Institute for Integrated Cell-Material Sciences

iCeMS Our World, Your Future

Kyoto University

Vol. 3
2017 January

contents

Image of molecules adsorbed to a metal copper surface, with formulas from the field of machine learning. When the adsorbed molecules organize into a straight line, we can produce a wire as fine as one-hundred-thousandth of a human hair. Employing mathematical models, we can identify the types of molecules predisposed to this orientation and ideal conditions for their alignment. Turn to page 6 to read the full story.

Feature Timeline:

Ten Years of iCeMS

Founded in 2007, iCeMS marks its 10th anniversary in 2017.
How have the seeds planted upon iCeMS' inception grown in the past ten years?
In this article we look back on the history of iCeMS.

The growth of the courtyard garden marks the swift passage of time.

2007

- iCeMS selected by MEXT as a **WPI Research Center**
- iCeMS founded
- The first iCeMS Seminar held

Prof. Norio Nakatsuji, Founding Director

The World Premier International (WPI) Research Center Initiative

A project launched in 2007 by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) to establish "globally visible" institutes with superb research environments and high quality results. Five institutes including iCeMS were selected as WPI Centers in 2007.

2008

- **The Center for iPS Cell Research and Application (CiRA) established as part of iCeMS**
  (Founding Director: Prof. Shinya Yamanaka)
- **The Science Communication Group (SCG) formed**
- The first **iCeMS Café** held

CiRA established

Science Communication Group

Works as a bridge between researchers and the public. Attracted much attention with its "Hands on with Stem Cells!" sugoroku (Japanese board game) released in 2015.

iCeMS Café

An opportunity for casual dialogue about science between iCeMS researchers and the public in a relaxed atmonphere.

2009

iCeMS Main Building

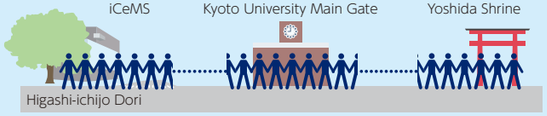
- **iCeMS Main Building completed**
- iCeMS Satellite at Gifu University established
- The first iCeMS retreat (researcher's camp) held

Piano in the iCeMS Lounge, a gift from the founding director

Participants at the 20 iCeMS Cafés to date

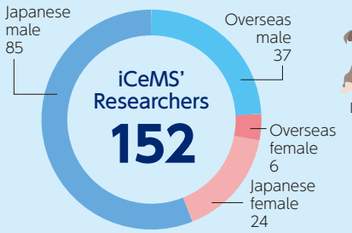
Cumulative total **543**

Enough to form a queue from iCeMS to the entrance of Yoshida Shrine!



(Job titles as of the dates of respective events)

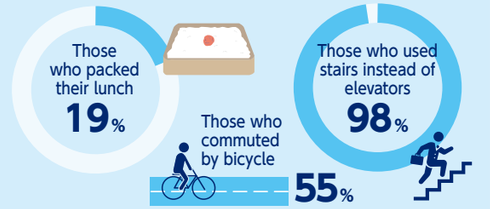
iCeMS' Reserachers



National origin of overseas researchers

Pets favored by researchers

A day in the life of researchers



Musical instruments owned by researchers

(Data as of April 1, 2016)

2010

- **Prof. Susumu Kitagawa listed as a Thomson Reuters Citation Laureate**
- The iCeMS Satellite at the Tata Institute of Fundamental Research National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem) in India opened
- The 10th iCeMS Café held

Thomson Reuters Citation Laureate

Thomson Reuters annually honors the authors of excellent papers cited with extreme frequency by other researchers. This serves as a clue to predicting Nobel Prize nominees!

iCeMS
WPI Centers : 6

Tree planted upon the inauguration of the NCBS-inStem Satellite. See how tall it has grown!

Joint Symposium with Heidelberg University

2011

- Project launched by Director Norio Nakatsuji et al. to achieve the practical use of ES cells
- Sugiyama Lab developed a DNA self-assembly system, the **"DNA origami"** method.
- Joint Symposium with Heidelberg University held in Heidelberg, Germany

DNA origami

DNA origami is the nanoscale folding of DNA strands to create two- or three-dimensional structures. The specificity of the interactions between complementary base pairs makes DNA a useful construction material.

