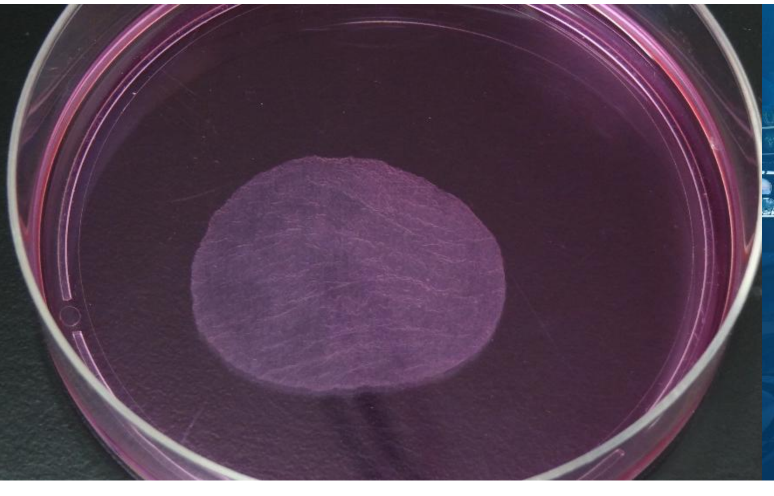
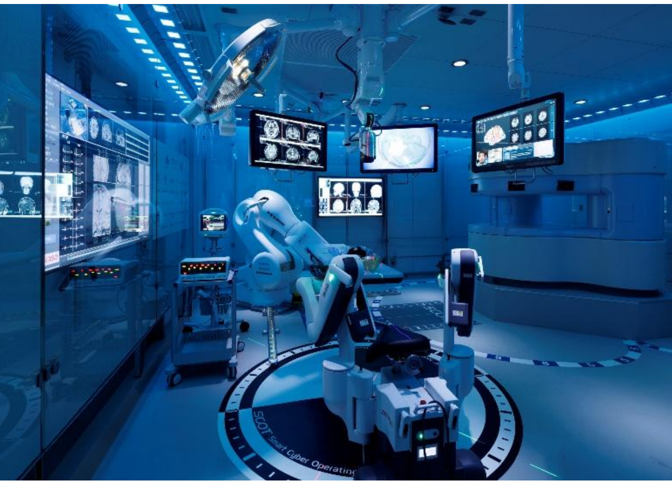
Institute of Advanced Biomedical Engineering and Science
Tokyo Women’s Medical University





Advanced Technology Leads People to Advanced Medicine

ABMES
Since 1969
Institute of Advanced BioMedical Engineering and Science
東京女子医科大学先端生命医科学研究所

History

1969 Launched “Institute for Medical Engineering” by Professor Shigeru MIURA as the first Director

1976 Reorganized as “Institute of Biomedical Engineering” by Professor Yasuhisa SAKURAI as the Director

1999 Professor Teruo OKANO as the Director

2001 Reorganized as “Institute of Advanced Biomedical Engineering and Science (ABMES)” by Professor Teruo OKANO as the Director
Established “Division of Advanced Biomedical Engineering and Science”, Graduate School of Medical Science

2008 Launched “Tokyo Women’s Medical University–Waseda University Joint Institution for Advanced Biomedical Sciences (TWIns)”

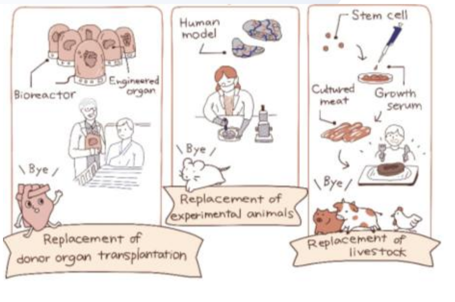
2010 Established “Cooperative Major in Advanced Biomedical Sciences” as Collaborated Graduate School with Waseda University

2016 Professor Tatsuya SHIMIZU as the Director

2017 The METI Minister’s Award in the 1st Japan Medical Research and Development Awards, co-awarded with Waseda University

2019 50th Anniversary of the establishment of the Institute

2025～ Creation of new advanced medicine and life sciences



The Director

For more than 50 years, the Institute of Advanced Biomedical Engineering and Science (ABMES), Tokyo Women’s Medical University has continuously promoted research and development through the fusion of interdisciplinary fields, and has extensively conducted research and education for creating new medical science and industries. In recent years, we have been actively engaged in life science research not only in the medical field but also in the food and space fields. For the advanced promotion of these research and development, we intend to foster young researchers who are fused across disciplines and strengthen industry-government-academia collaboration. All institute members will work together to pioneer the future life sciences and continue new challenge for the contribution to human life.

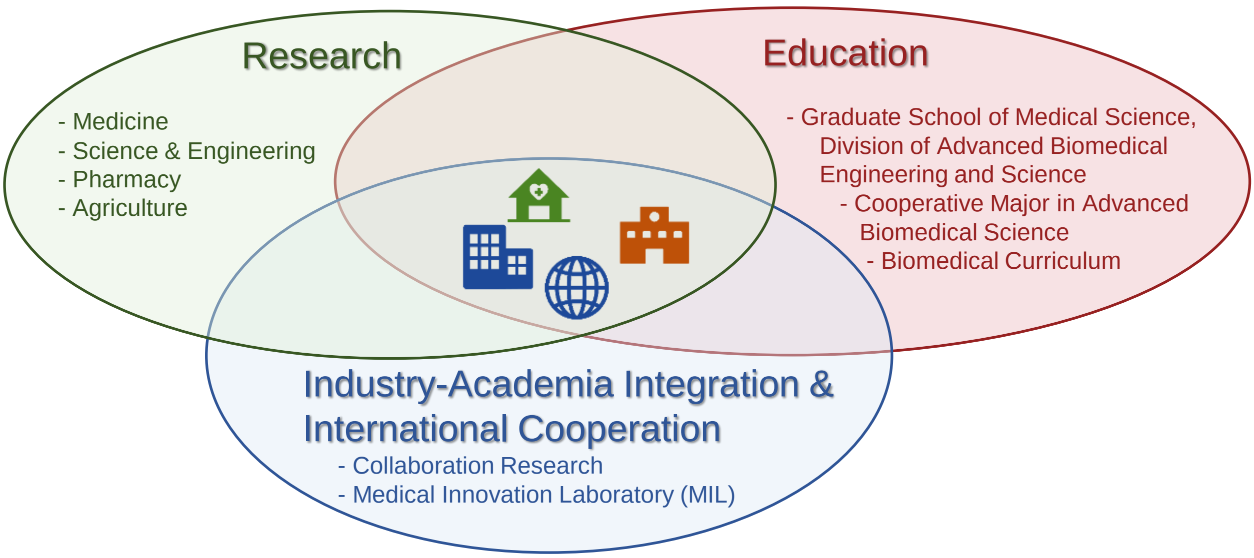
夢と信念

Dreams and Beliefs

Director & Professor
Tatsuya Shimizu, M.D., Ph.D

The Institute of Advanced Biomedical Engineering and Science (ABMES) promotes research and education in advanced medicine based on medicine-science-engineering-pharmacy and industry-academia integration, for contribution to the development of future medicine and medical industries.

In ABMES, medical doctors, researchers, and engineers are working together on the research and development of medical technologies under medicine-science-engineering-pharmacy-agriculture and industry-academia integrated environment for treating the patients of tomorrow



Focusing on Two Main Axes

Regenerative Medicine & Life Science

- Smart cell culture platforms for cell sheet tissue engineering
- Cell sheet-based tissue engineering & regenerative medicine
- Creation of novel cell-based therapy
- Human tissue & organ models
- Novel cell culture system for cell-based food production
- Life science research for space exploration
- Smart polymers for DDS and biomaterials

Advanced Techno-Surgery

- Smart Cyber Operating Theater: SCOT®
- Mobile medical treatment unit (Mobile SCOT)
- Surgical support robots and devices
- Risk assessment and patient safety addressed via AI analysis of intraoperative language function test
- Patient and public involvement (PPI) research initiatives
- Regulatory science in medical devices

Creation of New Surgical Devices through Advanced Science & Technology

Graduate School of Medical Science
Division of Advanced Biomedical Engineering and Science

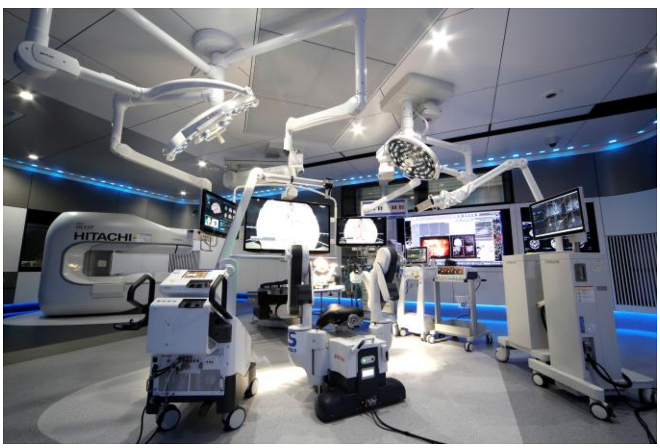
Advanced Techno-Surgery (FATS)

Educational Policy

Faculty of Advanced Techno-Surgery (FATS) conducts research and development aimed at realizing advanced healthcare through the utilization of cutting-edge technologies such as AI and robotics. In particular, our research on information-guided surgery, centered on intelligent operating rooms, integrates various modalities—including intraoperative MRI, OCT, photodynamic diagnosis, and functional testing—to improve surgical quality. We are also promoting the development of surgical support robots and therapeutic devices in collaboration with clinical departments, as well as clinical prediction using AI and remote support systems. Furthermore, we are working on the social implementation of technologies such as mobile SCOT and home healthcare robots. In addition, we place strong emphasis on regulatory science for medical devices, fostering human resources with a broad perspective through an integrated system that spans from basic research to clinical application and commercialization.

