultureware is controlled simply by changing the temperature.
- It is possible to recover intact cells, as extracellular matrix completely maintained without the use of trypsin or scrapers.
- Cells can be harvested in sheet form or in dispersed form depending on the purpose of use.
- Co-culturing with *UpCell*® makes it possible to obtain a structure that mimics biological tissues in vitro.



Introduction of the UpCell® Products

UpCell® Dish and Plate Type

The *UpCell*® dishes and plates we supply are used by many researchers worldwide for basic research in regenerative medicine using cell sheets. We also provide high and low detachment types with adjusted cell detachment.



UpCell® Insert Type

The use of *UpCell*® inserts makes it possible to fabricate cell sheets in a co-culture system that mimics the biological environment.



UpCell® Flask Type

It is possible to recover a large volume of cells in an area three times larger than that of *UpCell*® 10cm dishes. This product is designed for large-scale recovery of cells required for cell therapy that uses MSC, macrophages, and other cells.



UpCell® ADVANCE

UpCell® ADVANCE^{*1} is a product that has passed several quality control requirements for development of regenerative medicine and cell therapy products, and has been used to manufacture some regenerative medicine products. This product was registered on the “Master File for Devices (MAF^{*2,*3})” list of the U.S. Food and Drug Administration (FDA) in December 2022.

*1 : *UpCell*® ADVANCE has various safety testing data for each production lot, which is different from the cataloged product “*UpCell*®” that is limited to research use.

*2 : MAF is a system under which a manufacturers register various product specifications, including manufacturing know-how, with the FDA in advance as MAFs.

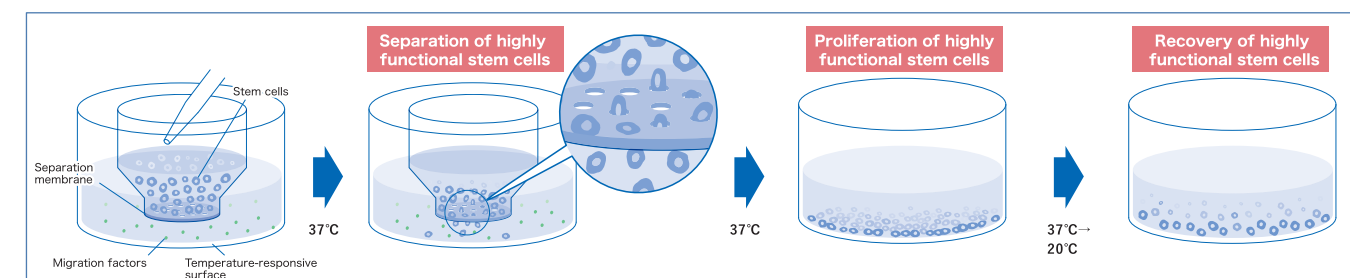
This enables pharmaceutical and medical device manufacturers to file sales licenses from FDA just by citing the MAF number.

*3 : MAF registration does not necessarily mean that the quality and safety of the product has been confirmed or evaluated by the FDA.

Highly Functional Stem Cells Recovery Kit VIVANT-CELL® -Pot with UpCell® Plate . . .

By seeding stem cells on a separation membrane with unique pores and applying migration factors, stem cells with high proliferative and regenerative abilities can be selectively collected.

Stem cells with high proliferative and regenerative abilities that have passed through the unique separation membrane adhere to the *UpCell*® plate and can be collected without damage by using temperature changes.



RepCell® Series

Temperature-responsive cell cultureware with Grid

RepCell® has the same performance and features as *UpCell*®, but also has a unique culture surface, a “grid-wall” structure that enables efficient recovery of a single cell and small cellular fragments without damaging them.



HydroCell® Series

Low cell binding cultureware

HydroCell® is based on the manufacturing technology of *UpCell*® and *RepCell*®, and its super hydrophilic polymer is firmly fixed to the cell culture surface. For embryoid and spheroid formation of iPS cells and cancer cells.



cellZscope® Series

Transepithelial/transendothelial Electrical Resistance (TEER) real-time measurement . . .

In response to the trend of banning animal testing that has spread from Europe to countries around the world, cellZscope® has been introduced by many pharmaceutical and cosmetics companies as an alternative evaluation method for skin corrosiveness in vitro, and is used with high reproducibility for toxicity and ADME evaluation of candidate compounds in pharmaceutical and cosmetic products.



ThermoPlate® IIISeries

UpCell®/RepCell® dedicated glass heater

ThermoPlate® is a transparent heating element made of hard glass. By placing *UpCell*® or *RepCell*® on this product, microscopic observation and medium exchange are possible while maintaining constant temperature of the cell culture surface on dishes and plates.