(Job titles as of the dates of respective events)

2012


Joint Symposium (Beijing)

iCeMS
WPI Centers : 9

- **Joint Symposium with the Center for Life Sciences (CLS) at Tsinghua and Peking Universities held in Beijing, China**
- **Co-hosted the World Stem Cell Summit 2013** (Florida, USA) **with Karolinska Institute and others**
- **Prof. Shinya Yamanaka awarded the Nobel Prize in Physiology or Medicine**


Press conference upon Nobel Laureate announcement

New Director appointed

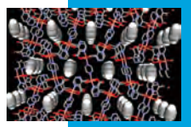

Prof. Susumu Kitagawa, Director

Biomaterials Science

2013

- **Prof. Susumu Kitagawa appointed as new Director of iCeMS**
- "Biomaterials Science" journal, co-published with the Royal Society of Chemistry (RSC), launched
- The 10th Japan-France Workshop on Nanomaterials and the first WPI Workshop on Materials Science (Kyoto) co-hosted by four WPI Centers in material science and Le Centre national de la recherche scientifique (CNRS), France
- **Porous materials that release gas molecules in response to light irradiation** developed by the research group led by Assoc. Prof. Shuhei Furukawa, Asst. Prof. Stéphane Diring and Director Susumu Kitagawa

\More Info! /
The developed porous coordination polymers (PCPs) were assembled using metal ions and organic links, which possess framework structures with one nanometer porosity. Nitric oxide trapped in pores can be released on-demand by light irradiation.



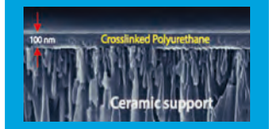
2014


E-MRS

- "The Chemistry of Life" online **edX lecture** opened by Prof. Motonari Uesugi
- **Four WPI institutes in material science participated in the European Materials Research Society (E-MRS) 2016 Spring Meeting** (Lille, France)
- Assoc. Prof. Easan Sivaniah's group **developed superior gas separation membrane materials.**

edX Lectures
Free online courses from more than 20 world-leading universities, including MIT and Harvard. iCeMS was the first Japanese institute to join this project. Around 26,000 students have taken Prof. Uesugi's lecture.

\More Info! /
Gas separation membranes are a technology proposed to separate carbon dioxide from exhaust gases. The team has successfully developed membrane materials which exhibit superior properties and greater durability at a lower cost than conventional membranes.



2015

- **Her Royal Highness Princess Maha Chakri Sirindhorn of Thailand visited iCeMS**


Princess Sirindhorn visiting iCeMS

- Assoc. Prof. Tatsuya Murakami's group developed a light-induced **method for controlling pain sensations in single neuronal cells.**

\More Info! /
When illuminated by near-infrared light, rod-shaped gold nanomaterials are capable of highly efficient heat generation. Engineering the surface of these nanomaterials with serum proteins effectively and safely delivers them to the plasma membrane of sensory neurons. Upon illumination of the gold-nanomaterial-bound cells, TRPV1, the primal heat-sensitive nociceptor in our body, can be locally heated to induce a pain signaling. This is the first demonstration of remote control of TRPV1 in intact neuronal cells.

- First Learning Lounge held
→ See page 11 for details
- Workshops linked to the "Think Like a Crow!" TV program on NHK Educational
- "Our World, Your Future" newsletter launched


"Think Like a Crow!" linked workshop


iCeMS Retreat (researchers' camp)

2016


Lecture by Prof. Jean-Marie Lehn

- Signing of the partnership agreement with Vidyasirimedhi Institute of Science and Technology (VISTEC), Thailand
- **200th iCeMS Seminar Special lecture by Prof. Jean-Marie Lehn, a Nobel Laureate in Chemistry**

Microscopes at iCeMS: 156


(Data as of April 1, 2016)

Access to iCeMS Main Entrance

From Kyoto City Bus Kyodai Seimon-mae stop :	10 steps
From the Kyoto University Main Gate :	283 steps
From the Keihan Line Demachiyanagi Station :	1,418 steps

Government subsidies over the past 10 years

JPY 12,739,467,588.-

The height in stacked one-yen coins:

Approx. 19,109,000 meters

about 5,060 times as high as Mt. Fuji

The biggest purchase

Leica Microsystems TCS SP5 STED (Stimulated Emission Depletion)

Price : JPY 138,390,000.-

This "super-resolution microscope" was developed by 2014 Nobel Prize Laureate Dr. Stefan Walter Hell. It visualizes detailed cellular structures and functions at a spatial resolution of more than 100 nanometers (ten-thousandth of one millimeter).