Research Theme

Surgical Strategy Systems（SCOT）



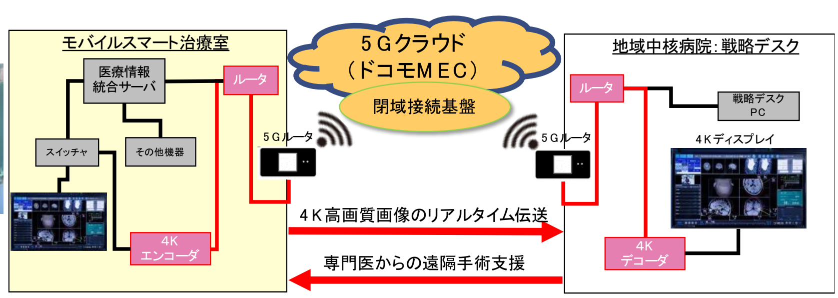
The Smart Operating Room, launched in 2019 at Tokyo Women's Medical University Hospital, is a next-generation surgical suite. The OPeLiNK Eye console integrates surgical field images, vital signs, and navigation data to support information sharing and risk reduction. By combining data such as navigation and brain function monitoring, it enables quick assessment of tumor malignancy and brain function, assisting in determining resection extent. These technologies are being evaluated and preclinical data collected at TWIns B1F.

（SCOT®：Smart Cyber Operating Theater）

Smart Operating Rooms Redefine the Concept of Hospitals: Mobile SCOT

We are developing a Mobile Treatment Unit—a mobile operating room that combines smart operating technologies with 5G communication. Equipped with advanced medical devices and surgical support systems, it enables high-quality emergency care even in remote regions. By allowing real-time collaboration among medical teams regardless of location, it makes prompt and accurate treatment possible. This represents a shift from “going to the hospital” to “the hospital coming to you.”

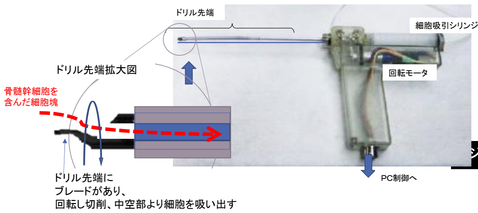
In-Vehicle Operating Room of Mobile SCOT



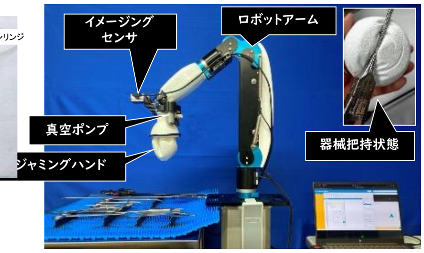
Implementation of Mobile SCOT in Healthcare Settings

Research and Development of Surgical Assistive Robots and Devices

As a “new hand” for surgeons, we are conducting research and development on laser surgical robots and novel surgical devices using ultrasound and laser technologies that surpass the precision, dexterity, and operability of the human hand by applying technologies from mechanical, electronic, information, and computer-assisted surgery engineering. Through a biomedical engineering approach, we explore the conceptual design, implementation methods, and functional utility of devices that support a wide range of diagnostics and treatments, including neurosurgery and abdominal surgery.



Minimally Invasive Bone Marrow Aspiration Device



Robotic Scrub Nurse

AIREC：AI driven Robot for Embrace and Care

AI-Based Risk Evaluation for Patient Safety during Intraoperative Language Function Testing

IEMAS, developed for intraoperative language testing during awake neurosurgery, supports safe surgery while preserving language function. The system is being advanced to more accurately localize language areas, predict complications, and automatically detect abnormal responses during free conversation. AI is also being used to evaluate its diagnostic support during language arrest.

Recording During Intraoperative Language Mapping

Technology-enabled PPI (Patient and Public Participation) Research Initiatives

Peer support is a system in which individuals with similar concerns or illnesses share their experiences and support one another. This study aims to utilize cutting-edge ICT technologies, such as AI and the metaverse, to create an accessible online environment for peer support. By doing so, we seek to reduce social isolation and stigma, while building a new healthcare-social model in which patients and citizens can actively participate.

Scenes from an Event Held in the Metaverse

Regulatory Science for Medical Devices

Despite domestic development, many Japanese medical devices—especially therapeutic ones—fail to reach practical use, leading to reliance on foreign products. Key challenges include risk-averse business practices and lack of evaluation criteria. Introducing Regulatory Science for Medical Devices, which incorporates early-stage data development, safety and efficacy evaluation, and stakeholder analysis, is essential. Many students are actively conducting research in this field and earning academic degrees.

※If you are considering graduate studies or would like to learn more about our research, please contact the Institute of Advanced Biomedical Engineering and Science.

※For detailed information such as admission requirements, please visit the website of the Graduate School of Medical Sciences.

TWMU FATS

Creation of Cell-based Future Medicine and Life Sciences

Graduate School of Medical Science
Division of Advanced Biomedical Engineering and Science

Life Sciences for Co-creating the Future

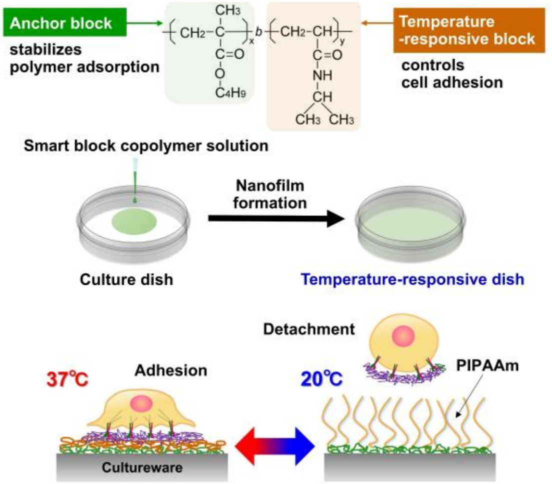
Educational Policy

Biomaterials are extremely diverse and are expected to contribute not only to medicine but also to the food field and the SDGs. As for regenerative medicine, recent advances accelerate research and development to create biomimicking tissues from cells, and the transplantation of regenerated tissues is also possible in the future. These engineered tissues are useful as tools for drug discovery and disease research instead of experimental animals. The development of tissue-engineered cellular foods has also attracted much attention as a solution to the global food crisis and food security issues. Meanwhile, food production and life science research in space are also important issues for the future space exploration. We extensively train researchers who can pioneer new areas of co-creation for the future via studying and practicing these fusion fields.

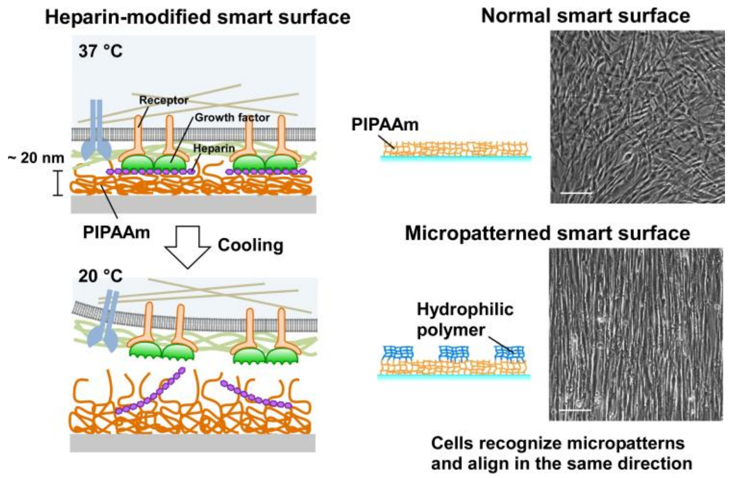
Research Theme

Next-generation Temperature-responsive Culture Platforms

Our group is developing the next-generation smart temperature-responsive poly(*N*-isopropylacrylamide) (PIPAAm)-immobilized culture platforms to produce cell sheets effectively. In particular, our researches include low-cost mass production of culture platforms, smart dishes bearing bioactive molecules (e.g., cell adhesion factors, growth factors, and antibodies), and surfaces for cell orientation or additional mechano-stress.