Transparent heating element
made of specially processed hard glass

Controller

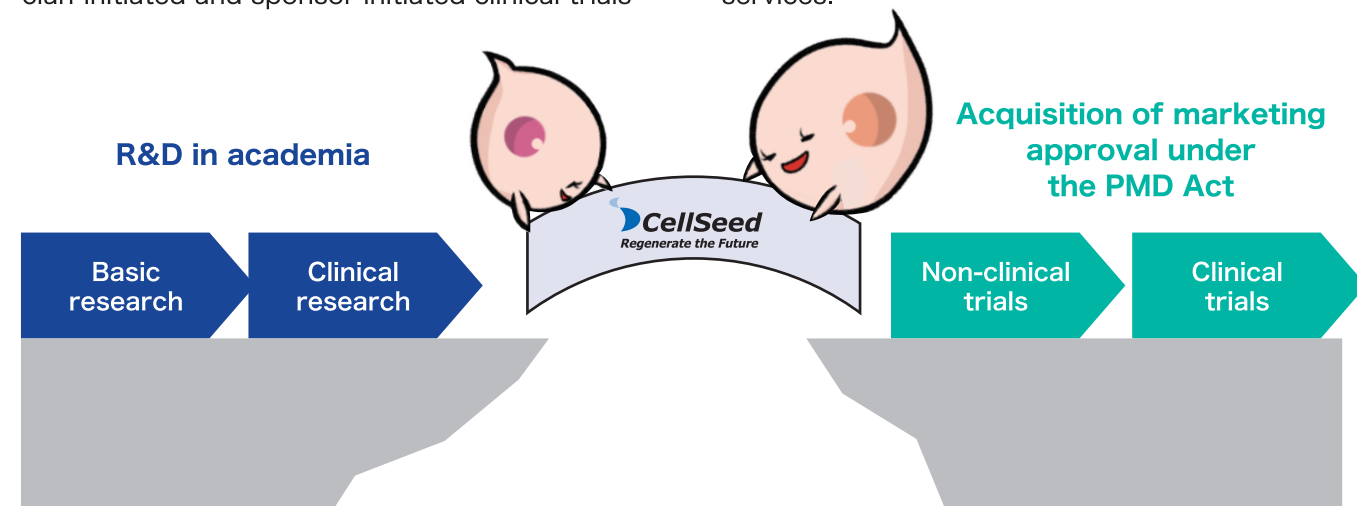
Regenerative Medicine Contract Manufacturing Services

In March 2017, CellSeed's Cell Processing Center acquired the approval to manufacture specified cell products, followed by the approval to manufacture regenerative medicine in October 2018. We are currently providing various contract services as a contract development and manufacturing organization (CDMO) for regenerative medicine. We will continue to provide safe, high-quality products and services with our experienced staff members.

Solve the Issues and Gaps for Our Clients

There are many cases where issues and gaps are encountered when applying seeds from universities and research institutes to clinical practice. One of the reasons is that the laws regulating clinical research and those regulating physician-initiated and sponsor-initiated clinical trials

conducted to obtain marketing approval of regenerative medicine products are different. CellSeed will solve these issues and gaps faced by our clients through our experience in developing regenerative medicine and providing contract services.



Details of Contract Services

Development of manufacturing methods and contract manufacturing for cell sheet products

- Development of cell sheet manufacturing methods
- Contract manufacturing of cell sheet products
- Quality testing of cell sheet products, etc.



Facility management and application support

- Support for preparing and submitting applications
- Support for document creation/consulting
- Support for operation and maintenance of facilities equipment/management system, etc.



Training of cell culturing technicians

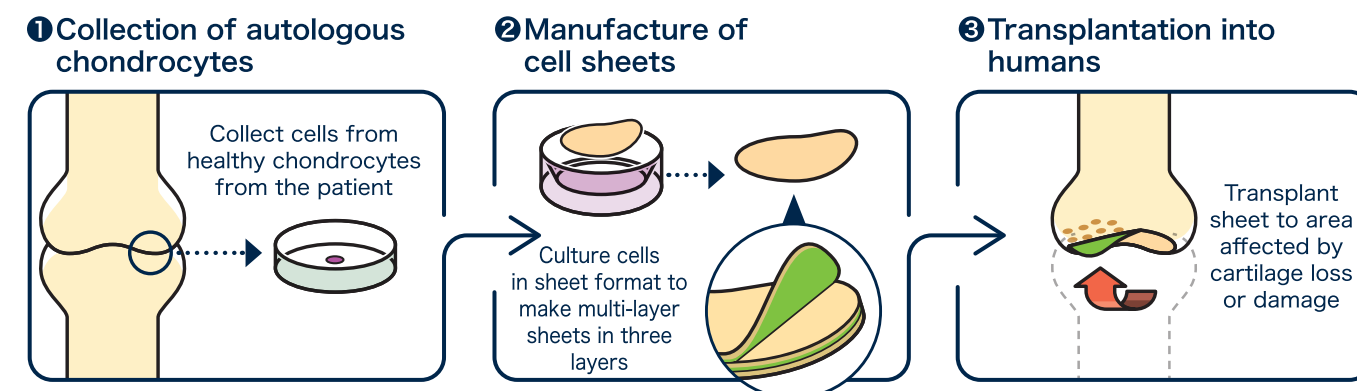
- Cell sheet culturing training
- Cell sheet harvesting training, etc.