The Gozan Okuribi bonfire observable from iCeMS: 4 mountains

- Daimonj
- Hidari Daimonji
- Funagata Mandoro
- Matsugasaki Myo-Ho (Ho)

A central processing unit (CPU), the brain of a computer, has eight billion transistors arranged on a five centimeter square substrate. Each transistor is about 20 nm, almost five thousandth the diameter of a human hair. Such minuscule and sensitive electronics require nanofabrication techniques to assemble and align atoms and molecules. Daniel Packwood has successfully developed such synthesis methods by utilizing theoretical chemistry that explain intricate molecular actions with mathematical models.

Daniel Packwood
Born in 1985 in Christchurch, New Zealand. Completed his PhD in chemistry at the College of Science of the University of Canterbury in 2010 and came to Japan as a chemistry postdoc of the Kyoto University Graduate School of Science. Has remained in his present position since 2016, after working for the Advanced Institute for Materials Research (AIMR) at Tohoku University.

Towards ultra-thin wires using mathematical models

Daniel Packwood

Junior Associate Professor

In contrast to his mastery of mathematics today, Packwood did not excel academically before entering the university. He barely passed the college entrance exam in New Zealand. "I struggled in mathematics, and I gave up learning Japanese - I had only chosen it because I was a big Super Nintendo fan [laughs]."

Friends' remarks motivated young Packwood. "Friends of mine said that math and chemistry would be too difficult for me. It was just a casual comment, but I felt insulted at that time for my scores were actually low." Packwood studied hard to prove his friends wrong and awakened to the appeal of chemistry and mathematics.

Charms of iCeMS: High-level research and flexible cross-disciplinary approaches

Packwood originally sought a research position in the West, but a conference in Japan opened his eyes to the high level of research here. "I immediately contacted a laboratory at Kyoto University." After spending one and a half years in Kyoto, he moved to the Advanced Institute for Materials Research (AIMR) at Tohoku University, another World Premier International Research Center. Since April 2016, he has been a member of iCeMS.

Packwood feels that the unpartitioned laboratories of iCeMS permit cross-disciplinary communications. "Sometimes my fellow researchers ask for my comments on fresh experimental data. New ideas occur to me one after another as I talk with them."

Next-generation wires as fine as one hundred-thousandth the size of a human hair

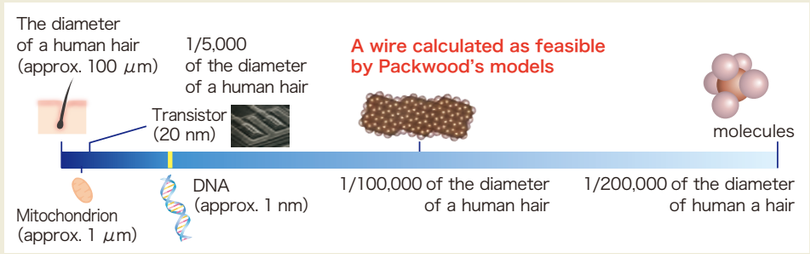
Packwood focuses on the study of "molecular self-assembly," a phenomenon seen in the growth of snow crystals or double-helical DNA, where molecules naturally organize into functional structures. He aims to apply this mechanism to nanotechnology. "If molecules lie on a straight line and become organized, we should be able to produce a wire as fine as one hundred-thousandth the size of a human hair. This will definitely contribute to the miniaturization of electronic devices." Utilizing predictions from an original mathematical model, Packwood has successfully identified the types of molecules predisposed to form straight lines, along with ideal temperature conditions for alignment. His achievements promise to lessen the need for time-consuming and costly experiments, a rewarding step forward.

While a few of his findings still require validation with experimental data, Packwood is quite optimistic. "iCeMS has an environment for collaboration, so I can readily demonstrate my theory through experiments. I am sure my study will bear more and more fruits from now. I hope to perfect a real product while being here at iCeMS."