Temperature-responsive culture dish via physical nanocoating of smart block copolymer



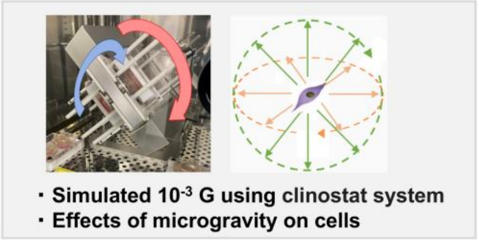
(Left) Heparin-immobilized temperature-responsive surface
(Right) Micropatterned smart surface for the controlled cell alignment

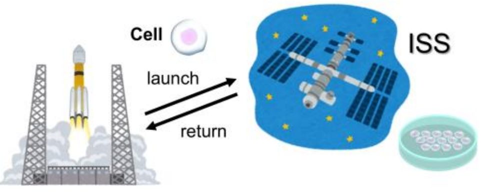
Life Science Research for Space Exploration

Astronauts who have stayed on the International Space Station (ISS) for long time periods are known to suffer from reduced bone density and muscle atrophy due to the effects of the microgravity environment. Considering that people will travel to space in the future, the elucidation of effects in a microgravity environment on living body and development of the related technologies are important issues.

Our group has found that the proliferation of human myoblasts is inhibited in a microgravity environment simulated using a clinostat system. These cultured cells show a property similar to that of aging, and further verification of the relationship between microgravity and muscle atrophy is under investigation. In collaboration with JAXA, we are also planning to culture human mesenchymal stem cells (MSCs) on the ISS laboratory. By analyzing gene expression and culture supernatant of cells cultured in space, the effects of microgravity in space on cells are expected to clarify.

Culture and differentiation of myoblasts under simulated microgravity

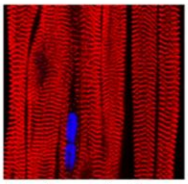




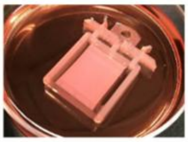
Culture, differentiation & omics analysis of MSCs at ISS

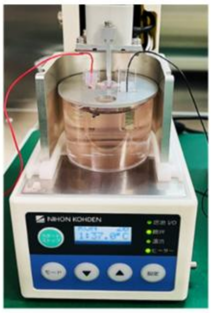
Development of Human Tissue & Organ Models

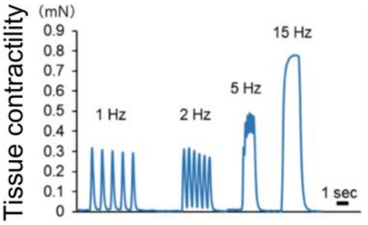
Our research group develops tissue and organ models based on cell sheet engineering. With the aim of regenerating functional muscle similar to living tissue, we are pursuing the construction of mechanically and physiologically mature muscle tissue governed by nerves by combining tissue engineering methods such as introduction of nerves and mechano-stress loading into muscle tissue with oriented myofibers. In addition, our researches include iPS cell-derived myocardial tissue models with beating and pump functions, new cancer tissue models and so on. These tissue and organ models are expected to be a useful alternative to experimental animals in drug discovery research and the elucidation of disease mechanisms.



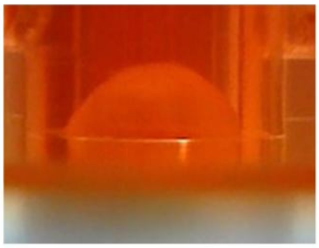
Skeletal muscle tissue



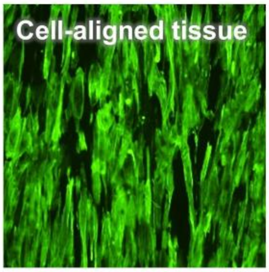


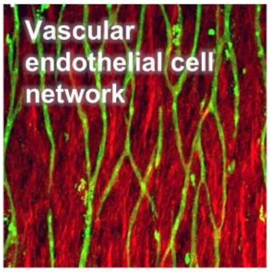


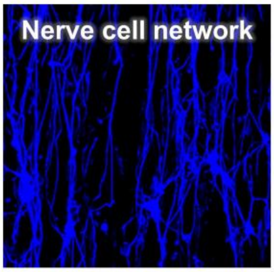
Contraction force measurement system using skeletal muscle tissue model



Dome-shaped myocardial tissue with autonomous pump function (miniature heart)





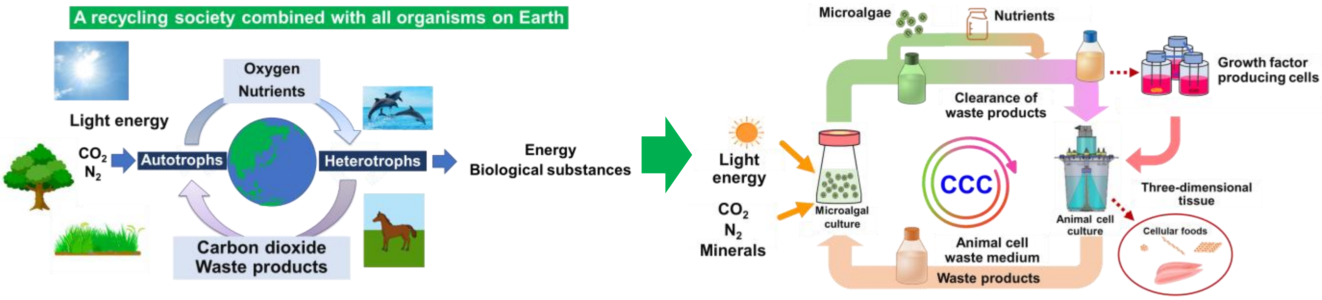


Engineered-tissue with vascular- and native-like microstructures

Symbiotic and Circular Cell Culture System for Cell-based Food Production

All organisms on the Earth form a symbiotic and recycling ecosystem through the exchange of materials. In pursuit of realizing circular-cell-culture (CCC) that incorporates this cycle into cell culture, we are conducting to utilize the culture medium, containing nutrients extracted from microalgae and secretions from several types of growth factor producing cells, for amplifying cells for food use. Subsequently, we aim to develop a game changing "cell-based food" that is equivalent in nutritional value and texture to livestock meat but more affordable than traditional forms by matured and thickened the amplifying cells using tissue engineering techniques. We will achieve to solve escalating global food shortages by developing a sustainable meat production system for reducing space requirements and environmental impact, based on the idea of substituting grain feedstocks with microalgae and livestock meats with cultured cells.

Cellular food



CCC system combined microalgae with animal cells incorporating the recycling system on the Earth into cell culture

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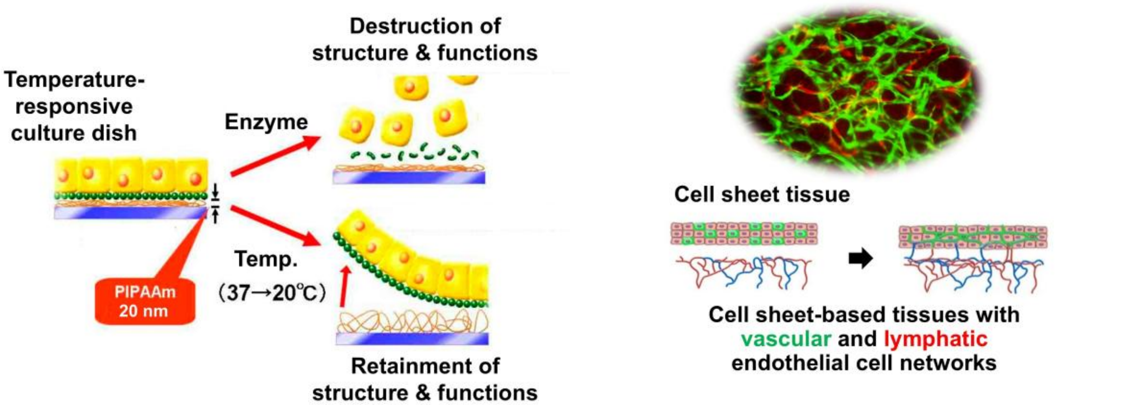
Creation of Tissues & Organs from Cells

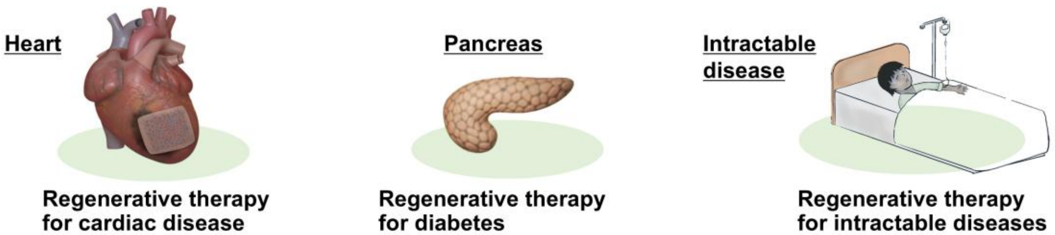
Graduate School of Medical Science
Division of Advanced Biomedical Engineering and Science

Tissue Regeneration

Educational Policy

Organ transplantation has long served as a critical treatment for patients with life-threatening conditions. However, challenges such as donor shortages and the lifelong use of immunosuppressive drugs with associated side effects remain unresolved. In response, regenerative medicine and tissue engineering have emerged as promising alternatives in the advancement of future medical therapies. Tissue engineering was first proposed in 1993 by R. Langer and J. Vacanti, who showed that cells seeded onto biodegradable scaffolds could regenerate three-dimensional tissue structures in the presence of growth factors. As stem cell biology continues to advance alongside tissue engineering, regenerative medicine is becoming an established interdisciplinary field. Its progress depends on the integration of medicine, science and engineering, and biology. We are committed to cultivating the next generation of researchers who will lead the development of novel concepts and innovative therapeutic strategies.





