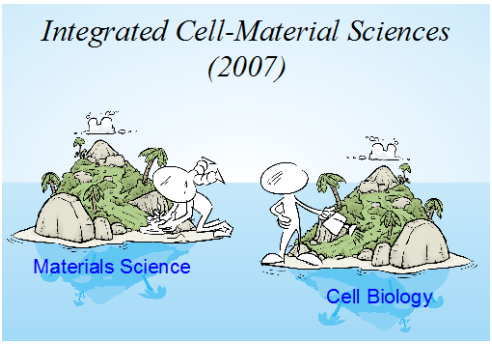
World Premier International Research Center Initiative (WPI)
Executive Summary (for Final Evaluation)

Host Institution	Kyoto University	Host Institution Head	Juichi Yamagiwa
Research Center	Institute for Integrated Cell-Material Sciences (iCeMS)	Center Director	Susumu Kitagawa

About filling out this form:
This summary is to be based on the Center's Progress Report and Progress Plan, with reference to the following items, prepare the summary within a space of **up to 6 pages.**

A. Progress Report of the WPI Center

I. Summary



iCeMS, in its 10 years program, has always set out to establish a unique place in science, at the interface of fundamental cell biology and materials science. This means that a fundamental approach is taken to the way that cell biology and materials can be combined to become relevant to global issues such as disease or diet, energy or the environment. This was a truly ambitious since the two fields could not be more different. Cell biology is the study of an evolved state with a complexity that we attempt to unravel to understand life. Material science is a state that grows more complex by our leaps of inspiration. In the integration of such diverse philosophies of science, we hold the tantalizing prospect of generating a new interdisciplinary field.

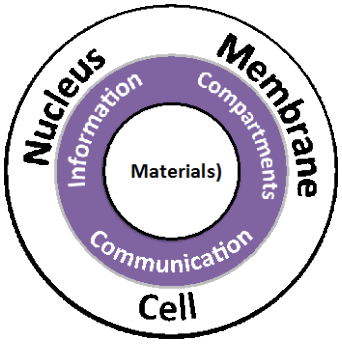
The WPI program at iCeMS was always about creating and spreading the creed of '**Global Awareness, Lateral Thinking, Iconoclastic actions'**. iCeMS has been an island of creative free thought in science and administration for the last 10 years, providing a catalyst for innovative change in the rest of Kyoto University's administrative system. We must continue to preserve this creed so it becomes deeply embedded within Kyoto University and indeed throughout the fabric of Japanese Universities.

Kyoto University had long considered the establishment of an overarching institute to capture the key precepts of iCeMS. In 2016 Kyoto University has successfully established the Institute for Advanced Study (IAS) under the leadership of Fields Medal winner Prof. Shigefumi Mori. The credibility of IAS was guaranteed by the inclusion of iCeMS to it as its flagship institute, and by securing the future participation of most of the current WPI-iCeMS senior PIs as well the very best of untenured young iCeMS researchers.

iCeMS can look proudly on its achievements, from its status within Kyoto University, as the place where traditions can be set-aside and replaced with new rules reflecting an internationalized research administration. It can reflect on its creation of an English language research environment with a 30% international researcher, and twice the national average of female researchers. It can bask in a constantly high level of research success, and the foresight of inviting a future Nobel prize winner as part of its world-class cadre of researchers. It can glow at the media attention the institute has garnered domestically. However now, looking forward, iCeMS is active in making sure the rest of the world knows what Japanese science knows, and which the WPI committee has acknowledged; that it is a world premier institute. This last step, the missing piece, is actually lacking across the spectrum of Japanese academia. *The biggest future priority for iCeMS is a successful systematic international communication of itself and WPI, Japanese Science's flagship international research program*.

II. Items

1. Overall Image of Your Center



At iCeMS, we gathered an exceptional collection of internationally known cell biologist, materials scientists and chemical biologist from Kyoto University, from Japan and from around the globe, who were equally motivated by this difficult but rewarding challenge. These eminent researchers were given the freedom to define, through their collaborations, the framework of what such a new interdisciplinary movement would like. Under the iCeMS leadership of Prof. Susumu Kitagawa, a world class leader in materials science, an equal dialogue was established between the key iCeMS field of cell biology and materials science to identify the core values of iCeMS in the last 10 years. This resulted bring focus to the natural process of developing iCeMS identity as "**Materials for Cell Elucidation and Control**". This encompasses a holistic interaction between materials and the three essential properties of cells and cell biology, **Cell Communication**, **Nucleus Information** and **Membrane Compartments**.

2. Research Activities

Cell Communication, **Nucleus Information** and **Membrane Compartments** can be succinctly described in this way:

(i) Nucleus Information:
The nucleus memorizes and processes centralized information in the cell. We strive to elucidate the dynamics and mechanisms of chromatin organization and transcription regulation during cell differentiation as well as reprogramming. By doing so, we can develop synthetic functional molecules, including those with photoinducible properties, to visualize and manipulate nuclear information processing.

(ii) Membrane Compartments:
Cellular membrane compartments mediate condensation and selection: inward and outward signaling cascades, energy conversion, and exchange of matter. We seek to understand the molecular mechanisms of these meso-domain reactions to develop molecular technologies for manipulating membrane functions by external stimuli such as light, magnetic field and heat.

(iii) Cell Communication:
Differentiation of stem cells into multicellular tissues is regulated by the communication between cells alone and cells with materials. We seek to uncover underlying mechanisms and develop scaffolds by molecular scale design for the reconstruction of functional cell architectures such as brain, muscle and germline tissues.

It is important to show that a combination of excellent researchers is more than the sum of its parts, in working for these goals. This has happened across the spectrum of iCeMS researchers, and to give some idea of that, we can say that

- iCeMS has **published 1439 peer reviewed papers**.
- 536 of these publications are considered the result of interdisciplinary collaboration.
- **One out of every five** of these has been within a high impact publication, such as *Science*, *Nature*, *Cell Reports* or other publications with impact factor >10.

Just a few of the high impact results can be mentioned here.

(i) Nucleus Information:
We now successfully control gene expression by interdisciplinary methods (combinations of biology, physics, and chemistry) to regulate cell fates. Collaborative research among iCeMS groups revealed that gene expression dynamics are important for the activity of transcription factors. For example, using optogenetics, we can effectively control the proliferation and differentiation of neural stem

cells. In other situations, we successfully activate pluripotency genes in mouse fibroblasts using synthetic molecules, whilst another study creates in-vitro eggs from stem cells.

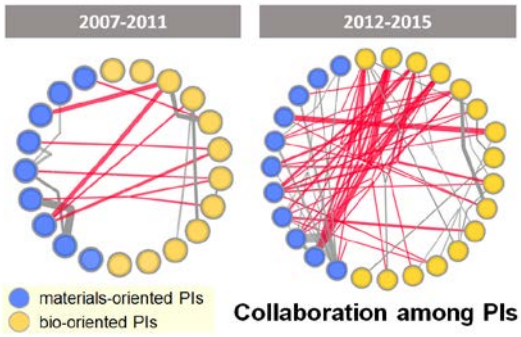
(ii) Membrane Compartments:

The collaboration among iCeMS researchers allows for the smooth transition from materials fabrications to cell biology investigations. The idea generated in iCeMS indeed stimulated chemists to produce a new material concept 'cell-inspired materials' and the Kitagawa group synthesized several porous coordination polymers (PCPs) with functions similar to compartmentalization concept Furthermore, newly synthesized photoactive PCPs that implement the light-triggered release of nitric oxide (NO) are being used to investigate and control the roles of NO as intracellular and intercellular signaling molecules, heralding a new chapter in gas biology.

(iii) Cell Communication:

Multidisciplinary collaboration among iCeMS and other scientists generated outstanding outcomes in manipulating cell fates and cell-material interactions. A combination of cell biology and material sciences revealed that the laminin fragment greatly improves human stem cell culture. Screening of chemical libraries and subsequent chemical synthesis identified small molecules that direct differentiation of pluripotent stem cells into cardiomyocytes and late-stage pancreatic β-cells. iCeMS collaborations also identified a molecule that promotes enhanced adhesion of cultured human cells.

3. Interdisciplinary Research Activities



At iCeMS, we put together cell biologist and materials scientists to achieve fundamental discoveries in these three focus areas. However, this does not guarantee they will instantaneously find the common language to work together. iCeMS has encouraged this interaction through focused funding schemes, monthly gatherings, annual retreats and even simply through the action of proximal working spaces. For example a **Cross-Disciplinary Research Task Force** explored original and innovative collaborative projects integrating functional smart materials with living cells. Every month many researchers including PIs and young researchers join to present research updates and to explore new areas for collaboration. Indeed we have been rewarded by an enhanced degree of materials-biology collaborations over the past 10 years. Moreover, the researchers are encouraged to present their work in ways that are accessible to those outside of the their field, through the **iCeMS Learning Lounge** series. As seen in the figure, initially such interdisciplinary collaboration were sparse, but in recent years, through a persistent effort, iCeMS has demonstrated greater, and continuously improving levels of interdisciplinarity, which invariably finds its impact within high visibility publications such as *Science*, *Nature* or *Cell Reports*.

4. International Research Environment

'Japan is a great place to visit' but anticipating cultural or language obstacles, foreigner researchers think twice before investing their vital research years in a Japanese institute. After only 10 years of the WPI-iCeMS program, that perception is changing.

iCeMS, from the very start, generated a senior international faculty list including those from CNRS (France), Heidelberg (Germany), Emory (United States), Max Planck (Germany) and Cambridge (UK). Overseas satellites and cooperative agreements were made with institutions in India (such as NCBS) or the States (UCLA) and indeed 15 highly productive international MOUs were established. iCeMS has been serving as the headquarters of the Asian Chemical Biology Initiative. This program, sponsored by JSPS "Asian CORE Program" since 2011, aims to establish Asian research hubs that conduct world-class research, and foster outstanding young researchers. This initiative is in cooperation with institutions including Seoul National University, Tsinghua

University and National University of Singapore. In addition, iCeMS is the 1st Japanese institute to join the EDX program, which originated in MIT, and its first course was taught by iCeMS deputy director, Prof. Uesugi, with a registration of 25,000 students.

iCeMS was the 1st WPI institute to establish the Kyoto Fellows program, a system now implemented across the WPI institutes, for attracting young talented scientists worldwide with an opportunity to establish a funded independent research group. All of Fellows have finished their five-year tenures and are now promoted in and outside of iCeMS. In keeping with merit-based promotion schemes less often associated with the hierarchical promotion system used in Japan. 29 young researchers (Assoc Prof, Junior Assoc Prof, Asst Prof, Research Associate) have been promoted at iCeMS and are actively engaged in research activities. Over its history, iCeMS has had three (of its five) tenured Professor-level positions occupied by women, or an international PI. Indeed, iCeMS has 30% quota of international researchers and a 25% quota of female researchers. The latter is striking in Japan where the national average of female researchers is typically half that value. In fact three of the five core iCeMS tenured faculty members are either female or international.

Sustaining such 'Internationality' required the establishing of a new research environment that permeated from the foundations of iCeMS. English was 'set' as the administrative language. An overseas researcher support office (ORSO) was created to assist foreign researchers in adapting to their new research environment and also to their lives in Japan.

iCeMS does not just retain its international researchers: it wants them to go out and spread the fame of iCeMS, through a number of JSPS supported visit programs. This enhances the international recirculation of iCeMS talented researchers and informs prospective researchers of our ability to host them; that *Japanese culture will actually enhance*, instead of impede, their ability to perform cutting edge international research.

5. Organizational Reforms

Briefly put, iCeMS is the place in Kyoto University where change happens, and ripples through the rest of the university. There are so many innovative aspects of iCeMS management that have been copied, intentionally so, within other parts of the university. There has not been a single large superficial organizational change but instead a series of deeper implementations. Even the simple requirement of making English the working language of the institute has sent forth more internationally-aware iCeMS administrative coordinators into the Kyoto University system. Another example is the imposition of a merit-based promotion and salary evaluation system, traditionally evaluated by administrative arm of Japanese universities. At iCeMS, such faculty evaluations are now evaluated in a formal way by the director.

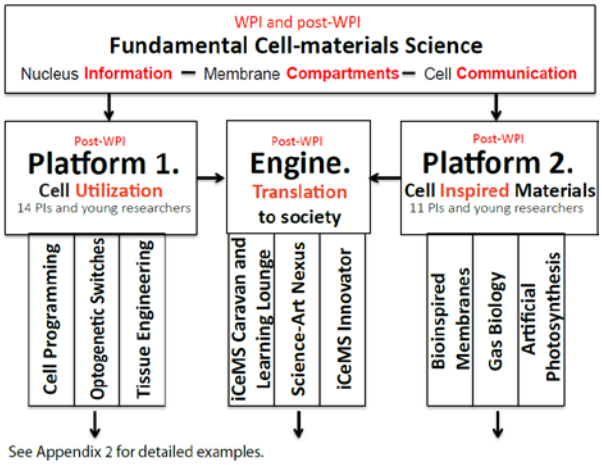
A further deep concept, started within iCeMS and permeating through Kyoto's administrative structure, is the concept of top-down management. Japanese university culture is broadly based around consensus-building, bottom-up decision making. It is a valuable process, and leads to a committed and sustained momentum in a particular organizational direction, once that consensus is reached. However what is lost is the speed and ability to become global change-agents. At iCeMS, there is a coupled effect of top-down leadership, with executive decisions made from the director and his board, as well as bottom-up consensus-driven changes led through monthly PI meetings; in both venues, new policies are proposed for final approval by the director.

To formulate more developed research strategy and gain large-scale competitive funding, at the encouragement of iCeMS, Kyoto University URA (KURA) was established in 2012, to serve the university community in streamlining research funding searches. Moreover, with the University's adaptation of iCeMS's ORSO principles, it became an easier for Kyoto University's general research community to deal with international affairs (such as immigration, housing etc).

As a final example, in 2007, just after Prof Yamanaka's discovery of human iPS cells, we swiftly established the iCeMS Center for iPS Cell Research and Application (CiRA). CiRA was recognized as a separate institute working outside of the fundamental scope of iCeMS, in 2012. iCeMS stands unique in the WPI academy, to have become the parent of another stand-alone institute.

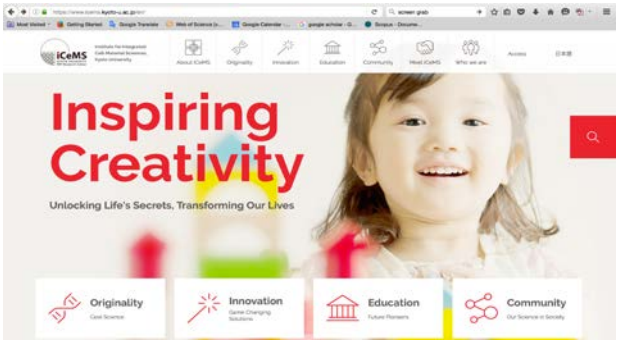
B. Progress Plan

1. Mid- to Long-term Research Objectives and Strategies Based on the Center's Research Results to Date



Scientists make up 0.1% of the world's population. The common person in the world is not interested in how a heart beats, but instead worries about what can be done if their child's heart stops beating. This is the dichotomy of fundamental and applied science. It is important to establish a credible and well-communicated link between the fundamental and applied aspect of smart cell-inspired materials. Importantly the post-WPI phase of iCeMS must accomplish this to justify future sustainable financial support of the institute. We do this through two platform concepts of **Utilization** of cells, **Inspiration** to materials and through an engine for its **Translation** to society.

- **Platform 1. Synthetic paradigms for cell programming and its utilization.** Major efforts in the fields of cell biology have been made toward understanding the molecular signals regulating cell differentiation and function and those orchestrating the cell-cell interactions in tissues. iCeMS, having pioneered such research at its most fundamental level, will continue it by developing new materials chemistries and technologies to monitor and control differentiation of stem cells into functional cells and tissues.
- **Platform 2. Breathing, cleansing and transformation through cell-inspired materials** Here we take on the cellular function of membrane compartments. Membrane compartments in living cells simultaneously "select" and "condense" molecules. Learning from sequential, integrated functions of cells in capturing, separating, transporting, storing, and transforming molecules. We will use this general Cell-Inspired theme to generate Smart Materials to achieve the equivalent of these membrane functionalities for application in healthcare, energy and the environment.
- **Translation Engine. A crucible for creativity.** Translation is now a key concept in biological and medical sciences, reflecting the connectivity between laboratory and medical practice. In Platform 1 and 2 we described some very crucial applications that can only be powered by breakthroughs in fundamental cell-material synergetic science. However, it is equally important to **translatively** educate the world to this activity.



By coordinating the "Translation Engine", we will bring WPI-iCeMS to a higher level of visibility than is available to fundamental science *only* based research. Such efforts are underway, with researchers encouraged to present their work in ways accessible to those outside of their field, and beyond the general scientific audience using modern media tools. A striking example of this is the **iCeMS Learning Lounge** series, which are available for the world to see on YouTube. Other examples are the **iCeMS Caravan**, with young researchers have made contact, with help from television networks, to far-flung schools.

iCeMS was the 1st WPI institute to develop social media tools such as Facebook and Twitter, Eureka Alert accounts and overseas press releases. We are reviving such leadership, such as the dramatic revival of the **iCeMS website**. This kind of visibility in turn will enhance the institute's sustainability to develop further impactful fundamental breakthroughs in cell-materials science.

2. Management System of the Research Organization

Leadership for future planning of iCeMS after WPI funding ends

At present, iCeMS has obtained 1.38 times more funding from external sources compared to its WPI budget. Acquisition of external funds will be critical to sustain iCeMS after the WPI program finishes. It is important to consider alternative means for funding the future of iCeMS's framework without a dependency on a few sources of funding. With an aim to follow the example of American institutions, Kyoto University is closely following the developments within the Japanese Diet concerning the use of charitable tax deductions. To this end, on June 1st 2015, iCeMS created the iCeMS Fund, utilizing the Kyoto University Fund framework. Framing iCeMS, through its translation of fundamental science to solutions to global issues, we are building towards a target of large scale endowments. Fifteen (very) small endowments have been donated at the preparatory stage but it illuminates the long road ahead. If achieved, it would be unprecedented in Japan, where no institute has received the level of endowment seen in the United States.

An essential issue is that WPI-iCeMS has reached science excellence but very poor visibility within an international setting. We are building more visible international links beyond the shores of Japan. For example following a visit by the Princess of Thailand in 2015, iCeMS will receive students in 2016, and a joint symposium with Kyoto University and the princess's flagship institute in Thailand, VISTEC, will occur in 2017, with the prospect of a endowed Chair representing VISTEC within iCeMS. A further program in development is the establishment of a satellite laboratory with CNRS, the French National funding federation. This will enhance the sustainability of funding European researchers at through their ability to apply for competitive European research funds such as ERS starter and advanced grants as well as participation in EU Horizon 2020 grants.

Japanese University-led Entrepreneurship culture is traditionally risk averse and this tends to reduce the pathway for development of early stage promising research. The common critique is that the fundamental work is too 'early-stage'. We are currently developing a broad program that will require the stake-holdership of various parties including the Kansai business community, local and central government to help incubate such early stage discoveries in cell materials science.

Retaining Youth, Key Personnel and Reorganization of research groups

In the aftermath of the non-extension of the WPI support, there was an unsurprising apprehension for the future of young independent iCeMS researchers, who accepting the risks associated with non-tenure, are the real seeds of the iCeMS creed of '**Globally Awareness, Lateral Thinking, Iconoclastic actions'**. Many have received national awards, or young researcher funds such as the prestigious Sakigake program. Director Kitagawa took firm steps to secure the future participation of most of the current WPI-iCeMS senior PIs and the very best of untenured young researchers, had their contracts extended to at least 2020. Moreover, iCeMS is currently reviewing candidates of international caliber for two tenured positions in the field of cell biology or chemical biology adding to the critical mass of iCeMS centric PIs required.

3. Center's Position within the Host Institution, and Measures Taken by Host Institution to Provide Resources to the Center

President Yamagiwa formulated the WINDOW concepts as future vision in 2015. WINDOW stands for; **W**ild and **W**ise; **I**nternational and **I**nnovative; **N**ature and **N**oble; **D**iverse and **D**ynamic; **O**riginal and **O**ptimistic; and **W**omen, leaders in the **W**orkplace. WPI is directly cited within WINDOW's Strategic Priority of being *'International and Innovative'* as follows. "We will establish a World Premier International Research Center (WPI Research Center) as a hub of front-line research at Kyoto University. Through the center, tentatively named the **Kyoto University Institute for Advanced Study** (**KUIAS**), we aim to facilitate the advancement of cutting-edge research that capitalizes on Kyoto University's particular strengths, cultivate the next generation of research professionals, and circulate outstanding research talent both within Japan and overseas." The present iCeMS will join in the KUIAS after WPI support ends in FY2016.

World Premier International Research Center Initiative (WPI)
Progress Report of the WPI Center (for Final Evaluation)

Host Institution	Kyoto University	Host Institution Head	Juichi Yamagiwa
Research Center	Institute for Integrated Cell-Material Sciences (iCeMS)	Center Director	Susumu Kitagawa

* Write your report within 30 pages. (The attached forms are in addition to this page count.) Keep the length of your report within the specified number of pages.

Common Instructions:

* Please prepare this report based on the current (31 March 2016) situation of your WPI center.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

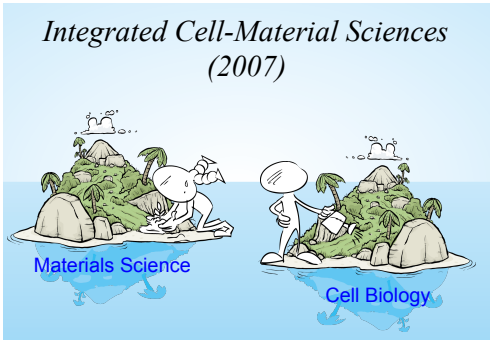
1. Overall Image of Your Center (write within 2 pages including this page)

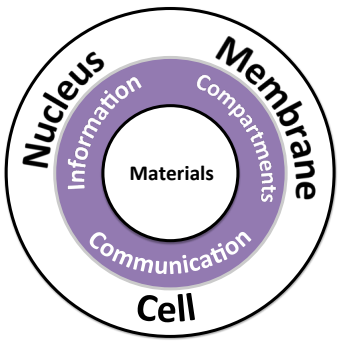
Describe the Center's current identity and overall image. For centers that have had a change in their directors, describe that transition and the effects of the change.

- On the sheets in [Appendix 1-1~7], list the Principle Investigators, and enter the number of center personnel, a chart of the center's management system, a campus map showing the center's locations on the campus, project funding, project expenditures, and WPI grant expenditures.

(a) Overall image of iCeMS

iCeMS, with its inception to the WPI program, in 2007, was proposed to establish a new fusion science between cell biology and materials science. This was a truly ambitious proposal since the two fields could not be more different. Cell biology is the study of an evolved state with a complexity that we attempt to unravel to understand the human condition. Material science is an evolving state that develops by small rational steps and inspired leaps of imagination. By uniting such disparate philosophies of science, we hold the tantalizing prospect of generating a truly new interdisciplinary field.

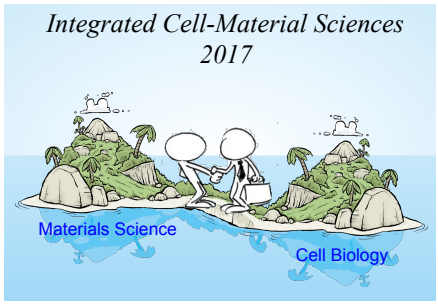




At iCeMS, we gathered an exceptional collection of internationally known cell biologist, materials scientists and chemical biologists from Kyoto University, from Japan and from around the globe, who were equally motivated by this difficult but rewarding challenge. These eminent researchers were given the freedom to define, through their collaborations, the framework of what such a new interdisciplinary movement would like. Five years after its inception, under the leadership of **Director Kitagawa in 2013**, a critical review of the institute's development was carried out, taking into consideration the future beyond the end of the WPI funding in FY2016. This resulted bring focus to the natural process of developing iCeMS identity as "**Materials for Cell Elucidation and Control**". This encompasses a holistic interaction between materials and the three essential properties of cells and cell biology: **Cell Communication**, **Nucleus Information** and **Membrane Compartments**.

iCeMS can look back on its achievements with a sense of pride, from its now-established status within Kyoto University, as the place where traditions can be set-aside and replaced with new rules reflecting an internationalized research administration. iCeMS can look back at a constantly high level of research success, and the foresight of inviting a future Nobel prize winner as part of its world-class cadre of researchers. However now, looking forward, iCeMS is active in making sure the rest of the world knows what Japanese science knows; that it is a world premier institute.

(b) A new era at iCeMS.



During the early years of iCeMS, the institute became mired in an almost semantic discussion with the working committee over its identity, especially over such terms as 'mesoscopic'. This threatened to derail the trajectory of the institute, and steps were taken to alter leadership to bring the important issue of the iCeMS identity into clearer focus. Under a new iCeMS leadership of Prof. Susumu Kitagawa, a world class leader in materials science, there was a more effective dialogue between the iCeMS's PIs working in the fields of cell biology and materials science. In doing so, it was possible to look past the questions of labels, and instead identify the core values of iCeMS in the last 10 years. Moreover this succession promulgated a new era where interactive, impact-oriented research at the interface of materials and cell biology could be promoted at a global level. The effects of this succession were significant:

(i) Strengthening institute management

Director Kitagawa appointed two deputy directors to support him at the executive level. One is a world-leading cell biologist **Ryoichiro Kageyama**, and the other is iCeMS Professor **Motonari Uesugi**, a highly-regarded chemical biologist in the United States and Japan with an exemplary record of uniting cell-material research. The institute's new leadership team, strong in both international and interdisciplinary contexts, is well placed to lead iCeMS in this new phase of its unified study crossing the boundaries between cells and materials.

(ii) Prioritizing research topics through focused funding and new eminent hires.

A portion of iCeMS funding was prioritized for the **acceleration** of outstanding projects in the areas multidisciplinary research. With such top-down pressure applied, the institute has rapidly yielded several such results in the highest quality scientific journals. Moreover, in 2013 iCeMS took measures to further strengthen the lineup of researchers, such as with the inclusion of world-renowned Kyoto University scientists **Ryoichiro Kageyama** (Institute for Virus Research) and **Mitinori Saitou** (Graduate School of Medicine), University of Heidelberg Professor **Motomu Tanaka** and **Easan Sivaniah** (Cambridge Univ.). Prof. Sivaniah was recently elevated to a tenured full professorship, a unique event within WPI's history, and indicative of the seriousness with which iCeMS takes its duty to provide a stable atmosphere for international faculty to thrive within the Japanese research system.

(iii) Leadership for future planning of iCeMS after WPI funding ends

Kyoto University had long considered the establishment of an overarching institute to capture the key precepts of iCeMS. However this consideration really crystallized in 2013 under Director Kitagawa's leadership in coordinating various University wide opinions on the new institute's mission. By April 2016 Kyoto University had successfully established the Institute for Advanced Study (KUIAS) under the leadership of Fields Medal winner Prof. Shigefumi Mori.

Director Kitagawa took rapid steps to ensure the credibility of KUIAS, guaranteeing the inclusion of iCeMS to it as its flagship institute, and by securing the future participation of most of the current WPI-iCeMS senior PIs. Moreover, the very best of untenured young researchers, whose futures had suddenly become precipitous at the natural end of the WPI funding for iCeMS, had their contracts extended to at least 2020. To date, eight such researchers have received this extension, with more to be included in FY2016. Moreover, iCeMS is currently reviewing candidates of international caliber for two tenured positions in the field of cell biology or chemical biology adding to the critical mass of iCeMS centric PIs required.

All of these events are a remarkable response to circumstances and is indicative of the efficient decision-making environment within iCeMS.

2. Research Activities (within 15 pages)

2-1. Research Results to Date

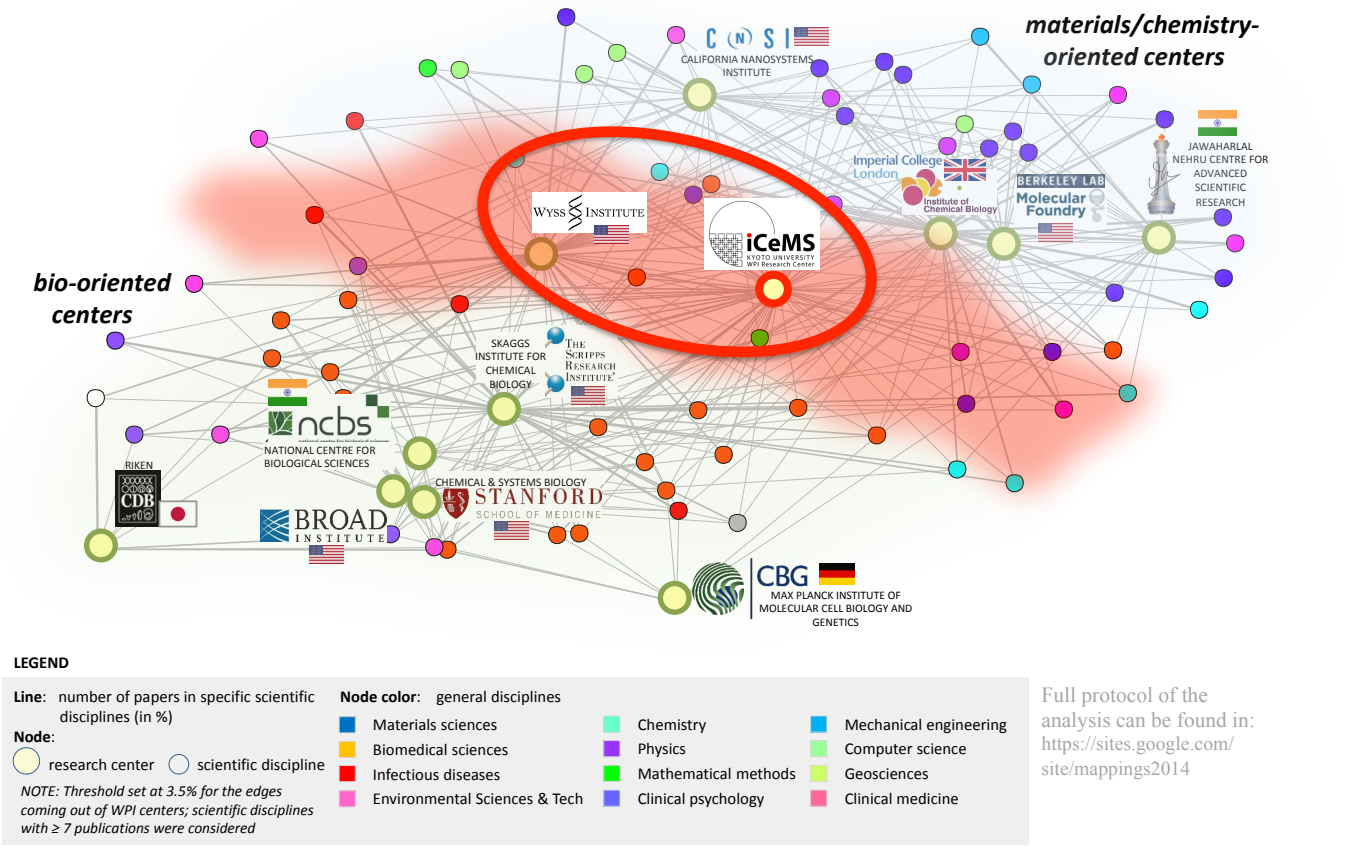
Describe issues of a global level that the Center has challenged, and give the results. Select 20 representative results achieved during the period from 2007 through March 2016. Number them [1] to [20] and provide a description of each. Place an asterisk (*) in front of those results that could only have been achieved by a WPI center.

- In Appendix 2-1, list the papers underscoring each research achievement (up to 40 papers) and provide a description of each of their significance.

(a) Over view of research at iCeMS

iCeMS, in its 10 years program has always set out to establish a unique place in science, at the interface of cell biology and materials science, but more specifically, to do so at a fundamental level. Our research is developed with an eye for immediate global issues such as disease or diet; however a fundamental approach is taken to the way that cell biology and materials can be combined to become relevant to these issues.

In fact, at the beginning of iCeMS's tenure there was no notable institute that had successful achieved such synergy. Of course there are world renowned institutes, such as the Broad Institute, or the Molecular Foundry at Berkeley, that combine both cell and materials components but typically the balance within those institutes is biased to one of these fields. As the figure below indicates, by analyzing the research outputs of several distinguished institutes claiming a Biological and Materials framework, iCeMS has almost singularly succeeded in establishing a true balance of Biology and Materials science within its framework. Notably, iCeMS is joined by one other institute, the Wyss Institute in Harvard, that was formed almost a year after iCeMS, having a similar level of funding, research faculty and facilities. Moreover, the Wyss Institute has a distinctly different role to iCeMS by instead focusing on bioengineering instead of fundamental research.

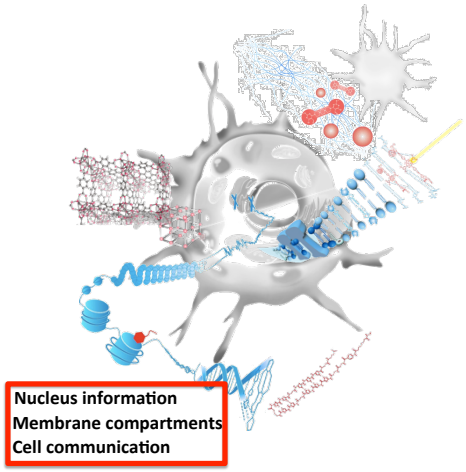


Full protocol of the analysis can be found in: https://sites.google.com/site/mappings2014

Let us consider how materials can interact with the three essential properties of cells and cell biology, **Cell Communication**, **Nucleus Information** and **Membrane Compartments**. It can be succinctly described in this way:

(i) Nucleus Information:

The nucleus memorizes and processes centralized information in the cell. We strive to elucidate the dynamics and mechanisms of chromatin organization and transcription regulation during cell differentiation as well as reprogramming. By doing so, we can develop synthetic functional molecules, including those with photoinducible properties, to visualize and manipulate nuclear information processing.



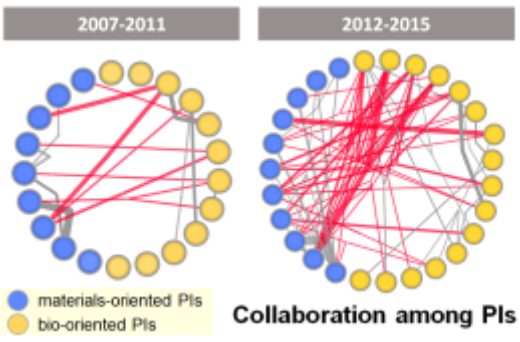
(ii) Membrane Compartments:

Cellular membrane compartments mediate condensation and selection: inward and outward signaling cascades, energy conversion, and exchange of matter. We seek to understand the molecular mechanisms of these meso-domain reactions to develop molecular technologies for manipulating membrane functions by external stimuli such as light, magnetic field and heat.