Example of Contract Services

Professor Masato Sato of Tokai University developed chondrocyte sheets with the aim of providing fundamental cure for knee osteoarthritis. Tokai University has been conducting treatment using

autologous chondrocyte sheets as the Advanced Medical Care B program from 2020 to 2024, and CellSeed has conducted the contract manufacturing of the autologous chondrocyte sheets.



Self-Pay Treatment Application Support

In 2023, Ikegami General Hospital began offering autologous chondrocyte sheet transplantation as a self-pay treatment. CellSeed provided support for the procedures necessary to start self-pay treatment, including the preparation of documents related to the provision plan for regenerative medicine. Additionally, we have been contracted to manufacture the cell sheets used for self-pay treatment at Ikegami General Hospital.

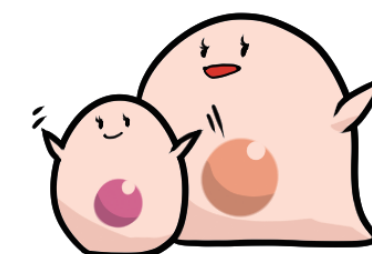


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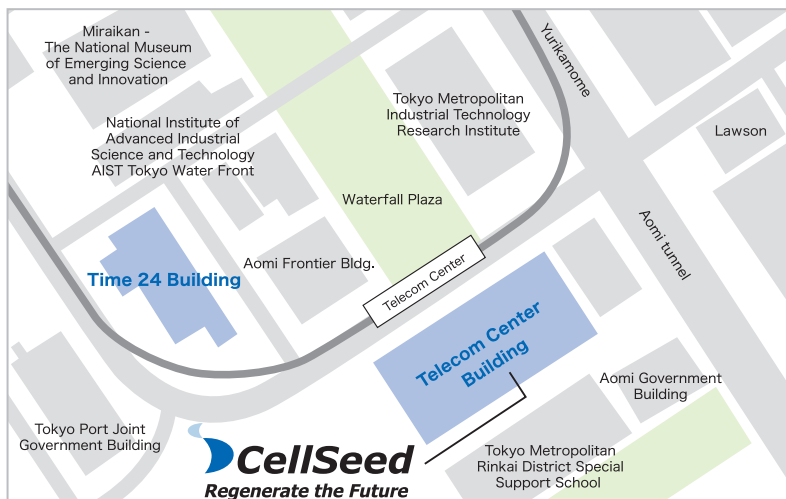


Track Record of Our Contract Services

- Contract manufacturing of autologous epithelial cell sheets for clinical research on regenerative medicine for congenital esophageal atresia postoperative anastomotic stricture
- Contract manufacturing of periodontal ligament cell sheets prepared from human (allogeneic) periodontal ligament-derived mesenchymal stromal cells for a physician-initiated clinical trial
- Cell sheet culturing and harvesting training



| | |
|------------------|---|
| Company name | CellSeed Inc. |
| Main businesses | Cell sheet regenerative medicine business Regenerative medicine support business |
| Head office | Telecom Center Building, East Tower 15F Aomi 2-5-10, Koto-ku, Tokyo 135-0064 Japan |
| Representative | Setsuko Hashimoto |
| Date established | May 2001 |
| Fiscal year end | December |
| Capital | 2,385 million yen |
| Employees | 35 (37% female) |
| Listed market | JASDAQ Growth (7776), Tokyo Stock Exchange |
| R & D | Cell Processing Center Telecom Center Building, East Tower 6F Aomi 2-5-10, Koto-ku, Tokyo Aomi Cell Cultureware Innovation Center Time 24 Building, Aomi 2-4-32, Koto-ku, Tokyo |



Telecom Center Station on the New Transit Yurikamome Line (directly connected to Telecom Center Building West Tower)

*To go to the East Tower 15th floor from the West Tower, head to the East Tower on the 2nd floor. (There is no passage between the West and East Towers on the 15th floor.)

CellSeed YouTube Channel

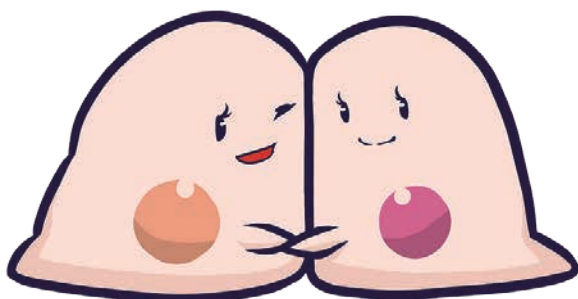
On our YouTube channel, we upload videos explaining how to prepare cell sheets and introducing our cell cultureware products as well as our business. We will upload more videos from time to time, so please check our new uploads.



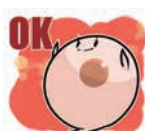
Introducing the Japanese idol of the world of cells from CellSeed!

Saibochan™

The cells of Saibochan have always been in your body, hoping you will notice them



LINE stamps are available now!



Celulun

The biggest cheering supporter for regenerative medicine and people's health.

A goofball who tries too hard and ends up making blunders, which makes him charming.



Shidomaru

Celulun's brother figure. A free-spirited mood maker who loves mimicking others and playing pranks.



Official merchandise is available now



Tote bag



Smartphone case