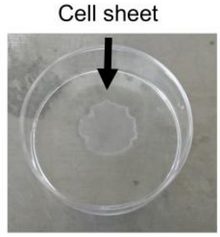
Medical doctors, scientific and pharmaceutical researchers, and corporate researchers are working together to promote research and development for innovative regenerative medicine.

Research Theme

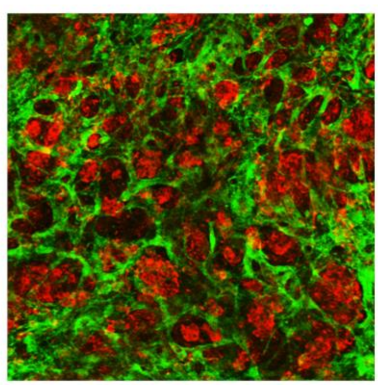
Regenerative Therapy for Diabetes

Diabetes is a disease that causes various complications throughout the body due to inadequate insulin secretion and insulin resistance. Our research group works on the research and development of cell sheets composed of insulin-secreting islet cells using temperature-responsive culture dish. As a new cell transplantation therapy for diabetes, we have been developing transplantable vascular-introduced islet cell sheets, which combine islet cells, mesenchymal stem cells, and vascular endothelial cells.

Cell sheet



Green: vascular endothelial cell
Red: pancreatic islet β cell

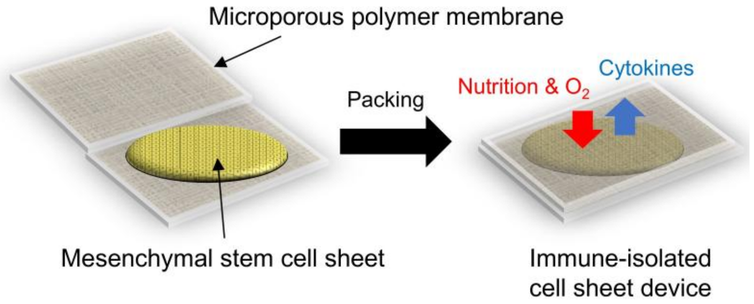


Pancreatic islet β cell sheet with vascular endothelial network

Transplantable Immuno-isolated Cell Sheet Device

Secretory factors (e.g., cytokines) from mesenchymal stem cells (MSCs) show some effects such as inflammatory suppression, angiogenesis, and immunomodulation. Therefore, these MSC-secreted factors attract much attention in regenerative medicine for especially inflammatory diseases.

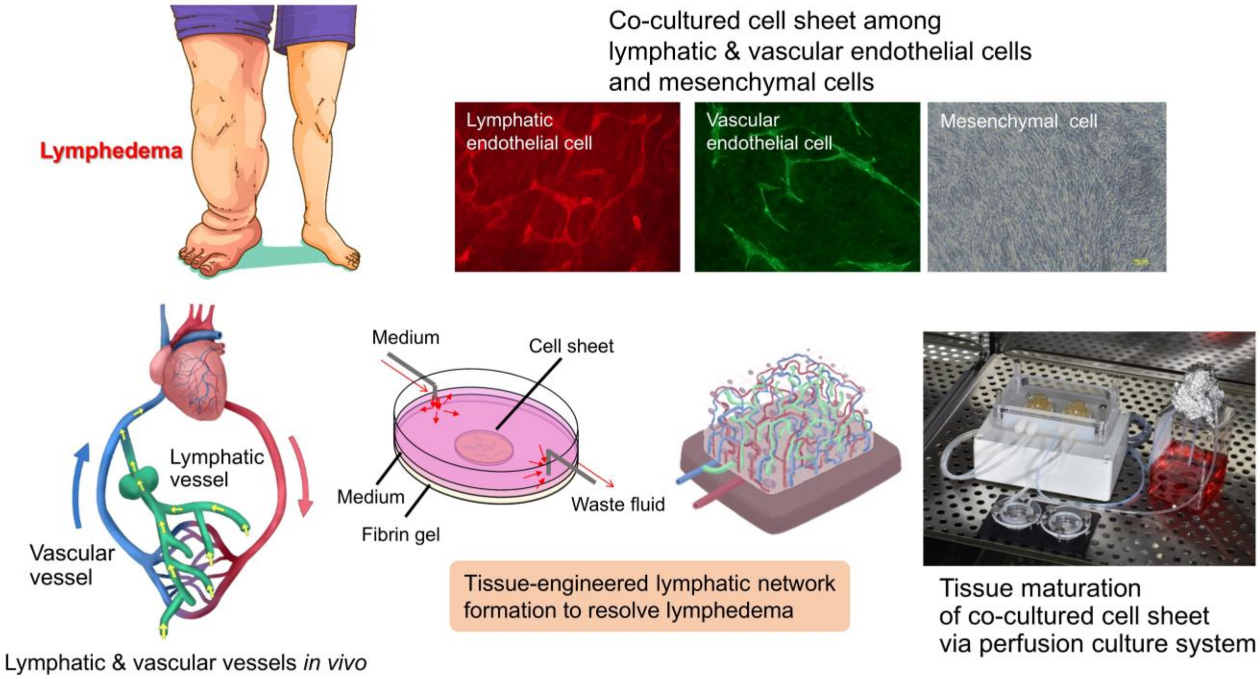
As academia-industrial collaboration, we currently work on a transplantable immuno-isolated MSC sheet device using a microporous polymer membrane. This device facilitates the molecular permeability (e.g., nutrition, O_2 and secretory factors) across the membrane pores, but inhibits the invasion of inflammatory cells from outside. Using this immuno-isolated MSC sheet device, the long-term sustained release of cytokines can be realized after *in vivo* transplantation.



Transplantable immuno-isolated MSC sheet device

Lymphatic and Vascular Engineered Tissue for Lymphedema Treatment

Lymphedema is a disease characterized by chronic swelling of the extremities due to excessive fluid accumulation, fibrosis of the tissues, accumulation of subcutaneous fat, decreased immune function, impaired wound healing, and increased risk of infection. In addition to changes in appearance, it may cause disability and be life-threatening. Once lymphedema develops, it often requires lifelong management, and no curative treatment has been established. Our research group works on the development of fundamental treatment for intractable lymphedema using a transplantable vascularized lymphatic tissue. The vascularized lymphatic tissue is expected to construct utilizing a perfusion culture system of co-cultured cell sheets with endothelial cell networks that construct lymphatic vessels and blood vessels, respectively. We aim to rapidly increase lymphatic capillary density by creating the transplantable lymphatic vascularized tissue that has the ability to pump lymphatic fluid, which is important for maintaining fluid homeostasis, and to drain it into veins.



Construction of engineered-tissue with blood capillary and lymphatic vessels

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TWMU

Collaboration with Waseda University for Research & Education

Collaboration for Research & Education and Joint Institution

For more than 50 years, Tokyo Women‘s Medical University (TWMU) and Waseda University have conducted joint researches in the fields of artificial organs, medical materials, and medical instrumentation, and have steadily cultivated medical-engineering collaboration between the two universities.

In April 2008, the Tokyo Women's Medical University-Waseda University Joint Institution for Advanced Biomedical Sciences (TWIns) has been established as a collaborative facility with the aim of realizing advanced medicine based on “medical-scientific fusion” and fostering human resources to play this role.

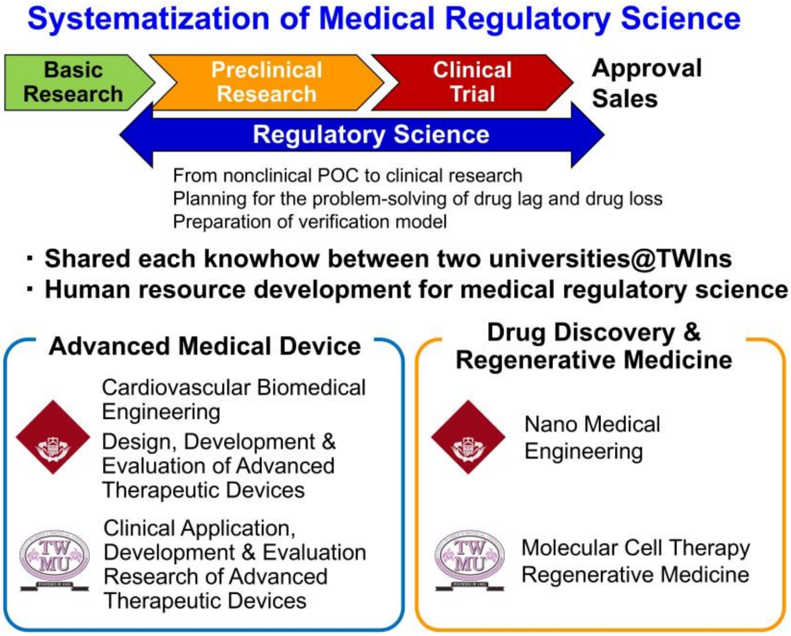
In 2010, we have also established the first in Japan joint graduate school doctoral program (Joint Department of Advanced Biomedical Sciences) with Waseda University for fostering human resources with knowledge and skills in medical regulatory science who will play a leading role in the development and realization of advanced medical devices, medical materials, regenerative medicine, and genomic medicine.