(iii) Cell Communication:

Differentiation of stem cells into multicellular tissues is regulated by the communication between cells alone and cells with materials. We seek to uncover underlying mechanisms and develop scaffolds by molecular scale design for the reconstruction of functional cell architectures such as brain, muscle and germline tissues.

At iCeMS, we put together cell biologist and materials scientists to achieve fundamental discoveries in these three focus areas. However, having such a collection of people does not mean that they will instantaneously find the common language that enables them to work together. iCeMS has worked hard to encourage this interaction through focused funding schemes, monthly gatherings, annual retreats and even simply through the action of proximal working spaces. Indeed we have been rewarded by an enhanced degree of materials-biology collaborations over the past 10 years. As seen in the figure, initially such interdisciplinary collaborations were sparse, but in recent years, through a persistent effort, iCeMS has demonstrated greater and continuously improving levels of interdisciplinarity.



Individually the researchers at iCeMS are world class in their field. And individually many of these researchers have shone through during their time at iCeMS. An extreme case in point would of course be the recognition in 2012 by the Nobel committee, of the research by Prof. Shinya Yamanaka, one of the original iCeMS PIs. Long before this, however, iCeMS had recognized the need to incubate Prof. Yamanaka's research, whilst allowing the institute to continue its more general mission of creating a world-class environment for interdisciplinary research of all types. With this in mind, iCeMS established a specific center for Prof. Yamanaka's research within iCeMS, fostering it, until it had the capability to establish itself as an independent center (CIRA) in 2010. However this rich vein of individual excellence runs through iCeMS; iCeMS PIs received more than a hundred top class awards over its ten year period and the

institute is determined to maintain a world-class research environment to elevate the next crop of world-class researchers.

We have demonstrated the interdisciplinarity of our actions. However it is altogether more important to demonstrate that this interdisciplinarity has led to research results that reach the highest levels of science, in terms of visibility and in terms of achievement. It is important to show that such combination of excellent researchers is more than the sum of its parts. Notably, we can say that:

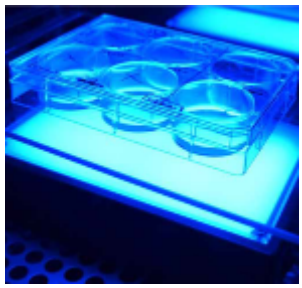
- iCeMS, to date has **published 1477 peer reviewed papers**.
- 537 of these publications are considered the result of interdisciplinary collaboration.
- **One out of every five o**f these has been within a high impact publication.

In the course of our institute's history, we have uncovered a number of molecular mechanisms of cellular processes for elucidating the regulation of stem cell proliferation and differentiation, and of meso-domain reactions in membrane compartments, resulting in the design and discovery of new materials for the control of cell physiology. iCeMS researchers have synthesized or discovered over 2,000 chemical compounds to date, including novel and unique cell-manipulating compounds such as porous coordination polymers (PCP), SAHA derivatives, adhesamine, Kyoto Probe 1 (KP-1), and ferrocene-porphyrin-fullerene linked triad (FPFT) many of which are described in detail below, where we list up to twenty different instances of high profile, interdisciplinary success.

(b) Representative results

I. Nucleus Information

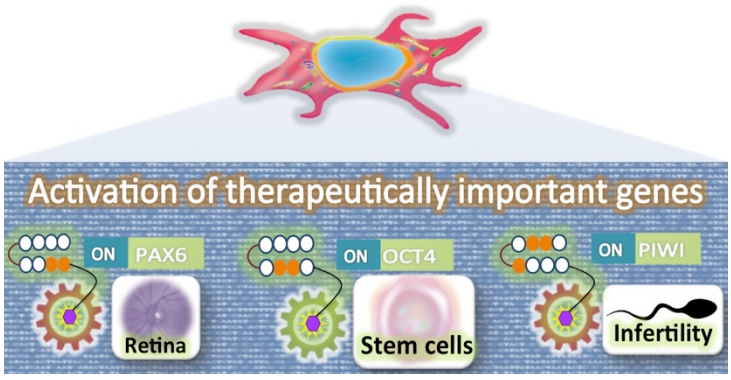
***[I-1] Control of fate in neural cells**



Neural stem cells have multipotency to give rise to three different cell fates, neurons, oligodendrocytes, and astrocytes, but the precise mechanism of neural stem cell control remains to be determined. We generated bioluminescence and fluorescence reporters to monitor the expression dynamics of each cell fate determination factor. Our optogenetic technology developed in this study offers a novel way to control neural stem cell proliferation and neuronal differentiation, demonstrating its applicability to the regenerative medicine. [*Science* 2013] [1]

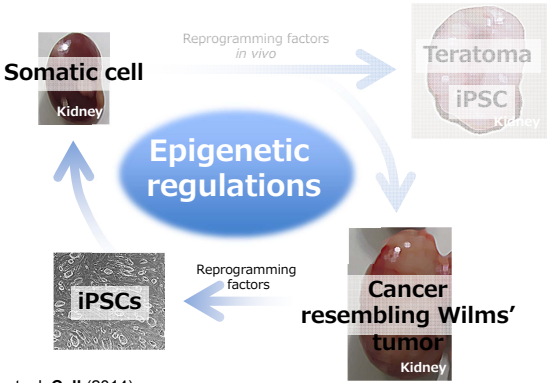
***[I-2] Artificial genetic switches**

Among the major classes of artificial transcriptional activators available for cellular reprogramming, small molecules have better clinical prospects over natural DNA binding proteins, as they are mostly non-immunogenic. We synthesized a new class of dual-functional small molecules for genome engineering termed `SAHA-PIP' with the ability to suppress or activate activity in genes related to autism, obesity, visual retinal function, HIV-silencing, or in stem-cell programming. Taken together, our results represent a successful model of DNA-based smart biomaterials capable of cell control through alteration of a genetic program in the nucleus. [*Angew. Chem.-Int. Edit.* (2013,2015)] [2,3]



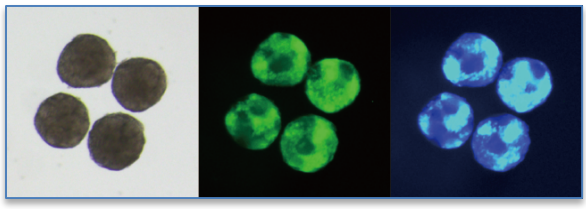
[I-3] Proving an epigenetic root of cancer

The technology for generating induced pluripotent stem cells (iPSCs) can be utilized to actively and globally manipulate the epigenetic regulation of differentiated cells. In this study, we have established an *in vivo* reprogramming system in which somatic cells can be reprogrammed into iPSCs in living mice. It has been widely accepted that cancer arises primarily through accumulation of genetic mutations. Our results provided a proof of concept for epigenetics-driven cancer that is independent of genetic transformation, and suggest that particular types of cancer can arise mainly as a result of epigenetic disruption triggered by dedifferentiation. [*Cell* 2014] [4]



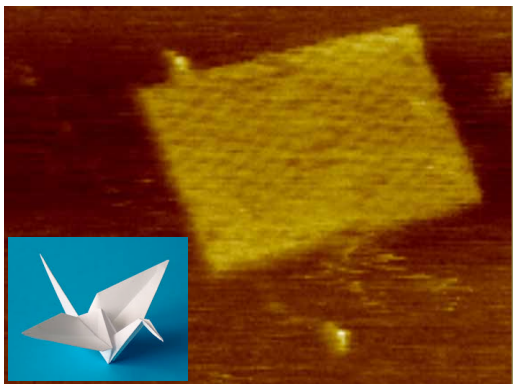
*[I-4] Identification of transcription factors sufficient for inducing the germ cell fate in epiblast cells in mice

This project offers a way to control germ cell fate by expressing appropriate transcription factors (TFs) *in vitro*. By using an *in vitro* PGC specification system that we have developed, we explored TFs that may be enough to sufficiently confer germ cell fate on precursor cells, epiblasts. We found that overexpression of three TFs led to PGC-like cells (TF-PGCLCs). Remarkably, upon transplantation into testes of neonatal mice lacking endogenous germ cells, TF-PGCLCs contributed to spermatogenesis and healthy offspring. Thus, this work provides a strong foundation for the TF-based control of *in-vitro* gametogenesis. [*Nature* 2013] [7]



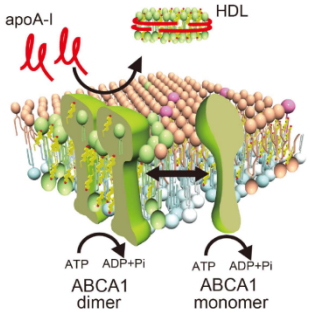
*[I-5] Origami meets DNA

Various meso-scale DNA structures can be designed by the DNA origami method, and manipulation of the molecular movement on the DNA structures is now possible. Real-time observation of the dynamic movement of single molecules using high-speed atomic force microscopy (AFM) revealed various enzymatic reactions such as DNA methylation, repair, and recombination and, structural changes of target DNA molecules including G-qaudruplex formation, duplex formation, and BZ transition at single molecule resolution. These results revealed that DNA origami can be used for the analysis of the biomolecules and creation of programmed functional materials. [*Nat. Nanotechnol.* (2011,2012), *Nat. Commun.* 2015] [8,9,10]



II. Membrane Compartments

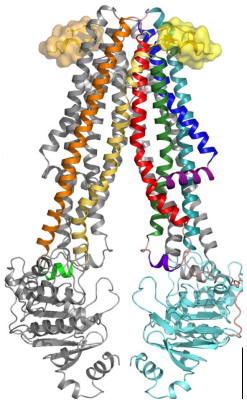
*[II-1]The fastest digital eyes



At iCeMS, we developed the world's fastest and longest single molecule tracking methodologies. Using these methods, we were able to show that the plasma membrane is a liquid which is hierarchically-organized, and -compartmentalized in a space scale of 3- 300 nm, right in the middle of the meso- scale, and that such a dynamic structure enables the plasma membrane function. [*Nat. Meth.* 2010; *J. Cell Biol.* (2011,2013), *Nat. Chem. Biol.* 2012] [11, 12, 13, 14]

***[II-2] Watching our cholestorol**

We are often reminded, of the dangers of cholesterol-rich foods. Yet, cholesterol is an indispensable component of our bodies, whose concentration is elaborately regulated, especially by lipid transporters. For example 'good' cholesterol (HDL) is invaluable in preventing heart disease and extending our health. Here at iCeMS, we have evaluated the important class of ABC proteins, such as ABCA1, that change distribution of membrane lipid compartments in the plasma membrane by moving lipid molecules and modulate cellular functions such as growth and migration. [*Angew. Chem.-Int. Edit* 2011, *Proc. Natl. Acad. Sci. U. S. A.* 2013] [15,16]

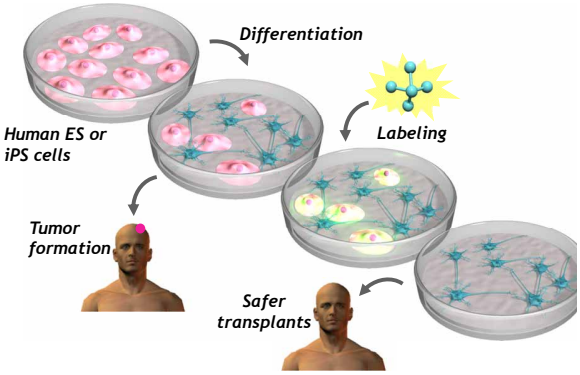


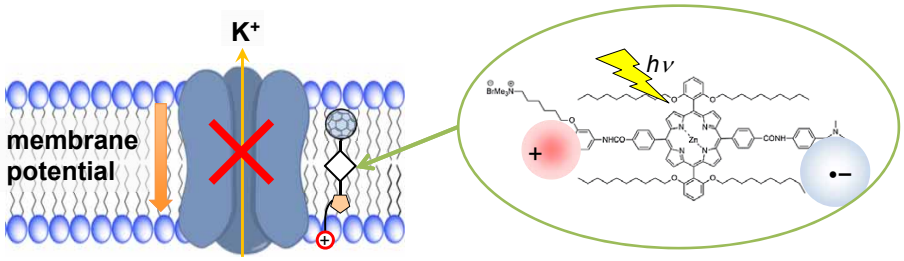
***[II-3] A cellular exit for the things we don't like**

Membranes define boundaries of a cell and cell compartments and separates the intra- from the extra compartmental environment. Transporters exchange materials via membranes, condense specific materials inside and eliminate nonessential, toxic materials. Here at iCeMS we revealed the functional mechanism of multidrug exporter MDR1, which eliminates various structurally unrelated toxic compounds from cells and maintains human health. We determined the structure of the protein at the highest resolution in the world. Such understanding is crucial to the identification of new chemicals that serve as MDR1 substrates. [*Proc. Natl. Acad. Sci. U. S. A.* 2014] [17]

***[II-4] KP-1, An invaluable tool for iPS 'gold prospectors'**

As induced Pluripotent Stem Cells gain traction in clinical applications, it becomes increasingly important to effectively identify which of the cells is actually an iPS cell. By making use of our world-class understanding of protein transporters, at iCeMS, we have created a molecular tool to label or even eliminate iPS cells. Specifically we developed a fluorescent molecule (Kyoto probe 1 [KP-1]) that very selectively and efficiently labels human pluripotent stem cells KP-1 may, in the future, be widely be used as a tool of choice in the field of stem cell biology. [*Cell Reports* 2014, *J Am Chem Soc.* 2014] [18, 36]





***[II-5] Synthetic antennae for our cells**

Ion channels transport ions selectively via membranes and play important physiological roles. The control of ion transport by light is an attractive strategy that allows targeted, fast control of precisely defined events in the biological membrane. At iCeMS, we developed a sophisticated optical antenna made of ferrocene, porphyrin and fullerene that uses light to alter plasma membrane potentials. This is the first optogenetic method for intact cell membranes and could in future be useful for controlling cell functions in a spatiotemporal manner, such as neuronal firing. *J. Am. Chem. Soc.* [2012] [19]

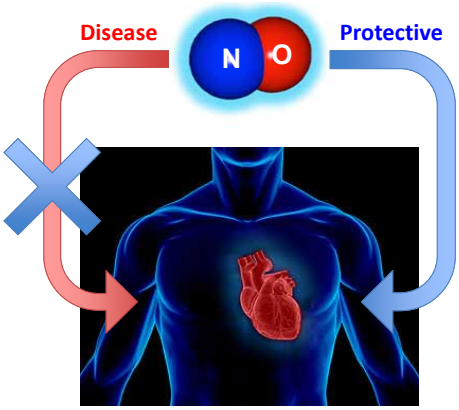
***[II-6] A Trojan horse for cells**

Delivering functional mesoscopic metallic materials to intracellular environments is a key step towards the cell-material integration; however, the precise localization of mesoscopic materials and the decrease of their cytotoxicity have been challenging. At iCeMS we overcome this issue by multistep surface engineering of mesoscopic materials that gave them 'stealth' qualities for biocompatiblity. A wide spectrum of mesoscopic metallic materials could be slipped past the cell membrane in this way. Then, guest materials could provide by photoirradiation, the control of various cellular and membrane functions, such as calcium influx without the need for prior genetic engineering of the target cells. [*Angew. Chem. Int. Ed.* 2015] [*ACS Nano* 2014] [20,21]

***[II-7] The super-terahertzer**

Rapid progress has recently been made in studying the "uncharted territory" of the terahertz electromagnetic spectrum. At iCeMS, we have developed the world's most powerful terahertz source, an orders of magnitude better than the rest. These results have attracted worldwide attention since 'terhertz' represents the "uncharted territory" of the electromagnetic spectrum. We now apply this technology to cell biology because the order of electric field generated by terahertz pulse is strong enough to locally manipulate the membrane potential of living cells. With the beautiful, non-invasive quality of terahrtz radiation, our work opens the door to never explored potentials developments in the field of interdisciplinary cell-material sciences. [*Nat. Commun.* 2011, *Nat. Photonics* 2013][22,23]

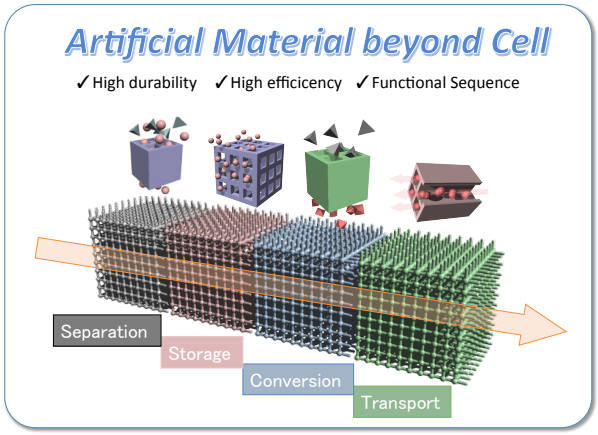
***[II-8] Piercing the frontiers of gas biology using porous materials**



Nitric oxide (NO) is an important signaling molecule that regulates physiological and pathological processes including vascular smooth muscle relaxation and neurotransmission. The rapid diffusion, membrane permeability and high reactivity of gases is the key of such molecules as a transmitter. However spatial and temporal delivery of NO had proved challenging and attempts at single-cell stimulation by NO had not yet been achieved. The Kitagawa group synthesized new porous coordination polymers that release NO upon laser irradiation. Compared to conventional molecule-based photoactive compounds, the framework materials give a very high NO payload, leading to new research opportunities to unveil the secret role of NO, in particular, at the required high concentration. [*Nat. Commun.* 2013] [24]

***[II-9] Cell-inspired porous materials**

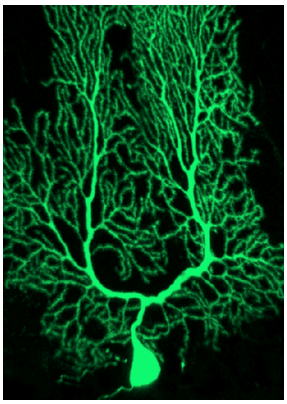
The simultaneous implementation of "selection" and "storage" of matter is a basic aspect in compartmentalization within cells. We create artificial materials called porous coordination polymers (PCPs) that efficiently and inherently store and select small molecules. However, we seek to mimic cellular systems that do this in massively sequential ways, and have developed several strategies to control the sequential storage and selection in such cell inspired compartments. [*Chem. Soc. Rev.* 2014, *Nat. Mater.* 2012, *Science 2013, Angew. Chem. Int. Ed. 2012*] [25, 26, 27, 28]



***[II-10] Cellular Self-Accelerating Processes as an inspiration for technology**

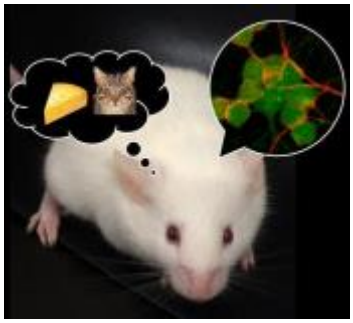
Gas separation is an important industrial process, and the discoveries of highly selective porous compounds are central to it. Nature shows the way to enhance selectivity through allosteric enhancement of substrate affinities to biological ligands. We take a similar approach of using soft porous materials, with adaptable pores, that synergetically enhance the selective adsorption of gases, yield materials with record performances. This superb function could not be realized without self-accelerating mechanism, opening up a new field of porous solids having cell-inspired functions. [*Nat. Mater.* 2010, *Science* 2014] [29, 30]

III. Cell Communication



***[III-1] The principles governing neuronal shapes and connectivity**

Neurons in the brain arborize, forming highly-patterned dendritic processes to form efficient neural circuits. The complex tree of dendritic processes is specifically shaped to facilitate access to synaptic counterparts within the tissue. An interdisciplinary approach is paramount to understand the phenomenology - utilizing cellular and molecular neurobiology and mathematical biology - for clarifying fundamental mechanisms of dendrite patterning in the developing brain. We demonstrated that the dendritic tree underwent dynamic remodeling influenced by neural activity of synaptic counterparts and physical interaction with other branches during postnatal maturation. [*Nat. Med. 2009, Development* 2012] [31, 32]

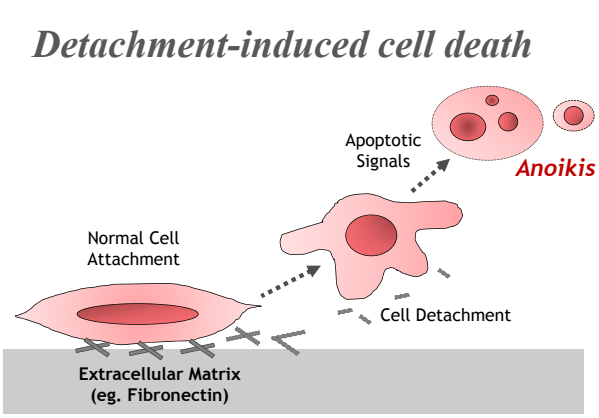


***[III-2] Molecular understanding of messengers in the brain**

The synapse is a structure between neurons through which a signal flows from one neuron to another. Synapses are typically formed between the axonal terminal of a neuron and the dendritic membrane of a target cell. Synaptic sites contain specific proteins that carry out the signaling processes. Neurons thus acquire mechanisms to deliver and localize functional proteins and messenger RNAs to synaptic compartments. We identified elements leading to mRNA localization to synaptic compartments in neuronal dendrites Furthermore, we developed a chemical approach to visualizing mRNA dynamics in living cells. [*Angew Chem Int Ed Engl. 2015, Proc. Natl. Acad. Sci. U. S. A.* 2012] [33,34]

***[III-3] Chemical tools for programming stem cells**

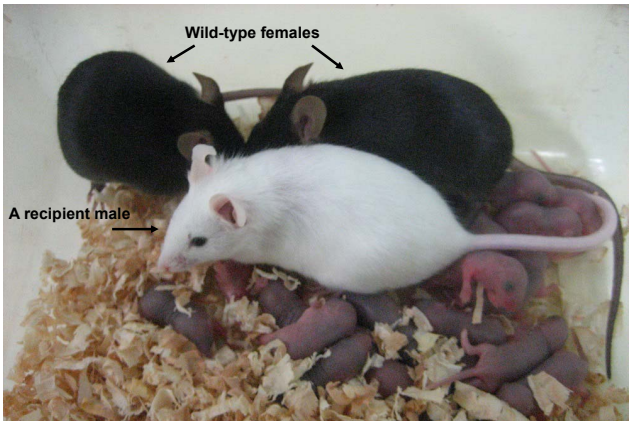
It is essential for future clinical application that we obtain control of the programmed differentiation of stem cells. Screening of chemical libraries and subsequent chemical synthesis identified small molecules that direct differentiation of pluripotent stem cells into cardiomyocytes and late-stage pancreatic T-cells. KY02111, one such library molecule, induces highly efficient differentiation of functional ventricular and pace maker cardiomyocytes from human pluripotent stem cells. This molecule allowed a record-breaking, defined, cytokine- and xeno-free method for the large-scale production of human cardiomyocytes. [*Cell Reports* 2012, *Nat. Chem. Biol.* 2014] [35, 37]



***[III-4] Novel methods for adhesion and expansion of cells**

Culturing human pluripotent stem cells originally required mouse feeder cells as a cell-adhesion substrates. Naturally such hPS cells cannot be used for clinincal application. By combining technologies from cell biology and material sciences, we found that the laminin fragment E8 greatly improves culturing human ES/iPS cells, permitting single cell passaging for effective cell expansion. Furthermore we identified a small molecule named 'adhesamine' from chemical libraries to clump together in solution, stabilizing it against *anoikis* both in vivo and in vitro. These new methods will contribute to stem cell therapy or cell therapy. [*Nat. Commun.* 2012, *J. Am. Chem. Soc 2013, Angew Chem Int Ed Engl. 2014]*. [38,39,40]

***[III-5]**
Generation of offspring from in-vitro generated eggs



This project opens the way to generate oocytes with the capacity to contribute to healthy offspring from in vitro primordial germ cell-like cells (PGCLCs) induced from female embryonic stem cells (ESCs)/induced pluripotent stem cells (iPSCs) in mice. We have demonstrated that by using appropriate combinations of cytokines and culture conditions, male ESCs/iPSCs are induced into epiblast-like cells (EpiLCs) and then into PGCLCs, which, upon transplantation into testes of neonatal mice lacking endogenous germ cells, contribute to spermatogenesis and healthy offspring. [*Cell* 2011] [5] Here, we next explored whether female PGCLCs bear the capacity to contribute to oogenesis and offspring. When transplanted under ovarian blusa of nude mice for four weeks, PGCLCs in reconstituted ovaries differentiated into oocytes at the germinal vesicle stage. Remarkably, these oocytes, through *in vitro* maturation and fertilization, contributed to healthy offspring. Thus, this work serves as a strong foundation for *in vitro* female gametogenesis. [*Science* 2012] [6]

2-2. Research Environment Including Facilities and Equipment

Describe the degree to which the Center has prepared a research environment appropriate for a world premier international research center, including facilities, equipment and support systems, and describe the functionality of that environment.

(a) Facilities and equipment

Because Kyoto University is located in a cultural and sightseeing zone of a historical city, several amenity restrictions are being imposed that, combined with limited university campus space, prevent the construction of new buildings. As a result, although performing research "Under the One Roof" — which is ideal for a WPI world research hub — is difficult to achieve, we are effectively utilizing research labs as shown below.

iCeMS Main Building and iCeMS Research Building. These buildings are conveniently located in Kyoto University's Main Campus, approximately 200 meters apart from each other, and together combine for 11,000 square meters of space. Most of the iCeMS researchers (115 researchers, 60%) make use of these buildings and the interdisciplinary research environment that is nurtured by open-lab and open-office space.

Center for Meso-Bio Single-Molecule Imaging (CeMI). Located in iCeMS Research Building and contributes to joint research.

Katsura Lab. Established in Kyoto University's Katsura Campus, 10 km west of iCeMS Main Building, this lab has 220 square meters of space. Several joint research projects are conducted in collaboration with 4 professors from Graduate School of Engineering there.

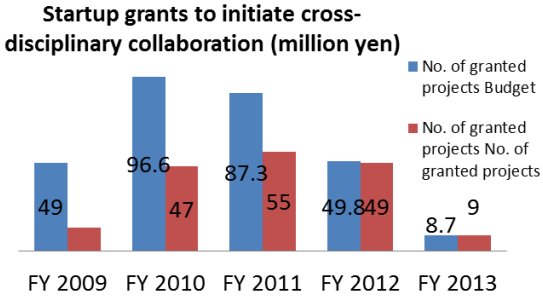
Advanced Chemical Technology Center in Kyoto (ACT Kyoto). ACT Kyoto is a research and development center for chemical research, which is in line with one of the Kyoto city policies of promoting the academy-industry-government cooperation. iCeMS rents lab space (595 square meters) for research and development of gas science technology.

Shared Equipment Support Office. The establishment of Shared Equipment Support Office in 2014 strengthened the management of the common equipment, and got to give researchers and technicians proper instructions. We gained a foothold of issues to be considered for effectively utilizing large-sized or shared equipment in the future. About the large-sized equipment purchased over 5 million yen, its information is shared within iCeMS for attempting common use, and furthermore its utilization and maintenance have been progressed as effective.

(b) Support System

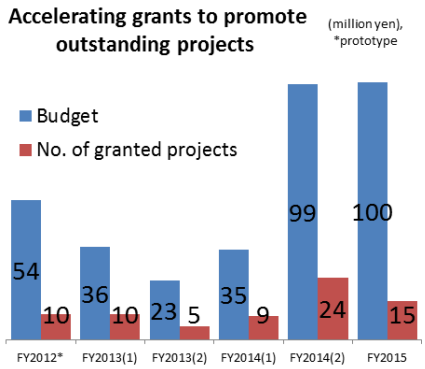
1. Startup grants to initiate cross-disciplinary collaboration

Small startup grants to initiate cross-disciplinary collaboration are provided to junior faculty and postdocs via "iCeMS Exploratory Grants for Junior Investigators," while the complementary "iCeMS Cross-Disciplinary Research Promotion Project" aids researchers in other departments of the university to start collaborative work with iCeMS researchers (the latter was expanded beyond the iCeMS as a result of a FY 2009 Site Visit suggestion).



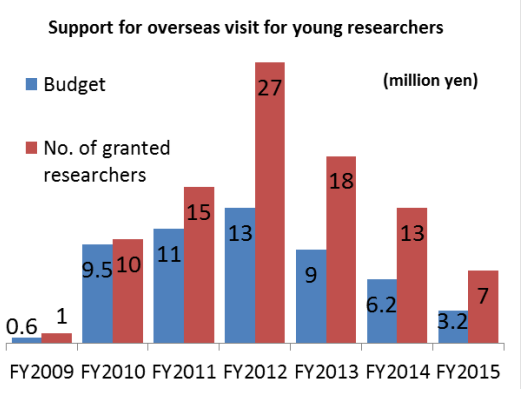
2. Accelerating grants to promote outstanding projects

Following the startup phase, in FY 2013 iCeMS undertook a new initiative to accelerate outstanding projects in certain areas of institute-initiated projects. Granted projects are expected to yield results within two years in the highest quality scientific journals.



3. Support for overseas visit for young researchers

Since 2010, iCeMS has supported more than 91 young researchers in earning opportunities to visit world-class institutions, opening the door to further international collaborations and careers with financial support from JSPS. The priority of the program has been shifted to assisting researcher career development from simply boosting international collaboration, and the program has been run successfully by iCeMS own budget since FY 2013.



4. Independent positions for young scientists worldwide

The iCeMS Kyoto Fellow position was established for young scientists worldwide with each fellow receiving a total annual budget of 20–30 million yen (including their own salary) and an opportunity to establish an independent lab group with a status of Assistant Professor or Research Associate. After their 5-year head-start at iCeMS, they are expected to continue and further their international scientific careers, or be promoted at Kyoto University. Such a process will help establish iCeMS as a prominent hub for building a global scientific career. Total 6 Fellows have been promoted in and outside of Kyoto University and accelerating research activities. For example, one became an Associate Professor of Kyoto University Graduate School of Biostudies and another became a Professor of Toyama Prefectural University Graduate School of Engineering.

5. Support for lab setup for new independent researchers

By absorbing the startup costs associated with setting up a laboratory environment for new independent researchers, iCeMS has demonstrated its commitment to helping these young researchers reach their full potential. Most notably, a startup fund equivalent to JPY 100 million, mainly covering equipment costs for a next generation optics system, was provided for Asst. Prof Carlton, an iCeMS Kyoto Fellow, who was hired to further develop optical microscopy technology used to examine mesoscopic cellular architectures. Assoc Prof Sivaniah also benefited from a renovated laboratory with a startup fund of JPY 40 million.

6. Encouraging young researchers' participation in education

- **Teaching classes.** Young researchers participate in teaching that is important for their career development. 16 young researchers have already started to teach courses for undergraduate and graduate students at Kyoto University. Additionally, 2 new educational courses for undergraduates, both with participation from several young iCeMS researchers, have been conducted.

- **Co-Mentor Program.** iCeMS PIs officially affiliated with Graduate Schools and supervising graduate students may choose to assign other faculty members (including iCeMS Kyoto Fellows) as "co-mentors" to their students in order to provide additional advice and guidance. Co-mentors can obtain significant experience and expertise in teaching graduate students, which is important for their career development.

- **Promotion to a tenured position at the Institute for Liberal Arts and Sciences.** Kyoto University has launched the new institute as one of the international strategies where more than one hundred overseas faculty members are employed as tenured staff to teach classes in English. The faculty members are allocated a tenure position at their primary-graduate school/institute and serve to teach at the new institute. Carlton (once hired as iCeMS Kyoto Fellow) has got this tenure position on December 2015.

2-3. Competitive and Other Funding

Describe the results of the Center's researchers to date in securing competitive and other research funding.

- In Appendix 2-2, describe the transition in acquiring research project funding, and note any external funding that warrants special mention.

From FY2007 to FY2015, iCeMS researchers acquired a total of **JPY 12,291 million** in research funds: 3,460 million from Grants-in-Aid for Scientific Research; 625 million from the Next-Generation Leading Research Funding Program; 6,744 million from sponsored research funding; and 1,462 million from other competitive research funding sources. For the last three years, the amount iCeMS has acquired is **1.33 times** greater than the support from WPI.

1. Large scale projects

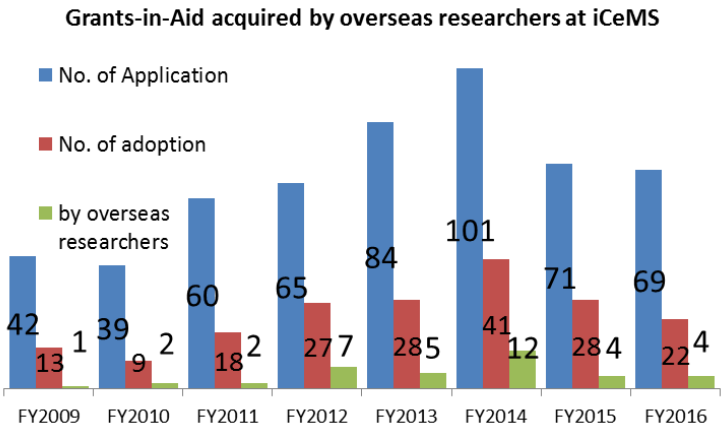
iCeMS scientists have acquired several large scale funding projects funded by Ministry of Economy, Trade and Industry's New Energy and Industrial Technology Development Organization (NEDO) and Japan Science and Technology Agency (JST). iCeMS has had 6 Sakigake fellows in its history, the best of the WPI institutes. Additionally several CREST programs have been won as well as participation in the IMPACT programs.

2. The Cabinet Office's Funding Program for Next Generation World-Leading Researchers (NEXT) program

From iCeMS, 5 projects were selected (Profs Harada, Uesugi, and Kengaku, and Assoc Profs Sengoku, and Ueno), ranked 5th out of 209 recipient departments across Japan, next only to the graduate school of engineering at the University of Tokyo (9 projects), Tohoku University (8), Osaka University (6), and the Tokyo Institute of Technology (6).

3. Grants-in-Aid acquired by overseas researchers at iCeMS

iCeMS has held annual workshops on how to obtain grants in English, resulting in a consistent increase in the number of applications (240% in six years, 42 to 101) as well as an increase in the number of awarded grants to overseas researchers (From 1 to 12 in six years). This is an important issue since actually JSPS is perhaps the easiest way for non-Japanese researchers to access Japanese funding. Other funding schemes tend to require a Japanese language proposal. Nonetheless, since most reviewers are Japanese for JSPS proposals and since proposal styles are unique for each country, it is important to educate the researcher on what is expected.