Developing mathematical formulas in his head

Pen, paper, and a computer are all Packwood needs to conduct basic research. He has filled hundreds notebooks since college. "I can write formulas in my head these days. Equations are like good friends to me. I memorize their every feature, just like I remember names, faces, voices." Sometimes he even starts calculations in his head. "Thinking about research all the time is part of being a researcher. It's the same as monks, who are monks all the time."

Packwood says that he felt more stress about his research in his twenties because of then-insufficient knowledge and experience to identify research targets. "But now, in my thirties, I have a broader range of methodologies to utilize, and can find solutions more quickly than before. And my research outcomes make my work all the more interesting. Research involves continual hardships with days of repeated failures, but once it bears fruit, it is very satisfying!"



At Koiwai Farm in Morioka, Iwate, in September 2014. Packwood has visited many places in Japan, from Wakkanai in the north to Nagasaki in the south. He particularly loves countryside richly endowed with nature. "Contact with nature makes me feel human again!"

"Animals have so many different shapes. How interesting!" Hasegawa's boyhood excitement motivates him even today. Driven by curiosity, he maintains a stance of "doing what I like", which now is investigating the mystery of animal body formation through stem cells. Stem cells can "differentiate" into various types of tissues/organ cells. Understanding and controlling such differentiation contributes innumerably to fields such as regenerative medicine and drug development. Fascinated by this quest, Hasegawa energetically pursues research in Japan, India and Australia.

Kouichi Hasegawa
Born in 1972 in Kumamoto, Japan. Graduated from Hiroshima University in 1995, with major in zoology from the Department of Biological Science. Received a PhD in 2000 from Kwansei Gakuin University Graduate School of Science. Held positions as Researcher with Institute for Frontier Medical Sciences, Kyoto University and Assistant Professor at Department of Cell and Neurobiology, University of Southern California. Has served as Junior Associate Professor of iCeMS Satellite at NCBS-inStem and Assistant Professor of NCBS-inStem in India since 2011, as well as Senior Researcher with Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne since 2014. Works as an advisory board for some entrepreneurial ventures.

Focus on your interests to lead the way

Kouichi Hasegawa

Program-Specific Research Center Junior Associate Professor

"Why do animals look so different from each other?" This simple question was how Hasegawa, born and raised close to nature in Tamana City of Kumamoto Prefecture, started towards research.

Hoping to study only animals

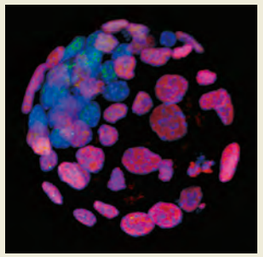
Hasegawa prioritizes what he likes, so much that people ask, "How can you be so careful in your experiments while being so careless about your daily life?" For this reason, he chose Hiroshima University, where he could specialize in zoology from year one.

Hasegawa's study convinced him that organized development was key to understanding animal morphology. Consequently, he wanted to conduct graduate study with Prof. Tsutomu Kinoshita. Just then, however, Prof. Kinoshita was promoted to Kwansei Gakuin University, where chemistry was mandatory in the postgraduate exam. Hasegawa, obsessed with biology, had hardly studied chemistry, but he still wanted to join. He intensely studied, successfully passed the chemistry exam, and realized his ambition to study embryology under Prof. Kinoshita. "He drilled into me the ABCs of research, including how to formulate a question, perform experiments and write a thesis and scientific manuscripts."

Encountering stem cell research and working overseas

In 2000, when Hasegawa completed his doctorate, Japan had scarce job openings. To pursue research further, rather than job hunting, he joined Dr. Norio Nakatsuji's laboratory, then at the Institute for Frontier Medical Sciences, Kyoto University. "At first I was in charge of preparing genetically engineered mice. As Prof. Nakatsuji recognized my experimental skills, I transitioned to deriving embryonic stem (ES) cells for monkey and human embryos."

Years later, at Prof. Nakatsuji's suggestion, Hasegawa applied to the laboratory of Prof. Martin Pera, a renown stem cell researcher. Prof. Pera was just leaving Australia to work in the United States, so Hasegawa followed him to the University of Southern California. There, under Prof. Pera's influence, he established his research style and mastered American research grant applications.