Our institute is continuously challenging to work for the creating new medical technologies and life sciences from Japan and to develop human resources who can play an active role worldwide.

TWMU−WASEDA Univ. Joint Graduate School Doctoral Program for Medical Regulatory Science

In the 21st century, there is a strong need to create medical regulatory science as a new science that integrates the rapidly advancing natural sciences such as medicine, medical engineering, and pharmaceutical sciences with the increasingly diverse humanities and social sciences.

The joint graduate school doctoral program “Cooperative Major in Advanced Biomedical Sciences” with Waseda University has been established as an academic program for medical regulatory science. We train human resources that can play a leading role in the development and realization of advanced medical devices, medical materials, regenerative medicine, and genomic medicine.



Recurrent Medical Education & Industry-Academia Collaboration

Biomedical Curriculum（BMC）

In order to introduce cutting-edge technologies necessary for medicine and medical care in response to social demands, it is essential to develop researchers and engineers who understand global-scale science and technology regarding both basic and advanced medicine and also bridge the gap between medicine and engineering. Our university has been offering the Biomedical Curriculum (BMC) for postgraduate medical education for more than 50 years, and has produced more than 2,100 graduates to date.

The BMC is a one-year public course designed to provide medical students with a systematic digest of the correct knowledge of all aspects of medicine that they spend four years studying, primarily for engineers in the fields of science, engineering, and pharmacology. The BMC offers not only seminars on the latest topics, but also hands-on training and field trips to experience the realities of basic medicine and medical care. In particular, BMC actively welcomes researchers and engineers from industry, and offers an up-to-date curriculum that incorporates basic medicine, clinical medicine, and biomedical engineering, which is a fusion of medicine and engineering.

Medical Innovation Laboratory（MIL）

The Institute for Advanced Biomedical Sciences promotes collaborative researches with various companies and external research institutions, and has established the Medical Innovation Laboratory (MIL) on the 3rd floor of TWIns, which can be used by companies and other organizations as a laboratory or experiment room.

In addition, with the aim of disseminating new medical technologies and life sciences from TWIns, the “Industry-Academia Collaboration Forum” is held to bring together companies and research institutions engaged in joint research to explore new research seeds, exchange opinions, and promote personnel exchange between different fields.

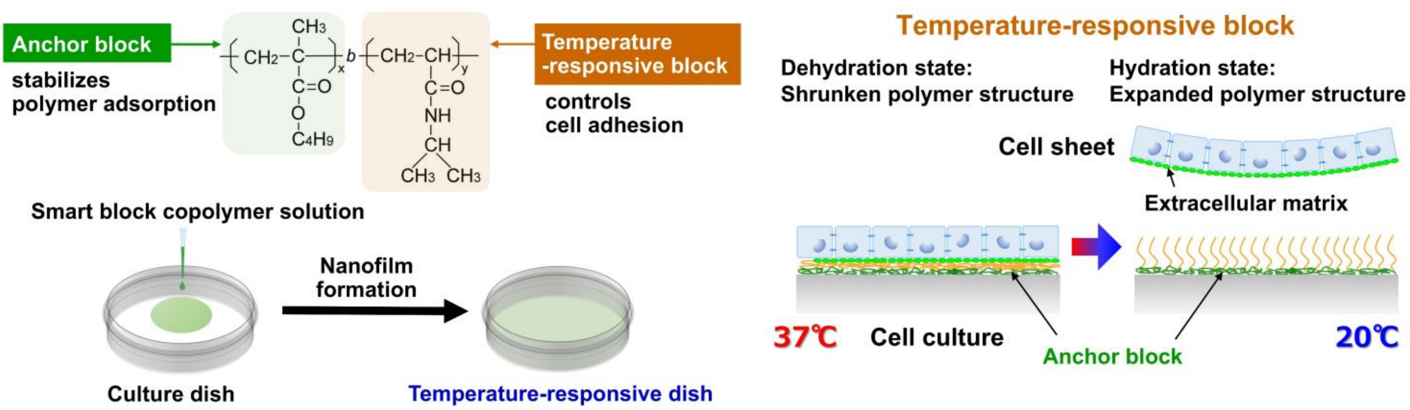
Research Introduction

Smart Culture Platforms for Regenerative Medicine

Temperature-responsive Culture Platforms via Polymer Coating Method

Our research group has developed the world's first temperature-responsive culture dishes with a nanothin film of poly(*N*-isopropylacrylamide) (PIPAAm). After cells are cultured to confluency at 37ºC, the cells can be recovered as a "cell sheet" by reducing temperature to 20ºC. The enzyme-free recovered cell sheets can be easily transplanted onto living tissues and be also stacked to create a three-dimensional tissues.

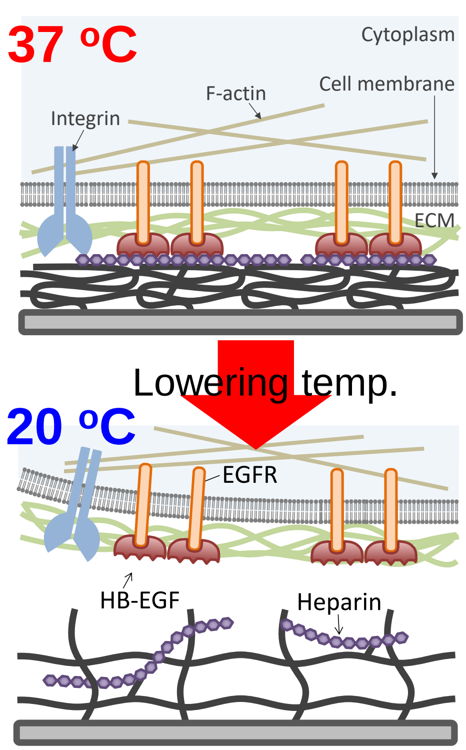
In recent decade, our group has proposed a novel fabrication method of temperature-responsive culture platforms via the physical nanocoating of smart block copolymers, called Smart Surface Cultureware (SSCW®) technology. Smart block copolymers contain hydrophobic blocks as polymer anchors which hydrophobically interact with cultureware surfaces. The SSCW shows a high water-stability even in cell culture environments with temperature changes. In addition, it is easy to control the film thickness on a nanometer scale by varying the polymer concentration in the coating solution, and thus the optimal smart surface can be customized for various cell types with different adhesive properties.



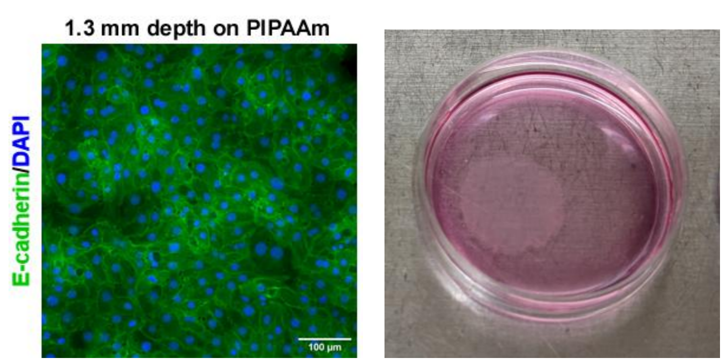
Fabrication method of temperature-responsive culture dish by physical coating of smart block copolymer.

Biomaterials for Cell Sheet-based Liver Tissue Engineering

Cell sheet technology holds promise as an efficient means of transplanting hepatocytes for congenital metabolic liver diseases and acute liver failure. Heparin-immobilized thermoresponsive culture surfaces can bind heparin-binding EGF-like growth factor (HB-EGF) with enhanced stability and activity, resulting in the maintenance of cultured hepatocyte functions such as albumin secretion. At the same time, they allow the detachment as a sheet with lowering temperature due to decreased affinity interaction. Furthermore, subcutaneous transplantation of VEGF-secreting hepatocyte sheets by delivery of mRNA encoding vascular endothelial growth factor (VEGF) has improved the engraftment of transplanted sheets. By using biomaterials-based approaches, we aim to construct transplantable liver tissue efficiently while maintaining hepatic functions.



Heparin-immobilized temperature-responsive culture surface for both tethering growth factor and detaching cells by lowering the temperature.



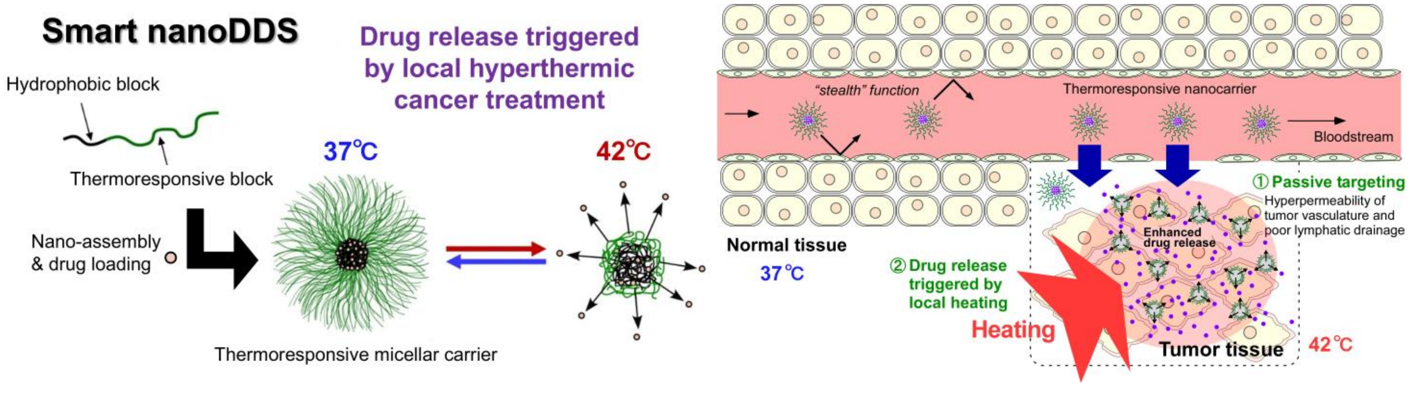
Rat hepatocyte sheet using a temperature-responsive culture dish.
Hepatocytes having cell-cell junctions (left) and transplantable hepatocyte sheet tissue (right).