2-4. State of Joint Research

Describe the results of joint research conducted with other research organizations both in and outside Japan.

(a) NCBS, InStem in Bangalore, India

The iCeMS satellite lab in Bangalore on stem cell research and single molecule imaging was established in as **the Institute for Stem Cell Biology and Regenerative Medicine (inStem)** at the **National Centre for Biological Sciences (NCBS)** new building, completed in June 2012. Assoc Prof Suzuki, for single molecule imaging, and Senior Lecturer Hasegawa, for stem cell research, conduct research activities there as group leaders. The research groups published 25 papers, five of which appeared in journals with IF 10 or more. Their work at NCBS and inStem are highly regarded and the terms of their contracts have been extended.

(b) UCLA California NanoSystems Institute (CNSI)

iCeMS has been promoting active collaboration with CNSI as a partner institution since 2010. Research groups led by Profs Susumu Kitagawa and Omar Yaghi on porous materials, and Assoc Prof Ueno and Prof James Gimzewski on biomaterials STM and AFM have been conducting collaborative research. Furthermore research groups led by Prof Hashida, Prof Imahori and Assoc Prof Murakami and Prof Fuyuhiko Tamanoi have discussed future collaborations on drug delivery. These collaborations have already resulted in papers such as:

(c) Center for Meso-Bio Single-Molecule Imaging (CeMI)

CeMI was established to promote effective collaboration via the shared use of large scale and/or unique equipment among iCeMS researchers and collaborating scientists from other departments and organizations. In addition to leading-edge commercial laser scanning microscopes, CeMI-built stations are in operation: four, single fluorescent-molecule tracking (SFMT) stations, each with distinct and specific capabilities, including simultaneous three-color SFMT, photoactivation; the world's fastest frame-rate at 10 kHz (all operable for live cells at 37°C in 5% CO^2 atmosphere); a terahertz near-field microscope with the world's fastest image acquisition rate (10 Hz).
Highlights of CeMI's achievements since its establishment include the following:

(d) Domestic satellite: the Faculty of Applied Biological Sciences, Gifu University

One domestic satellite laboratory was established at Gifu University in 2008, in order to add a world leader in glyco-chemistry. As an iCeMS PI, Prof Makoto Kiso collaborates and interacts with other members of the iCeMS in the area of glyco-technology and its application to cell biology. Since its establishment, over 300 carbohydrate derivatives were synthesized and a total of 76 papers have been published from the Kiso group. Representative papers in three main research domains are listed below.

(e) Katsura Laboratory

During the FY2011 Site Visit, one of the suggestions iCeMS received was to promote joint research in polymer chemistry. In response, iCeMS has opened a 220 m^2 shared-use laboratory on Kyoto University's Katsura campus, in collaboration with four professors from the university's Graduate School of Engineering at its core. Some notable progress has already being achieved, such as in the Imahori, Mori, and Murakami groups demonstration of effective control over cell functions utilizing the photoinduced charge-separated state for the first time, and the Kitagawa, Chen and Wang groups using a living cell made by the Mori group for working on a new PCP-based cell-stimulation platform that releases nitric oxide by photoactivation. This cell-stimulation platform was utilized to control the growth of neurites in neuronal cells, successfully regulating the neurite length by the photo-release of nitric oxide, a signaling molecule known to regulate neuron development. Mori lab also developed fluorescent thermosensors to visualize temperature inside cells. This was applied to monitor the fluctuation of the temperature within mitochondria in response to chemical stimuli, revealing the temperature heterogeneity within a single cell for the first time.

In summary, iCeMS has produced 1477 peer-reviewed papers with an iCeMS affiliation from 2007 to December 2015.

- 24% (328) of those were published with co-authors affiliated with overseas institutes
- 33% (457) with co-authors affiliated with Japanese institutes other than Kyoto University
- 23% (322) with co-authors affiliated with other departments at Kyoto University
- 9% (128) were co-authored within iCeMS

This demonstrates the institute's highly positive attitude towards collaborative research activities.

2-5. Appraisal by Society and Scientific Organizations

Describe how society and/or scientific organizations in and outside Japan have recognized the Center's research achievements. In Appendix 2-3, list the awards received and invitational lectures given by the Center's researchers.

(a) Eminent awards received.

60 iCeMS researchers have received 125 awards since the establishment of the institute. The most outstanding awards are as follows:

1. Nobel prize to Prof Yamanaka

iCeMS PI and CiRA Director Prof Yamanaka was awarded the 2012 Nobel Prize in Physiology or Medicine together with Sir John B Gurdon, University of Cambridge, for the discovery that mature cells can be reprogrammed to become pluripotent.

2. 2010 Thomson Reuters Citation Laureate to Profs Kitagawa and Yamanaka

iCeMS then Deputy Director Prof Kitagawa (Chemistry) and iCeMS PI and CiRA Director Prof Yamanaka (Physiology or Medicine) were awarded 2010 Thomson Reuters Citation Laureates. Laureates typically rank among the top one-tenth of one percent (0.1%) of researchers in their fields, based on citations of their published papers over the last two decades.

3. Profs Heuser and Yamanaka elected to U.S. National Academy of Sciences

iCeMS PI and Prof Heuser and iCeMS PI and CiRA Director Prof Yamanaka were elected as members of the U.S. National Academy of Sciences in May 2011.

(b) Invited Distinguished talks

Director Kitagawa was invited to the Symposium Celebrating 125 Years of Angewandte Chemie (a journal with the highest IF in the field of chemistry, excluding review journals) in March 2013 as a speaker together with two Nobel laureates and several other leaders in the field. Invited talks were delivered to 2,000 audience members and broadcasted worldwide.

(c) World Stem Cell Summit

iCeMS has been actively involved in co-organizing and participating in World Stem Cell Summit since 2012, the second largest congress of stem cell research in the USA. **Founding Director Nakatsuji** contributed as one of the co-chairs and was invited to give the plenary in FY2015 in a row to experts in the stem cell and regenerative medicine fields. iCeMS organized the "Japan Symposium" in the recent two years, inviting a panel of experts from academia and industry.

(d) Outreach activities organized by Science Communication Group (SCG)

SCG, led by Specially-Appointed Prof Kato, has held "iCeMS Cafes" since 2008. The Cafe is designed as an outreach activity supporting iCeMS young researchers to gain experience in communicating with the public. More than one hundred early-career researchers joined the events. SCG has provided an original "Dialogue skills Training Program" prior to the Cafe. The program is now being used by Kyoto University, Hiroshima University, Nara Institute of Science and Technology (NAIST), and the JST's Center for Science Communication. Our outreach activities are expanding from one institute's challenge to a nation-wide practice for bridging researchers and the public. Furthermore, SCG has carried out the research and development project, which is for purpose of connecting needs and opinions of the public to the policy process, named "PESTI". This project was one of the R&D program: "Science of Science, Technology and Innovation Policy" of JST-RISTEX. PESTI contribute to the STI policy-making process on MEXT and local governments.

2-6. Feeding Research Outcomes Back into Society

2-6-1. Applications of research results

Describe the applications created from research results, their effect in spawning innovation, intellectual properties (IPs) obtained, and joint research activities conducted with corporations, etc.

(a) Industrialization of research results. One of the successful examples of starting up and nurturing a business at iCeMS is ReproCELL. ReproCELL Inc. was established by an entrepreneur in 2003 with the goal of contributing to the health and welfare of the general public through the development of stem cell technologies and is now listed on the JASDAQ Stock Exchange. Many of ReproCELL's technologies were developed by iCeMS Founding Director Nakatsuji, a stem cell pioneer. ReproCELL develops diverse products, with an underlying theme that focuses on stem cell

technology, to address the needs of researchers and clinicians. This product range encompasses reagents for ES/iPS cells and stem cell-derived functional cells.

(b) Patent acquisition. The present status of patent acquisition at Kyoto University's iCeMS for 2013-2015 is as follows: Number of applications 112; PCT (Patent Cooperation Treaty) applications 36; and issued patents 21. The income from intellectual property of iCeMS from the year 2007 to 2015 has reached a total of JPY 29 million. SACI (Office of Society-Academia Collaboration for Innovation) will support patent-related issues and collect patent royalties.

(c) Collaborative work with industry. iCeMS has actively collaborated with industry. The total funding acquired by collaborative research for 199 projects has reached JPY 952 million. The number of projects and research funding has soared to 229% and 369%, respectively, in nine years.

(d) New facility at Rakunan-shinto. iCeMS opened a new lab at the Advanced Chemical Technology Center in Kyoto (ACT Kyoto), located in Rakunan-shinto which is in the southern part of Kyoto City, 10 km from iCeMS Main building. Act Kyoto bridges industry, regional government and academia, and was selected as a Local Innovation Promoting Region by the regional activation program run by MEXT and METI. Here, **iCeMS plays a leading role in local revitalization** by promoting Kyoto Next-Generation Energy Systems Creation Strategy.

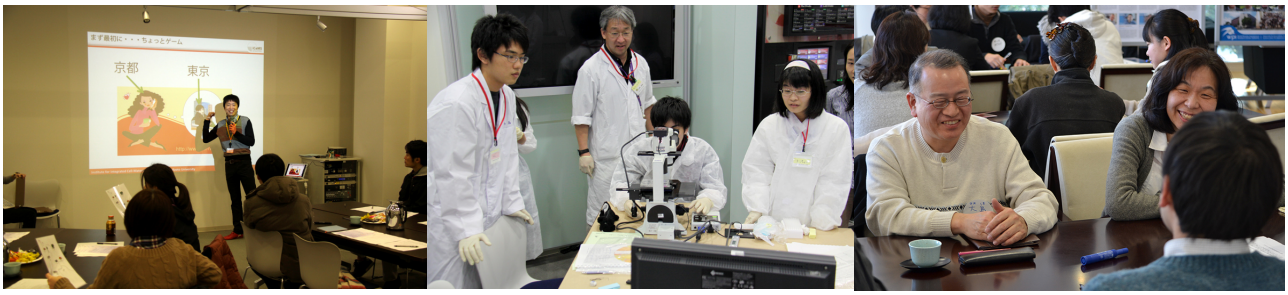
2-6-2. Achievements of Center's outreach activities

If the Center has conducted its own unique outreach activities, describe those worthy of special mention.

- In Appendix 2-4, list and describe media coverage, press releases, and reporting.

(a) Outreach activities organized by Science Communication Group (SCG)

SCG have held hands-on iCeMS-CiRA joint stem cell classrooms for high school students and high school teachers since 2009. To date, more than 700 people have participated in this program. For these efforts, SCG received a Commendation for Science and Technology by MEXT in 2014. The concept of these activities was applied to science educational TV programs by NHK. In addition, SCG have been developing science workshops for children by using these TV programs. The activities awarded Knowledge Innovation Award 2nd by Knowledge Capital in 2015.



(b) Social media utilization. iCeMS was the first WPI institute to utilize social media for effective science communication. At the 2014 Chicago AAAS meeting, iCeMS played a pivotal role in launching the official WPI facebook page to reach out to international audiences, where the use of social media is a common practice. This outreach medium became a standard platform for all WPI institutes to engage the public by posting notable events and research findings.

(c) Booths featuring hands-on activities. The iCeMS Science Communication Group and public relations section exhibited a booth that featured action figure crafting activities for participants at the Science Agora held in Tokyo in November, 2013. Through interpersonal communication, iCeMS promoted understanding of frontier research to over 450 participants over the course of two days. Similarly, iCeMS public relations exhibited a booth for high school students to learn about porous

coordination polymers with the aid of magnetic objects at the WPI joint-symposium held in Sendai in December, 2013. The event attracted over 600 participants.

(d) edX Lectures. **Prof Uesugi** initiated a lecture series "Chemistry of Life" in April 2014 through a new online educational approach called "Massive Open Online Courses (MOOC)" offered by edX. Prof Uesugi's lecture has been taken by more than 25,000 students from the world. This is the first lecture series provided by a Japanese University using edX. edX is a non-profit educational consortium created by founding partners Harvard University and Massachusetts Institute of Technology (MIT) in 2012, and offers a variety of free interactive online classes from top-level universities in fields such as law, computer science, history and artificial intelligence. It is composed of more than 70 schools, nonprofit organizations and corporations, and boasts over 7 million registered users worldwide.

3. Interdisciplinary Research Activities (within 3 pages)

3-1. "Top-down" Undertakings toward Creating New Interdisciplinary Domains

(a) Director succession. To take the institute to a higher level of cell-material integration, iCeMS decided to implement a more materials science approach under the leadership of Prof Kitagawa, to build upon the primarily cell science approach of iCeMS during the first five years under the leadership of Prof Nakatsuji.

(b) New PIs hired and new junior PI's promoted. iCeMS has taken measures to strengthen its lineup of researchers, in response to WPI Program Committee and Site Visit Working Group remarks questioning the strength of the institute's cell science team. Three new PIs, Profs **Kageyama, Saitou, Tanaka and Assoc Prof Sivaniah** joined the iCeMS and were allocated adequate lab space and postdoc researchers. We also promoted 5 young researchers to junior PI's.

(c) Startup grants for young researchers. iCeMS has provided two types of small startup grants to initiate interdisciplinary collaboration within the institute and within university. The grant for collaboration within the institute was merged into the **Accelerated Research Projects** for FY2013, marking a shift from the institute's startup phase into one focusing on promoting targeted research projects. Meanwhile the latter grant for collaboration within the university has been continued, albeit with a reduced total budget.

(e) Open-Offices and Open-Laboratory. Open laboratory and office space contributes to an environment suitable for adapting to dynamic research styles. For instance, even a short stay researcher would be able to drive joint research when visiting iCeMS immediately upon arrival. In addition, the Support Office for Common Use Equipment is contributing to this environment by making it increasingly more convenient for researchers to conduct experiments.

(f) Task forces established for interdisciplinary research. In order to promote interdisciplinary research and to focus its prioritized research areas, iCeMS has established appropriate task force teams, as called for by the situation and in a timely manner.

- **Cross-Disciplinary Research Task Force.** Original and innovative cross-disciplinary collaborative projects integrating functional smart materials with living cells including stem cells were conducted among the Kitagawa, Imahori, Takano, Kiso, Chen, Kusumi, Ueda, Harada, Heuser, Kengaku, and Nakatsuji Labs. In 2012, every month many researchers including PIs and young researchers join to present research updates and to explore new areas for collaboration.

- **Future Challenge Task Force.** This task force was established February 2014 to clarify the identity of iCeMS, an issue that has been raised in follow-up reports and at a meeting with the Program Director, Program Officer and representative of MEXT. This task force is also to identify challenging targets which the institute will achieve after WPI funding ends.

(g) Annual iCeMS retreats for all research staff

Annual iCeMS retreats have been held since 2009, for the purpose of sharing on-going, unpublished multidisciplinary research activities thorough poster presentations and short talks, including iCeMS researchers from the widest possible variety of backgrounds. This once-a-year opportunity has contributed significantly to the generation of new collaborations and the acceleration of on-going multidisciplinary projects. Numbers of attendees and poster presentations reached its peak in FY2013, having increased by 253% (83 to 210) and 379% (39 to 148) respectively.

(i) Biomaterials Science

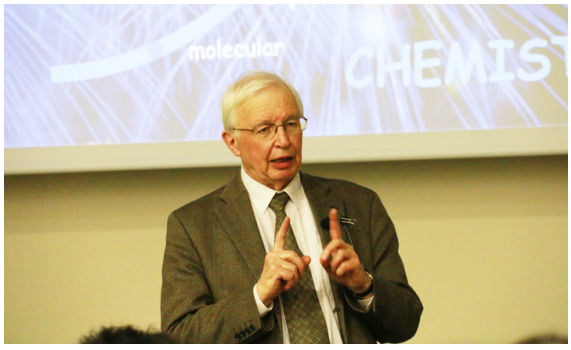
In January 2012, iCeMS began an important new project to contribute to the further development of cell-material integration research as well as mesoscopic sciences by launching a new international journal, Biomaterials Science, in collaboration with RSC. 512 articles and 34 issues have appeared in the online journal as of the end of March 2016. Biomaterial Science has become the 10th of 33 journals in journal ranking of International Scientific Index 'Materials Science, Biomaterials' Category.

3-2. State of "Bottom-up" Undertakings from the Center's researchers toward Creating New Interdisciplinary Domains

Young researchers are voluntarily conducting various kinds of Cross-disciplinary activities. There is a growing number of such activities, as the researchers come to realize that iCeMS becomes a more interesting place through a combination of top-down and bottom down actions.

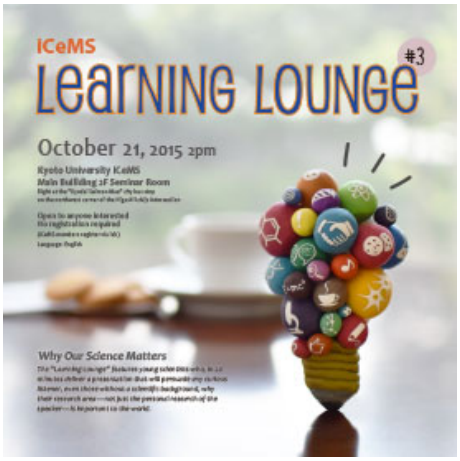
iCeMS International Seminar Series.

iCeMS has hosted more than 200 seminars, conducted in English, since its inception in 2007. Eighty seven percent of these seminars have featured speakers from overseas institutes representing 22 countries. The speakers are invariably of world class pedigree and iCeMS has implemented a system where the speakers will spend time during their visit to have discussions with members of iCeMS, to ensure he or she leaves with an impression of the activities at iCeMS. At the 200th such seminar series we had the pleasure of hosting Prof. Lehn, a Nobel Prize winner in chemistry, who led workshops with both students and young faculty.



Young Scientists' Colloquia & Happy Hour Series.
This is a cross-disciplinary series of informal scientific talks and social gatherings, which are open to all scientists interested in attending a casual forum for exchanging ideas and getting to know other researchers. The idea for the colloquia was born out of a series of informal Friday happy hours initiated by the iCeMS Kyoto Fellows. Since 2012, ten colloquia have been held, attracting an average of 21 researchers.

iCeMS Science 101. This is an informal monthly meeting, organized by postdocs, to facilitate communication among young scientists who are starting their careers and coming from diverse research backgrounds. It serves as a tutorial for general education rather than specific research studies and provides a foundation for researchers to conduct interdisciplinary studies. Four evening meetings have been held since it was launched in October 2013, attracting an average of 17 attendees.



iCeMS "The Learning Lounge". iCeMS commenced a new seminar series The "Learning Lounge" on June 29, 2015 and six Learning Lounge have been held. In these 15-minute talks featuring two speakers every session, young scientists will present their research in a way that is relatable to those outside of their field. Each talk will be recorded and where possible, publicized online. The biggest point is that the speakers must persuade any average intelligent person, even without a scientific background, why their research area - not the personal research of the speaker - is important to the world. These presentations are becoming popular online, and one such video is linked here (Add web LINK), receiving nearly 2000 views in the last few months.

iCeMS Caravan. iCeMS Caravan is a collective effort by young iCeMS researchers to spread an awareness of their research efforts beyond the normal reaches of scientific PR. For example, a group of young PIs and researchers, led by Dr. Katsuda of the Uesugi laboratory went in April 2016 to the remote island of Goto in the west of Japan to explain "the mechanism (karakuri) of study" emerged from their interdisciplinary research approaches and to motivate young students in high-schools to aware what the background of study is. The visit is entirely funded by sponsorship, and has received coverage from the local Nagasaki NHK affiliate, with hopes of the program being distributed nationwide. The program has already resulted in small donations to the iCeMS fund, reflecting the start of iCeMS strategy to generate a nationwide grass-roots support for iCeMS long-term sustainability.

3-3. Results of Research in Fused Research Fields

Describe the Center's record and results by interdisciplinary research activities.
- In Appendix 3, list the main papers published (up to 20 papers) on the Center's interdisciplinary research and provide a description of each of their significance.

(a) Overall evaluation

Due to self-evaluation, the institute has produced 211 highly interdisciplinary and 362 interdisciplinary peer-reviewed papers, 148 (26%) of which have appeared in IF 10+ journals. In order to evaluate more quantitatively, we applied the established bibliometric measure proposed by Porter & Rafols, and analyzed interdisciplinary indices of iCeMS research, comparing them with those of other WPI centers. Indices consist of **Integration** (the average interdisciplinarity of ***cited*** papers ***by*** each publication from a WPI-institute and **Diffusion** (the average interdisciplinarity of ***citing*** papers ***to*** each publication from a WPI-institute). iCeMS Integration and Diffusion indices are 0.598 and 0.527 respectively which are both 2nd among 6 WPI centers.

(b) Representative results of interdisciplinary research

20 representative papers are described in Appendix 3. Three outstanding interdisciplinary research results are as follows.

(i) Nucleus Information:

We now successfully control gene expression by interdisciplinary methods (combinations of biology, physics, and chemistry) to regulate cell fates. Collaborative research among iCeMS groups revealed that gene expression dynamics are important for the activity of transcription factors. Using a new light technology, we showed that oscillatory expression of the transcription factor Ascl1 activates cell proliferation whereas sustained expression of Ascl1 promotes neuronal differentiation [*Science* 2013]. We also synthesized small molecules, SAHA-PIP, consisting of sequence-specific pyrrole-imidazole polyamides and the histone deacetylase inhibitor SAHA. One such compound successfully activates pluripotency genes in mouse fibroblasts [*Sci Rep* 2012], while another induces germ cell genes [*Angew. Chem.-Int. Edit.* 2013].

(ii) Membrane Compartments:

The collaboration among iCeMS researchers allows for the smooth transition from materials fabrications to cell biology investigations. The idea generated in iCeMS indeed stimulated chemists to produce a new material concept 'cell-inspired materials' and the Kitagawa group synthesized several porous coordination polymers (PCPs) with functions similar to compartmentalization concept [*Angew. Chem.-Int. Edit.* 2011, *Nat. Mater.* 2012, *Science* 2013, *Science* 2014]. Furthermore, newly synthesized photoactive PCPs that implement the light-triggered release of nitric oxide (NO) was integrated into cell culture substrates and iCeMS biologists are using them to control a localized cell stimulation system to investigate the roles of NO as intracellular and intercellular signaling molecules, thus towards gas biology applications [*Nat. Commun.* 2013].

(iii) Cell Communication:

Multidisciplinary collaboration among iCeMS and other scientists generated outstanding outcomes in manipulating cell fates and cell-material interactions. For example, screening of chemical libraries and subsequent chemical synthesis identified small molecules that direct differentiation of pluripotent stem cells into cardiomyocytes [*Cell Reports* 2012] and late-stage pancreatic β -cells [*Nat. Chem. Biol.* 2014]. A combination of cell biology and material sciences also revealed that the laminin fragment E8 greatly improves human ES/iPS cell culture for effective cell expansion [*Nat. Commun.* 2012]. iCeMS collaborations also identified a small molecule named "adhesamine' that promotes adhesion of cultured human cells and revealed its mechanism of action [*J. Am. Chem. Soc.* 2013, *Angew. Chem.-Int. Edit.* 2014].

4. International Research Environment (within 4 pages)

4-1. International Circulation of Best Brains

4-1-1. Center's record of attracting and retaining top-world researchers from abroad

Describe the participation of top-world researchers as PIs and the residing of joint researchers at the Center.

- In Appendix 4-1, give the number of overseas researchers among all the Center's researchers, and the yearly transition in their numbers.

(a) iCeMS prominent PIs from overseas

1. **Prof John Heuser**: an internationally recognized authority on electron microscopy, was named a National Academy of Sciences Member in May 2011.
2. **Prof Yong Chen**: a research director of CNRS at the Ecole Normale Supérieure of Paris, contributed

to a number of European research projects.

3. **Prof Motomu Tanaka**: a professor of University of Heidelberg, an internationally recognized authority on Biological Physics, received the Philipp Franz von Siebold Prize in 2013.
4. **Prof Konstantin Agladze**: USA-based Russian Biophysicist left to join MIPT (Moscow Institute of Physics and Technology).
5. **Prof Takashi Hiiragi**: Highly regarded Developmental Biologist, hired from Max-Planck Institute for Molecular Biomedicine, left to join EMBL (The European Molecular Biology Laboratory) after 5 years at iCeMS.

(b) Visitors

There are many world-renowned scholars and visitors who have visited for short stays, not exceeding three months, to conduct joint research. Also iCeMS has been host to a number of celebrity and high profile visitors. A notable example of this, within the last year was the visit of **Her Royal Highness Princess Maha Chakri Sirindhorn of Thailand**; a consequence of this visit was the establishing of an MOU for future collaborations with a prominent Thai institute and iCeMS.

4-1-2. Employment of young researchers at the Center and their job placement after leaving the Center

Describe the Center's employment of young researchers, including postdoctoral researchers, and the positions they acquire after leaving the Center.

- In Appendix 4-2~4, enter the following:
  - The state of international recruitment for postdoctoral researchers, applications received, and selections made
  - The percentage of postdoctoral researchers from abroad
  - The positions that postdoctoral researchers acquire after leaving the Center

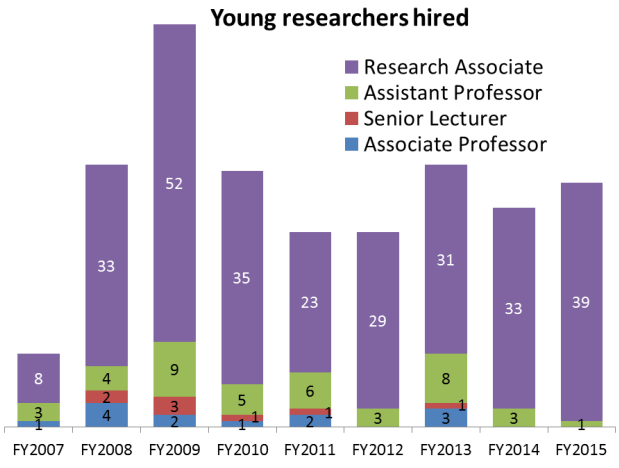
(a) iCeMS Kyoto Fellows and iCeMS Associate Kyoto Fellows hired

Since FY 2009 iCeMS has been attracting young talented scientists worldwide with a total annual budget of 20–30 million yen and an opportunity to establish an independent research group. A total of 96 candidates, which consist of 70% from overseas scientists, have applied for the positions. All of Fellows have finished their five-year contact and get promoted in and outside of iCeMS.

(b) Young researchers hired, promoted or transferred.

From the level of post-doc to associate professor, nearly 350 researchers have been hired at iCeMS over the years. Since its establishment, 29 young researchers (Assoc Prof, Junior Assoc Prof, Asst. Prof, Research Associate) have been promoted at iCeMS and are actively engaged in research activities.

- Promotion to Professor: 2
- Promotion to Associate Professor: 9
- Promotion to Junior Associate Professor: 3
- Re-contract as Assistant Professor from Research Associate: 15



175 of 203 (86.2%) scientists who left iCeMS

have found new positions inside and outside of Japan, and 36 (20.6%) have relocated overseas. To address the issue of brain circulation abroad, we initiated a new Seminar Tour program in 2013 — in addition to the overseas visits program — to encourage young and promising researchers to turn their attention to international opportunities.

4-1-3. Overseas satellites and other cooperative organizations

In Appendix 4-5, describe the state of the Center's agreements concluded with overseas satellites and other cooperative organizations.

We have already mentioned two highly successful international cooperations with the **National Centre for Biological Sciences (NCBS)** and the **Institute for Stem Cell Biology and Regenerative Medicine (inStem)** in Bangalore, India as well as the **UCLA California NanoSystems Institute (CNSI)**, USA. Further to this, we have activities in Europe and Asia such as.

- **Heidelberg University, Germany.** First formed in 2011, the Japanese-German University Presidents' Conference (German-Japanese HeKKSAGOn Universities Consortium, consisting of Heidelberg University, Göttingen University, Karlsruhe Institute of Technology, Tohoku University, Osaka University, and Kyoto University) continues to meet annually. Kyoto University works especially closely with Heidelberg University in the area of cell-material integration, resulting in the Heidelberg-Kyoto joint symposium "Crossing Boundaries: Stem Cells, Materials, and Mesoscopic Sciences" held in Heidelberg in July 2011. Prof Nakatsuji also gave a lecture for a summer school held at Heidelberg University from September 17-26, 2012. It was the first summer school of the Japanese-German network HeKKSaGOn, and the title was "Crossing Borders: Unraveling Principles of Life with Quantitative Tools". The 2nd HeKKSaGOn summer school was held at Karlsruhe Institute of Technology in September 2014, and Prof Kusumi gave a lecture for the school. As a concrete result of these collaborations, Prof M Tanaka of Heidelberg was appointed as an iCeMS PI beginning in FY2013. After joining iCeMS, Tanaka has further accelerated Japan-German academic exchanges; in FY2015 he led Kyoto Winter School 2016 and an exchange program for students and young researchers. In addition, at the university-wide level, Kyoto University established an overseas office within Heidelberg University Campus in May 2014. Administrative staff and a university research administrator (URA) have been allocated to the center to promote cooperation among the HeKKSaGOn Consortium.

- **Vidyasirimedhi Institute (VISTEC), Thailand.** On February 29 2016 , we exchanged a MoU with VISTEC, Thailand. VISTEV was established in 2015 by full financial support of PTT Public Company Limited. VISTEC has the mission to increase the Thailand's competitiveness and foster the best people in science and technology to ensure guide sustainable development and increase prosperity in Thailand. We will not only aim to e xchange graduate students and researchers but also establish the VISTEC endowed chair where joint researches on gas and oil and other energy related technologies will be conducted. iCeMS will hold Kyoto University International Symposium on February 2 and 3 2017 at VISTEC with Her Royal Highness Princess Maha Chakri Sirindhorn's in attendance.

4-2. Center's Record of Holding International Symposia, Workshops, Research Meetings, Training Meetings and Others

・ In Appendix 4-6, describe the main international research meetings held by the Center.

For the main international research meetings held by iCeMS, see Appendix 4-6. Some major symposia are as follows

(a) Heidelberg-Kyoto joint symposium "Crossing Boundaries: Stem Cells, Materials, and Mesoscopic Sciences"

As mentioned above, the Heidelberg-Kyoto joint symposium "Crossing Boundaries: Stem Cells, Materials, and Mesoscopic Sciences" was held in Heidelberg in July 2011. 34 speakers from the iCeMS joined the meeting and the number of participants totaled 296. This symposium featured mesoscopic sciences of cell-material integration, an area which Heidelberg University and Kyoto University work especially closely with each other.

(b) Kick-off Symposium for Biomaterials Science

As stated in P.19 3-1-(i), iCeMS launched a new international journal, Biomaterials Science, in collaboration with RSC and, together, held a joint kick-off symposium for the journal Biomaterials Science in Kyoto in March 2013. 13 speakers from iCeMS joined the workshop, and the total number of attendees was 157. It also included remarks by WPI Program Director Dr Toshio Kuroki, iCeMS Founding Director Nakatsuji, and Managing Editor Niamh O'Connor. Several members of the editorial board delivered presentations, along with members of the iCeMS Academic Advisory Committee.

(c) Japan-France workshop on nanomaterials co-hosted by 4 WPI institutes

Four World Premier International Research Center Initiative (WPI) institutes and France's National Center for Scientific Research (CNRS) co-hosted the 10th annual workshop on nanomaterials between Japan and France in Kyoto in June 2013. Four speakers from iCeMS joined the workshop, and the total number of attendees was 82. iCeMS also co-hosted the 11th workshop in Rennes, France in May 2015 and five speakers from iCeMS delivered oral presentations. The workshop has been promoting researchers from both countries to exchange scientific ideas, foster interdisciplinary collaborations, and forge new connections since 2000.

(d) International Symposium on Nanobiotechnology

The symposium series was initiated in 2007 by the California NanoSystems Institute (CNSI) of the University of California, Los Angeles and the Center for NanoBio Integration (CNBI) at the University of Tokyo. iCeMS has joined this symposium since 2010 as one of the core members.

4-3. System for Supporting the Research Activities of Overseas Researchers

・ Describe the Center's preparations to provide an environment conducive for overseas research to concentrate on their work, including for example living support in various languages or living support for their families. （照会：ORSO）

(a) Overseas Researchers Support Office

The Overseas Researchers Support Office was established in FY2009 to assist foreign researchers in quickly and smoothly adapting not only to their new research environment but also to their new lives in Japan. They specifically provide assistance with immigration procedures, residence status updates, housing arrangements and other matters related to daily life.

(b) iCeMS Housing Guarantor System launched

For enhancing the international environment of the institute, iCeMS launched a Housing Guarantor System in October 2012 to fulfill the role of guarantor when international scientists lease housing for mid- to long-term stays. Joint guarantors are often requested for leases, a custom that has been a persistent barrier for researchers from overseas who have difficulty finding a Japanese guarantor at the time of their arrival. iCeMS has partnered with several cooperative housing agencies in the area in order to improve the move-to-Japan experience.

4-4. Others

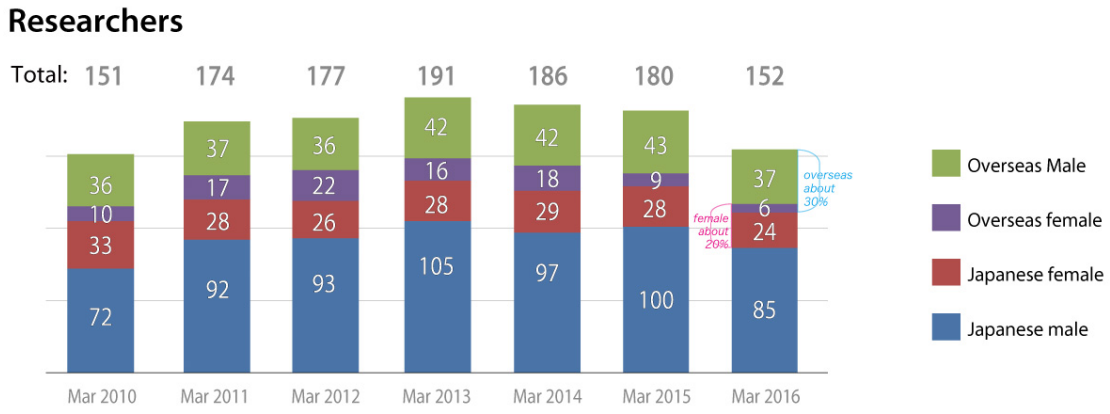
- Describe the Center's policy for sending Japanese researchers overseas to gain international experience, and give examples of how the Center is working to create career paths for its researchers within a global environment of researcher mobility.