A stained embryo at initial cellular differentiation from a fertilized egg; future somatic cells in green are distinguishable from future placenta cells in red.

Hasegawa at a wedding with his colleagues in India. "Experiencing diverse cultures and perspectives in India is quite fun and helps me in expanding my views—though it does often bring conflicts to my work."

Traveling and research across three countries

In the aftermath of the economic crisis of 2008, Hasegawa was called back to Japan by Prof. Nakatsuji, then director of iCeMS. He asked Hasegawa to launch an iCeMS satellite laboratory at the National Centre for Biological Sciences (NCBS) in India. "I was quite puzzled, but I am not a kind of person who rejects someone's requests [laughs]."

NCBS had ample start-up funds, but its facilities were still under construction. Kyoto, on the other hand, had facilities but not enough research funds for Hasegawa at the mid-year. He was at a loss as to how to proceed when Prof. Pera contacted him to ask for help launching a laboratory at the University of Melbourne. Hasegawa immediately accepted his request and headed for Australia. "The start-up was certainly a hard work, but I was able to use an adjacent lab to conduct my experiments in my spare time. The three months I spent there were very fulfilling, and I successfully completed two papers."

Hasegawa loves motorcycling. Driving through the American wilderness offers a chance to re-examine himself in comparison to the greatness of nature.

Since then, Hasegawa is mainly based in Kyoto and India, flying back and forth between the two almost monthly and visiting Australia on a regular basis. "In fact, I just came back from India yesterday! I conduct my research in those three places, but what I do is totally different because each location has its own facility condition, fund status and research climate." In Kyoto, he conducts basic research on stem cells, whereas in India he utilizes stem cell differentiation to search for cures for malaria or other diseases. "Now that I have a base in India, I definitely want my research to help Indian people. And I also hope that my basic research in Japan, as a foundation for medical treatment and technology, will help many patients."

iCeMS Fund — Help us grow

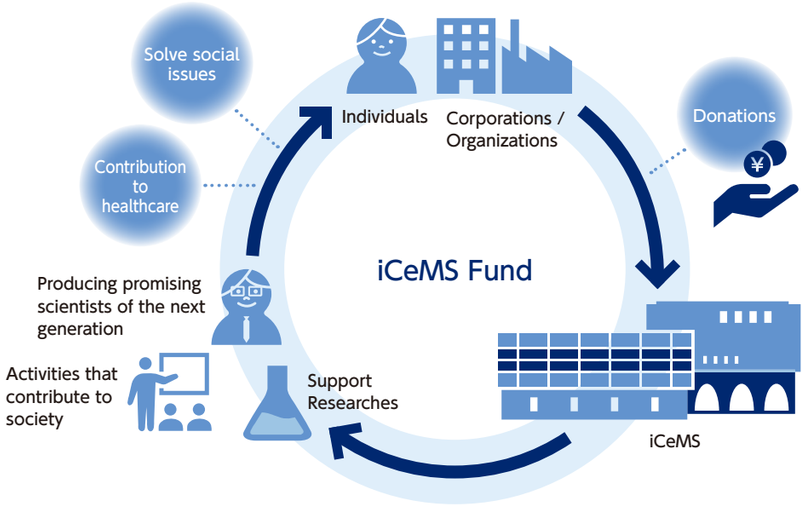
At iCeMS, we develop new insights into the principles of life that distinguish living things from non-living things, and harness these ideas to create bio-inspired super materials and devices that will revolutionize health-care, medicine, industry and the Environment to create a sustainable world for us all.

Whilst much of the work we do here is Pure Science, we are absolutely certain that our research combining high-level chemistry, cell biology and physics, at the border between materials and life, will meaningfully impact the world in which we live.

The research we carry out at iCeMS will help doctors to fight such perennial problems as heart disease, cancer, and degenerative brain conditions, as well as develop invaluable new medicines and therapies. Our revolutionary work also addresses key issues such as global warming, pollution, over-dependency on fossil fuels, and the availability of clean drinking water.