Research Introduction

Smart Polymers for Biomedical Applications

■ Smart NanoDDS for Cancer Therapy

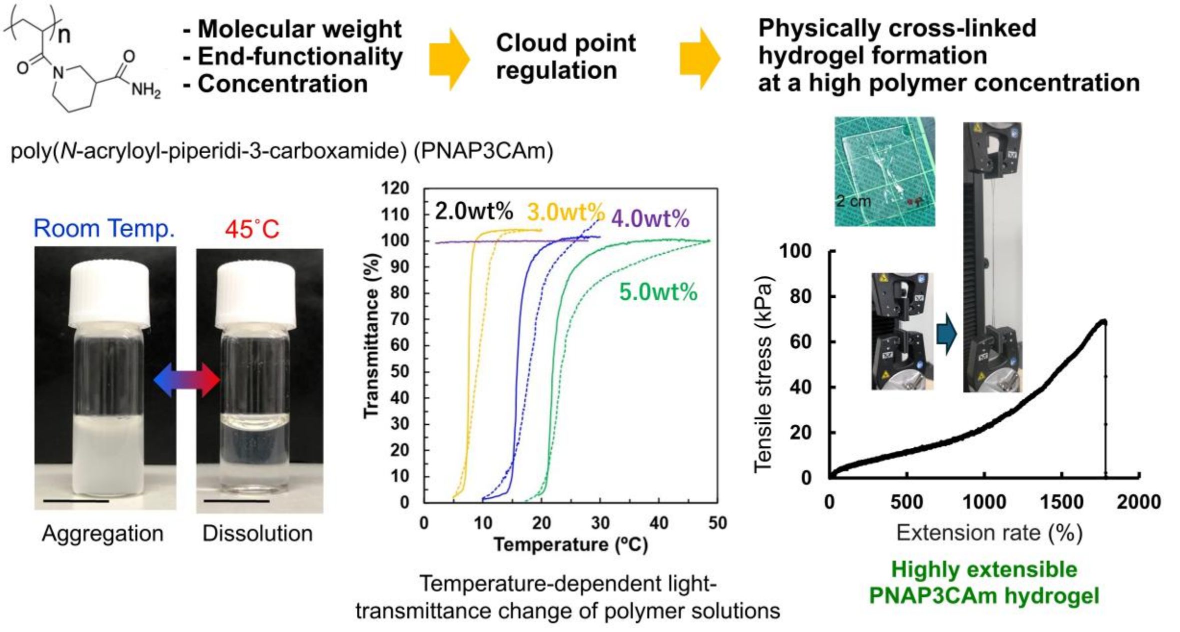
Polymeric micelles formed from amphiphilic block copolymers have a particle size of several tens of nanometers and can encapsulate hydrophobic drugs inside cores. To date, the development of drug delivery systems (DDS) using nano drug carriers is under investigation, taking advantage of the characteristic nanoparticle accumulation phenomenon (Enhanced Permeability and Retention effect) at solid tumors. We have designed temperature-responsive nano drug carriers which can trigger drug release in combination with cancer thermotherapy (heating of the body to around 42^{o}C). After the drug carriers are accumulated in the cancer tissue, energy irradiation is applied only to the affected area, enabling spatial and temporal control of local drug release for the improvement of treatment efficiency as well as side effect reduction.



Smart cancer therapy using thermoresponsive nanocarrier combined with local hyperthermia

■ New Smart Polymers for Biomaterials

Our research group has developed a novel temperature-responsive polymer, poly(*N*-acryloyl-piperidi-3-carboxamide) (PNAP3CAm) exhibiting an upper critical solution temperature (UCST) even under the physiological condition. PNAP3CAm shows to aggregate and precipitate at a temperature below its cloud point, whereas to hydrate and dissolve at a higher temperature due to the temperature-dependent formation/dissociation of inter- and intramolecular hydrogen bonding among their polymer chains. In addition, based on this property of hydrogen bonding formation, we successfully created physically crosslinked hydrogels that exhibit high transparency, high extensibility, and self-healing properties upon temperature stimulation. We are currently investigating the detailed mechanism of UCST expression of PNAP3CA and creating the PNAP3CAm-based biomaterials as well as designing new UCST-type polymers.

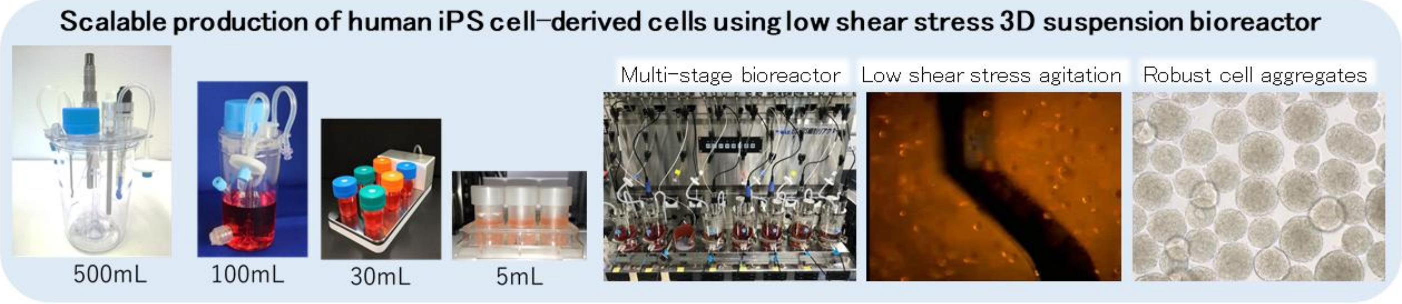


PNAP3CAm as novel UCST-type polymer and its hydrogel with highly extensible property

Research Introduction

Mass Production System for Human iPS Cells

Human iPS cells attract worldwide attention as a promising cell source for regenerative medicine, drug discovery, and disease research. On the other hand, the stable mass production of target cells is indispensable for their practical use and acceleration of research and development. In our industry-academia collaborative research, our research group has successfully performed in high-density mass culture of human iPS cell aggregates by low-share stress agitation. In addition to hardware development, we have also succeeded in mass production of undifferentiated human iPS cells, and iPS-derived cardiomyocytes, pancreatic islet cells, and thyroid follicular cells.

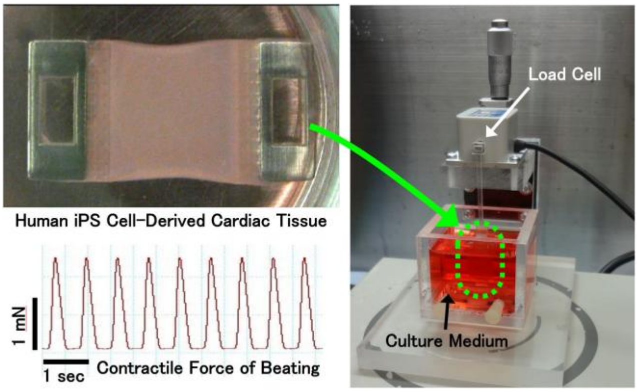


Mass production system for human iPS cells

Human Tissue & Organ Models

■ Human Cardiac Tissue Model and Contractility Measurement System

Animal models have been used in disease and drug discovery research. However, it is desired to develop tissue models that more closely resemble human organisms. Our research group has developed a system for measuring the contractile force of beating cardiac tissues generated from human iPS cell-derived cardiac cells. This system is used for evaluating drug efficacy and cardiotoxicity on commercial service in collaboration with a joint research company. We also work on the application of this system to the evaluation of contractile function of cardiac tissues for transplantation *in vivo* and pathological research as a model of pathological tissue.

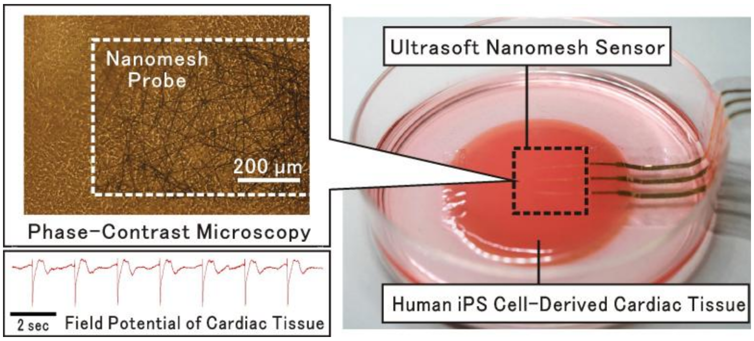


Contractility measurement system for cardiac tissue model

■ Soft Nanomesh Sensor for Measuring Surface Potential of Self-beating Cardiac Tissues

By utilizing of iPS cells and cell sheet engineering, it has become possible to create human myocardial tissue that beats as strongly like a living heart tissue.