(a) The iCeMS-JSPS Overseas Visit Program for Young Researchers

The iCeMS-JSPS Overseas Visit Program for Young Researchers has been implemented since 2010 with aims to 1) provide opportunities for young iCeMS researchers to conduct research at overseas institutes, 2) to strengthen participants' international competitiveness, and 3) to enhance iCeMS' role as an international hub for researchers in related fields. To date, 78 researchers have earned opportunities to visit world-class institutions, opening the door to further international collaborations and careers. Since FY2013, the priority of the program has shifted to career development in contrast to simply boosting international collaboration efforts, and has been successfully run using iCeMS own budget.

(b) Seminar tours for promotion

Seminar tours for promotion have been implemented since 2013 to evaluate the eligibility of a candidate for career advancement. The candidate visits three overseas institutions to conduct seminars, and examiners at each institution make evaluations with an international perspective. Based on these evaluations, the Executive Board carefully considers and reaches a final decision. Total seven candidates went on seminar tours so far and some of them got promoted to a tenured Associate Professor of Kyoto University and to a tenured Professor of Toyama Prefectural University, after promotions at iCeMS.



As a result of all these varied programs, iCeMS has overseen a remarkable enhancement of the international environment for researchers, with nearly 30% of its researchers being non-Japanese.

5. Organizational Reforms (within 3 pages)

5-1. Decision –Making System in the Center

- Describe the strong leadership that the director is giving the Center's operation and its effect, and the division of roles and authority between the Center and its host institution.

(a) Management under strong leadership of the Director

Top down decision-making is made by the Executive Board (the Director, two Deputy Directors, PI Chairman and Admin Director) about matters related to personnel affairs, budget and management — excluding university level management matters and appointment of the iCeMS Director (directly appointed by the President).

Because initiating interdisciplinary research and getting breakthroughs in science are challenging, strong leadership by the Director is critical for success. Particularly, in the early stages after iCeMS' inauguration, **Founding Director Nakatsuji** was dedicated to exploring collaborations with many iCeMS' members and establishing an interdisciplinary research environment.

In **Accelerated Research Projects** initiated in 2013, **Director Kitagawa** takes initiatives to decide

on the research topics. With his strong leadership, quick decision-making and prioritized budget allocation have been successfully achieved. Also as described in 1, his decisive leadership has made iCeMS research mission more transparent.

Under the leadership of the Director, **decision-making is faster**, particularly in the cases of promotion/termination of researchers and allocation of lab space and budget.

5-2. Arrangement of Administrative Support Staff and Effectiveness of Support System

- Describe the assignment of the Center's administrative support staff who have English language and other specialized skills, effort made in establishing the support system, and the system's effectiveness.

(a) Professionals hired in International Affairs and Planning

iCeMS has hired professionals with a wealth of experience in international public relations at overseas and Japanese public sectors and Master of Professional Studies in Strategic Public Relations holder, at the International Affairs and Planning Section for internationalization of iCeMS. In addition, the institute hired a public relations University Research Administrator (URA) to enhance the global visibility of iCeMS. The URA has a PhD and is able to comprehend and communicate the institute's scientific findings to the general public.

(b) Professionals hired in Research Planning

Two senior researchers are employed in the Research Planning Section to oversee the management of large-scale projects, support the acquisition of new large-scale project funds, and advance open innovation with industry via the Open Innovation Task Force and Industrial Advisory Committee (Refer to Appendix 1-3). In addition, an URA has been hired by iCeMS to improve the procurement of external funding in the form of grants.

(c) Industry-government-academia collaboration management by the Innovation Management Group (IMG)

IMG, led by Assoc Prof Sengoku, was exploring novel modes, models, and methods for advancing innovation management in order to realize the promise of leading edge inventions and discoveries for society. IMG had been conducting social implementation initiatives for advanced cross-sector partnerships by designing new and improved collaboration systems between public and private sectors. These initiatives are being conducted in partnership with Kyoto SMI (Smart Materials & Innovation), a satellite NPO and subsidiary of the WPI-iCeMS. After Assoc Prof Sengoku left iCeMS in 2014, IMG was merged together with Research Planning Section.

(d) Public outreach by the Science Communication Group (SCG)

SCG initiated numerous outreach efforts, such as science cafés, hands-on iCeMS-CiRA joint stem cell classrooms, hands-on exhibitions at science festivals hosted by the Cabinet Office (two days in March 2013), and lectures for middle and high school students (more than 5 times in FY2012). SCG offered a "Dialogue Skills Training Program" for young iCeMS' scientists. This program has been adopted by the Center for Science Communication of the Japan Science & Technology Agency (JST) as its communication program for scientists. SCG activity on iCeMS classrooms was highly evaluated and commended by MEXT in 2014 as Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology (文部科学大臣賞).

5-3. System Reforms Advanced by WPI Program and Their Ripple Effects

Concisely itemize the system reforms made to the Center's research operation and administrative organization, and describe their background and results. Describe the ripple effects that these reforms have on the host institution. (Describe the ripple effects on other institutions.)

(a) System reforms achieved at iCeMS

There are a variety of system reforms being undertaken at iCeMS, some of which are listed below.

1. Internationalization

(i) Use of English as the official language;
(ii) Global recruitment;
(iii) 30% overseas researchers;
(iii) Strengthening of International Public Relations and Oversea Affairs and Planning staff;
(iv) Establishment of the Overseas Researchers Support Office;
(v) Over 50% English-speaking administration staff;
(vi) Active MoU exchange with 15 world-renowned partner institutions;
(vii) 44 international symposia held;
(viii) 200 international seminars;
(ix) International journal newly published (Biomaterials Science with RSC);
(x) English-language workshops on obtaining competitive grants;

2. Interdisciplinary research support and open collaboration with industries

(i) Open office and open lab policies;
(ii) Establishing Research Planning Section,
(ii) and Innovation Management Group (IMG) ;
(iv)and Science Communication Group (SCG);
(iii) Collaboration with KURA;
(iV) Establishing Industrial Advisory Board;
(v) Outreach activities;
(v) Annual retreats;

3. Management

(i) Director decision making;
(ii) Merit-based salary system;
(iii) Hiring not limited by the retirement age;
(iv) Budget allocation on prioritized researches;
(v) Strict and fair personnel strategy;
(vi) Cooperative management with researchers by various committees ;

(b) Ripple effects on Kyoto University management

Kyoto University is making a great effort to embody the National University Reform Plan under the leadership of former President Matsumoto (until September 2014) and present President Yamagiwa (from October 2014). iCeMS has been the front runner and the testbeds of these system reforms. The new paradigm created by iCeMS has been highly evaluated and has strongly influenced plans for these Kyoto University reforms described below.

1. Kyoto University international strategy

Kyoto University has formulated a new international strategy, the 2x by 2020 Initiatives on September 2013. 2x by 2020 is the slogan of the new International Strategy by means of which Kyoto University aims to double its international indices in research, education and international service by the year 2020. Goals are clarified in terms of quantity and deadline as WPI missions.

2. Kyoto University level administrative reform

On July, 2013 Kyoto University has undertaken substantial administration reforms, such as the relocation and centralization of staff, new positions for supporting education and research, and implementation of rigorous evaluation and training systems to increase the efficiency of administration. iCeMS has become to support and accelerate internationalization far beyond iCeMS to the Graduate School of Advanced Integrated Studies in Human Survivability (Shishu-Kan) and the Institute for Liberal Arts Studies (ILAS), newly established in FY2013. In ILAS, more than one hundred of oversea faculties are employed as tenured staff to teach classes in English.

iCeMS' rich accumulated experience in internationalization is anticipated to have a large impact on these new institutions. For example, 10 bilingual administrative staff are allocated to ILAS, some of whom are now on the job training at iCeMS.

3. Kyoto University Research Administration

KURA (Kyoto University Research Administration) was established at the university in 2012, and subsequently hired nearly 46 university research administrators (URAs). With its pioneering experience such as in its work with the Innovation Management Group, iCeMS' Research Planning Section has been playing an important role in collaborating with KURA.

4. Kyoto University Vision for the future: WINDOW

President Yamagiwa formulated the WINDOW concepts as a vision for the future on August, 2015. WINDOW is the first letters for the following six words; W: wild and wise, I: International and innovative, N: Nature and Noble, D: Diverse and Dynamic, O: Original and Optimistic and W: Women, Leaders in the Workplace. WPI is directly cited within WINDOW's 2nd Strategic Priority 2-2 of being 'International and Innovative' as follows. "We will establish a World Premier International Research Center (WPI Research Center) as a hub of front-line research at Kyoto University. Through the center, tentatively named the Kyoto University Institute for Advanced Study we aim to facilitate the advancement of cutting-edge research that capitalizes on Kyoto University's particular strengths, cultivate the next generation of research professionals, and circulate outstanding research talent both within Japan and overseas".

5. Personnel management

Introduction of a new salary system including cross-appointment scheme and annual salary system is partially introduced in FY2014 into Kyoto University's personnel management. Abolishment of the retirement age has been implemented in other institutes such as CiRA and Shishu-kan and will be expanded to other organizations.

5-4. Support by Host Institution

The following two items concern the support that the host institution provides the Center, including those items of support that it committed to at the time of the initial project proposal submittal or in its revised commitment following the project's interim evaluation. Describe the functional measures that the host institution has taken to sustain and advance the Center's project.

5-4-1. Record of host institution support and its effects

In Appendix 5-1, describe the concrete measures being taken by the host institution.

Kyoto University declared at the time of the initial project proposal to secure measures to support iCeMS research activities, and has secured them.

5-4-2. Position of the Center within the host institution's mid-term plan

To Appendix 5-2, attach the cover sheets of the host institution's "Mid-term objectives" and/or "Mid-term plan" and parts of these documents related to the WPI Center.

Kyoto University launched, on August 2015, a plan to establish the **Institute for Advanced Study (KUIAS)**. KUIAS established on April 2016 and the present iCeMS will join the KUIAS in April 2017 as one of the core institution of the KUIAS.

5-5. Others

Describe efforts advanced to foster young researchers (e.g., start-up funding, autonomous research environment) and to enlist female researchers.

In Appendix 5-3, give the transition in the number of female researchers.

iCeMS has taken the following efforts to foster young researchers.
(a) Startup grants to initiate cross-disciplinary collaboration: P.11 2-2-(b)-1, P.17 3-1-(c)
(b) Acceleration of outstanding projects: P.2 1-(b)-2-(ii), P.11 2-2-(b)-2, P.25 5-1-(b)-2
(c) Support for overseas visit for young researchers: P.11 2-2-(b)-3, P.24 4-4
(d) Independent positions for young scientists worldwide: P.12 2-2-(b)-4

6. Others

In addition to the above 1-5 evaluation items, only if there is anything else that deserves mention regarding the center project's progress, please note it.

(a) Strengthening collaboration with CiRA

In FY 2007, just after **Prof Yamanaka**'s discovery of human iPS cells, iCeMS Director swiftly the Center for iPS Cell Research and Application under the auspices of iCeMS, marking a major advance in the effort to apply human stem cell research to the field of regenerative medicine. As CiRA developed over time, to its present focus on **on clinical applications of iPS cells**, Kyoto University established CiRA as the 14th university institute outside of the predominantly fundamental scope of iCeMS. This is fantastic research output of iCeMS, again unique to the WPI institutes, to have given birth to another stand-alone institute. Nonetheless six CiRA scientists have iCeMS affiliations, performing basic and multidisciplinary research related to iPS cells in conjunction with iCeMS colleagues. Moreover, CiRA PI and iCeMS Professor Yamada and CiRA PI and iCeMS Kyoto Fellow Yamamoto both engage in the management of this institute as participants in iCeMS Board of PI meetings.

(b) Asian Chemical Biology Initiative

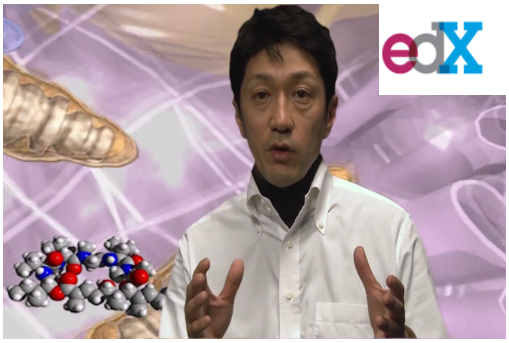
iCeMS has been serving as the headquarters of the Asian Chemical Biology Initiative. This program, sponsored by JSPS "Asian CORE Program" since 2011 (5-year term), aims to establish Asian research hubs that conduct world-class research, and foster outstanding young researchers. This initiative is being orchestrated by iCeMS **Prof Uesugi** in cooperation with institutions in Asia, including Seoul National University, Tsinghua University and National University of Singapore. The main goals of this initiative are as follows.

1. To establish a world-visible core of "Chemical Biology originating from Asian countries" led by Japan's initiatives.

2. To recruit talented graduate students from emerging Asian countries to Chemical Biology. More than 70 top-notch chemical biology professors from Japan, Korea, China, Singapore, Hong Kong and India have already joined this initiative. Since the launch of this initiative, more than 100 international students have applied for interviews to study in Japan, and it resulted in more than 10 of them actually coming to study in Japan.

(c) Kyoto University joined edX program

Kyoto University announced on May 21, 2013 its alliance with **"edX,"** making it the first Japanese university to take part in the non-profit educational consortium. The first course offered by Kyoto University's "*KyotoUx*" series is taught by iCeMS deputy director and Institute for Chemical Research **Prof. Uesugi**, titled the "**The Chemistry of Life**." Prof. Uesugi also provided the first "flipped class" in the long history of Kyoto University education.



(d) Creation of iCeMS Fund

On June 1st, iCeMS created the iCeMS Fund, utilizing Kyoto University Fund framework. We are aiming to maintain and develop our research activities and scientific achievements for solving environmental problems and contributing to new medications, and calling for financial supports for public. 15 endowments have been donated at the preparatory operation stage and this shows high expectations for our institute.

7. Center's Response to Results of FY2015 Follow-up (including Site Visit Results)

* Describe the Center's Response to Results of FY2015 Follow-up. Note: If you have already provided this information, please indicate where in the report.

The Program Committee gave us three recommendations which we should keep in mind to continue our research.

- **Although the scientific achievement is high, truly visible results, which will be regarded as iCeMS landmarks, may be missing.**
- **It is necessary to devise a concrete future plan of iCeMS as a major part of KUIAS, which will commence next April.**
- **It is understandable that the fusion of material science and cell biology is quite difficult and contains various directionalities. However, still, the aim of iCeMS seems a little too divergent. More focused subjects would be desirable in view of the size reduction of the institute after the current WPI program funding.**

Kyoto University announced that the new institute called Institute for Advanced Studies (KUIAS) will start on April, 2016. The management principles of the KUIAS are as follows:

- Serve as a global center of excellence where world-renowned scholars can join for collaborative research
- Act as a global hub to promote world-class research and investigate proto-sciences
- Provide an environment where select, talented Kyoto University scientists can devote time to their research interests and where young, promising researchers are nurtured
- Exist under the university president's leadership in order to act as a sustainable testbed for implementing university reforms and to apply them university-wide

The present iCeMS will join in the KUIAS after WPI support ends in FY2016. Kyoto University promised to provide the iCeMS with 5 tenure posts, 10 tenure track posts and 5 overseas researchers' posts in addition to administration personnel and facilities maintenance expense.

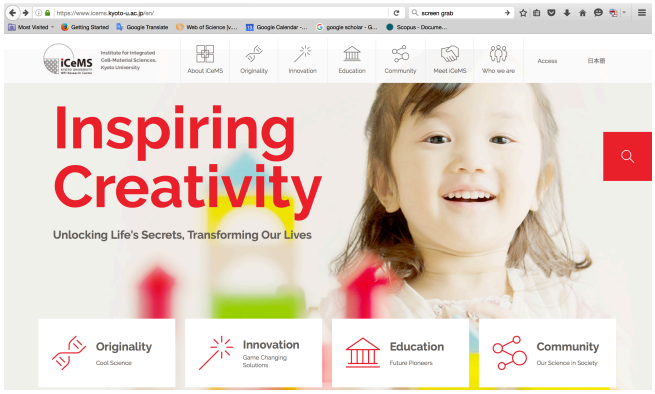
By considering the scale of financial and personnel support given by Kyoto University and of external funding amount iCeMS can acquire, New iCeMS after FY2017 will be shrunk in number of researchers (reduced from 146 (at present) to 106). Number of PI's who will participate in the New iCeMS is 9 and their names are listed in Appendix-1 of Progress Plan.

After the WPI funding ends in FY2017, we have clearly identified two challenging research areas described below and will attain more goal-oriented results under the director's leadership.

- **Platform 1. Synthetic paradigms for cell programming and its utilization.**
- **Platform 2. Breathing, cleansing and transformation through cell-inspired materials**

These are described in detail in the future plan section. However briefly these themes indicate a more impact motivated purpose to achieve recognition for how our cutting edge fundamental science can play a vital, tangible role in society. In addition, and iCeMS is playing a significant attention to enhancing the visibility of it research and institute by incorporating an engine for the translation of these activities to society.

- **Translation Engine. A crucible for creativity.**



iCeMS has made fantastic results of true global significance. However to date it has not made a more sophisticated attempt to translate this fact to world. It is notable to point out, that our failure is symptomatic of Japanese academia's failure, across the spectrum of Japanese Universities which are relentlessly generating cutting edge research but who fail to properly adapt to the modern system of promoting research to the wider, international audience using more sophisticated PR machinery. We are addressing this issue by overhauling our public relations machine**, and indeed there is already evidence of this, through the revision of the iCeMS website**, and with significant plans for further changes described in the future plan.

World Premier International Research Center Initiative (WPI)

Appendix 1-1. FY 2015 List of Principal Investigators

NOTE:
・Underline names of investigators who belong to an overseas research institution.
・In case of researchers not listed in the latest report, attach Appendix1-1a, "Biographical Sketch of a New Principal Investigator".

<Results at the end of FY2015>

Principal Investigators Total: 25

Name (Age)	Affiliation (Position title, department, organization)	Academic degree, specialty	Working hours (Total working hours: 100%)				Starting date of project participation	Status of project participation (Describe in concrete terms)	Contributions by PIs from overseas research institutions
			Work on center project		Others				
			Research activities	Other activities	Research activities	Other activities			
Center Director Kitagawa, Susumu (64)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Coordination Chemistry	75%	15%		10%	Oct. 1, 2007	Usually stays at the institution.	
Nakatsuji, Norio (66)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Stem Cell Biology	40%	50%	5%	5%	Oct. 1, 2007	Usually stays at the institution.	
Uesugi Motonari (49)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Chemical Biology	80%	10%		10%	Oct. 1, 2007	Usually stays at the institution.	
Kageyama, Ryoichiro (59)	Professor, Institute for Virus Research, Kyoto University	M.D. Ph.D. Developmental Biology	15%	10%	65%	10%	Feb. 2, 2013	Participates at the 25% effort level. 75% devoted to the Institute for Virus Research.	

Ueda, Kazumitsu (62)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Cellular Bio-chemistry	80%	10%		10%	Oct. 1, 2007	Usually stays at the institution.	
Chen, Yong (59)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University Research Director, Ecole Normale Supérieure, CNRS	Ph.D. Nanobiotechnology	30%	10%	50%	10%	Mar. 1, 2008	Participates in the institution at the 40% effort level. (Frequency of visits to Japan: 2 times and 17 days in FY2015)	
Hashida, Mitsuru (64)	Professor, Graduate School of Pharmaceutical Sciences, Kyoto University	Ph.D. Drug Delivery Systems	40%	10%	40%	10%	Jan. 1, 2008	Participates at the 50% effort level. 50% devoted to the Graduate School of Pharmaceutical Sciences.	
Imahori, Hiroshi (54)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Organic Chemistry	80%	10%		10%	Oct. 1, 2007	Usually stays at the institution.	
Kengaku, Mineko (49)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Developmental Neurobiology	90%	10%			Oct. 1, 2008	Usually stays at the institution.	
Kiso, Makoto (68)	Professor, Faculty of Applied Biological Sciences, Gifu University	Ph.D. Glycotechnology	80%	10%		10%	Oct. 1, 2007	Joins a video conference from Gifu University once a month. Usually stays at Gifu University satellite.	
Saitou, Mitinori (45)	Professor, Graduate School of Medicine, Kyoto University	M.D. Ph.D. Germ Cell Biology	15%	5%	70%	10%	Jan. 16, 2013	Participates at the 20% effort level. 80% devoted to the Graduate School of Medicine.	

Sugiyama, Hiroshi (59)	Professor, Graduate School of Science, Kyoto University	Ph.D. Chemical Biology	15%	5%	70%	10%	Apr. 1, 2008	Participates at the 20% effort level. 80% devoted to the Graduate School of Science.	
Tanaka, Motomu (45)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	M.D. Ph.D. Biological Physics	40%		50%	10%	Apr. 1, 2013	Participates at the 40% effort level. (Frequency of visits to Japan: 9 times and 215 days in FY2015)	
Harada, Yoshie (56)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Single-Molecule Physiology	90%	10%			Mar. 1, 2008	Usually stays at the institution.	
Heuser, John (73)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University Professor, Washington University School of Medicine	M.D. Biophysics	50%		40%	10%	Nov. 16, 2009	Participates in the institution at the 50% effort level. (Frequency of visits to Japan: 4 times and 145 days in FY2015)	
Kusumi, Akihiro (63)	Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Single-Molecule Cell Biophysics	80%	10%		10%	Oct. 1, 2007	Usually stays at the institution.	
Tanaka, Koichiro (53)	Professor, Graduate School of Science, Kyoto University	Ph.D. Terahertz Optical Science	15%	5%	70%	10%	Apr. 1, 2008	Participates at the 20% effort level. 80% devoted to the Graduate School of Science.	
Yamanaka, Shinya (53)	Professor, iPS Cell Research and Application (CiRA), Kyoto University Senior Investigator, Gradstone Institutes	M.D. Stem Cell Biology	4%	1%	75%	20%	Oct. 1, 2007	Participates at the 5% effort level. 95% devoted to the CiRA.	

Kato, Kazuto* (55)	Professor, Graduate School of Medicine, Osaka University)	Ph.D., Bioethics, Science Communication	4%	1%	50%	45%	Nov. 1, 2008	Usually attend meetings at the center once or twice in a month, and/or give supervision to the group members through video conference from the main affiliation (Osaka University) once or twice a month.	
Carlton, Peter* (42)	Program-Specific Research Center Associate Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph. D. Molecular and Cell Biology	90%	10%			Mar. 1, 2010	Usually stays at the institution.	
Murakami, Tatsuya (46)	Program-Specific Research Center Associate Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. (Eng.), Nanobio-science	90%	10%			Jan. 1, 2009	Usually stays at the institution.	
Sivaniah, Easan (44)	Associate Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph. D. Physics	90%	10%			July 1, 2013	Usually stays at the institution.	
Suzuki, Kenichi (47)	Program-Specific Research Center Associate Professor, Institute for Integrated Cell-Material Sciences, Kyoto University	Doctor of Engineering, Cell Biophysics	75%	5%	15%	5%	Apr 17, 2011	Stays at National Centre for Biological Sciences(NCBS) / Institute for Stem Cell Biology and Regenerative Medicine (inStem) satellite 5-6 times a year, and at center during other periods	
Kim, Franklin (38)	iCeMS Kyoto Fellow, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Chemistry	90%	10%			Dec. 16, 2010	Usually stays at the institution.	
Wang, Dan Ohtan (40)	iCeMS Kyoto Fellow, Institute for Integrated Cell-Material Sciences, Kyoto University	Ph.D. Neuroscience	90%	10%			May 1, 2011	Usually stays at the institution.	

Researchers unable to participate in project in FY 2015

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken

Biographical Sketch of a New Principal Investigator in FY 2015

Name (Age)	
Current affiliation (Position title, department, organization)	
Academic degree, specialty	

Research and education history

Achievements and highlights of past research activities *(Describe qualifications as a top-caliber researcher if he/she is considered to be ranked among the world's top researchers.)*

Achievements

(1) International influence

a) Guest speaker, chair, director, or honorary member of a major international academic society in the subject field, b) Holder of a prestigious lectureship, c) Member of a scholarly academy in a major country, d) Recipient of an international award(s) , e) Editor of an influential journal etc.

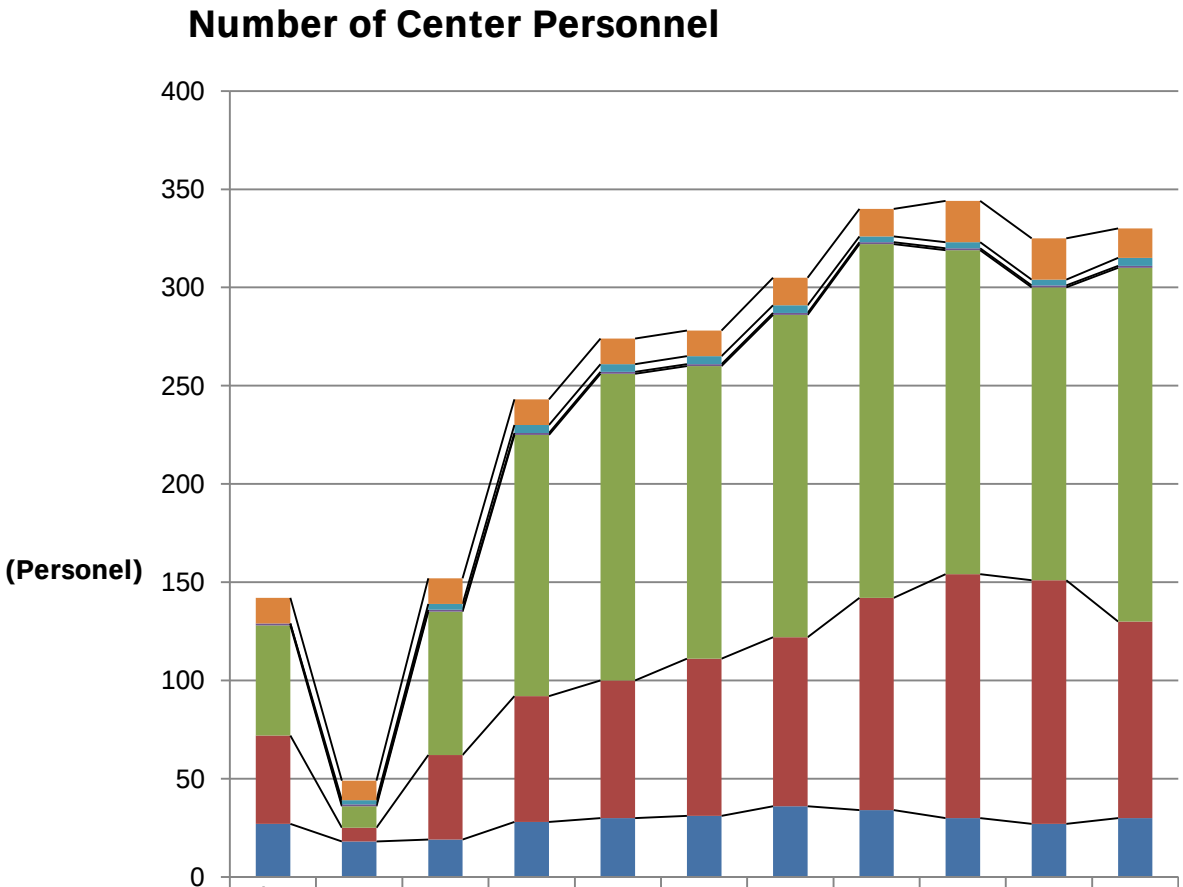
(2) Receipt of large-scale competitive fundings *(over past 5 years)*

(3) Article citations *(Titles of major publications, and number of citations.)*

(4) Others (Other achievements that indicate qualification as a top-caliber researcher, if any.)

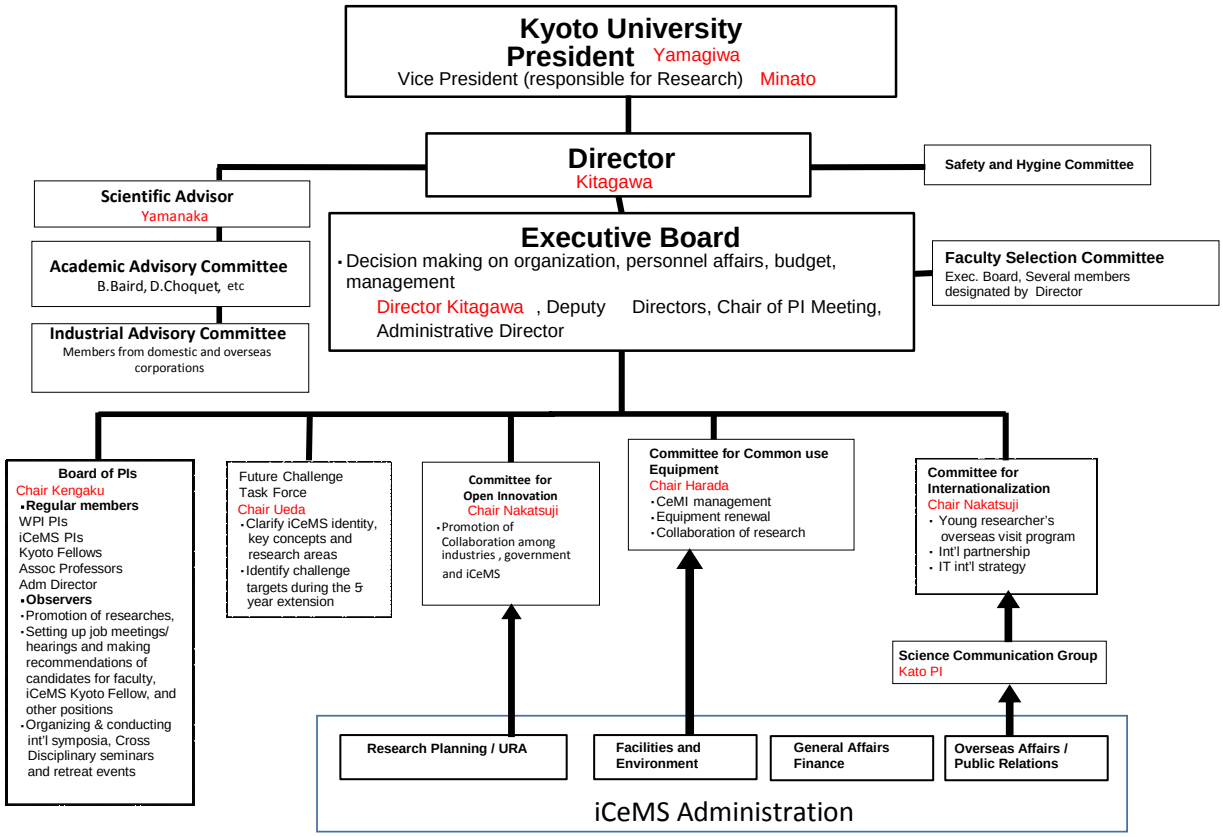
World Premier International Research Center Initiative (WPI)
Appendix 1-2. Annual Transition in the Number of Center Personnel

*Make a graph of the annual transition in the number of center personnel since the start of project.