Generous gifts from donors like you provide the financial and moral support needed to continue and develop this research at the cutting edge of modern science. We are not merely content to improve existing technologies, but seek to affect paradigm shifts in the way science may benefit humanity.

Help us to help the world. Together we can make a difference because we care.



Kyoto University Fund webpage

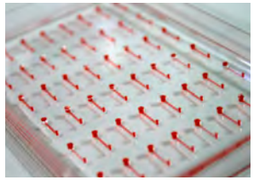
http://www.en.kikin.kyoto-u.ac.jp/funds-in-operation/icems/

iCeMS in brief

• Research Highlights •

A unique device to create a small and optimal 3D environment for human pluripotent stem cells

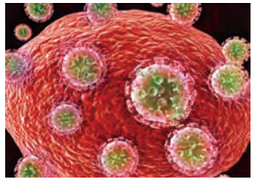
The research group led by Prof. Yong Chen and Assoc. Prof. Ken-ichiro Kamei have developed a microfluidic device with a number of advantages for controlling cellular microenvironmental factors. A thermo-responsive hydrogel, which can transform between solution and gel by changing temperature, combined with the microfluidic device allows for the creation of an artificial 3D cellular microenvironment for hPSC culture and analysis.



The microfluidic device (1 cm length, 1 mm width, 200 μm height)

New fluorescent probes help solve cell membrane mystery

The research group led by Profs. Makoto Kiso, Akihiro Kusumi and Assoc. Prof. Kenichi Suzuki have observed raft domains—active sections of the cell membrane—in live cells for the first time. They observed how gangliosides form raft domains with cholesterols and a special receptor protein, CD59, from the class of GPI-anchored receptors. Now, researchers can begin to investigate how toxins, bacteria and viruses invade cells through these raft domains.



An illustration of HIV/AIDS viruses surrounding and attacking a host cell

Copyright : William Roberts/123rf

• What's new? •

Extension Lectures for High School Students: iCeMS Caravan's "The Mechanism for Learning"

Starting with an ice-breaker

Young iCeMS researchers conducted an active-learning educational program for high school students called "iCeMS' Caravan." The Caravan attempts to provide high school students with a chance to experience the process of transforming knowledge into wisdom, conveying ideas to other people, and the "mechanisms for learning" that are hidden in these processes. At the beginning of each session, researchers provide basic knowledge. The students then create their own ideas through group work, finishing with an easy-to-understand presentation that follows the structure of scientific manuscript.

"Learning Lounge"

The "Learning Lounge" features young scientists who deliver a 20-minute presentation to persuade any curious listener, even those without a scientific background, that their research area is important to the world. Each talk is recorded and when possible, publicized online. You can watch Learning Lounge talks by visiting the following URL;
http://www.icems.kyoto-u.ac.jp/en/community/lounge/
You are welcome to join the Learning Lounge. No registration is required. Please check our website for details.

#1 - June 29, 2015
Dr. Ken-ichiro Kamei "My Life as A Microchip"*
Dr. Koh Nagata "What Did You Eat Yesterday? —How to Manage Your Cholesterol"*

#2 - August 3, 2015
Dr. Ganesh Pandian Namasivayam "Nature-inspired Cure for the Incurable—Coming Soon?"*
Dr. Marcel Hörning "What is a Heart Attack?"*

#3 - October 21, 2015
Dr. Aya Sato-Carlton "How Is Your DNA Passed Onto Your Children?"*
Dr. Hideki Hirori "Making Invisible Worlds Visible"*

#4 - November 19, 2015
Dr. Yuta Takano "Powering the People with Nano Solar Cells"*
Dr. Yoji Kojima "Decoding the Keys of Our Life Cycle"*

#5 - February 25, 2016
Mr. Hirotaka Nakatsuji "Golden Rods & Guided Robots: Your 'Nano Doctors' Healing from Within"*
Ms. Ikumi Oomoto "Seeing is Believing; What Happens in the Brain?"*

#6 - March 31, 2016
Dr. Akihisa Yamamoto "Sticky Moments in Biology"*
Dr. Georgia Kafer "Protecting Your DNA Code"*

#7 - Apri 27, 2016
Dr. Kouichi Hasegawa "Making Malaria the Last Century's Problem"*
Dr. Daniel Packwood "Nanotechnology by Herding Molecules —Hints from Theory"*

#8 - July 28, 2016
Dr. Ayami Joh "Every Little Bit Counts in Human Interaction"
Dr. Alfonso Avila-Robinson "Seeing the Dynamics of Science Convergence"

#9 - September 28, 2016
Dr. Patrick Larpent "Nano-Pockets to Trap Carbon Dioxide"
Dr. Wan-Ting Hong "Zoo from Lorises' Point of View"

#10 - November 24, 2016
Dr. Junjun Li "Catch Me If You Can"
Dr. Yoshihiko Fujita "Gene Switch: Asking Cells, 'Who are You?'"