Our research group has developed the world's first ultra-flexible nanomesh sensor that can measure the surface potential of beating human myocardial tissue, collaborated with Prof. Someya's groups at the University of Tokyo. This measurement system can be used for drug efficacy and toxicity testing of compounds without using experimental animals, and for functional evaluation of cardiac muscle tissue to be produced for regenerative medicine. Based on this technology, research is also expected to expand into the development of highly functional implanted tissues and bio-actuators that integrate electronics.



Soft nanomesh sensor to measure surface potential of cardiac tissues

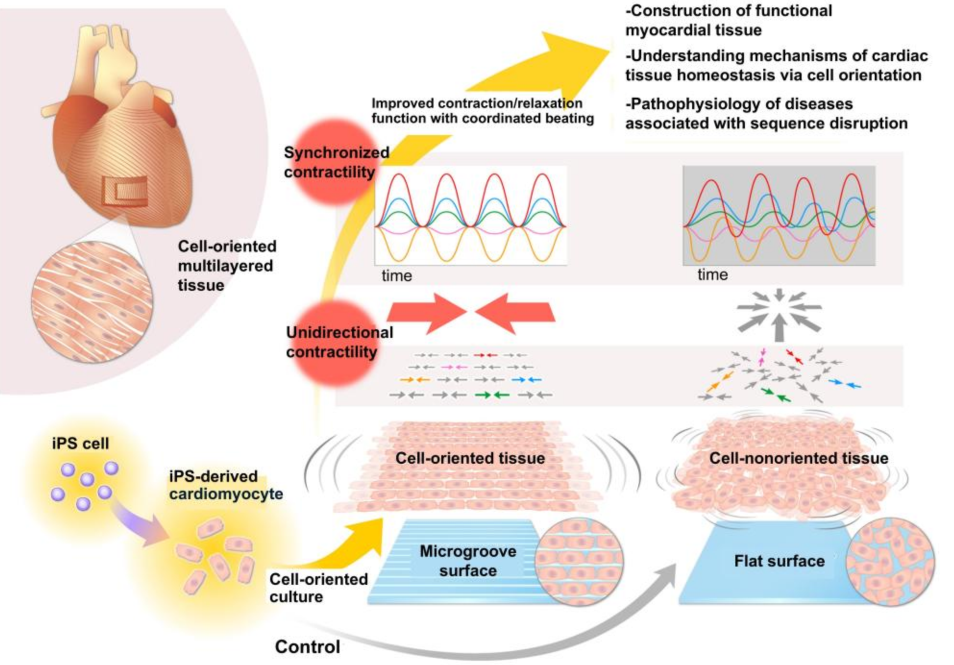
Research Introduction

Human Tissue & Organ Models

Human Cardiac Tissue Model with Controlled Cell Orientation

The construction of biomimicking cardiac tissues is an important issue not only for regenerative medicine, but also for applications in disease and drug discovery research and in understanding the living heart. Although the heart has a tissue structure with oriented cardiomyocytes, the effect and mechanism on the contractile and relaxing functions of the tissue as a whole have not been clarified.

We have successfully produced human cardiac tissue models with controlled cardiomyocyte orientation. The oriented cardiomyocytes show unidirectional contractility-relaxation, and thus this function of the whole tissue is enhanced by promoting synchronous contraction. This finding is expected not only to be applied to the construction of various medical cardiac tissues, but also to clarify the relationship between the disorder of cell arrangement and abnormalities in contraction and relaxation property and proarrhythmic effects in the pathogenesis of cardiac diseases.

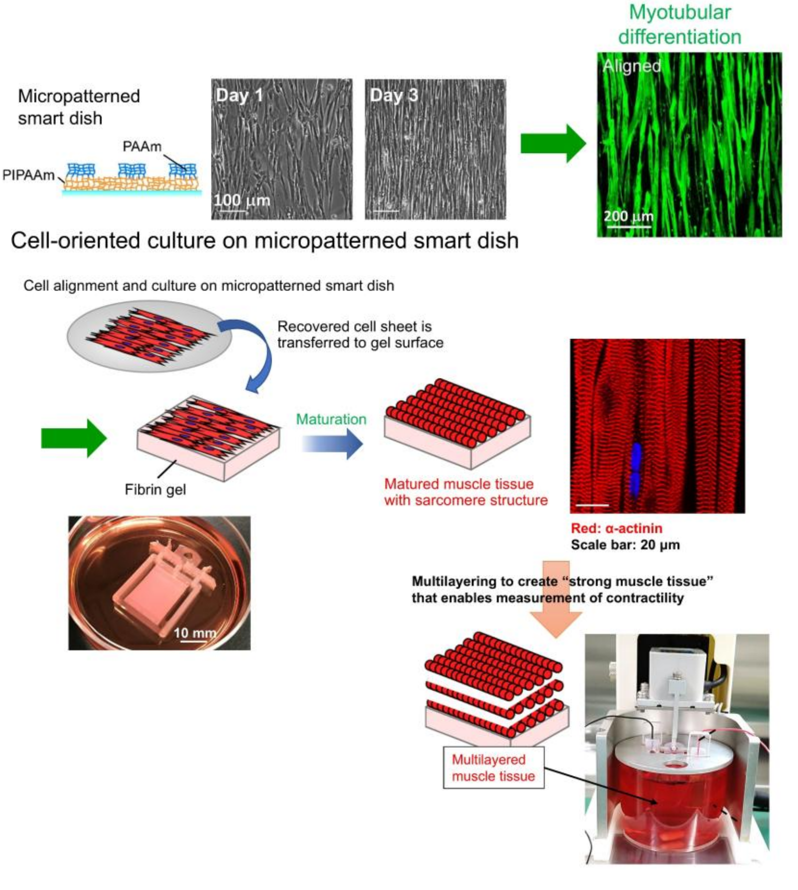


Human cardiac tissue model with controlled cell orientation improves contractile and relaxing functions

3D Human Skeletal Muscle Tissue Model and Contractility Measurement System

Based on cell sheet engineering, our group has successfully produced a three-dimensional human skeletal muscle tissue model that structurally and functionally mimics living muscle tissue via oriented myofiber formation. In addition, a system to measure the muscle contraction via electrical stimulation of the tissue has been also constructed. This system facilitates the real-time detection of drug effects on muscle tissue based on the contraction force change and can be applied to the development of treatments for intractable muscle diseases.

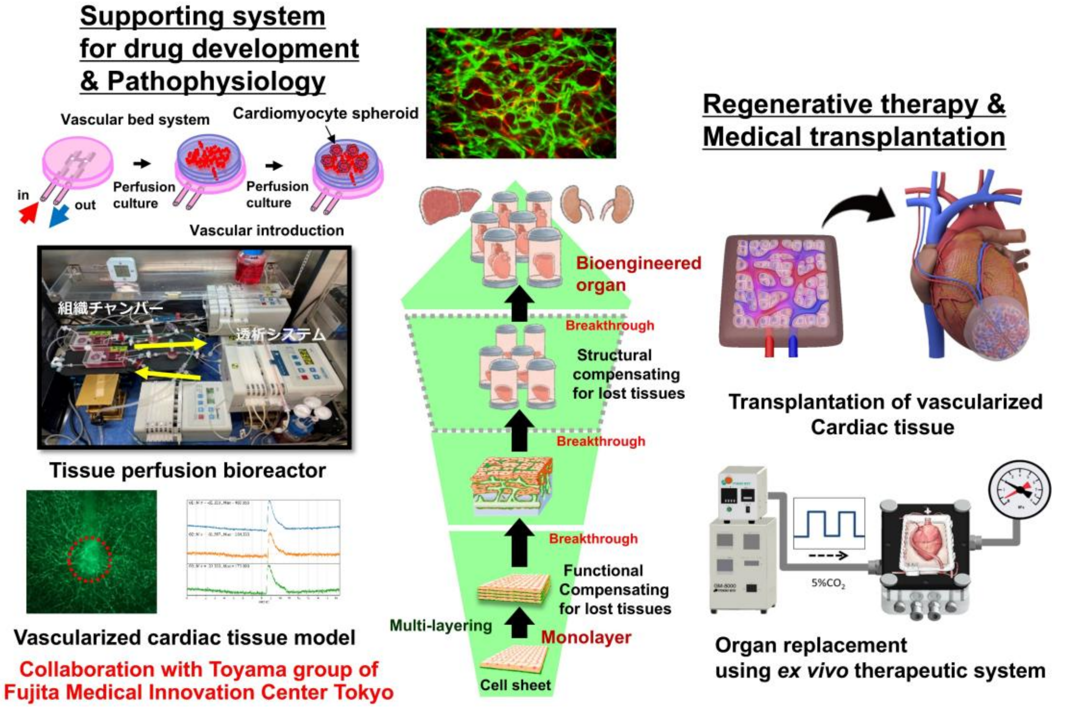
On the other hand, the living skeletal muscle receives nerve-derived signals to move, and thus any abnormality in the nerve tissue will also affect or cause abnormalities in the muscle tissue. Our group has previously shown that the neurons elongate dendrites along the same direction as the muscle fibers in the co-culture between the oriented muscle fibers and human iPS cell-derived neurons. The construction of neuro-muscular tissue with physiologically connected neuro-muscular junctions is expected to contribute to the investigation of the causes of neuro-muscular diseases and the development of treatments.