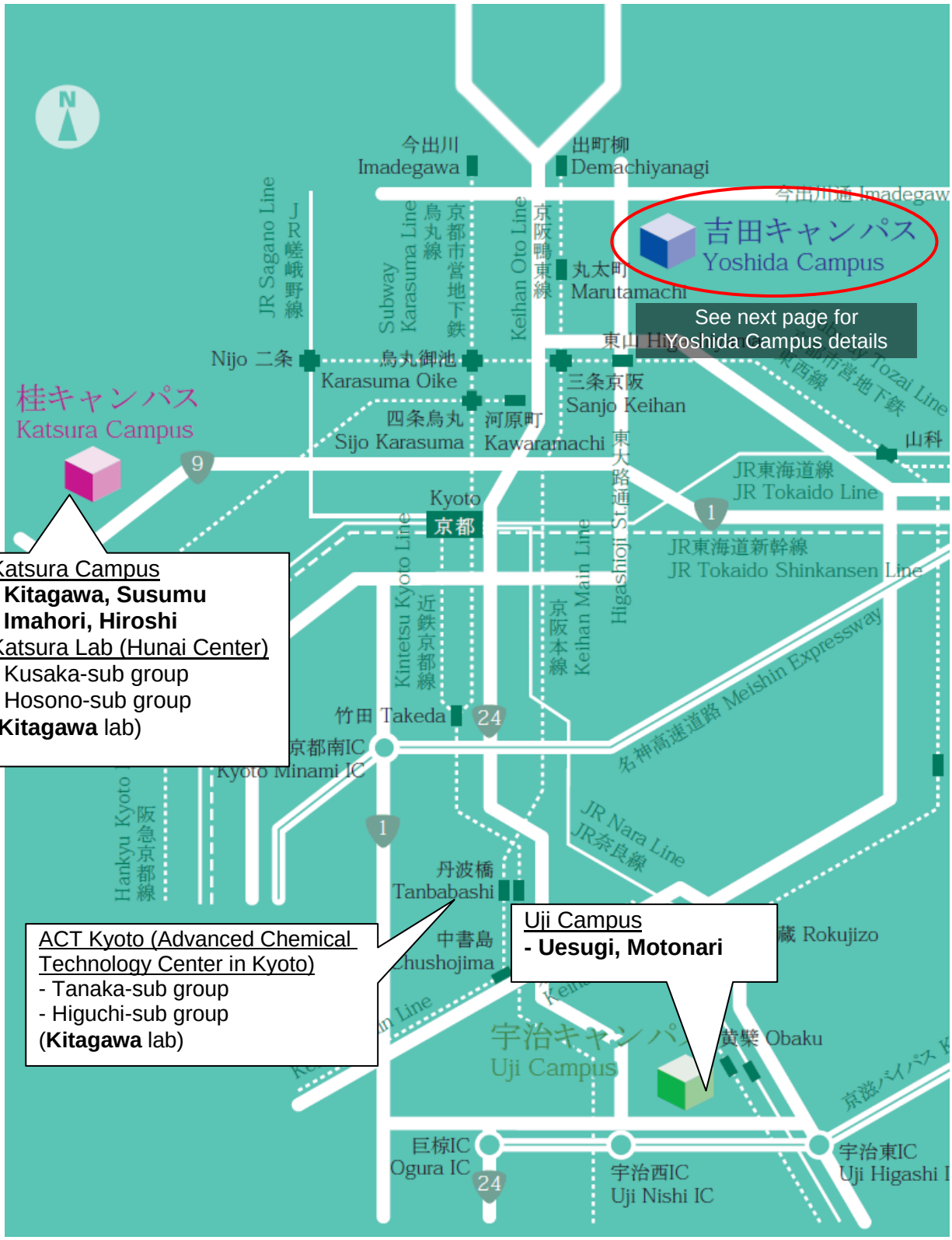
	(At beginning)	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	(Final goal)
PI：Researchers from within host institution	13	10	13	13	13	13	14	14	21	21	15
PI：Foreign researchers invited from abroad	0	2	3	4	4	4	4	3	3	3	4
PI：Researchers invited from other Japanese institutions	1	1	1	1	1	1	1	1	1	1	1
Other researchers	56	11	73	133	156	149	164	180	165	149	180
Research support staffs	45	7	43	64	70	80	86	108	124	124	100
Administrative staffs	27	18	19	28	30	31	36	34	30	27	30

World Premier International Research Center Initiative (WPI)
Appendix 1-3. Diagram of Management System

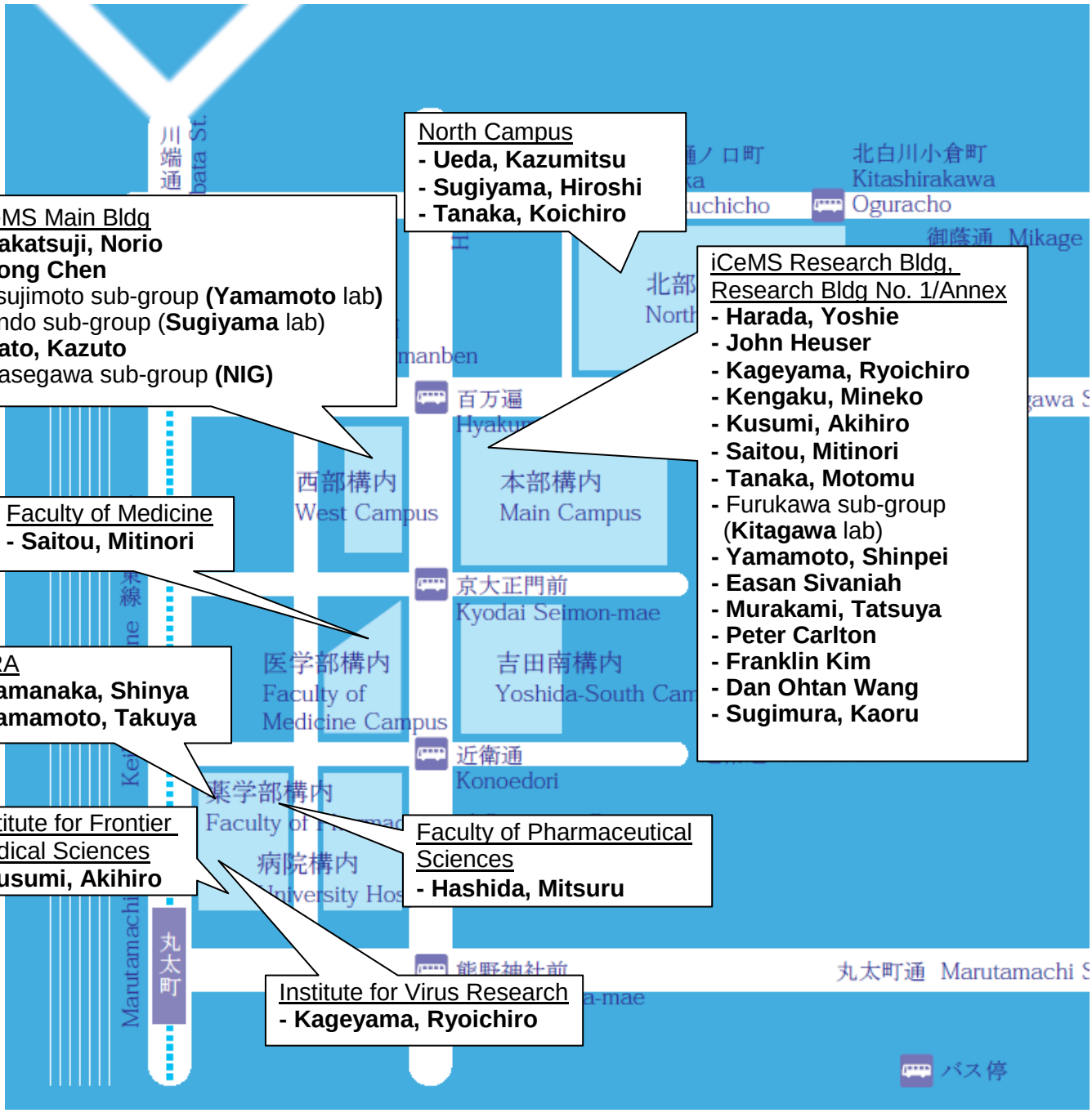


World Premier International Research Center Initiative (WPI)

Appendix 1-4. Campus map

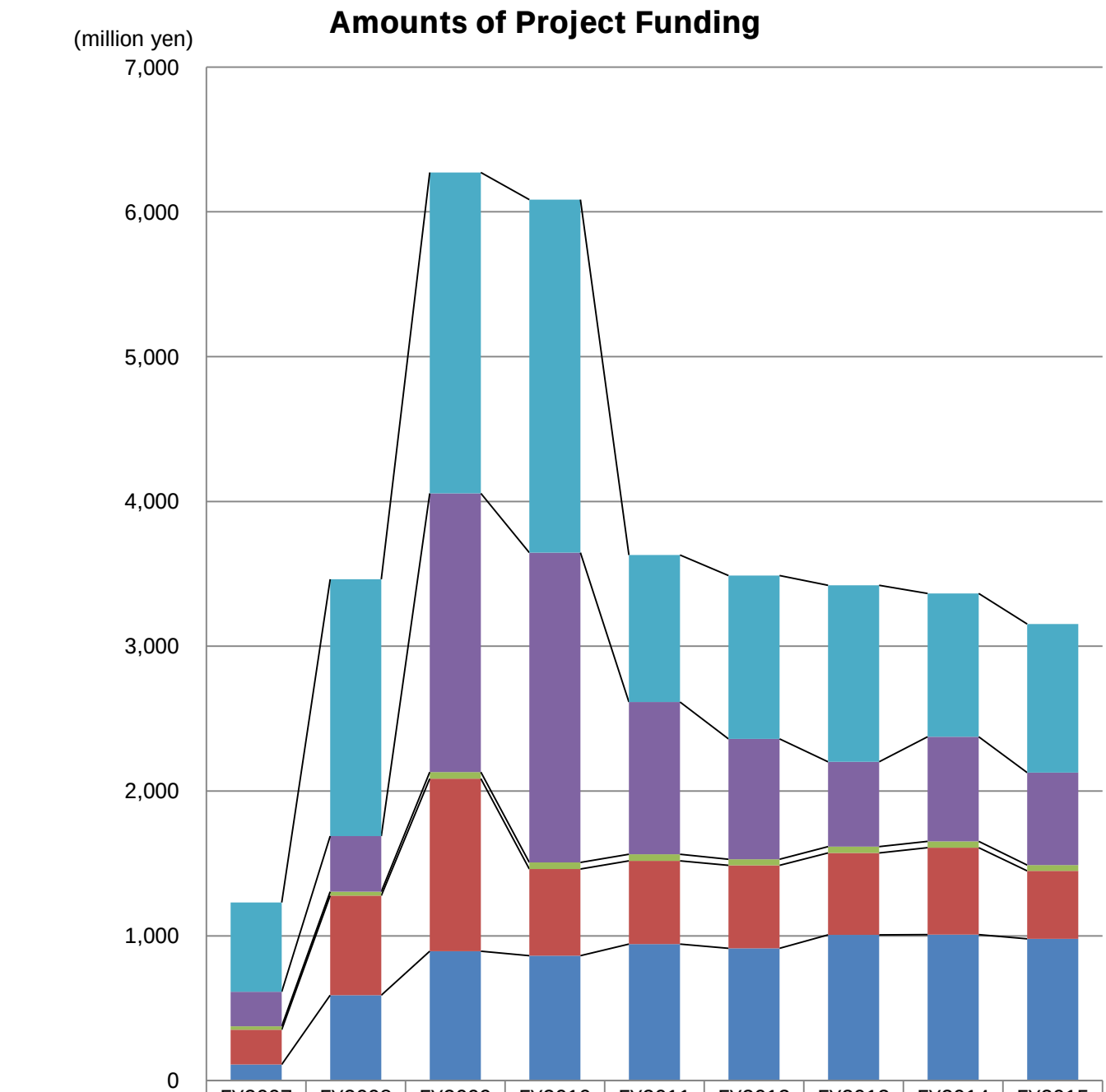


Yoshida Campus



World Premier International Research Center Initiative (WPI)
Appendix 1-5. Annual Transition in the Amounts of Project Funding

*Make a graph of the transition in the number of overall project funding.



	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	FY2015
Research projects	618	1,774	2,217	2,437	1,015	1,129	1,219	990	1026
Equipment	237	384	1,924	2,140	1,051	831	585	722	639
Travel	24	27	46	45	46	42	44	43	39
Project activities	241	687	1,191	600	575	574	565	600	469
Personnel	111	590	894	862	943	913	1,007	1009	980

Appendix 1-6. FY2015 Project Expenditures (the exchange rate used: 1USD=100JPY)

i) Overall Project Funding

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	38
	Principal investigators (no. of persons): 22	195
	Other researchers (no. of persons): 98	454
	Research support staffs (no. of persons): 93	132
	Administrative staffs (no. of persons): 42	161
	Total	980
Project activities	Gratuities and honoraria paid to invited principal investigators	0
	Cost of dispatching scientists (no. of persons): 38	76
	Research startup cost (no. of persons): 25	108
	Cost of satellite organizations (no. of satellite organizations):	50
	Cost of international symposiums (no. of symposiums): 3	4
	Rental fees for facilities	44
	Cost of consumables	26
	Cost of utilities	59
	Other costs	102
	Total	469
Travel	Domestic travel costs	8
	Overseas travel costs	19
	Travel and accommodations cost for invited scientists (no. of domestic scientists): 29 (no. of overseas scientists): 46	11
	Travel cost for scientists on secondment (no. of domestic scientists): (no. of overseas scientists): 3	1
	Total	39
Equipment	Depreciation of buildings	118
	Depreciation of equipment	521
	Total	639
Other research projects	Projects supported by other government subsidies, etc.	70
	Commissioned research projects, etc.	618
	Grants-in-Aid for Scientific Research, etc.	338
	Total	1026
Total		3153

Ten thousand dollars

WPI grant	1,286
Costs of establishing and maintaining facilities	4
Establishing new facilities (Number of facilities: 1) Costs paid:	3
Repairing facilities (Number of facilities: 1) Costs paid:	1
Others	
Cost of equipment procured	77
Name of equipment: Super-resolution confocal laser scanning microscopy) Number of units: 1 Costs paid:	58
Name of equipment: Imaging plate reader Number of units: 1 Costs	5
Others	14

ii) Costs of Satellites and Partner Institutions

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of persons): 1	
	Other researchers (no. of persons): 1	
	Research support staffs (no. of persons): 6	
	Administrative staffs (no. of persons): 0	
	Total	33
Project activities		14
Travel		2
Equipment		1
Other research projects		9
Total		59

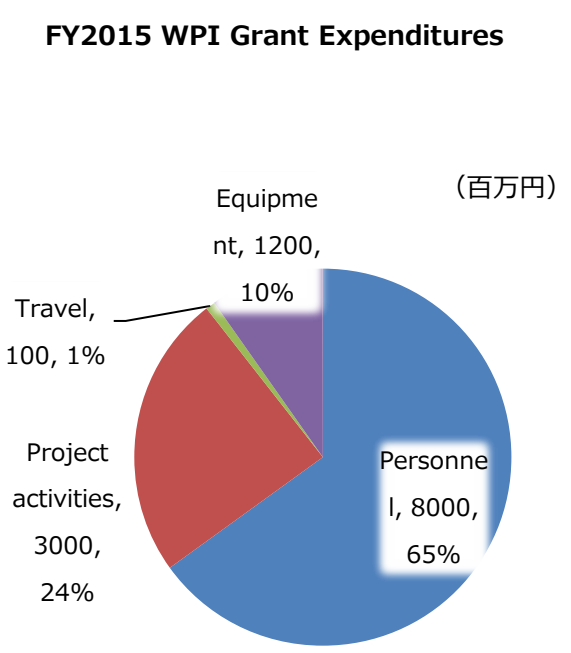
World Premier International Research Center Initiative (WPI)

Appendix 1-7. FY2015 WPI Grant Expenditures (the exchange rate used: 1USD= 100JPY)

i) Overall Expenditures

* Describe a circle graph for cost items.

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	15
	Principal investigators (no. of person) 22	90
	Other researchers (no. of person) 98	423
	Research support staffs (no. of person) 93	132
	Administrative staffs (no. of person) 42	103
	Total	763
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of person) 0	0
	Cost of dispatching scientists (no. of person) 38	76
	Research startup cost (no. of person) 25	108
	Cost of satellite organizations (no. of satellite organization) 1	50
	Cost of international symposiums (no. of symposiums) 3	4
	Rental fees for facilities	33
	Cost of consumables	16
	Cost of utilities	60
	Other costs	71
	Total	418
Travel	Domestic travel costs	4
	Overseas travel costs	14
	Travel and accommodations cost for invited scientists (no. of domestic scientists) 29 (no. of overseas scientists) 46	5
	Travel cost for scientists on secondment (no. of domestic scientists) 0 (no. of overseas scientists) 3	1
	Total	24
Equipment	Cost of equipment procured	81
	Total	81
Total		1286



ii) Costs of Satellites and Partner Institutions

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of person) 1	
	Other researchers (no. of person) 1	
	Research support staffs (no. of person) 6	
	Administrative staffs (no. of person) 0	
	Total	33
Project activities		14
Travel		2
Equipment		1
Total		50

Kyoto University

iCeMS

World Premier International Research Center Initiative (WPI)
Appendix 2-1. List of Papers Underscoring Each Research Achievement

* List papers underscoring each research achievement listed in the item 2-1 “Research results to date” (up to 40 papers) and provide a description of the significance of each (within 10 lines).
* For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is the same. If a paper has many authors, underline those affiliated with the Center.
* If a paper has many authors (say, more than 10), all of their names do not need to be listed.
* Place an asterisk (*) in front of those results that could only have been achieved by a WPI center.

*I-1. Oscillatory control of factors determining multipotency and fate in mouse neural progenitors

*1. Imayoshi, I; Isomura, A; Harima, Y; Kawaguchi, K; Kori, H; Miyachi, H; Fujiwara, T; Ishidate, F; Kageyama, R; Oscillatory Control of Factors Determining Multipotency and Fate in Mouse Neural Progenitors; *Science* 342, 1203-1208 (2013) [IF 31.0]

This project enables gene expression control by light illumination to regulate stem cell differentiation. Neural stem cells have multipotency to give rise to three different cell fates, neurons, oligodendrocytes, and astrocytes, but the precise mechanism of neural stem cell control remains to be determined. We here generated bioluminescence and fluorescence reporters to monitor the expression dynamics of each cell fate determination factor. In collaboration with CEMI microscopy specialists, we revealed that the expression of these factors oscillates in neural stem cells, whereas the expression of one of them becomes sustained during cell fate choice. By using a new optogenetic method, we successfully showed that oscillatory expression of the proneural factor Ascl1 activates neural stem cell proliferation, whereas sustained expression of Ascl1 induces neuronal differentiation.

*I-2. Successful development of artificial genetic switches using DNA-based synthetic small molecules

2. Han, L; Pandian, GN; Junetha, S; Sato, S; Anandhakumar, C; Taniguchi, J; Saha, A; Bando, T; Nagase, H; Sugiyama, H; A Synthetic Small Molecule for Targeted Transcriptional Activation of Germ Cell Genes in a Human Somatic Cell; *Angew. Chem.-Int. Edit.* 52, 13410-13413 (2013) [IF 13.7]

In this study carried out in human fibroblasts, we identified that a SAHA-PIP called K was capable of triggering unusual transcriptional activation of the typically conserved PIWI gene that regulates the meiotic process. This first ever report on a germ cell gene switch is a successful representative model that substantiates the scope of iCeMS, which aims to achieve `materials for cell control`. This paper was selected as a `Hot paper` by the editor for the importance of this work in a rapidly evolving field of high current interest.

*3. Han, L; Pandian, GN; Chandran, A; Sato, S; Taniguchi, J; Kashiwazaki, G; Sawatani, Y; Hashiya, K; Bando, T; Xy, Y; Qian, X; Sugiyama, H; A synthetic DNA-binding domain guides distinct chromatin modifying small molecules to activate an identical gene network; Angew Chem Int Ed 54, 8700-8703 (2015) [IF 11.261]

Transcriptionally permissive marks are acquired more reliably by activating the epigenetic writers like histone acetyl transferases (HATs) than by blocking the erasers like histone deacetylases (HDACs). Unlike the broad array of targeting small molecules for histone deacetylases (HDACs), few modulators are known for histone acetyltransferases (HATs), which play a central role in transcriptional control. As a novel chemical approach to induce selective HAT-regulated genes, Sugiyama lab conjugated a DNA-binding domain (DBD) “I” to N-(4-chloro-3-trifluoromethyl-phenyl)-2-ethoxy-benzamide (CTB), an artificial HAT activator. In vitro enzyme activity assays and microarray studies were used to demonstrate that distinct functional small molecules could be transformed to have identical bioactivity when conjugated with a targeting DBD. This proof-of-concept synthetic strategy successfully validates the switchable functions of

HDACs and HATs in gene regulation and provides a molecular basis for developing versatile bioactive ligands. This is an interdisciplinary research of chemistry and cell biology.

I-3. Proof of concept for epigenetics-driven cancer development through artificial manipulation of epigenetic regulation

4. Ohnishi, K; Semi, K; Yamamoto, T; Shimizu, M; Tanaka, A; Mitsunaga, K; Okita, K; Osafune, K; Arioka, Y; Maeda, T; Soejima, H; Moriwaki, H; Yamanaka, S; Woltjen, K; Yamada, Y; Premature Termination of Reprogramming In Vivo Leads to Cancer Development through Altered Epigenetic Regulation; *Cell* 156, 663-677 (2014) [IF 32.0]

It is widely accepted that cancer develops through accumulation of genetic mutations. Taking advantage of iPSC technology, this paper provided a proof of concept that cancer can arise predominantly through altered epigenetic regulations.

*I-4. Identification of transcription factors sufficient for inducing the germ cell fate in epiblast cells in mice

*5. Hayashi, K; Ohta, H; Kurimoto, K; Aramaki, S; Saitou, M; Reconstitution of the mouse germ cell specification pathway in culture by pluripotent stem cells.; *Cell* 146, 519-532 (2011) [IF 32.0]

This work demonstrates the reconstruction of the mouse germ cell specification pathway in culture using pluripotent stem cells. Embryonic stem cells (ESCs)/induced pluripotent stem cells (iPSCs) are induced into epiblast-like cells (EpiLCs) and then into primordial germ cell-like cells (PGCLCs) with capacity to contribute to spermatogenesis and healthy offspring. This work serves as a robust foundation for in vitro gametogenesis from pluripotent stem cells.

*6. Hayashi, K; Ogushi, S; Kurimoto, K; Shimamoto, S; Ohta, H; Saitou, M; Offspring from Oocytes Derived from in Vitro Primordial Germ Cell-like Cells in Mice; *Science* 338, 971-975 (2012) [IF 31.0]

This paper reports the generation of healthy offspring from oocytes derived from in vitro primordial germ cell-like cells induced from embryonic stem cells or induced pluripotent stem cells in mice. This work was selected as one of the 10 breakthrough achievements in 2012 by Science.

*7. Nakaki, F; Hayashi, K; Ohta, H; Kurimoto, K; Yabuta, Y; Saitou, M; Induction of mouse germ-cell fate by transcription factors in vitro; *Nature* 501, 222-226 (2013) [IF 38.6]

This paper reports the identification of transcription factors that are sufficient to induce, upon in vitro epiblast-like cells generated from embryonic stem cells, primoridial germ cell-like cells with capacity for spermatogenesis.

*I-5. Single molecule imaging and manipulation using meso-scale DNA origami structures

8. Wickham, SFJ; Endo, M; Katsuda, Y; Hidaka, K; Bath, J; Sugiyama, H; Turberfield, AJ; Direct observation of stepwise movement of a synthetic molecular transporter; *Nat. Nanotechnol.* 6, 166-169 (2011) [IF 34.0]

A DNA transportation system with a mobile DNA nanomachine (DNA motor) was constructed on a DNA origami surface. The track with multiple ssDNAs (stators) was introduced onto the DNA origami tile to observe the movement of a DNA motor strand. Time-dependent movement of the motor strand along the motor track was observed. Furthermore, the stepwise movement of the motor strand was directly visualized by high-speed AFM. The detailed AFM analysis revealed that the distance of the motor-strand movement

corresponded to the distance between the adjacent stators, indicating that the movement occurred stepwise on the track.

*9. Wickham, SFJ; Bath, J; Katsuda, Y; Endo, M; Hidaka, K; Sugiyama, H; Turberfield, AJ; A DNA-based molecular motor that can navigate a network of tracks; *Nat. Nanotechnol.* 7, 169-173 (2012) [IF 34.0]

To control the programmable movement of the DNA motor strand, a branched track was constructed on the DNA origami tile, and three branching points and four final destinations were created. The block strands were introduced at both sides of the branching points to control the direction of the DNA motor. When the specific block strands were removed by the corresponding release strand, the motor strand moved to reach the final destination, which was observed using AFM and the fluorescence quenching method. The DNA motor can be precisely delivered to the defined destination by following the programmed instructions.

*10. Suzuki, Y; Endo, M; Sugiyama, H; Lipid bilayer-supported two-dimensional self-assembly of DNA origami nanostructures; *Nat. Commun.* 6, 8052 (2015) [IF 11.5].

Self-assembly is a ubiquitous approach for design and fabrication of novel supermolecular architectures. We describe a strategy to assemble DNA origami nanostructures into two-dimensional lattices on the lipid bilayer. We demonstrate that the bilayer-adsorbed origami units are mobile on the surface and can self-assemble into large lattices with micrometer size in their lateral dimensions. By using high-speed AFM imaging technique, a variety of dynamic processes such as growth and reorganization of lattices were successfully visualized. The surface modifiability of the assembled lattice was also proven by in situ decoration with streptavidin molecules. Our approach provides a new strategy for preparing versatile scaffold for nanofabrication and paves the way for organizing functional nanodevices in a micrometer space.

*II-1. New single-molecule tracking methods elucidated the hierarchical meso-scale compartment architecture of the plasma membrane for signal transduction

*11. Tanaka, KAK; Suzuki, KGN; Shirai, YM; Shibutani, ST; Miyahara, MSH; Tsuboi, H; Yahara, M; Yoshimura, A; Mayor, S; Fujiwara, TK; Kusumi, A; Membrane molecules mobile even after chemical fixation; *Nat. Methods* 7, 865-866 (2010) [IF 23.6]

Chemical crosslinking has been extensively used for immobilizing membrane-associated molecules and cytoskeletal molecules in optical and electron microscopy in virtually all the biomedical fields. We critically reevaluated this method, and reported that under general crosslinking conditions, membrane molecules are hardly immobilized, and described new methods useful for many membrane proteins.

*12. Nishimura, H; Ritchie, K; Kasai, RS; Morone, N; Sugimura, H; Tanaka, K; Sase, I; Yoshimura, A; Nakano, Y; Fujiwara, TK; Kusumi, A; Biocompatible fluorescent silicon nanocrystals for single-molecule tracking and fluorescence imaging; *J. Cell Biol.* 202, 967-983 (2013) [IF 10.8]

Fluorescence microscopy is used extensively in cell biological and biomedical research, but it is plagued by three major problems with the presently available fluorescent probes: photobleaching, blinking, and large size. In this research, these problems have been basically solved by developing biocompatible, red-emitting silicon nanocrystals (SiNCs) with a 4.1-nm hydrodynamic diameter, conjugated to biomolecules precisely at a 1:1 ratio, which neither blinked nor photobleached for at least 5 h. Using the SiNCs, it became possible for the first time to observe the internalization process of receptor molecules at the single-molecule level and to reveal the micron-scale mosaicism in the plasma membrane.

*13. Kasai, RS; Suzuki, KGN; Prossnitz, ER; Koyama-Honda, I; Nakada, C; Fujiwara, TK; Kusumi, A; Full characterization of GPCR monomer-dimer dynamic equilibrium by single molecule imaging; *J. Cell Biol.* 192, 463-480 (2011) [IF 10.8]

The G-protein-coupled receptors (GPCRs) represent the largest superfamily in human genome and more than half of the drug development cost is now spent for drugs that can modulate the GPCR functions. However, the exact mechanism for its function remains unknown. We found a GPCR forms transient homodimers, with a lifetime of 90 ms, and succeeded in fully characterizing its monomer-dimer dynamic equilibrium, first time ever for any membrane molecules. This work is important in GPCR research as well as in the methodology development for determining the dynamic equilibrium in the membrane.

*14. Suzuki, KGN; Kasai, RS; Hirosawa, KM; Nemoto, YL; Ishibashi, M; Miwa, Y; Fujiwara, TK; Kusumi, A; Transient GPI-anchored protein homodimers are units for raft organization and function; *Nat. Chem. Biol.* 8, 774-783 (2012) [IF 13.0]

The sterol-dependent mesoscale domains in cellular membranes, called raft domains, have been controversial, including their very existence. In this work, advanced single-molecule tracking developed in the Kusumi and CeMI groups revealed the interactions among some of the most rudimentary units from which rafts may originate (glycosylphosphatidylinositol-anchored receptors [GAR] and cholesterol), clarifying that lipid- and protein-based interactions jointly contribute to form the transient GAR homodimer rafts in the plasma membrane. These homodimer rafts act as the basic units for generating more stable signaling rafts and their signal transduction activities. Understanding these interactions helps to develop long-evolving and still debated models of raft domains.

*II-2. Mechanism of modulating membrane lipid distribution by lipid transporter

*15. Tamai, H; Ando, H; Tanaka, HN; Hosoda-Yabe, R; Yabe, T; Ishida, H; Kiso, M; The Total Synthesis of the Neurogenic Ganglioside LLG-3 Isolated from the Starfish Linckia laevigata; *Angew. Chem.-Int. Edit.* 50, 2330-2333 (2011) [IF 13.7]

This paper describes the first total synthesis of highly neuritegenic glycolipid LLG-3 which was found in starfish and the first demonstration of neuritegeneration induced by the synthetic LLG-3. To achieve the first total synthesis, the most crucial, common issue in glycolipid syntheses, that is, the chemical conjugation of sugar chain (glycan) and lipid was mainly addressed. As a result, an expedient approach to the glycolipid framework has been successfully established, which was designated as glucosyl ceramide cassette approach, in this study. In addition, a reliable method for constructing complex sialic acid-containing glycan has been developed. By harnessing the two important synthetic methods, the target molecule has been successfully synthesized. This innovation provided the core technology of glycolipid synthesis, which allowed us to develop a wide spectrum of fluorescent ganglioside probes for single molecule imaging of lipid raft.

*16. Nagata, KO; Nakada, C; Kasai, RS; Kusumi, A; Ueda, K; ABCA1 dimer-monomer interconversion during HDL generation revealed by single-molecule imaging; *Proc. Natl. Acad. Sci. U. S. A.* 110, 5034-5039 (2013) [IF 9.7]

The generation of high-density lipoprotein (HDL), one of the most critical events for preventing atherosclerosis, is mediated by the ATP binding cassette protein A1 (ABCA1) located on the plasma membrane. Using single-molecule tracking, we found that ABCA1 forms a dimer as it accumulates cholesterol in/around the ABCA1molecule, where two molecules of apoA1 is recruited and form a pair, presumably during the process of receiving the accumulated cholesterol from ABCA1, and eventually making a nascent HDL. This was achieved by close collaboration between Ueda and Kusumi groups, which was made possible by iCeMS.

*II-3. Mechanism of multi-drug transport

*17. Kodan, A; Yamaguchi, T; Nakatsu, T; Sakiyama, K; Hipolito, CK; Fujioka, A; Hirokane, R; Ikeguchi, K; Watanabe, B; Hiratake, J; Kimura, Y; Suga, H; Ueda, K; Kato, H; Structural basis for gating mechanisms of a eukaryotic P-glycoprotein homolog; *Proc. Natl. Acad. Sci. U. S. A.* 111, 4049-4054 (2014) [IF 9.7]

MDR1 exports various hydrophobic chemicals in an ATP-dependent manner and determines their absorption and distribution in the body, and is involved in multidrug resistance (MDR) in tumors. To understand the mechanism of the multidrug transport is important for designing drugs of good bio-availability and efficient cancer chemotherapy. Ueda group, in collaboration with Kato group, determined the high-resolution crystal structures of a eukaryotic MDR1 homolog and revealed the detailed architecture. The structure revealed i) how MDR1 takes hydrophobic toxic compounds into the protein, ii) how MDR1 recognizes structurally unrelated various compounds and iii) how MDR1 exports them out of cells.

*II-4. A chemical probe that labels human pluripotent stem cells

*18. Hirata, N; Nakagawa, M; Fujibayashi, Y; Yamauchi, K; Murata, A; Minami, I; Tomioka, M; Kondo, T; Kuo T; Endo, H; Inoue, H; Sato, S; Ando, S; Kawazoe, Y; Aiba, K; Nagata, K; Kawase, E; Chang, Y; Suemori, H; Eto, K; Nakauchi, H; Yamanaka, S; Nakatsuji, N; Ueda, K; Uesugi, M; A chemical probe that labels human pluripotent stem cells; *Cell Reports* 6, 1165-1174 (2014) [IF 8.4]

Screening of fluorescent chemical libraries with human induced pluripotent stem cells (iPSCs) identified a fluorescent molecule (Kyoto probe 1 [KP-1]) that selectively labels human pluripotent stem cells. Our mechanistic analyses indicated that the selectivity results primarily from a distinct expression pattern of ABC transporters in human pluripotent stem cells and from the transporter selectivity of KP-1. KP-1 may widely be used as a tool in the field of stem cell biology.

*II-5. Utilization of photoinduced charge-separated state of donor-acceptor linked molecules for regulation of cell membrane potential and ion transport

*19. Numata, T; Murakami, T; Kawashima, F; Morone, N; Heuser, JE; Takano, Y; Ohkubo, K; Fukuzumi, S; Mori, Y; Imahori, H; Utilization of Photoinduced Charge-Separated State of Donor-Acceptor Linked Molecules for Regulation of Cell Membrane Potential and Ion Transport; *J. Am. Chem. Soc.* 134, 6092-6095 (2012) [IF 10.7]

We have successfully controlled the membrane potential and ion transport across the PC12 cell membrane by using ferrocene− porphyrin− fullerene triad molecules, cell penetrating high density lipoprotein (HDL), This is the first optogenetic method utilizing the photoinduced charge-separated state of D−A-linked molecules on the intact cell membrane.

*II-6. Thermosensitive Ion Channel Activation by Surface-Engineered Mesoscopic Nanoparticles

*20. Murakami T; Nakatsuji H; Morone N; Heuser J E; Ishidate F; Hashida M; Imahori H; Mesoscopic Metal Nanoparticles Doubly Functionalized with Natural and Engineered Lipidic Dispersants for Therapeutics; *ACS Nano.* 8, 7370-7376 (2014) [IF 12.1]

Surface engineering of mesoscopic metal nanoparticles to increase biocompatibility and cell interaction is important for improvement of their therapeutic properties. We established a strategy to stabilize mesoscopic metal nanoparticles and to enhance their cell interaction by stepwise addition of

(Z)-9-octadecenoate (oleate) and a cell-penetrating peptide-fused high-density lipoprotein (cpHDL). The cpHDL-bound gold nanorods (AuNRs) were internalized greater than 80 times more efficiently than poly(ethylene glycol)-conjugated AuNRs and were able to elicit cancer cell photoablation.

*21. Nakatsuji H; Numata T; Morone N; Kaneko S; Mori Y; Imahori H; Murakami T; Thermosensitive Ion Channel Activation in Single Neuronal Cells by Using Surface-Engineered Plasmonic Nanoparticles; *Angew. Chem. Int. Ed.* 54, 11725-11729 (2015) [IF 11.3]

Controlling cell functions using external photo-responsive nanomaterials has enormous potential for the development of cell-engineering technologies and intractable disease therapies, but the former currently requires genetic modification of the target cells. We presented a method using plasma-membrane-targeted gold nanorods (pm-AuNRs) prepared with a cationic protein/lipid complex to activate a thermosensitive cation channel, TRPV1, in intact neuronal cells. Highly localized photothermal heat generation mediated by the pm-AuNRs induced Ca^{2+} influx solely by TRPV1 activation. In contrast, the use of previously reported cationic AuNRs that are coated with a conventional synthetic polymer also led to photoinduced Ca^{2+} influx, but with serious membrane damage. Our method provides a photoactive platform without the need for prior genetic engineering of the target cells.

*II-7. Study on the generation of ultra-intense THz pulse sources and nonlinear spectroscopy

22. Hirori, H; Shinokita, K; Shirai, M; Tani, S; Kadoya, Y; Tanaka, K; Extraordinary carrier multiplication gated by a picosecond electric field pulse; *Nat. Commun.* 2, 594 (2011) [IF 10.0]

The study of carrier multiplication has become an essential part of many-body physics and materials science as this multiplication directly affects nonlinear transport phenomena, and has a key role in designing efficient solar cells and electroluminescent emitters and highly sensitive photon detectors. Here we show that a 1-MV/cm electric field of a terahertz pulse, unlike a DC bias, can generate a substantial number of electron–hole pairs, forming excitons that emit near-infrared luminescence. The bright luminescence associated with carrier multiplication suggests that carriers coherently driven by a strong electric field can efficiently gain enough kinetic energy to induce a series of impact ionizations that can increase the number of carriers by about three orders of magnitude on the picosecond time scale.

23. Kampfrath, T; Tanaka, K; Nelson, KA; Resonant and nonresonant control over matter and light by intense terahertz transients; *Nat. Photonics* 7, 680-690 (2013) [IF 27.3]

Electromagnetic radiation in the terahertz (THz) frequency range is a fascinating spectroscopic tool that provides resonant access to fundamental modes, including the motions of free electrons, the rotations of molecules, the vibrations of large molecules such as proteins and DNAs, and the relaxations of polar liquids such as water. As a result, THz waves have been extensively used to probe such responses with high sensitivity. However, owing to recent developments in high-power sources, scientists have started to abandon the role of pure observers and are now exploiting intense THz radiation to engineer transient states of matter. This Review provides an overview and illustrative examples of how the electric and magnetic fields of intense THz transients can be used to control matter and light resonantly and non-resonantly.