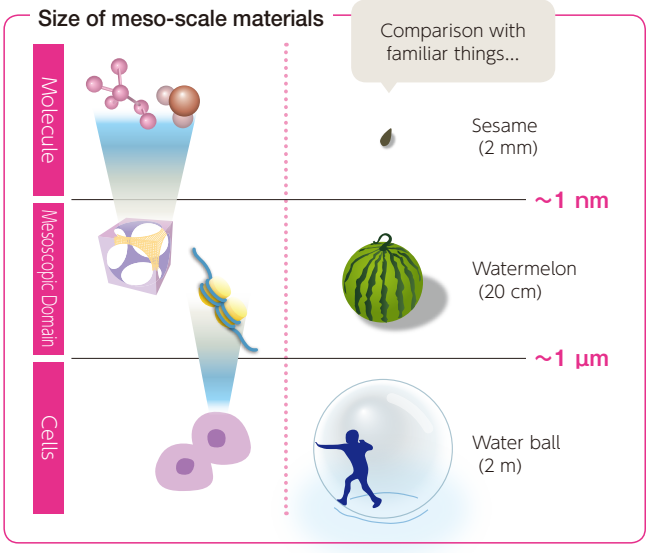
* Marked talks can be watched on the web.

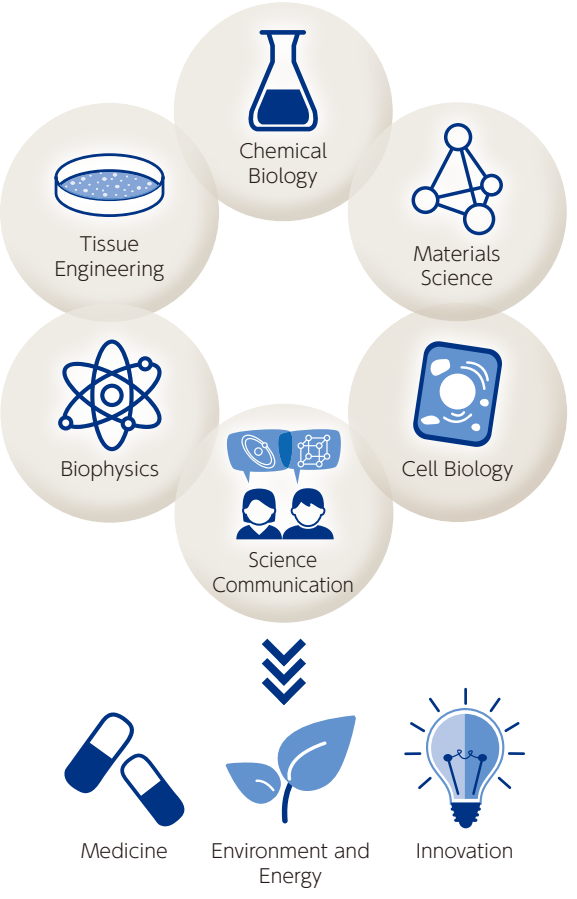
Explore the secrets of life and innovate for the good of society

iCeMS' Mission

- Explore the secrets of life by creating compounds to control cells
- Create life-inspired new materials for the future

Global warming. Pollution. Disease. Aging. These major concerns can no longer be countered by traditional single discipline-based research. At iCeMS, cell biologists, biophysicists, chemists, material scientists, physicists, and bioengineers share ideas and work together to devise new ways to integrate cells and materials, all for the greater good. We find inspiration through collaboration. We leverage our critical mass of scientific and technological knowledge into purposeful, transformative innovations for the practical benefit of society.





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