Research Introduction

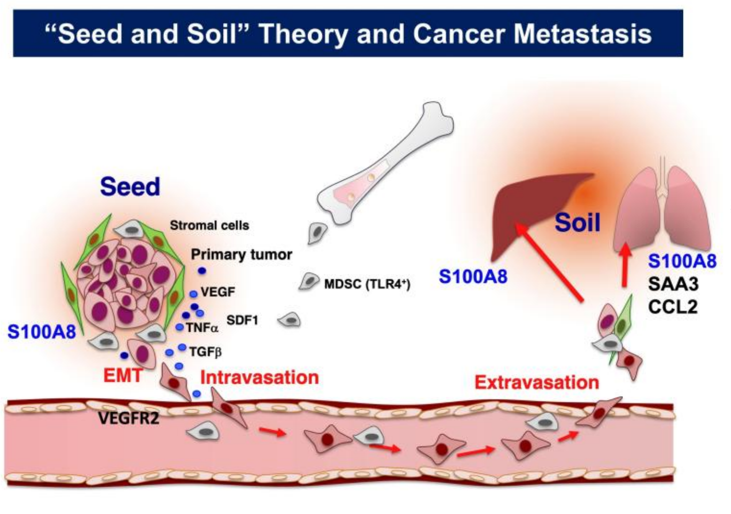
Vascularized 3D Tissue Models

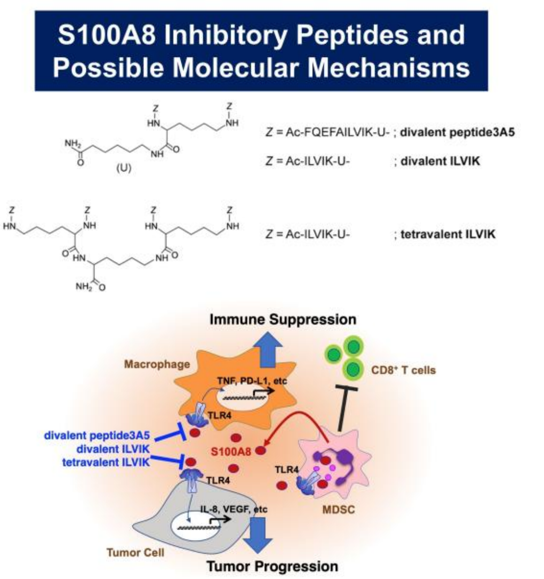
Simply repeating the layering of cell sheets will result in limited tissue thickness due to lack of oxygen and nutrients inside the tissue and accumulation of waste products. Our research group has devised a technology to create a network of blood vessels in tissues by *in vivo* grafting cell sheets, and finally successfully constructed thick three-dimensional tissues. To realize this technology *in vitro*, we are currently developing a vascular network delivery system using vascular beds and tissue perfusion bioreactors.



Development of Novel Cancer Drugs against Tumor Microenvironment

The major causes of cancer deaths are probably due to metastasis to distant organs, and thus effective therapies for metastatic cancer are desired. It is considered that the formation of a premetastatic niche similar to tumor microenvironment promotes metastasis. S100A8, one of endogenous ligands for Toll-like receptor 4 (TLR4), induces the recruitment of bone marrow-derived suppressor cells to the surrounding of tumor and distant organs, which promote metastasis. In addition, the overexpression of TLR4 has been reported in various cancer cells, and the suppression of S100A8 function is expected to inhibit cancer progression and metastasis. We have identified peptides and low-molecular-weight compounds that competitively inhibit the binding of S100A8 to TLR4, and found multivalent S100A8 inhibitory peptides suppress the tumor growth in tumor-bearing mice.



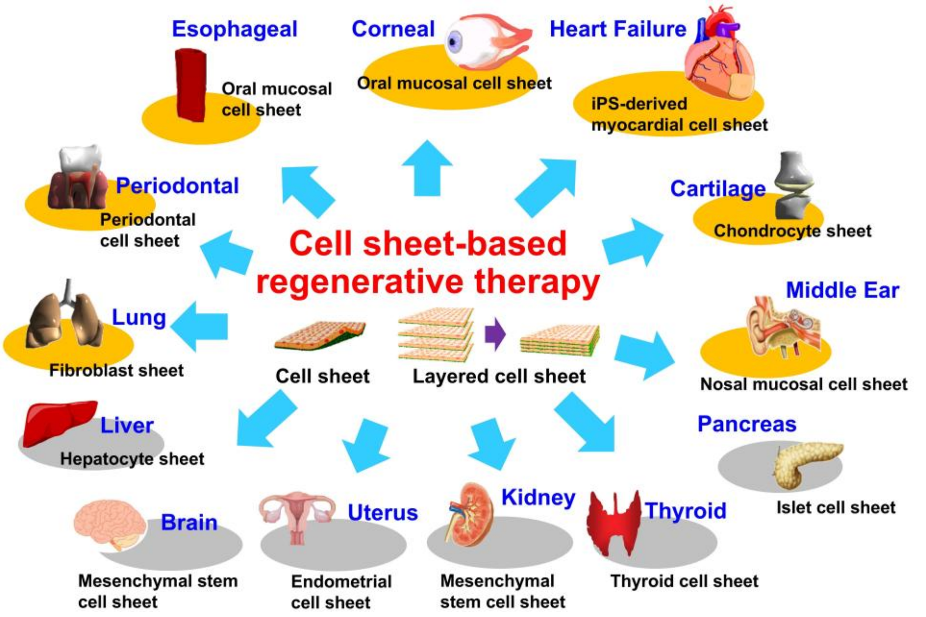


Deguchi A, *et al*, **Cancer Gene Ther,** 30, 2023

Research Introduction

Cell Sheet-based Regenerative Medicine

Enzyme-free recovered "cell sheets" retain adhesive proteins that act as biological glues. Therefore, cell sheets can be transplanted into living tissues by simply attaching them. We have been promoting cell-sheet-based regenerative medicine for various tissues and organs.



■ Ischemic Brain Disease Therapy

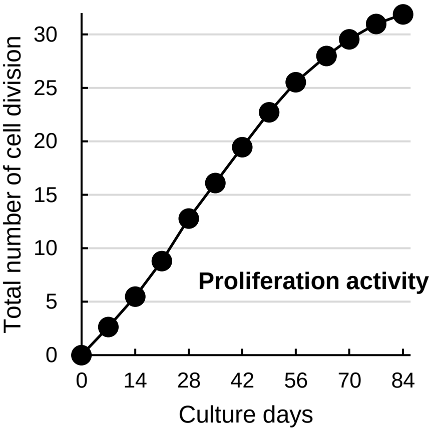
In collaboration with the Department of Neurosurgery of our medical hospital, our group are developing a novel therapy for cerebrovascular disorders. We have transplanted mesenchymal stem cell sheets into a rat cerebral infarction model, and reported that they can induce angiogenesis and nerve regeneration in the ischemic brain, leading to improvement of behavioral disorders. Currently, we are conducting research for clinical application to cerebral infarction and vascular dementia.

■ Pulmonary Air Leak Closure Surgery

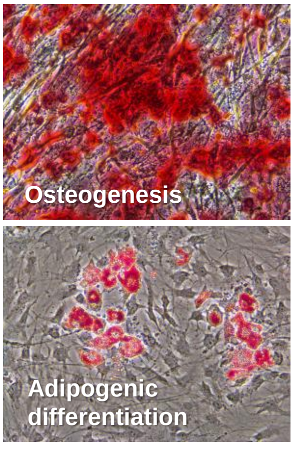
No surgical technique has been developed to completely prevent pulmonary air leaks as the one of the complications after lung resection. In collaboration with the Department of Pulmonary Surgery of TWMU, we have revealed that fibroblast sheets are effective as a biosealant to prevent postoperative air leaks. We are currently working to establish a treatment for the closure of lung air leaks by transplantation of autologous skin-derived fibroblast sheets.

Development of Cell-based Muscular Dystrophy Therapy

Muscular dystrophy is a progressive genetic disorder that causes gradual muscle deterioration. Duchenne muscular dystrophy (DMD) is the most common form of the disease, affecting 3 to 5 per 100,000 people in Japan. Mesenchymal stem cells (MSCs) are known to be involved in tissue repair and suppression of inflammation, and are expected to be a DMD treatment. In collaboration with the Department of Pediatrics and the Institute for Experimental Animals, the University of Tokyo, Meiji University, and Kyoto Animal Testing Center, we are evaluating the contribution of MSC transplantation, which has proliferative and differentiation potential, to the improvement of DMD using animal models of DMD. Based on this investigation, we aim to properly evaluate the efficacy of MSC transplantation and to link it to future clinical applications.



Differentiation potency



Weekday 8:30 a.m. – 6:00 p.m.
Saturday 8:30 a.m. – 1:00 p.m.
Close 3rd Saturday, Sunday, & Public Holidays etc.

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