*II-8. Localized cell stimulation by nitric oxide using a photoactive porous coordination polymer platform

*24. Diring, S; Wang, DO; Kim, C; Kondo, M; Chen, Y; Kitagawa, S; Kamei, K; Furukawa, S; Localized cell stimulation by nitric oxide using a photoactive porous coordination polymer platform; *Nat. Commun.* 4, 2684 (2013) [IF 10.0]

Nitric oxide (NO) is one of the most investigated gasotransmitters, having important roles in numerous signaling events as well as therapeutic potentials. However, the development of releasing systems that allow spatial and temporal control over the delivery remains challenging. Collaboration among iCeMS scientists generated a new photoactive porous coordination polymer, which allows for a controlled release of nitric oxide upon light irradiation. Organizing a photoactive ligand into a three-dimensional porous structure induced a drastic increase in the photoreactivity and in the amount of released NO. The technology permitted a precisely controlled delivery of NO at the cellular level via localized near-infrared two-photon laser activation. This unique approach provides a tool for better understanding the physiological role of NO.

*II-9. Structuring of porous coordination polymers in the mesoscale towards creation of cell-inspired materials

*25. Furukawa, S; Reboul, J; Diring S; Sumida K; Kitagawa, S; Structuring of metal-organic frameworks at the mesoscopic/macroscopic scale; *Chem. Soc. Rev.* 43, 5700-5734 (2014) [IF 24.9]

Besides the structural designability of PCPs at the molecular length scale, the researchers in this field very recently made important advances in creating more complex architectures at the mesoscopic/macroscopic scale, in which PCP nanocrystals are used as building units to construct higher-order superstructures. The structuring of MOFs in such a hierarchical order certainly opens a new opportunity to improve the material performance via design of the physical form rather than altering the chemical component. This review highlights these superstructures and their applications by categorizing them into four dimensionalities, zero-dimensional (0D), one-dimensional (1D), two-dimensional (2D), and three- dimensional (3D) superstructures.

*26. Reboul, J; Furukawa, S; Horike, N; Tsotsalas, M; Hirai, K; Uehara, H; Kondo, M; Louvain, N; Sakata, O; Kitagawa, S; Mesoscopic architectures of porous coordination polymers fabricated by pseudomorphic replication; *Nat. Mater.* 11, 717-723 (2012) [IF 35.8]

This paper describes a method for the formation of mesoscopic architectures made of PCPs with designed morphology in both two and three dimensions. Inspired by geological processes, this method relies on the replacement of a sacrificial metal oxide priory shaped via a sol-gel procedure by an analogous PCP architecture. In particular, the replication of macroporous alumina aerogels resulted in a PCP architecture with hierarchical porosity in which the hydrophobic micropores of the PCP and the mesopores/macropores inherited from the parent aerogels synergistically enhanced the material's selectivity and mass transfer for water/ethanol separation.

27. Sakata, Y; Furukawa, S; Kondo, M; Hirai, K; Horike, N; Takashima, Y; Uehara, H; Louvain, N; Meilikhov, M; Tsuruoka, T; Isoda, S; Kosaka, W; Sakata, O; Kitagawa, S; Shape-Memory Nanopores Induced in Coordination Frameworks by Crystal Downsizing; *Science* 339, 193-196 (2013) [IF 31.0]

Flexible porous coordination polymers change their structure in response to molecular incorporation but recover their original configuration after the removal of guest. We demonstrated that crystal downsizing of twofold interpenetrated frameworks regulates the structural flexibility and induces a framework shape-memory effect. In addition to the two structures that contribute to the sorption process (that is, a closed phase and a guest-included open phase), we isolated an unusual, metastable open dried phase when downsizing the crystals to the mesoscale, and the closed phase was recovered by thermal treatment. The successful isolation of two interconvertible empty phases, the closed phase and the open dried phase, provided switchable sorption properties with or without gate-opening behavior.

28. Hirai. K; Furukawa. S; Kondo, M; Uehara, H; Sakata, O; Kitagawa. S; Sequential functionalization of porous coordination polymer crystals; *Angew. Chem. Int. Ed.* 50, 8057-8061 (2011) [IF 13.7]

Chemists fabricate materials by integrating two or more distinct chemical functionalities into a single platform, leading to a multifunctional property that conventional single-phase material can never achieved. We introduce the concept of compartmentalization utilized in living cells into porous coordination polymers (PCPs) and synthesized the materials that simultaneously implement two key properties of compartmentalization: selection and condensation. We developed the synthetic strategy to grow a shell PCP on the surface of a core PCP to fabricate a core-shell PCP crystal, in which the shell totally covers the core. Using the shell with narrow pores and the core with large pores, we realized an integrated property of selectivity and storage; the shell selectively extracted cetane molecules from its branched isomer (isocetane) and the core worked as a container to concentrate extracted cetane.

***II-10. Self-Accelerating Gas Trapping in a Soft Nanoporous Crystal**

*29. Sato, H; Kosaka, W; Matsuda, R; Hori, A; Hijikata, Y; Belosludov, RV; Sakaki, S; Takata, M; Kitagawa, S; Self-Accelerating CO Sorption in a Soft Nanoporous Crystal; *Science* 10, 167-170 (2014) [IF 31.0]

Carbon monoxide (CO) is a central resource for industry, and the discovery of a porous compound with high selectivity toward CO is scientifically and technologically important. The Kitagawa group developed a new soft nanoporous crystalline material that selectively adsorbs CO with adaptable pores, along with the first crystallographic evidence that CO molecules can coordinate with Cu2+ ions. The unprecedented high selectivity was achieved by the synergetic effect of the local interaction between CO and accessible metal sites and a global transformation of the framework. This transformable crystalline material enabled the separation of CO from a mixture with nitrogen, a gas that is the most competitive to CO. The dynamic and efficient molecular trapping and releasing system is reminiscent of sophisticated biological systems such as heme proteins.

30. Sato, H; Matsuda, R; Sugimoto, K; Takata, M; Kitagawa, S; Photoactivation of a nanoporous crystal for on-demand guest trapping and conversion; *Nat. Mater.* 9, 661-666 (2010) [IF 35.8]

The discovery of a new porous compound with unique properties is scientifically and technologically important. However, the functional species used in this context are limited to those that are sufficiently inert to not spoil the porous structures. In this work, the Kitagawa group showed a new strategy to achieve a crystalline porous material with the pore surface regularly decorated with highly reactive ‘bare’ nitrenes that are photonically generated from stable ‘dormant’ precursors at will. The bare triplet nitrenes were accessible to and reacted with adsorbed oxygen or carbon monoxide molecules, which showed not only activation of the pore surface, but also a high probability of chemical trapping and conversion of guest molecules by light stimulation on demand.

***III-1. Establishment of an interdisciplinary approach for understanding principles and mechanisms governing neuronal differentiation within cellular communities**

31. Yamada, M; Yoshida, Y; Mori, D; Takitoh, T; Kengaku, M; Umeshima, H; Takao, K; Miyakawa, T; Sato, M; Sorimachi, H; Wynshaw-Boris, A; Hirotsune, S; Inhibition of calpain increases LIS1 expression and partially rescues in vivo phenotypes in a mouse model of lissencephaly; *Nat. Med.* 15, 1202-U132 (2009) [IF 22.9]

LIS1 is a causal gene for a genetic brain malformation type I lissencephaly. Kengaku group and coworkers proposed a new therapeutic approach for this disease using a calpain inhibitor that inhibited LIS1 proteolysis and rescued abnormal brain formation in Lis1 heterozigous mutant mice.

32. Fujishima, K; Horie, R; Mochizuki, A; Kengaku, M; Principles of branch dynamics governing shape characteristics of cerebellar Purkinje cell dendrites; *Development* 139, 3442-3455 (2012) [IF 6.5]

Branch patterns of neuronal dendrites greatly vary depending on their function in the neural circuit. In this paper, we analyzed dynamics of dendritic arborization in developing neurons by live-imaging and quantitative morphometry. Using a combination of molecular biology and mathematical modeling, Kengaku group identified an important contribution of contact-mediated branch retraction in the formation of non-overlapping dendrites.

*III-2. Identification of a cis-acting element that localizes mRNA to synaptic compartments in neurons

*33. Meer, EJ; Wang, DO; Kim, S; Barr, I; Guo, F; Martin, KC; Identification of a cis-acting element that localizes mRNA to synapses; *Proc. Natl. Acad. Sci. U. S. A.* 109, 4639-4644 (2012) [IF 9.7]

mRNA localization and regulated translation can spatially restrict gene expression to each of the thousands of synaptic compartments formed by a single neuron. While cis-acting RNA elements have been shown to direct localization of mRNAs from the soma into neuronal processes, less is known about signals that target transcripts specifically to synapses. We have identified a 66-nucleotide element in the 5'UTR of sensorin that is necessary and sufficient for synaptic mRNA localization. Mutational and chemical probing analyses reveal a role for secondary structure in this process.

34. Sato, S; Watanabe, M; Katsuda, Y; Murata, A; Wang, DO; Uesugi, M; Live-Cell Imaging of Endogenous mRNAs with a Small Molecule; *Angew Chem Int Ed Engl.* 54, 1855-8 (2015) [IF 11.3]

Determination of subcellular localization and dynamics of mRNA is increasingly important to understanding gene expression. A new convenient and versatile method is reported that permits spatiotemporal imaging of specific non-engineered RNAs in living cells. The method uses transfection of a plasmid encoding a gene-specific RNA aptamer, combined with a cell-permeable synthetic small molecule, the fluorescence of which is restored only when the RNA aptamer hybridizes with its cognitive mRNA. The method was validated by live-cell imaging of the endogenous mRNA of β-actin. Application of the technology to mRNAs of a total of 84 human cytoskeletal genes allowed us to observe cellular dynamics of several endogenous mRNAs including arfaptin-2, cortactin, and cytoplasmic FMR1-interacting protein 2. The RNA-imaging technology and its further optimization might permit live-cell imaging of any RNA molecules.

*III-3. Chemical tools for directed differentiation of pluripotent stem cells

*35. Minami, I; Yamada, K; Otsuji, TG; Yamamoto, T; Shen, Y; Otsuka, S; Kadota, S; Morone, N; Barve, M; Asai, Y; Tenkova-Heuser, T; Heuser, JE; Uesugi, M; Aiba, K; Nakatsuji, N; A small molecule that promotes cardiac differentiation of human pluripotent stem cells under defined, cytokine- and xeno-free conditions; *Cell Reports* 2, 1448-1460 (2012) [IF 8.4]

A multidisciplinary collaboration among Nakatsuji, Uesugi, and Heuser groups discovered, through chemical library screening and organic synthesis, a small molecule that boosts cardiomyogenesis. The discovery of the molecule named KY02111 led to a novel, defined method to induce differentiation of functional ventricular and pace maker cardiomyocytes at high efficiency from human pluripotent stem cells including ES and iPS cell lines. This cytokine- and xenon-free method is currently considered as the most suited technology for production of human cardiomyocytes for clinical application.

*36. Kuo, TF; Mao, D; Hirata, N; Khambu, B; Kimura, Y; Kawase, E; Shimogawa, H; Ojika, M; Nakatsuji, N; Ueda, K; Uesugi, M; Selective Elimination of Human Pluripotent Stem Cells by a Marine Natural Product Derivative; *J Am Chem Soc.* 136, 9798-801 (2014) [IF 10.7]

One of the current obstacles to stem cell therapy is the tumorigenic potential of residual undifferentiated stem cells. The present study reports rediscovery of a synthetic derivative of okadaic acid, a marine polyether toxin, as a reagent that selectively induces the death of human pluripotent stem cells. Cell-based screening of 333 cytotoxic compounds identified methyl 27-deoxy-27-oxookadaate (molecule 1) as a substrate of two ATP-binding cassette (ABC) transporters, ABCB1 (MDR1) and ABCG2 (BCRP), whose expression is repressed in human embryonic stem cells and induced pluripotent stem cells. The results demonstrate that selective elimination of human pluripotent stem cells can be achieved by designing cytotoxic small molecules with appropriate ABC-transporter selectivity.

37. Sakano, D; Shiraki, N; Kikawa, K; Yamazoe, T; Kataoka, M; Umeda, K; Araki, K; Mao, D; Matsumoto, S; Nakagata, N; Andersson, O; Stainier, D; Endo, F; Kume, K; Uesugi, M; Kume, S; VMAT2 identified as a regulator of late-stage beta-cell differentiation; *Nat. Chem. Biol.* 10, 141-148 (2014) [IF 13.0]

Cell replacement therapy for diabetes mellitus requires cost-effective generation of high-quality, insulin-producing, pancreatic β cells from pluripotent stem cells. Screening of a chemical library identified reserpine and tetrabenazine (TBZ), both vesicular monoamine transporter 2 (VMAT2) inhibitors, as promoters of late-stage differentiation of Pdx1-positive pancreatic progenitor cells into Neurog3 (referred to henceforth as Ngn3)-positive endocrine precursors. VMAT2-controlled monoamines, such as dopamine, histamine and serotonin, negatively regulated β-cell differentiation. When ES cell-derived β cells were transplanted into AKITA diabetic mice, the cells reversed hyperglycemia. This work provides a basis for the understanding of β-cell differentiation and its application to a cost-effective production of functional β cells for cell therapy.

III-4. Novel methods for adhesion and expansion of cells

*38. Miyazaki, T; Futaki, S; Suemori, H; Taniguchi, Y; Yamada, M; Kawasaki, M; Hayashi, M; Kumagai, H; Nakatsuji, N; Sekiguchi, K; Kawase, E; Laminin E8 fragments support efficient adhesion and expansion of dissociated human pluripotent stem cells; *Nat. Commun.* 3, 1236 (2012) [IF 10.0]

Culture of human pluripotent stem cells originally required mouse feeder cells as a cell-adhesion substrate. Defined and xeno-free substrate is essential for clinical application of human pluripotent stem cells. Cell adhesion molecule laminin is one of such currently used substrate. However, it is a very large molecule that can be denatured easily, making disadvantages in quality control, production cost and handling. Nakatsuji group and others found that the laminin fragment E8 can support human ES/iPS cell culure much better than the whole laminin molecule. This technology enabled single cell passaging for more effective cell expansion. This work may contribute to various applications of human ES/iPS cells.

39. Frisco-Cabanos, HL; Watanabe, M; Okumura, N; Kusamori, K; Takemoto, N; Takaya, J; Sato, S; Yamazoe, S; Takakura, Y; Kinoshita, S; Nishikawa, M; Koizumi, N; Uesugi, M; Synthetic Molecules that Protect Cells from Anoikis and Their Use in Cell Transplantation; *Angew Chem Int Ed Engl.* 53, 11208-13 (2014) [IF 13.7]

One of the major problems encountered in cell transplantation is the low level of survival of transplanted cells due to detachment-induced apoptosis, called anoikis. The present study reports on the chemical synthesis and biological evaluation of water-soluble molecules that protect suspended cells from anoikis. The synthetic molecules bind to and induce clusters of integrins and heparan-sulfate-bound syndecans, two classes of receptors that are important for extracellular matrix-mediated cell survival. Molecular biological analysis indicates that such molecules prolong the survival of suspended NIH3T3 cells, at least in part, by

promoting clustering of syndecan-4 and integrin β1 on the cell surface, leading to the activation of small GTPase Rac-1 and Akt. In vivo experiments using animal disease models demonstrated the ability of the molecules to improve cell engraftment. The cluster-inducing molecules may provide a starting point for the design of new synthetic tools for cell-based therapy.

*40. Takemoto, N; Suehara, T; Frisco, HL; Sato, S; Sezaki, T; Kusamori, K; Kawazoe, Y; Park, SM; Yamazoe, S; Mizuhata, Y; Inoue, R; Miller, GJ; Hansen, SU; Jayson, GC; Gardiner, JM; Kanaya, T; Tokitoh, N; Ueda, K; Takakura, Y; Kioka, N; Nishikawa, M; Uesugi, M; Small-Molecule-Induced Clustering of Heparan Sulfate Promotes Cell Adhesion; *J. Am. Chem. Soc.* 135, 11032-11-39 (2013) [IF 9.7]

Adhesamine is an organic small molecule that promotes adhesion and growth of cultured human cells by binding selectively to heparan sulfate on the cell surface. Mechanistic analysis showed that multiple adhesamine molecules cooperatively bind to heparan sulfate and induce its assembly, promoting clustering of heparan sulfate-bound syndecan-4 on the cell surface. Animal studies showed that adhesamine improved the viability and attachment of transplanted cells in mice. Further studies could lead to the design of assembly-inducing molecules for use in cell biology and cell therapy.

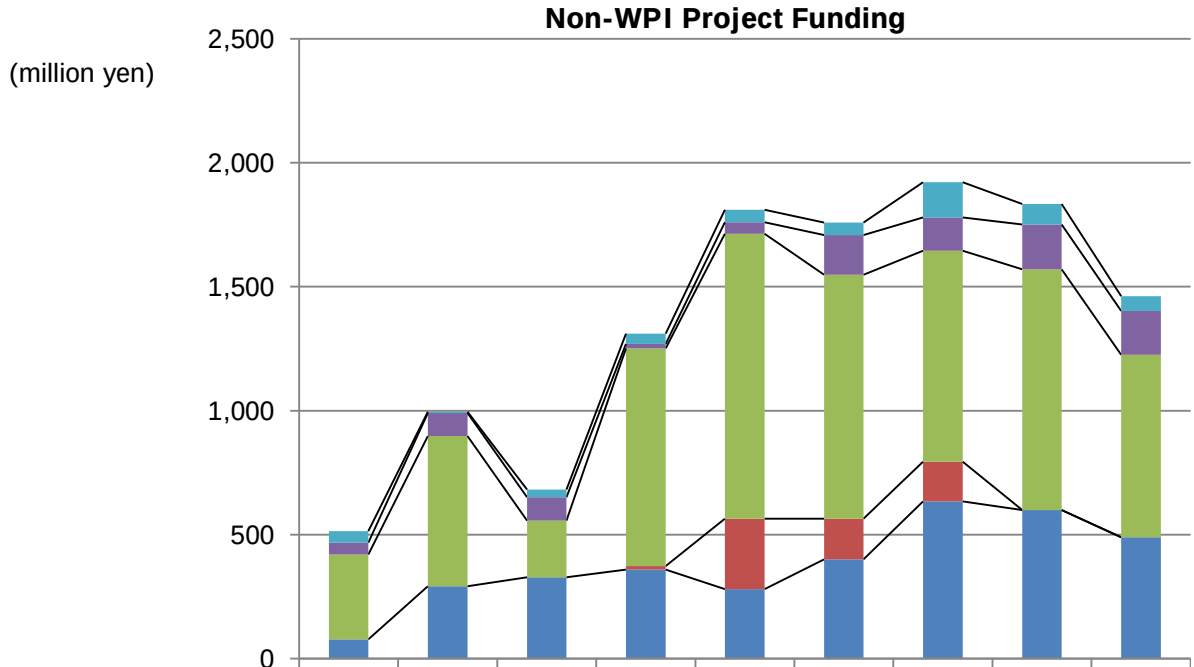
*** [III-5] Generation of offspring from oocytes derived from in vitro primordial germ cell-like cells in mice**

*6.

*7.

World Premier International Research Center Initiative (WPI)
Appendix 2-2. Annual Transition in Non-WPI Project Funding (Grants)

*Make a graph of the annual transition in non-WPI project funding (grants). Describe external funding warranting special mention.



	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	FY2015
Donations	46	6	31	41	51	50	143	83	59
Collaborative Research funding	48	92	94	19	46	161	134	181	177
Sponsored Research Funding (including NEDO)	342	606	229	877	1,149	983	851	971	736
Funding Program for Next Generation World-Leading Researchers (NEXT)				15	285	165	160	0	0
Grats-in-Aid for Scientific Research	78	292	328	359	280	400	634	599	490

[External funding warranting special mention]

1
[Prof Nakatsuji, 2007/10-2010/3]
Ministry of Economy, Trade and Industry's New Energy and Industrial Technology Development Organization (NEDO) programs for Gene Functions R&D (JPY 224 million)

2
[Prof Kitagawa, 2010/3-2013/2]
Ministry of Economy, Trade and Industry's New Energy and Industrial Technology Development Organization (NEDO) programs for Green Sustainable Chemical Process (JPY 617 million)

3
[Prof Takano, 2010/3-2011/3]
Ministry of Economy, Trade and Industry's New Energy and Industrial Technology Development Organization (NEDO) programs for Rare Metal R&D (JPY 65 million)

4
[Prof Ueda, 2010/8-2015/3]
National Agriculture and Food Research Organization (NARO), Bio-oriented Technology Research Advancement Institution's (BRAIN) funding program, Fundamental research for innovation creation (JPY 59 million, not yet fixed due to single year contract)

5
[Prof Nakatsuji, 2011/3-2014/3]
Ministry of Economy, Trade and Industry's New Energy and Industrial Technology Development Organization (NEDO) programs for Industry Application for Human Stem Cell (JPY 956 million)

6
[Prof Koichiro Tanaka, 2012/4-2015/3]
Japan Science and Technology Agency (JST) program of Strategic Basic Research Programs (CREST) (JPY 130 million)
7
[Prof Kitagawa, 2012/10-2016/3]
Japan Science and Technology Agency (JST) program for Advanced Catalytic Transformation program for Carbon utilization (ACT-C) (JPY 242 million, not yet fixed due to single year contract)

8
[Prof Kitagawa, 2013/4-2014/3]
Japan Science and Technology Agency (JST) program for Exploratory Research for Advanced Technology (ERATO) (JPY 65 million)

9
[Prof Kitagawa, 2013/12-2018/3]
Japan Science and Technology Agency (JST) ACCEL program for Molecular Control (JPY 823 million, not yet fixed due to single year contract)

10
[Prof Koji Tanaka, 2012/11-2014/3]
Minister of Economy, Trade and Industry (METI) program for Solar Hydrogen R&D (JPY 174 million)

11
[Prof Takano, 2012/10-2014/3]
Minister of Economy, Trade and Industry (METI) program for Nano-particles R&D (JPY 51 million)

12
[Prof Uesugi, 2011/2-2014/3]
Cabinet Office's Funding Program for Next Generation World-Leading Researchers (NEXT) program for Control and Analysis of Cells by Synthetic Small Molecules (JPY 163 million)

13
[Prof Ueno, 2011/2-2012/3]
Cabinet Office's Funding Program for Next Generation World-Leading Researchers (NEXT) program for Cell Function Control (JPY 82 million)

14
[Prof Kengaku, 2011/2-2014/3]
Cabinet Office's Funding Program for Next Generation World-Leading Researchers (NEXT) program for Mechanisms Underlying the Critical Period Plasticity of Dendrite Arborization and Neural Circuit Formation (JPY 120 million)

15
[Prof Harada, 2011/2-2014/3]
Cabinet Office's Funding Program for Next Generation World-Leading Researchers (NEXT) program for Development of a Novel Single-Molecule Imaging Technique using Fluorescent Diamond Nanoparticles and its Application to Biomolecule Observation (JPY 150 million)

16
[Assoc Profs Sengoku, 2011/2-2014/3]

Cabinet Office's Funding Program for Next Generation World-Leading Researchers (NEXT) program for Integrative Innovation Management Research, Human Resources Development, and Support for Commercialization in the Stem Cell Science and Technology Sphere (JPY 109 million)

17
[Prof Takano, 2008/4-2010/3]
Grants-in-Aid for Scientific Research (S) program for Search of New Material Development and the Chemical / Physical Function (JPY 28 million)

18
[Prof Ueda, 2008/4-2013/3]
Grants-in-Aid for Scientific Research (S) program for Search of Lipid Transportation (JPY 161 million)

19
[Prof Imahori, 2013/4-2018/3]
Grants-in-Aid for Scientific Research (S) program for Utilization of Photoinduced Charge-Separated (JPY 217 million)

20
[Prof Ueda, 2013/4-2018/3]
Grants-in-Aid for Scientific Research (S) program for Elucidation of the ABC Protein (JPY 207 million)

21
[Prof Kitagawa, 2013/4-2018/3]
Grant-in-Aid for Specially Promoted Research program for Chemistry of Hierarchical Coordination Space (JPY 579 million)

22
[Prof Nakatsuji, Prof Uesugi, Junior Assoc Prof Hasegawa, Assoc Prof Sengoku, 2014/4-2016/3]
Ministry of Economy, Trade and Industry's New Energy and Industrial Technology Development Organization (NEDO) programs for Systematic Development of Cell Production and Processing, and of Tissue- Engineered Medical Products for Industrial Application of Tissue Engineering (JPY 271 million)

23
[Assoc Profs Ohtan, 2014/10-2016/3]
Japan Science and Technology Agency (JST) program for Impulsing Paradigm Change through Disruptive Technologies Program (imPaCT) for Creation of Novel Value through Systematic Creation of Serendipity (JPY 50 million)

24
[Prof Uesugi, 2014/12-2016/3]
Ministry of Education, Culture, Sports, Science and Technology- Japan (2014), Japan Agency for Medical Research and Development (AMED) (2015) for Drug Discovery Targeted for Transcription (JPY 80 million)

25
[Prof Sivaniah, 2015/4-2016/3]
Japan Science and Technology Agency (JST) program for Creating Start-ups from Advanced Research and Technology (START) for Industrial Development of Novel Membrane Filter(JPY 77 million)

26
[Prof Kusumi, 2015/4-2018/3]
Japan Science and Technology Agency (JST) program of Strategic Basic Research Programs (CREST) for Dynamic Analysis of Synapse Molecular by Single Molecular Tracing Method (JPY 50 million)

27
[Prof Koji Tanaka, 2014/4-2017/3]
Collaborative research for Development of Process Technology for Chemical Products from Carbon Dioxide, Solar Hydrogen with Photo Catalyst (JPY 223 million)

28
[Assis Prof Yamamoto, 2014/4-2017/3]
Collaborative research for Magnetic Material of High Efficient Motor for Future Automobile, Technical Research and Development of Bulk Body from Ferrum Nitride (JPY 183 million)

29
[Prof Kitagawa, 2013/4-2018/3]
Grant-in-Aid for Specially Promoted Research program for Chemistry of Hierarchical Coordination Space (JPY 579 million)

World Premier International Research Center Initiative (WPI)
Appendix 2-3. Major Awards, Invited Lectures, Plenary Addresses (etc.)(within 2 pages)

1. Major Awards

*List main internationally-acclaimed awards received/unofficially announced in order from the most recent.
* For each, write the recipient's name, name of award, and year issued.
In case of multiple recipients, underline those affiliated with the center.

<PIs>

1) Yong Chen, **Nanoimprint Pioneer Award** (2015)
2) Susumu Kitagawa, **Marco Polo della Scienza Italiana** (2015)
3) Motomu Tanaka, **Philipp Franz von Siebold Award** (2014)
4) Mitinori Saitou, **Japan Academy Medal** (2014) and four others
5) Susumu Kitagawa, **RSC de Gennes Prize** (2013)
6) Norio Nakatsuji, **Fellow of Royal Society of Chemistry** (2013) and one other
7) Mitsuru Hashida, **Life-time Achievement Award (Journal of Drug Targeting)** (2012) and three others
8) Shinya Yamanaka, **Nobel Prize in Physiology or Medicine** (2012) and 39 others
9) John Heuser, **National Academy of Sciences Full Member** (2011) and two others
10) Motonari Uesugi, **German Innovation Award "Gottfried Wagener Prize 2010"** (2011)
11) Akihiro Kusumi, **Science and Technology Film & Video Festival Best Research and Development Video Award** (2011)
12) Susumu Kitagawa, **2010 Thomson Reuters Citation Laureates (2010)** and nine others
13) Kazumitsu Ueda, **Japan Bioscience, Biotechnology and Agrochemistry Society Award** (2010)
14) Hiroshi Imahori, **The 25th Osaka Science Prize (2007)** and one other

<Young scientists>

15) Hideki Hirori, **The 6th German Innovation Award "Gottfried Wagener Prize 2014"** (2014)
16) Shuhei Furukawa, **The Chemical Society of Japan Award for young Chemist** (2014)
17) Hiroshi Sato, **PCCP Prize** (2014)
18) Yasuhiro Yamada, **CiRA Award** (2014)
19) Nobuhiro Yanai, **Quadrant Award First Prize** (2013)
20) Hideki Hirori, **The 7th Young Scientist Award of the Physical Society of Japan** (2012)
21) Hiromune Ando, **Japan Society for Bioscience, Biotechnology, and Agrochemistry Award** (2012)
22) Ganesh N. Pandian, **AAAS Days of Molecular Medicine Young Investigator Award** (2011)
23) Yuta Takano, **Best Lecture Award for the Fourth Competition Kanto Division of the Chemical Society of Japan** (2011)
24) Koh Nagara, **ABC2010 Young Investigator Award** (2010)
25) Kazutoshi Takahashi, **Yukawa-Tomonaga Memorial Prize** (2009)
26) Takafumi Ueno, **Young Scientists' Prize for Science and Technology by the Japanese Minister of Education, Culture, Sports, Science and Technology** (2008)

2. Invited Lectures, Plenary Addresses (etc.) at International Conferences and International Research Meetings

* List up to 20 main presentations in order from most recent.
*For each, write the lecturer/presenter's name, presentation title, conference name and date(s)

1) Susumu Kitagawa, Dynamic Structures and Properties of Porous Coordination Polymers/Metal-Organic Frameworks, **12th International Conference on Materials Chemistry (MC12)** (July20-23, 2015)
2) Ryoichiro Kageyama, Molecular control of neural stem cells, **9th World Congress of International Brain Research Organization (IBRO)** (July 7-10, 2015)
3) Motonari Uesugi, Synthetic Molecules for Cell Biology and Cell Therapy, **The 51th International Conference on Medicinal Chemistry (RICT 2015) - "Drug Discovery and Selection - Understanding Targets and Mechanisms"** (July 1-3, 2015)
4) Mineko Kengaku, Mechanical basis of cell motility control in the developing brain, **25th 2014 International Symposium on Micro-NanoMechatronics and Human Science**, (November 9-13, 2014)
5) Kenichi Suzuki, the Very Fast Steps for Raft Formation and Function, Revealed by Single-MoleculeImaging, **Gordon Research Conference** (January 12, 2014)
6) Norio Nakatsuji, Stem Cell Open Innovation in Japan: Industry-Academia Collaboration on Stem CellLarge-Scale Production and Quality Control, **World Stem Cell Summit 2013** (December 4-6, 2013)
7) Easan Sivaniah, Advanced Polymer Membranes for Gas and Liquid Separations, **Swiss-KyotoSymposium** (November 21-22, 2013)
8) Yoshie Harada, Development of a New Single-Molecule Imaging Technique Using Fluorescent DiamondNanoparticles, **New Advances in Optical Imaging of Live Cells and Organisms** (August 20-23, 2013)
9) Mitinori Saitou, Mechanism and Reconstitution in Vitro of Germ Cell Specification in Mice, **ISSCR 11thAnnual Meeting** (June 12-15, 2013)
10) Motomu Tanaka, Spatio-Temporal Evolution in Diseases and Development, **Self-Organization andEmergent Dynamics in Active Soft Matter** (February 18-20, 2013)
11) Shinya Yamanaka, Induction of Pluripotency by Defined Factors, **Novel Lecture in Physiology orMedicine** (December 7, 2012)
12) Koichiro Tanaka, Nonlinear Carrier Dynamics Induced by Intense Terahertz Wave, **37th InternationalConference on Infrared, Millimeter and Terahertz Waves (IRMMW-THz2012)** (September 23-28, 2012)
13) Kazumitsu Ueda, Mechanism of Cholesterol Efflux by ABCA1, **FASEB Meeting: New Frontiers inTransport ATPases** (June 3-8, 2012)
14) John Heuser, the Central Role of Electron Microscopy in the Birth of Modern Cell Biology, **HewsonSwift Memorial Lecture for the Department of Molecular Genetics and Cell Biology** (May 7, 2012)
15) Kazuto Kato, Conceptual and Practical Considerations for Material and Data Sharing in Stem CellResearch - Lessons from Human Genome Research, **Qatar International Conference on Stem Cell Science and Policy** (February 27-March 1, 2012)
16) Yong Chen, Biomimetic Engineering of in Vitro Cellular Microenvironments, **10th InternationalConference on Nanoimprint and Nanoprint Technology** (October 19-21, 2011)
17) Hiroshi Sugiyama, Chemical Biology that Controls DNA Structure and Function, **CIPSM Fest ofBiological Chemistry** (September 15-16, 2011)
18) Mitsuru Hashida, New Technologies Impacting Drug Discovery, **World Congress of Pharmacy andPharmaceutical Sciences 2011** (September 3-8, 2011)
19) Akihiro Kusumi, Organizing Principle of the Plasma Membrane: Three-Tiered Meso-Scale DomainArchitecture Revealed by Single-Molecule Tracking, **The 8th European Biophysics Congress** (August 23-27, 2011)
20) Hiroshi Imahori, Photoinduced Energy Transfer and Charge Separation in Donor-Acceptor LinkedSystems, **8th International Conference on Excitonic Processes in Condensed Matter** (EXCON'08) (June 22-27, 2008)

World Premier International Research Center Initiative (WPI)

Appendix 2-4. List of Achievements of Center's Outreach Activities

* Using the table below, show the achievements of the Center's outreach activities from FY2007 through FY2015 (number of activities, times held).

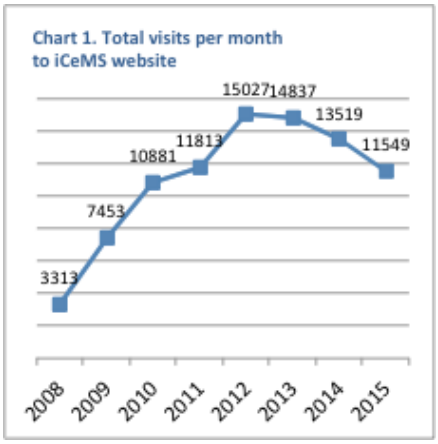
Activities	FY2007 (number of activities, times held)	FY2008 (number of activities, times held)	FY2009 (number of activities, times held)
PR brochure, pamphlet	0	1	1
Lectures, seminars for general public	7	35	30
Teaching, experiments, training for elementary and secondary school students	0	4	12
Science cafe	0	5	2
Open houses	0	0	1
Participating, exhibiting in events	0	1	4
Press releases	0	17	15

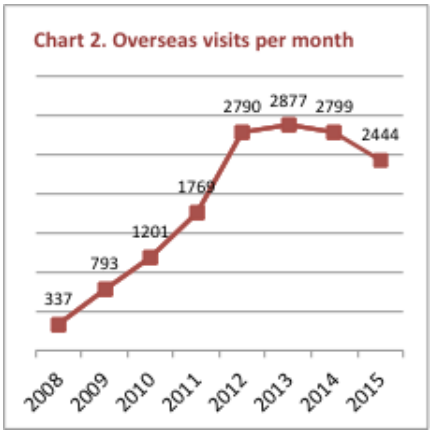
Activities	FY2010 (number of activities, times held)	FY2011 (number of activities, times held)	FY2012 (number of activities, times held)
PR brochure, pamphlet	2	5	3
Lectures, seminars for general public	57	30	27
Teaching, experiments, training for elementary and secondary school students	30	22	26
Science cafe	4	6	8
Open houses	4	0	0
Participating, exhibiting in events	12	3	5
Press releases	23	14	13

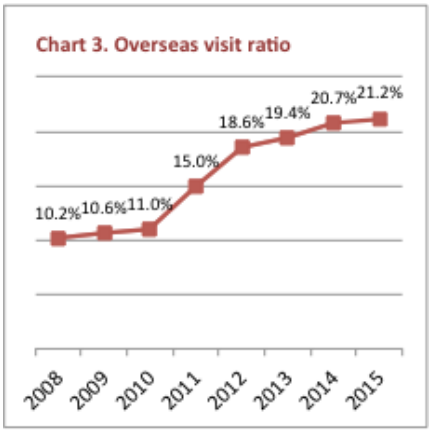
Activities	FY2013 (number of activities, times held)	FY2014 (number of activities, times held)	FY2015 (number of activities, times held)
PR brochure, pamphlet	4	4	5
Lectures, seminars for general public	16	34	37
Teaching, experiments, training for elementary and secondary school students	20	25	19
Science cafe	6	1	9
Open houses	0	1	2
Participating, exhibiting in events	11	26	13
Press releases	12	20	18

Special Achievements: International visibility

a) Web traffic analysis
Number of visitors to the iCeMS website dramatically increased immediately after Professor Shinya Yamanaka's receipt of the Nobel Prize in 2012. Although the total access rate has slowly declined since the spike(Chart 1), the number of access remains higher than before 2012 (Chart 2). The proportion of access from overseas is on a continued rise, indicating iCeMS is keeping a constant rate of interest in the international community(Chart 3).







b) Social media utilization
iCeMS is also committed to utilizing social media, such as Twitter, YouTube, and Facebook. In particular Facebook has aided in raising iCeMS' visibility: the iCeMS Facebook page drove 2,023 visits to the iCeMS website in 2014. The page also garnered 7,396 views (the number of times iCeMS updates are seen by Facebook users) per month in 2015, showing its increasing number compared to 2014 (6,979 views).

c) World Stem Cell Summit
For the forth consecutive year, iCeMS co-organized and participated in the 2015 World Stem Cell Summit, an event held in Atlanta, USA, that attracted 1,000 visitors from industry, academia, and government of 40 countries. Prof. Nakatsuji gave a welcome speech at the opening ceremony, well as a lecture at the Japan

Symposium to an international audience. An iCeMS booth also attracted industry leaders interested in forging potential partnerships. Other iCeMS' members gave poster presentations and were part of the awards evaluation committee.

List of Media Coverage of Projects carried out between FY 2007 – 2015

(within 2 pages)

* Select main items of press releases, media coverage, and reports for FY 2007-2015 (especially by overseas media)

1) Japan

No.	Date	Type media (e.g., newspaper, magazine, television)	Description
1	Mar 14, 2008	[newspaper] The Nikkei	(Nakatsuji) Nine-tenths of Japanese conformant with fifty people's worth of cells
2	May 2, 2008	[newspaper] Yomiuri Shimbun	(Yamanaka) Time Magazine selects Prof. Yamanaka as one of the world's 100 most influential people
3	Jun 26, 2009	[newspaper] Nikkan Kogyo Shimbun	(Tanaka) Kyoto Univ and Aisin Seiki Co., Ltd. develop high efficiency terahertz pulses using a commercial sub-picosecond fiber laser.
4	Apr 18, 2011	[TV] TV Tokyo: World Business Satellite	(Nakatsuji, Yamanaka, iCeMS) The business of iPS cells: Changing the path to new drug development
5	Aug 30, 2011	[TV] NHK	(Kitagawa) Prof Kitagawa of Kyoto U and his research into capturing gasses
6	Oct 9, 2012	[newspaper] Mainichi Shimbun	(Yamanaka, iCeMS) Nobel prize in physiology or medicine goes to Shinya Yamanaka and British scientist
7	Mar 21, 2013	[TV] NHK World	(Nakatsuji) Generating iPS business
8	Oct 28, 2013	[newspaper] The Nikkei Sangyo Shimbun	(Kitagawa) Nitric oxide release triggered by UV rays: Kyoto U invents medical tool that may enable effective production of iPS cells
9	Nov 1, 2013	[newspaper] The Nikkan Kogyo Shimbun	(Kageyama) Kyoto U discovers gene rhythm determines brain cell fate
10	July 1, 2014	[newspaper] The Nikkei	(Kitagawa) Kyoto University develops novel material to purify gas and collect CO2

11	Sep 11, 2014	[newspaper] The Nikkan Kogyo Shimbun	(Sivaniah) Kyoto U creates cross-link structure for gas separation membranes, gas permeability increased 100 times fold, selectivity doubled
12	July 17, 2015	[TV] NHK	(Saitou) Kyoto U develops method to create cells for reproduction from iPS cells efficiently

2) Overseas

No.	Date	Type media (e.g., newspaper, magazine, television)	Description
1	Nov 21, 2007	[newspaper] The Times	(Yamanaka) Breakthrough as iPS cells are produced from skin, not embryos
2	Nov 24, 2007	[newspaper] The Washington Post	(Yamanaka) Stem cell breakthrough
3	Dec 11, 2007	[newspaper] The New York Times	(Yamanaka) Risk taking is in his genes
4	May 12, 2008	[magazine] TIME	(Yamanaka) Yamanaka & Thomson putting an end to the ES cell debate
5	Aug 28, 2008	[magazine] Medical Tribune	(Nakatsuji) Accurate and simple screening of drug-induced QT prolongation using myocardial cell derived from ES cell
6	Jun 1, 2009	[web] Thomson Reuters Science Watch	(Yamanaka, iCeMS) Interview to Prof. Shinya Yamanaka, director of the CiRA at the iCeMS.
7	Oct 21, 2009	[web] Reuters	(Yamanaka) iPierian to collaborate with Johns Hopkins University on 3.7 million dollars NIH grand opportunities grant
8	May 5, 2010	[TV] CNN	(Yamanaka) Scientists use pig embryos to create stem cells
9	Jan 23, 2012	[web]Discovery News	(Sugiyama, iCeMS) Motor Made of DNA Runs on Tracks
10	Sep 04, 2014	[web] Engineering (Canada)	(Sivaniah) To clean air and beyond: Catching greenhouse gases with advanced membranes
11	Oct 16, 2014	[web] World Industrial Reporter (USA)	(Kim) Kyoto Devises Versatile Way to Build 3D Materials of the Future
12	Oct 23,	[web] Big News	(Carlton) Single protein behind successful

	2014	Network (USA)	fertilisation
13	July 15, 2015	[web] Medical News Today	(Wang) Visualizing RNA activity within brain tissues for efficient discovery of drugs

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Appendix 3. List of Papers of Representative of Interdisciplinary Research Activities

* List **up to 20 papers** that underscoring each interdisciplinary research activity and give brief accounts (within 10 lines).
* For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is the same. If a paper has many authors, underline those affiliated with the Center.
* If a paper has many authors (say, more than 10), all of their names do not need to be listed.

I. Manipulation of Nucleus Information

1. Han, L; Pandian, GN; Junetha, S; Sato, S; AnandhaKumar, C; Han, L; Saha, A; Nagase, H; Sugiyama, H;; A synthetic small molecule for targeted transcriptional activation of germ cell genes in a human somatic cell; *Angew Chem Int Ed* 52, 13410-13413 (2013)

   Meiosis is a highly specialized cell-division process in multicellular eukaryotes that is specific to germ cells and do not occur in somatic cells like skin cells. Here, we identified that a SAHA-PIP called K capable of triggering unusual transcriptional activation of the PIWI gene that regulates the meiotic process. This first ever report on a germ cell gene switch is a successful representative model that substantiates the scope of iCeMS, which aims to achieve `materials for cell control`. This paper was selected as a `Hot paper` by the editor for the importance of this work in a rapidly evolving field of high current interest. This is an interdisciplinary research of chemistry and cell biology.

2. Pandian, GN.; Taniguchi, J; Junetha, S; Sato, S; Han, L; Saha, A; AnandhaKumar, C; Bando, T; Nagase, H; Vaijayanthi, T; Taylor, R; Sugiyama, H; Distinct DNA-based epigenetic switches trigger transcriptional activation of silent genes in human dermal fibroblasts; *Sci Rep* 4, 3843 (2014)

   Artificial transcriptional activators must encompass both DNA recognition and functional modules to rewire misregulated transcriptional networks. The sugiyama lab has been developing such dual-functional small molecules called SAHA-PIPs as DNA-based epigenetic switches. In this study, we demonstrate through microarray studies and functional analysis about the remarkable ability of thirty-two distinct SAHA-PIPs to trigger the transcriptional activation of exclusive clusters of genes including KSR2, the obesity gene and SEMA6A, the retinal 'ON' circuit factor. Our proof-of-concept study demonstrates the possibility to develop these kind of DNA-based epigenetic switches as `iCeMS developed materials` for controlling the transcription of silent genes associated with cell fate and/or the genes of therapeutic importance. This paper was highlighted in various portals including one in GEN EN News. This is an interdisciplinary research of chemistry and cell biology.

3. Pandian, GN.; Sato, S; Chandran, A; Taniguchi, J; Takashima, K; Syed, J; Han, L; Saha, A; Bando, T; Nagase, H; Sugiyama, H; Identification of a Small Molecule that Turns `ON` the Pluripotency Gene Circuitry in Human Fibroblasts; *ACS Chem Biol* 9, 2729-2736 (2014)

   Noncoding RNAs like microRNAs (miRNAs) are attractive therapeutic targets as they demonstrate tissue-specific expression and sequence conservation across species, however, they are often considered 'undruggable'. In this study, through the independent line of evidences from genome and epigenome analysis, Sugiyama lab identified a SAHA-PIP termed `I` as the first-ever small molecule capable of inducing the OCT-3/4 regulated pluripotency gene circuitry and miR-302 family. Long-term incubation studies generated alkaline phosphatase positive cells with an induction efficiency of 0.06%±0.03% in 21 days to suggest partial reprogramming. This study suggests the possibility of developing SAHA-PIPs as tools to distinctively activate cell fate regulating microRNAs and regulate cell fate. This is an interdisciplinary research of chemistry and cell biology.

4. Han, L; Pandian, GN; Chandran, A; Sato, S; Taniguchi, J; Kashiwazaki, G; Sawatani, Y; Hashiya, K; Bando, T; Qian, X; Sugiyama, H; A synthetic DNA-binding domain guides distinct chromatin modifying small molecules to activate an identical gene network; *Angew Chem Int Ed* 54, 8700-8703 (2015)

Unlike the broad array of targeting small molecules for histone deacetylases (HDACs), few modulators are known for histone acetyltransferases (HATs), which play a central role in transcriptional control. As a novel chemical approach to induce selective HAT-regulated genes, Sugiyama lab conjugated a DNA-binding domain (DBD) "I" to *N*-(4-*c*hloro-3-trifluoromethyl-phenyl)-2-ethoxy-benzamide (CTB), an artificial HAT activator. In vitro enzyme activity assays and microarray studies were used to demonstrate that distinct functional small molecules could be transformed to have identical bioactivity when conjugated with a targeting DBD. This proof-of-concept synthetic strategy successfully validates the switchable functions of HDACs and HATs in gene regulation and provides a molecular basis for developing versatile bioactive ligands. This is an interdisciplinary research of chemistry and cell biology.

3. Nakaki, F; Hayashi, K; Ohta, H; Kurimoto, K; Yabuta, Y; Saitou, M; Induction of mouse germ-cell fate by transcription factors in vitro; *Nature* 501, 222-226 (2013)

This paper reports the identification of transcription factors that are sufficient to induce, upon *in vitro* epiblast-like cells generated from embryonic stem cells, primoridial germ cell-like cells with capacity for spermatogenesis. This is an interdisciplinary research of molecular biology, informatics (biophysics), and reproductive technology.

4. Imayoshi, I; Isomura, A; Harima, Y; Kawaguchi, K; Kori, H; Miyachi, H; Fujiwara, T; Ishidate, F; Kageyama, R; Oscillatory Control of Factors Determining Multipotency and Fate in Mouse Neural Progenitors; *Science* 342, 1203-1208 (2013)

In this study, time-lapse imaging analysis showed that the expression of multiple fate determination factors oscillates in multipotent neural stem cells, whereas one of them becomes dominant and sustained during cell fate choice. By using an interdisciplinary approach, which can control gene expression with blue light illumination, we successfully showed that oscillatory expression of the proneural factor Ascl1 activates neural stem cell proliferation, whereas sustained expression of Ascl1 induces neuronal fate choice. Thus, a single factor exhibits contradictory functions, promoting stem cell proliferation vs. neuronal differentiation, by changing the oscillatory vs. sustained gene expression. This light technology offers a new way to control cell proliferation and differentiation by changing blue light illumination patterns, showing its applicability to regenerative medicine. This is an interdisciplinary research of Cell Biology and Physics in iCeMS.

II. Manipulation of Membrane Compartments

5. Nagata, KO; Nakada, C; Kasai, RS; Kusumi, A; Ueda, K; ABCA1 dimer-monomer interconversion during HDL generation revealed by single-molecule imaging; *Proc. Natl. Acad. Sci. U. S. A.* 110, 5034-5039 (2013)

Single molecule analysis using TIRF microscopy in collaboration with the Kusumi group revealed that monomer-dimer interconversion of the ATP binding cassette protein A1 (ABCA1) occurs on the plasma membrane during the generation of high-density lipoprotein (HDL), one of the most critical events for preventing atherosclerosis. ABCA1 temporarily forms a dimer as it accumulates cholesterol in/around the ABCA1 molecule, where two molecules of apoA-I, a lipid acceptor in blood, is recruited and form a pair, presumably during the process of receiving the accumulated cholesterol from ABCA1, and eventually making a nascent HDL. This study will facilitate our understanding of the detailed mechanism of HDL generation and developing a way of preventing atherosclerosis. This is the achievement of the integration of cell biology and physics in iCeMS.

6. Nishimura, H; Ritchie, K; Kasai, RS; Morone, N; Sugimura, H; Tanaka, K; Sase, I; Yoshimura, A; Nakano, Y; Fujiwara, TK; Kusumi, A; Biocompatible fluorescent silicon nanocrystals for single-molecule tracking and fluorescence imaging; *J. Cell Biol.* 202, 967-983 (2013)

   Fluorescence microscopy is used extensively in cell biological and biomedical research, but it is plagued by three major problems with the presently available fluorescent probes: photobleaching, blinking, and large size. In this research, these problems have been essentially resolved by developing biocompatible, red-emitting silicon nanocrystals (SiNCs) with a 4.1-nm hydrodynamic diameter, conjugated to biomolecules precisely at a 1:1 ratio, which neither blinked nor photobleached for at least 5 h. Using the SiNCs, it became possible for the first time to observe the internalization process of receptor molecules at the single-molecule level and to reveal the micron-scale mosaicism in the plasma membrane. This is the achievement of the integration of cell biology and physics in iCeMS.

7. Kasai, RS; Suzuki, KGN; Prossnitz, ER; Koyama-Honda, I; Nakada, C; Fujiwara, TK; Kusumi, A; Full characterization of GPCR monomer-dimer dynamic equilibrium by single molecule imaging; *J. Cell Biol.* 192, 463-480 (2011)

   The G-protein-coupled receptors (GPCRs) represent the largest superfamily in the human genome and more than half of the drug development investments are now spent for drugs that can modulate the GPCR functions. However, the exact mechanism for its function remains unknown. We found that a GPCR forms transient homodimers, with a lifetime of 90 ms, and succeeded in fully characterizing its monomer-dimer dynamic equilibrium, which is the first time for any membrane molecule. This work is important in GPCR research as well as in the methodology development for determining the dynamic equilibrium in the membrane. This is the achievement of the integration of cell biology and physics in iCeMS.

8. Tanaka, KAK; Suzuki, KGN; Shirai, YM; Shibutani, ST; Miyahara, MSH; Tsuboi, H; Yahara, M; Yoshimura, A; Mayor, S; Fujiwara, TK; Kusumi, A; Membrane molecules mobile even after chemical fixation; *Nat. Methods* 7, 865-866 (2010)

   Chemical crosslinking has been extensively used for immobilizing membrane-associated molecules and cytoskeletal molecules in optical and electron microscopy in virtually all the biomedical fields. We critically reevaluated this method, and reported that under general crosslinking conditions, membrane molecules are hardly immobilized, and described new methods useful for many membrane proteins. This is the achievement of the integration of cell biology and physics in iCeMS.

9. Suzuki, KGN; Kasai, RS; Hirosawa, KM; Nemoto, YL; Ishibashi, M; Miwa, Y; Fujiwara, TK; Kusumi, A; Transient GPI-anchored protein homodimers are units for raft organization and function; *Nat. Chem. Biol.* 8, 774-783 (2012)

   Advanced single-molecule tracking developed in our laboratory revealed that lipid- and protein-based interactions jointly contribute to form the transient homodimer rafts of the glycosylphosphatidylinositol-anchored receptors in the plasma membrane. These homodimer rafts act as the basic units for generating more stable signaling rafts and their functions. Understanding these interactions helps to develop long-evolving and still debated models of raft domains. This is an achievement made possible by the integration of cell biology and physics in iCeMS. This is the achievement of the integration of cell biology and physics in iCeMS.

10. Diring, S; Wang, DO; Kim, C; Kondo, M; Chen, Y; Kitagawa, S; Kamei, K; Furukawa, S; Localized cell stimulation by nitric oxide using a photoactive porous coordination polymer platform; *Nat. Commun.* 4, 2684 (2013)

Nitric oxide (NO) is, a crucial signaling molecule with highly site-specific and concentration-dependent activities. The Kitagawa group synthesized spatiotemporally controllable NO releasing platforms based on photoactive porous coordination polymers (PCPs) and demonstrated that the organization of poorly reactive motives into PCP structures affords increased photoreactivity. In collaboration with the Chen and Wang groups, we embedded photoactive PCP crystals in a biocompatible polymer matrix and achieved precise control of NO delivery at a cellular level by two-photon laser activation. The biological relevance of the exogenous NO produced by the PCPs is demonstrated by an intracellular calcium change, mediated by a NO-responsive plasma membrane channel protein. This is truly an interdisciplinary study of state-of-the-art materials chemistry with bioengineering and cell biology.

11. Reboul, J; Furukawa, S; Horike, N; Tsotsalas, M; Hirai, K; Uehara, H; Kondo, M; Louvain, N; Sakata, O; Kitagawa, S; Mesoscopic architectures of porous coordination polymers fabricated by pseudomorphic replication; *Nat. Mater.* 11, 717-723 (2012)

Size and shape control of crystalline PCP is necessary for the application to Cells. This paper describes a method for the formation of mesoscopic architectures made of PCPs with designed morphology in both two and three dimensions. Inspired by pseudomorphic mineral replacement events, this method relies on the replacement of a sacrificial metal oxide priory shaped via a sol-gel procedure by an analogous PCP architecture. In particular, the replication of macroporous alumina aerogels resulted in a PCP architecture with hierarchical porosity that enhanced the material's selectivity and mass transfer for water/ethanol separation. This new synthetic method will allow for the fabrication of hollow structures, which compartmentalize the space similarly to cells and implement the sequential selection-condensation protocols, thus the creation of cell-inspired materials. This resulted from intensive discussions between chemists and cell biologists.

12. Nakatsuji H; Numata T; Morone N; Kaneko S; Mori Y; Imahori H; Murakami T; Thermosensitive Ion Channel Activation in Single Neuronal Cells by Using Surface-Engineered Plasmonic Nanoparticles; *Angew. Chem. Int. Ed.* 54, 11725-11729 (2015) [IF 11.3]

The Murakami, Imahori and Mori groups presented a method using plasma-membrane-targeted gold nanorods (pm-AuNRs) prepared with a cationic protein/lipid complex to activate a thermosensitive cation channel, TRPV1, in intact neuronal cells. Highly localized photothermal heat generation mediated by the pm-AuNRs induced Ca^{2+} influx solely by TRPV1 activation. In contrast, the use of previously reported cationic AuNRs that are coated with a conventional synthetic polymer also led to photoinduced Ca^{2+} influx, but with serious membrane damage. The interdisciplinary approache provides a photoactive platform without the need for prior genetic engineering of the target cells. This is truly an interdisciplinary collaboration between materials science and cell biology.

13. Koshiyama, T; Shirai, M; Hikage, T; Tabe, H; Tanaka, K; Kitagawa, S; Ueno, T; Post-Crystal Engineering of Zinc-Substituted Myoglobin to Construct a Long-Lived Photoinduced Charge-Separation System; *Angew. Chem.-Int. Edit.* 50, 4849-4852 (2011)

An artificial photoinduced electron-transfer system has been constructed by accumulating redox cofactors in a protein crystal. Inspired by natural photosynthesis, the Kitagawa and Ueno groups utilized as host matrices myoglobin crystals with inner voids, into which two distinct ruthenium redox complexes, each for oxidation or reduction process, can be incorporated in an organized fashion. With the K. Tanaka group, the interdisciplinary research team identified that both redox cofactors have low reorganization energies, as observed similarly to native photosynthesis, which leads to the drastic

increase of a half-life time of a charge-separated state with a half-life 2800 times longer than that in organic solution. The interdisciplinary research between protein chemistry and photophysics generates a new design concept of an artificial photosynthetic system based on cell-inspired materials. This is the achievement of the integration of chemistry and cell biology.

14. Igarashi, R; Yoshinari, Y; Yokota, H; Sugi, T; Sugihara, F; Ikeda, K; Sumiya, H; Tsuji, S; Mori, I; Tochio, H; Harada, Y; Shirakawa, M; Real-Time Background-Free Selective Imaging of Fluorescent Nanodiamonds in Vivo; *Nano Lett.* 12, 5726-5732 (2012)

By combining single molecule fluorescence measurement and optically detected magnetic resonance, the iCeMS interdisciplinary research team has successfully established a powerful method not only for eliminating extrinsic signals completely in fluorescence measurement for higher organisms, but also for realizing real-time observation of fluorescent nanodiamonds. This is the fruitful result of excellent cooperation between physicists skilled at operating instrumentation and biologists paying close attention to sample preparations.

15. Sakata, Y; Furukawa, S; Kondo, M; Hirai, K; Horike, N; Takashima, Y; Uehara, H; Louvain, N; Meilikhov, M; Tsuruoka, T; Isoda, S; Kosaka, W; Sakata, O; Kitagawa, S; Shape-Memory Nanopores Induced in Coordination Frameworks by Crystal Downsizing; *Science* 339, 193-196 (2013)

A physical form of inorganic materials is known to affect the material property; for instance, metallic gold shows a catalytic property only when being downsized into a few nanometer size. The iCeMS researchers demonstrated, for the first time, that inorganic-organic hybrid materials also provide a novel property simply by downsizing the materials into the mesoscale. The Kitagawa group targeted flexible PCPs that change their structure in response to molecular incorporation and showed that the crystal downsizing regulates the structural flexibility and induces a shape-memory effect in the coordination frameworks only at the mesoscale (a few tens of nanometers). Experimental physicists in iCeMS were heavily involved in supporting this new discovery by providing a phase transition theory and a wide range of characterization techniques. This resulted from intensive discussions between chemists and physicists.

16. Numata, T; Murakami, T; Kawashima, F; Morone, N; Heuser, JE; Takano, Y; Ohkubo, K; Fukuzumi, S; Mori, Y; Imahori, H; Utilization of Photoinduced Charge-Separated State of Donor-Acceptor-Linked Molecules for Regulation of Cell Membrane Potential and Ion Transport; *J. Am. Chem. Soc.* 134, 6092-6095 (2012)

The iCeMS interdisciplinary research team has successfully controlled the membrane potential and ion transport across the cell membrane by synthetic ferrocene−porphyrin−fullerene triad molecules. The Imahori group synthesized molecules with a very long photoinduced charge separated state and the Murakami group delivered this molecules into the plasma membrane of PC12 cells by high density lipo protein (HDL). By collaborating with cell biologists in iCeMS, the research team for the first time achieved the generation of photoinduced ion flux through the cell membrane using the synthetic donor acceptor molecules with photoinduced charge-separated state. This new approach suggested by iCeMS researchers gives an impact on the society of optogenetics, which regulates a variety of cell functions, in particular neuronal functions, by light irradiation. This is the fruitful outcome of excellent cooperation of chemists, physicists, and cell biologists in iCeMS.

III. Manipulation of Cell Communication

17. Hirata, N; Nakagawa, M; Fujibayashi, Y; Yamauchi, K; Murata, A; Minami, I; Tomioka, M; Kondo, T; Kuo T; Endo, H; Inoue, H; Sato, S; Ando, S; Kawazoe, Y; Aiba, K; Nagata, K; Kawase, E; Chang, Y;

Suemori, H; Eto, K; Nakauchi, H; Yamanaka, S; Nakatsuji, N; Ueda, K; Uesugi, M; A chemical probe that labels human pluripotent stem cells; *Cell Reports* 6, 1165-1174 (2014)

This institute-initiated project combined expertise from four groups in iCeMS (Uesugi, Ueda, Nakatsuji, and Yamanaka) and two groups in CiRA (Eto and Inoue) to develop a chemical tool useful for stem cell biology. Screening of fluorescent chemical libraries with human induced pluripotent stem cells (iPSCs) identified a fluorescent molecule (Kyoto probe 1 [KP-1]) that selectively labels human pluripotent stem cells. Multidisciplinary mechanistic analyses indicated that the selectivity results primarily from a distinct expression pattern of ABC transporters in human pluripotent stem cells and from the transporter selectivity of KP-1. KP-1 may widely be used as a tool in the field of stem cell biology. This is the achievement of the integration of chemistry and cell biology.

18. Minami, I; Yamada, K; Otsuji, TG; Yamamoto, T; Shen, Y; Otsuka, S; Kadota, S; Morone, N; Barve, M; Asai, Y; Tenkova-Heuser, T; Heuser, JE; Uesugi, M; Aiba, K; Nakatsuji, N; A Small Molecule that Promotes Cardiac Differentiation of Human Pluripotent Stem Cells under Defined, Cytokine- and Xeno-free Conditions; *Cell Reports* 2, 1448-1460 (2012)

A multidisciplinary collaboration among Nakatsuji, Uesugi, and Heuser groups discovered, through chemical library screening and organic synthesis, a small molecule that boosts cardiomyogenesis. The discovery of the molecule named KY02111 led to a novel, defined method to induce differentiation of functional ventricular and pace maker cardiomyocytes at high efficiency from human pluripotent stem cells including ES and iPS cell lines. This cytokine- and xenon-free method is currently considered as the most suitable technology for production of human cardiomyocytes for clinical application. This is the achievement of the integration of chemistry and cell biology.

19. Takemoto, N; Suehara, T; Frisco, HL; Sato, S; Sezaki, T; Kusamori, K; Kawazoe, Y; Park, SM; Yamazoe, S; Mizuhata, Y; Inoue, R; Miller, GJ; Hansen, SU; Jayson, GC; Gardiner, JM; Kanaya, T; Tokitoh, N; Ueda, K; Takakura, Y; Kioka, N; Nishikawa, M; Uesugi, M; Small-Molecule-Induced Clustering of Heparan Sulfate Promotes Cell Adhesion; *J. Am. Chem. Soc.* 135, 11032-11039 (2013)

Adhesamine is an organic small molecule that the Uesugi group previously discovered to promote adhesion and growth of cultured human cells by binding selectively to heparan sulfate on the cell surface. A multidisciplinary collaboration among Uesugi, Ueda, and others revealed its mesoscopic mechanism of action. Chemical and cell biological analysis showed that multiple adhesamine molecules cooperatively bind to heparan sulfate and induce its assembly, promoting clustering of heparan sulfate-bound syndecan-4 on the cell surface. Animal studies showed that adhesamine improved the viability and attachment of transplanted cells in mice. Further studies could lead to the design of assembly-inducing molecules for use in cell biology and cell therapy. This is the achievement of the integration of chemistry and cell biology.

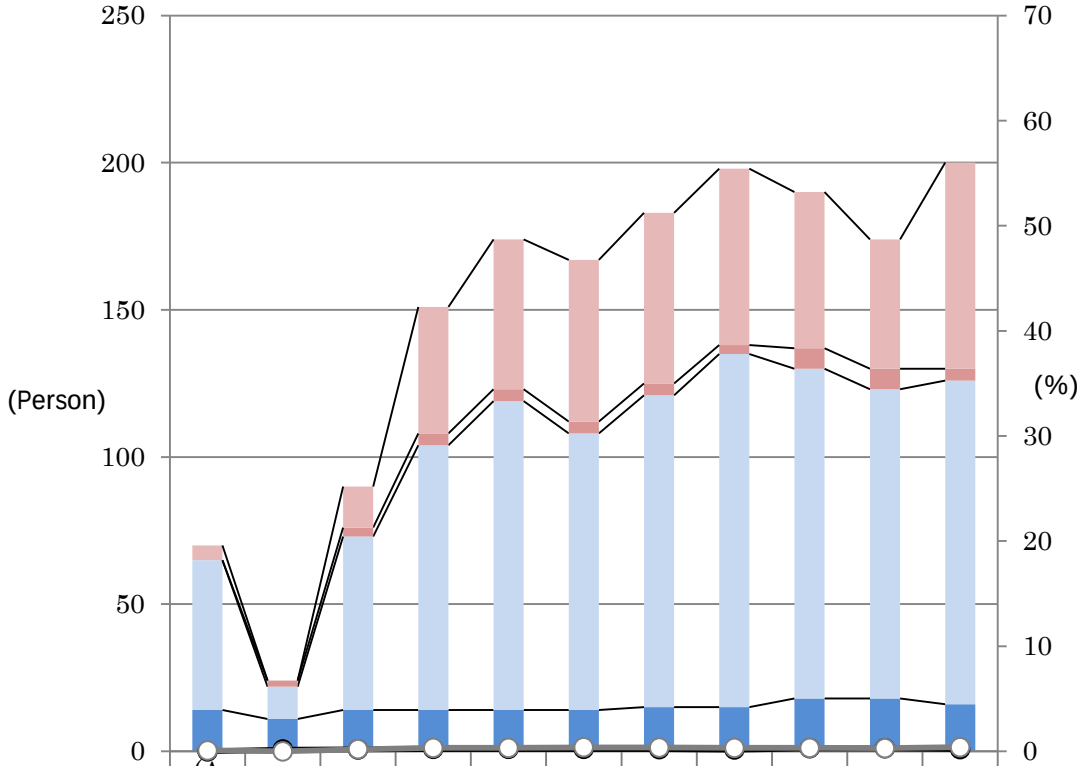
20. Wickham, SFJ; Bath, J; Katsuda, Y; Endo, M; Hidaka, K; Sugiyama, H; Turberfield, AJ; A DNA-based molecular motor that can navigate a network of tracks; *Nat. Nanotechnol.* 7, 169-173 (2012)

DNA is a material that conveys information. Clever use of its properties leads to the design of intelligent materials. The Sugiyama group and others designed a branched motor-track on a DNA origami scaffold and controlled the movement of a DNA motor with programmable instructions. To control motor strand movement, a branched track was constructed on the DNA origami scaffold, and three branching points and four final destinations were created. Block strands introduced at both sides of the branching points controlled the direction of the DNA motor. The DNA passed the two branching points, meaning that the two releasing strands can determine the pathway and destinations in a programmed fashion. The DNA motor was found at the predefined destinations by following the programmed instructions. This system could be further used for programmed drug delivery into cells. This is the achievement of the integration of chemistry and cell biology.

World Premier International Research Center Initiative (WPI)
Appendix 4-1. Number of Overseas Researchers and Annual Transition

*Make a graph of the transition in the number of overseas researchers since the application.

Number of Overseas Researchers



	(At beginning)	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	(Final goal)
Researchers from abroad	5	0	14	43	51	55	58	60	53	44	70
PIs from abroad	0	2	3	4	4	4	4	3	7	7	4
Japanese researchers excluding PIs	51	11	59	90	105	94	106	120	112	105	110
Japanese PIs	14	11	14	14	14	14	15	15	18	18	16
Ratio of PIs from abroad	0.0%	15.4%	17.6%	22.2%	22.2%	22.2%	21.1%	16.7%	28.0%	28.0%	20.0%
Ratio of researchers from abroad	8.9%	0.0%	19.2%	32.3%	32.7%	36.9%	35.4%	33.3%	32.1%	29.5%	38.9%

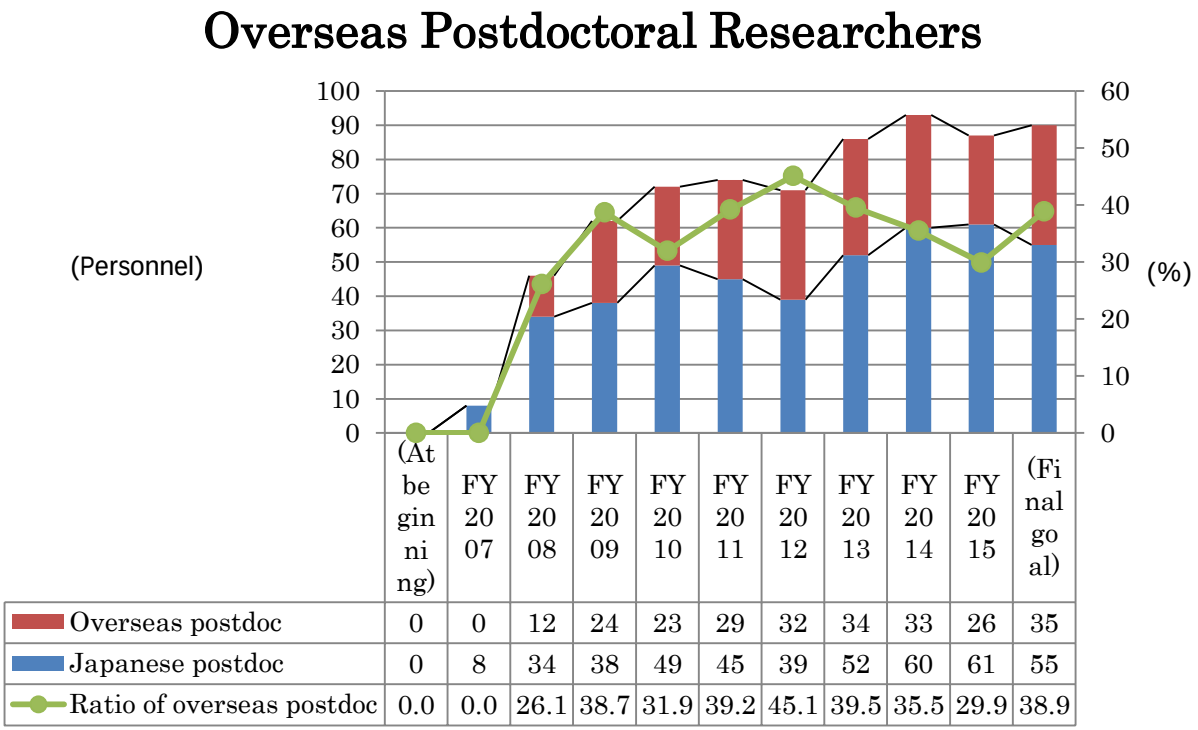
World Premier International Research Center Initiative (WPI)
Appendix 4-2. Postdoctoral Positions through Open International Solicitations

- In the column of number of applications and number of selection, put the number and percentage of overseas researchers in the < > brackets.

FY	number of applications	number of selection
FY2007	51 < 20, 39.2%>	8 < 0, 0%>
FY2008	62 < 14, 22.6%>	33 < 6, 18.2%>
FY2009	183 < 144, 78.7%>	52 < 13, 25.0%>
FY2010	190 < 180, 94.7%>	35 < 10, 28.6%>
FY2011	402 < 393, 97.8%>	23 < 11, 47.9%>
FY2012	337 < 329, 97.7%>	29 < 10, 34.4%>
FY2013	161 < 159, 98.8%>	31 < 17, 54.8%>
FY2014	364 < 350, 96.2%>	31 < 10, 32.3%>
FY2015	361 < 347, 96.1%>	33 < 12, 36.4%>

World Premier International Research Center Initiative (WPI)
Appendix 4-3. Number of Overseas Postdoctoral Researchers and Annual Transition

*Make a graph of the transition in the number of overseas postdoctoral researchers since the application.



	(At beginning)	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	(Final goal)
Overseas postdoc	0	0	12	24	23	29	32	34	33	26	35
Japanese postdoc	0	8	34	38	49	45	39	52	60	61	55
Ratio of overseas postdoc	0.0	0.0	26.1	38.7	31.9	39.2	45.1	39.5	35.5	29.9	38.9

World Premier International Research Center Initiative (WPI)

Appendix 4-4. Status of Postdoc Employment at Institutions of Postdoctoral Researchers

*List each researcher in 1 line. If the list exceeds this form, please add extra pages.

Japanese Postdocs

	Period of project participation	Previous Affiliation Position title (Country)	Next Affiliation Position title (Country)
1	2008/2/1 - 2008/12/19	British Consulate-General Osaka , Assistant to Science Attache (Japan)	Consulate General of the United States Osaka (Japan)
2	2008/4/1 - 2008/12/31	Japan Science and Technology Agency (JST) , Research Associate (Japan)	Japan Biological Informatics Consortium , Research Associate (Japan)
3	2008/4/1 - 2009/1/15	Kyoto University Institute for Frontier Medical Sciences, Part-time Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
4	2008/4/1 - 2009/1/31	JST CREST, Research Associate (Japan)	University of Alberta Dept of Chemistry, Postdoctoral Fellow (USA)
5	2008/4/1 - 2009/2/28	Kyoto University Graduate School of Science, Doctoral Student (Japan)	Chiba University , Specially Appointed Assistant Professor (Japan)
6	2008/4/1 - 2009/3/31	Kyoto University , JSPS Fellow (Japan)	Osaka University Department of Science, Postdoctoral Researcher (Japan)
7	2008/7/1 - 2009/3/31	Kyoto University Center for Law Temperature and Materials Sciences, Part-time Research Associate (Japan)	Kyoto University Center for Law Temperature and Materials Sciences, Assistant Professor (Japan)
8	2008/8/1 - 2009/3/31	Baylor College of Medicine, USA , Postdoctoral Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
9	2008/12/8 - 2009/3/31	Nagoya University Graduate School of Medicine, Assistant Professor (Japan)	Showa University Graduate School of Pharmacy, Lecturer (Japan)
10	2008/3/1 - 2009/5/31	Kyoto University Institute for Chemical Research, Research Associate (Japan)	JST , Research Associate (Japan)
11	2009/5/1 - 2009/10/31	Cancer Institute Hospital , Clinical Fellow (Japan)	University of Toronto The Hospital for Sick Children, Postdoctoral Researcher (Canada)
12	2009/4/1 - 2010/1/31	Gifu University Graduate School of Medicine, Associate Professor (Japan)	Kyoto University iCeMS, Professor (Japan)
13	2007/12/17 - 2010/3/31	Orion Registrar Japan , Assistant to the President (Japan)	Kyoto University iCeMS, Staff (Japan)
14	2008/1/1 - 2010/3/31	Kyoto University Institute for Frontier Medical Sciences, Assistant Research Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
15	2008/4/1 - 2010/3/31	Kyoto University Institute for Frontier Medical Sciences, Research Associate (Japan)	Kyoto University Center for iPS Cell Research and Application (Japan)

16	2008/4/1 - 2010/3/31	Kyoto University Grad School of Science, Assistant Research Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
17	2008/6/1 - 2010/3/31	Namiki Hospital , Physician (Japan)	Kyoto University Center for iPS Cell Research and Application, Senior Lecturer (Japan)
18	2008/6/1 - 2010/3/31	Sumitomo Dainippon Pharma Intellectual Property Department, Manager (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
19	2008/6/16 - 2010/3/31	Kyoto University Hospital, Technical Support Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
20	2008/10/1 - 2010/3/31	JST Life Science Unit, Fellow (Japan)	Kyoto University Center for iPS Cell Research and Application (Japan)
21	2008/10/27 - 2010/3/31	Japan Times Osaka Branch, Writer (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
22	2008/11/1 - 2010/3/31	Kyoto University Institute for Frontier Medical Sciences, Assistant Research Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
23	2008/12/1 - 2010/3/31	Tokyo Metropolitan Geriatric Hospital , Part-time staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
24	2009/2/23 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
25	2009/4/1 - 2010/3/31	JST , Technical Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
26	2009/4/1 - 2010/3/31	Kyoto University iCeMS, Part-time Research Associate (Japan)	Japan Foundation for Neuroscience and Mental Health , Research Associate (Japan)
27	2009/4/1 - 2010/3/31	Ministry of Foreign Affairs , Officer (Japan)	Kyoto University Center for iPS Cell Research and Application (Japan)
28	2009/4/1 - 2010/3/31	JST CREST, Assistant Research Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
29	2009/4/1 - 2010/3/31	Kyoto University Grad School of Medicine, Research Associate (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
30	2009/4/1 - 2010/3/31	JST , Technical staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
31	2009/4/1 - 2010/3/31	OncoTherapy Science Inc Intellectual Property Department, Group Leader (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
32	2009/4/1 - 2010/3/31	NTT West , Temporary staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Specially appointed staff (Japan)
33	2009/4/1 - 2010/3/31	JST , Technical staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
34	2009/4/1 - 2010/3/31	Human Resocia , Temporary staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Specially appointed staff (Japan)

35	2009/4/1 - 2010/3/31	Kyoto University Hospital, Office Assistant (Japan)	Kyoto University Center for iPS Cell Research and Application, Assistant Professor (Japan)
36	2009/4/1 - 2010/3/31	student	Kanazawa University School of Pharmaceutical Sciences, Assistant Professor (Japan)
37	2009/4/1 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
38	2009/5/1 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
39	2009/7/1 - 2010/3/31	Avant Inc , Secretary (Japan)	Kyoto University Center for iPS Cell Research and Application, Specially appointed staff (Japan)
40	2009/7/1 - 2010/3/31	Tokyo CRO Inc Osaka Branch, Application Research Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Specially appointed staff (Japan)
41	2009/8/1 - 2010/3/31	Maruyama Mokuzai Inc , Academic Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
42	2009/9/1 - 2010/3/31	RIKEN Research Center for Allergy and Immunology, Research Associate (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
43	2009/9/7 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
44	2009/10/1 - 2010/3/31	Ohishi Shuzo , Officer (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
45	2009/11/1 - 2010/3/31	Akita Prefectural Health & Environment Center , Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
46	2009/11/1 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
47	2009/12/1 - 2010/3/31	The National Center of Neurology and Psychiatry Institute of Neuroscience, Research Associate (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
48	2010/1/1 - 2010/3/31	Foundation for Biomedical Research and Innovation , Research Associate (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
49	2010/1/1 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
50	2010/1/1 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
51	2010/3/1 - 2010/3/31	Kyoto University Institute for Chemical Research, Research Fellow (Japan)	Kyoto University iCeMS, Research Associate (Japan)
52	2008/4/1 - 2010/4/30	Kyoto University Grad School of Informatics, Research Associate (Japan)	Kyoto University Museum, Assistant Research Staff (Japan)

53	2010/4/1 - 2010/6/11	Kyoto University iCeMS, Research Associate (Japan)	Osaka University The Institute of Scientific and Industrial Research, Postdoctoral Research Associate (Japan)
54	2008/4/1 - 2010/6/15	Toray Research Center for Material Science, Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
55	2008/9/1 - 2010/6/30	Kyoto University Institute for Frontier Medical Sciences, Lecturer (Japan)	unknown Grad School of Medicine, Assistant Research Staff (Japan)
56	2008/8/1 - 2010/7/31	Nagoya University Research Center for Material Science, COE Researcher (Japan)	Kyoto University iCeMS, Research Associate (Japan)
57	2008/8/1 - 2010/7/31	Nagoya University Research Center for Material Science, Part-time Research Associate (Japan)	Kyoto University iCeMS, Research Associate (Japan)
58	2010/4/1 - 2010/7/31	Japan Science and Technology Agency (JST) ICORP, Research Associate (Japan)	Kyoto University Graduate School of Medicine, Assistant Professor (Japan)
59	2010/8/1 - 2010/11/30	Kyoto University iCeMS, Research Associate (Japan)	Kyushu University Graduate School of Science, Assistant Professor (Japan)
60	2009/12/1 - 2010/11/30	Kyoto University Institute for Virus Research, Assistant Research Staff (Japan)	unknown
61	2008/4/1 - 2011/3/31	Tokyo Medical and Dental University Institute of Biomaterials and Bioengineering, COE Specially appointed researcher (Japan)	Tohoku University Graduate School of Engineering, Associate Professor (Japan)
62	2008/4/1 - 2011/3/31	Kyoto University Institute for Frontier Medical Sciences, Research Associate (Japan)	Kyoto University iCeMS, Research Associate (Japan)
63	2009/6/1 - 2011/3/31	Kyoto University Graduate School of Medicine, Part-time Research Associate (Japan)	Kyushu University Graduate School of Medicine, Assistant Professor (Japan)
64	2010/1/1 - 2011/3/31	Kyoto University Institute for Research in Humanities, Research Associate (Japan)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
65	2010/4/1 - 2011/3/31	Japan Science and Technology Agency (JST) ICORP, Research Associate (Japan)	Kyoto University Institute for Frontier Medical Sciences, Assistant Professor (Japan)
66	2010/4/1 - 2011/3/31	The University of Tokyo Graduate School of Frontier Sciences, JSPS Fellow (Japan)	Keio University Graduate School of Science and Technology, Assistant Professor (Japan)
67	2010/4/1 - 2011/3/31	Kyoto University iCeMS, JSPS Research Fellow (Japan)	Osaka University Graduate School of Engineering and Science, Assistant Professor (Japan)
68	2010/4/1 - 2011/3/31	Kyoto University Fukui Institute for Fundamental Chemistry, Professor (Japan)	Kyoto University Fukui Institute for Fundamental Chemistry, Research Associate (Japan)
69	2010/6/16 - 2011/3/31	unknown	Kyoto University Fukui Institute for Fundamental Chemistry, Research Associate (Japan)
70	2010/7/1 - 2011/3/31	Texas A&M University Dept of biochemistry and Biophysics, Research Assistant (USA)	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)

71	2010/10/16 - 2011/3/31	Kyoto University iCeMS, Assistant Research Staff (Japan)	Kyoto University Fukui Institute for Fundamental Chemistry, Research Associate (Japan)
72	2009/4/1 - 2011/4/30	RIKEN Brain Science Institute, Research Associate (Japan)	Kanazawa University Cancer Research Institute, Research Associate (Japan)
73	2008/5/16 - 2011/5/15	RIKEN Center for Developmental Biology, Research Staff (Japan)	unknown
74	2010/7/1 - 2011/7/31	McKinsey & Company , Business Analyst (Japan)	Mitsui & CO., Ltd (Japan)
75	2011/2/1 - 2011/8/31	University of Pittsburgh College of Science and Engineering, Postdoctoral Researcher (USA)	Kumamoto University Faculty of Life Sciences, Assistant Professor (Japan)
76	2011/5/18 - 2011/9/4	Kyoto University Graduate School of Medicine, Office Assistant (Japan)	Catenion GmbH , Full-time (Germany)
77	2009/11/1 - 2011/9/30	Gifu Pharmaceutical University Dept of Pharmaceutical Science, Assistant Professor (Japan)	Sizuoka prefectural Institute for Environmental Hygiene , Manager (Japan)
78	2011/4/1 - 2011/9/30	Osaka University Institute for Protein Research , Part-time staff (Japan)	unknown
79	2009/4/1 - 2011/11/30	Kyoto University Graduate School of Science, JSPS Research Fellow (Japan)	University of Tsukuba Graduate School of Pure and Applied Sciences, Assistant Professor (Japan)
80	2009/4/1 - 2012/1/31	RIKEN Brain Science Institute, Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
81	2011/4/1 - 2012/2/29	Kyoto Institute of Technology Insect Biomedical Research Center, Research Associate (Japan)	Tokyo Institute of Technology Graduate School of Bioscience and Biotechnology (Japan)
82	2010/8/1 - 2012/3/30	Kyoto University iCeMS, Research Associate (Japan)	Tokyo Institute of Technology Graduate School of Bioscience and Biotechnology, Assistant Professor (Japan)
83	2008/4/1 - 2012/3/31	Max-Planck Institute for Molecular Biomedicine , Postdoctoral Fellow (Japan)	Osaka University , Specially Appointed Assistant Professor (Japan)
84	2008/4/1 - 2012/3/31	Nagoya Bunri University College of NBU, Lecturer (Japan)	Dokkyo Medical University Graduate School of Medicine, Lecturer (Japan)
85	2010/7/1 - 2012/3/31	student	Kyoto University iCeMS, JSPS Fellow (Japan)
86	2011/5/1 - 2012/3/31	Kyoto University Pioneering Research Unit for Next Generatin, Research Associate (Japan)	Kyoto University Institute for Chemical Research, Research Associate (Japan)
87	2011/8/10 - 2012/8/26	McKinsey & Company , Associate (Japan)	McKinsey & Company Japan Branch, Consultant (Japan)
88	2011/10/1 - 2012/10/31	Rennes 1 University , Postdoctoral Fellow (France)	University of Tokyo The Institute for Solid State Physics, Specially Appointed Assistant Professor (Japan)
89	2012/10/8 -	Nagoya University Research Center for Material Science,	Kyoto University iCeMS, Research Associate (Japan)

	2012/11/15	Assistant Professor (Japan)	
90	2010/4/1 - 2012/11/30	NPO Stem Cell Institute HTS Group, Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
91	2011/4/18 - 2012/12/31	Advantage Science , Part-time staff (Japan)	unknown
92	2012/4/1 - 2013/1/1	Japan Biological Informatics Consortium , JSPS Fellow (Japan)	Fukushima Medical University Medical-Industrial Translational Research Center, Assistant Professor (Japan)
93	2008/2/1 - 2013/1/31	Kyoto University Grad School of Medicine, Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
94	2008/3/1 - 2013/2/28	The University of Tokyo Grad School of Arts and Science, Research Support Staff (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
95	2008/3/1 - 2013/2/28	Kyoto University Center for the Promotion of Excellence in Higher Education, Lecturer (Japan)	Kyoto University iCeMS, Research Associate (Japan)
96	2013/4/1 - 2013/4/30	Kyoto University Graduate School of Science, JSPS Fellow (Japan)	University of Groningen , Doctoral research fellow (Netherlands)
97	2010/4/1 - 2013/6/30	Kyoto University , JSPS Fellow (Japan)	Tokushima University Graduate School of Pharmacy, Assistant Professor (Japan)
98	2011/4/1 - 2013/9/30	Kyoto University Institute for Chemical Research, Postdoctoral Researcher (Japan)	n/a
99	2012/12/1 - 2013/11/17	Kyoto University Institute for Frontier Medical Sciences, Research Associate	unknown
100	2010/6/24 - 2014/2/28	United Energy Consulting , President	Kyoto University iCeMS, Specially Appointed Research Associate (Japan)
101	2011/4/1 - 2014/2/28	Hokkaido University Grad School of Pharmacy, Assistant Professor (Japan)	Kyoto University Institute for Chemical Research, Assistant Professor (Japan)
102	2013.4.1 - 2014.4.30	Kyoto University Graduate School of Agriculture, Office Assistant (Japan)	Japan Atomic Energy Agency, Researcher (Japan)
103	2013.4.1 - 2014.5.31	Student (Japan)	Tokyo Institute of Technology Interdisciplinary Graduate School of Science and Engineering, Assistant Professor (Japan)
104	2009.9.1 - 2015.3.31	Nagoya University Ecotopia Science Institute, Researcher (Japan)	Institut Curie Centre de Recherche, Researcher (France)
105	2010.4.1 - 2015.3.31	ReproCELL, Engineer (Japan)	Kyoto Stem Cell Innovation (Japan)
106	2010.7.1 - 2014.7.3	Nara Institute of Science and Technology Graduate School of Biological Sciences, Engineer (Japan)	The Institute of Medical Science, The University of Tokyo, Academic Support Specialist (Japan)

107	2011.1.16 - 2014.9.30	Kyoto University Graduate School of Science, Researcher (Japan)	Tokushima University Institute of Socio-Arts and Sciences, Lecturer (Japan)
108	2011.7.16 - 2015.3.31	Kyoto University Institute for Frontier Medical Sciences, Researcher (Japan)	n/a
109	2012.4.1 - 2014.3.31	Nara Women's University Faculty of Human Life and Environment, Lecturer (Japan)	Yamaguchi University Faculty of Global Science Studies, Assistant Professor (Japan)
110	2012.4.1 - 2016.3.31	Kyoto University Museum, Assistant Teaching Staff (Japan)	Osaka University Center for the Study of Communication Design, Assistant Professor (Japan)
111	2012.4.1 - 2016.3.31	Institute for Molecular Science, Professor (Japan)	Kyoto University Graduate School of Agriculture, Researcher (Japan)
112	2012.6.1 - 2015.3.31	University of South California Department of Biochemistry and Molecular Biology Keck School of Medicine, Postdoc (US)	n/a
113	2012.11.19 - 2015.3.31	Northwestern University College of Chemistry, JSPS fellow (US)	n/a
114	2013.5.1 - 2015.3.31	Showa Chemical Industry Co.,Ltd. R&D Department, Researcher (Japan)	n/a
115	2013.4.1 - 2015.3.31	Australian National Center for the Public Awareness of Science, Casual Academic Staff (Australia)	British Consulate General Osaka Science and Innovation Section, Science & Innovation Officer (Japan)
116	2013.4.1 - 2015.9.30	Osaka University Graduate School of Medicine, Assistant Technical Staff (Japan)	Kyoto University Center for iPS Cell Research and Application, Assistant Professor (Japan)
117	2013.4.1 - 2014.9.30	Kyoto University Center for iPS Cell Research and Application, Office Assistant (Japan)	The University of Tokyo Institute for Solid State Physics, Assistant Professor (Japan)
118	2013.5.1 - 2016.3.31	TAIHO Pharmaceutical Co., Ltd. Corporate Strategy Division	Cmic-Holdings Executive Officer (Japan)
119	2013.6.1 - 2015.3.31	Tohoku University AIMR, Assistant Teaching Staff (Japan)	n/a
120	2014.4.1 - 2015.3.31	Kyoto University Center for iPS Cell Research and Application, Researcher (Japan)	Kyoto University Center for iPS Cell Research and Application, Researcher (Japan)
121	2014.4.1 - 2016.3.31	RIKEN Researcher (Japan)	Nagoya University Graduate School of Engineering, Assistant Professor (Japan)
122	2014.4.1 - 2016.3.31	Kyoto University Institute for Chemical Research, Lecturer (Japan)	Okayama University Graduate School of Natural Science and Technology, Adjunct Lectuerer (Japan)
123	2014.4.1 - 2016.3.31	Kyoto University iCeMS, ,Assistant Teaching Staff (Japan)	Kyoto University iCeMS, Researcher (Japan)
124	2014.4.16 - 2014.5.31	Student (Japan)	Massachusetts Institute of Technology Department of Chemistry, JSPS Fellow (US)

125	2014.5.1 - 2015.3.31	Student (Japan)	n/a
126	2014.6.1 - 2016.3.31	National Cerebral and Cardiovascular Center Research Institute, Research Associate (Japan)	n/a
127	2014.8.16 - 2015.6.30	Kyoto University iCeMS, JSPS Fellow (Japan)	The University of Adelaide School of Physical Sciences, Postdoc (Australia)
128	2015.1.16 - 2015.10.31	Max-Planck-Institut Molekulare Physiologie Abteilung Chemische Biologie, Researcher (Germany)	Kyoto University Institute for Chemical Research, Assistant Professor (Japan)
129	2015.4.1 - 2016.3.31	Hokkaido University Institute for Catalysis, Postdoc (Japan)	Yakuju Co., Ltd., Pharmacist (Japan)
130	2015.4.1 - 2016.3.31	n/a	n/a
131	2015.4.1 - 2016.3.31	Student (Japan)	Sumitomo Chemical, Health and Crop Sciences Research Laboratory, Researcher (Japan)
132	2015.4.1 - 2016.3.31	n/a	Kyoto University Graduate School of Agriculture, Researcher (Japan)
133	2015.4.1 - 2016.3.31	Kyoto University Graduate School of Science, Researcher (Japan)	Doshisha University Faculty of Life and Medical Sciences, Adjunct Lecturer (Japan)
134	2015.4.1 - 2015.11.30	Kyoto University Graduate School of Science, Researcher (Japan)	Kyoto University Graduate School of Science, Researcher (Japan)
135	2015.4.1 - 2016.3.31	n/a	Kyoto University Graduate School of Medicine, Researcher (Japan)
136	2015.5.1 - 2015.6.30	Kyoto University Yoshida-South Campus Administrative Office, Specialist Staff (Japan)	Wakayama Medical University, Lecturer (Japan)
137	2015.8.1 - 2016.3.31	Kyoto University Graduate School of Agriculture, Researcher (Japan)	Kyoto University Graduate School of Agriculture, Researcher (Japan)
138	2015.9.1 - 2016.3.31	Student (Japan)	Okinawa Institute of Science and Technology Graduate University, Technical Staff (Japan)
139	2015.10.1 - 2016.3.31	Kyoto University Graduate School of Pharmaceutical Sciences, Researcher (Japan)	Kyoto University Institute for Chemical Research, Assistant Professor (Japan)
140	2016.1.25 - 2016.3.31	Doshisha University Graduate School of Brain Science, Adjunct Researcher (Japan)	n/a

Overseas Postdocs

	Period of project participation	Previous Affiliation Position title (Country)	Next Affiliation Position title (Country)
1	2008/4/1 - 2008/5/31	Tokyo Metropolitan Institute of Medical Science , Part-time Research Associate (Japan)	University of Texas Medical Branch, Researcher (USA)
2	2008/4/1 - 2008/7/31	Chalmers University of Technology Department of Experimental Physics, (Sweden)	Chalmers University of Technology Department of Experimental Physics, , Assistant Professor (Sweden)
3	2008/4/1 - 2009/6/30	Kyoto University Graduate School of Science, Part-time Research Associate (Japan)	Indian Institute of Technology , Assistant Professor (India)
4	2008/4/1 - 2009/6/30	student	Rutgers University College of Pharmaceutical Science, Postdoctoral Fellow (USA)
5	2009/6/1 - 2009/10/31	Ibaraki University Graduate School of Engineering, Postdoctoral Fellow (Japan)	Kyoto University iCeMS, Research Associate (Japan)
6	2009/10/1 - 2010/1/31	Pohang University of Science and Technology Graduate School of Chemistry, Postdoctoral Associate (Korea)	Kyoto University iCeMS, Research Associate (Japan)
7	2009/7/1 - 2010/2/28	Osaka Prefecture University , Visiting l Research Associate (Japan)	Lanzhou University College of Chemistry ad Chemical Engineering, Associate Professor (China)
8	2008/8/16 - 2010/3/31	unknown	Kyoto University Center for iPS Cell Research and Application, Research Associate (Japan)
9	2009/7/1 - 2010/9/30	Tohoku University The Advanced Institute for Materials Research (AIMR), Assistant Professor (Japan)	China Petrochemical Corporation , Senior Engineer (China)
10	2009/3/1 - 2010/12/31	student	CNRS ENSAT, Postdoctoral Research Associate (France)
11	2010/10/1 - 2010/12/31	Kyoto University Graduate School of Engineering, Student (Japan)	Kyushu University Institute for Materials Chemistry and Engineering, Research Associate (Japan)
12	2010/4/5 - 2011/1/14	AFG Biosolutions, Inc , Scientist (USA)	unknown
13	2009/9/9 - 2011/2/28	Kyoto University Graduate School of Medicine, Doctoral Student (Japan)	unknown
14	2010/2/1 - 2011/2/28	Kyoto University iCeMS, Research Associate (Japan)	Samsung Advanced Institute of Technology, Research Scientist (Korea)
15	2009/11/16 - 2011/3/31	Washington University School of Medicine Neurobiology and Psychiatry, Research Assistant (USA)	Kyoto University iCeMS, Research Associate (Japan)
16	2010/6/1 - 2011/3/31	Tata Institute of Fundamental Research , Postdoctoral Research Fellow (India)	Kyoto University Fukui Institute for Fundamental Chemistry, Research Associate (Japan)
17	2010/9/1 -	unknown (Japan)	Kyoto University Fukui Institute for Fundamental Chemistry, Research Associate

	2011/3/31		(Japan)
18	2011/3/28 - 2011/9/30	Central South University Affiliated Haikou Hospital of Xiangya Medical College, Medical Doctor (China)	Hainan Province Haikou Municipal People's Hospital , Physician (China)
19	2009/10/1 - 2012/3/31	Wuhan University College of Chemistry and Molecular Science, Lecturer (China)	Wuhan University College of Chemistry and Molecular Science, Lecturer (China)
20	2010/4/1 - 2012/3/31	Stanford University Stanford University and Regenerative Medicine , Research Assistant	Karolinska Institute, , Graduate Student, (Stockholm, Sweden)
21	2009/10/1 - 2012/7/31	Harfang Microtechnique , Technician (UK)	McGill University , Doctoral Research Fellow (Canada)
22	2009/11/1 - 2012/7/31	New Mexico University , Research & teaching Assistant (USA)	Kyoto University iCeMS, Assistant Professor (Japan)
23	2011/1/16 - 2012/7/31	Kyoto University ERATO Kitagawa Integrated Pores Project, Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
24	2011/2/1 - 2012/7/31	ELLA-CS(company dealing with development and sales of medical devices(stents)) , medical devices(stents)) (Czech)	Kyoto University Museum, Research Associate (Japan)
25	2011/1/16 - 2012/9/21	Russian Academy of Science Laboratory of Cellular neurobiology Institute of Cell Biophysics, Postdoctoral Researcher (Russia)	Brandeis University , Postdoctoral Associate (USA)
26	2012/4/1 - 2012/10/31	unknown	Nanjing University State Key laboratory of Pharmaceutical Biotechnology School of Life Sciences, Associate Professor (China)
27	2011/8/16 - 2012/11/15	student	Kyoto University iCeMS, JSPS Overseas Fellow (Japan)
28	2012/7/1 - 2012/11/30	Tokyo Institute of Technology Graduate School of Innovation Management, Research Student (Japan)	Wuhan East Lake Hi-Tech Development Zone Management Committee Investment Promotion Department, Investment Director (China)
29	2011/6/1 - 2012/12/31	The University of Tokyo Graduate School of Science, Specially appointed Research Associate (Japan)	Vignan University , Assistant Professor (India)
30	2008/4/1 - 2013/1/31	Kyoto University Grad School of Science, Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor (Japan)
31	2009/11/1 - 2013/3/31	Kyoto iCeMS, Research Associate (Japan)	University of Nova Gorica Dvorec Lanthieri (Slovenia)
32	2011/7/1 - 2013/3/31	Kyoto University , Research Assistant (Japan)	n/a
33	2011/8/1 - 2013/7/31	Seoul National University Center for Agricultural Biomaterials , Postdoctoral Researcher (Korea)	Ewha Womans University Center for Intelligent NanoBio Materials, Assistant Professor (Korea)
34	2013/7/1 -	Osaka University , Student (Japan)	Kyoto University iCeMS, Research Associate (Japan)

	2013/8/31		
35	2009/10/1 - 2013/9/30	Kumamoto University Institute for Molecular Embryology and Genetics, Research Associate (Japan)	Keio University Graduate School of Medicine, Assistant Professor (Japan)
36	2011/12/1 - 2013/9/30	Kyoto University iCeMS, JSPS Research Fellow (Japan)	Kyoto University iCeMS, Research Associate (Japan)
37	2012/10/1 - 2013/10/15	student	Kyoto University iCeMS, JSPS Researcher (Japan)
38	2013/10/1 - 2013/10/31	Kyoto University iCeMS, Research Associate (Japan)	The University of Iowa Molecular Physiology and Biophysics, Carver College of Medicine, , Postdoc Scholar (USA)
39	2011/9/1 - 2013/12/31	GenScript Corporation , Technical Account manager (USA)	Qualtec Institute for Biochemistry, Research Associate (Japan)
40	2010/1/1 - 2014/2/28	Niigata University Grad School of Science and Technology, Research Associate (Japan)	Kyoto University iCeMS, Assistant Professor
41	2013/3/1 - 2014/2/28	St. Mary's College , Lecturer (USA)	University of Nebraska Medical Center College of Pharmacy, Postdoctoral Research Associate (USA)
42	2013.10.1 - 2015.3.31	Kyoto University iCeMS, Assistant Teaching Staff (Japan)	Kyoto University Graduate School of Agriculture, Researcher (Japan)
43	2012.7.1 - 2014.6.30	National Center for Biological Sciences, Researcher (India)	Nagoya University Graduate School of Engineering, Researcher (Japan)
44	2012.5.1 - 2015.11.30	Student (China)	n/a
45	2013.10.16 - 2015.3.31	Student (Japan)	National Institute for Materials Science, Posdoc (Japan)
46	2011.4.1 - 2016.3.31	Kyoto University iCeMS, Researcher (Japan)	Kyoto University iCeMS, Researcher (Japan)
47	2011.10.16 - 2015.3.31	The first high school of Kuailuan, Teacher (China)	University of Liverpool Department of Chemistry, Postdoctoral Researcher (UK)
48	2012.3.1 - 2015.12.31	Kyoto University Institute for Chemical Research, Researcher (Japan)	Institute for Bioengineering of Catalonia Nanoscopy for Nanomedicine Group, Researcher (Spain)
49	2012.5.1 - 2014.8.31	National University of Singapore Faculty of Dentistry, Researcher (Singapore)	n/a
50	2012.9.1 - 2015.5.31	German Military Service (Germany)	n/a
51	2013.4.16 - 2016.3.31	Beijing BD Star Navigation Co.,Ltd. , Assistant Purchaser (China)	Guangdong University of Technology, Adjunct Lecturer (China)
52	2013.5.1 - 2016.3.31	Regeron,Inc., Lecturer (Korea)	Okayama University Graduate School of Natural Science and Technology, Assistant Professor (Japan)

53	2013.9.1 - 2014.10.31	Kyoto University iCeMS, Researcher (Japan)	n/a
54	2013.10.1 - 2015.3.31	Osaka University Researcher (Japan)	n/a
55	2014.1.16 - 2014.11.30	ReproCELL, Research Scientist (US)	Palk Institute for Chemical Research, Research Professor
56	2014.4.1 - 2015.3.31	n/a	n/a
57	2014.8.1 - 2015.8.31	Max Planck Institute of Colloids and Interfaces , Alexander von Humboldt Postdoc (Germany)	Chinese Academy of Sciences , Project Professor(Tenure-track) (China)
58	2014.9.1 - 2016.3.31	Kyoto University iCeMS, JSPS Fellow (Japan)	Kyoto University Graduate School of Biostudies, Researcher (Japan)
59	2014.11.1 - 2015.11.30	Ecole Polytechnique Federal Lausanne(EPFL) Laboratory of Photonics and Interfaces(LPI), External collaborator (Switzerland)	University of Amsterdam Van't Hoff Institute for Molecular Sciences(HIMS) (Nederland)
60	2015.4.1 - 2015.9.30	Kyoto University iCeMS, JSPS Fellow (Japan)	Tongii University Shanghai , Distinguished Research Fellow (China)
61	2015.4.1 - 2016.1.14	Kyoto University iCeMS, Assistant Teaching Staff (Japan)	n/a
62	2015.7.1 - 2015.8.28	n/a	East China University of Science and Technology, Lecturer, (China)
63	2015.11.16 - 2016.1.31	Kyoto University iCeMS, JSPS Fellow (Japan)	Jiangsu Normal University School of Chemistry and Chemical Engineering, Lecturer（China)

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Appedex 4-5. List of the Cooperative Research Agreements Outside Japan

1. Counterpart of an Agreement: California NanoSystems Institute (CNSI), UCLA
   Name of an Agreement:
   Memorandum of understanding Between the Regents of the University of California, on Behalf of Its Los Angeles Campus, USA, and on Behalf of the California Nanosystems Institute (CNSI) and the Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University
   Dates of an Agreement: 15 March, 2010
   Summary of an Agreement:
   Exchange of researchers, administrative staff and students, research collaboration, joint symposium, exchange of information

2. Counterpart of an Agreement: National Centre for Biological Science, Tata Institute of Fundamental Research (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem)
   Name of an Agreement:
   Memorandum of understanding Between the National Centre for Biolofical Sciences of Tata Institute of The National Centre for Biological Sciences of Tata Institute of Fundamental Research Bangalore and the Institute for Stem Cell Biology And Regenerative Medicine and the Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University
   Dates of an Agreement: 28 April, 2010
   Summary of an Agreement:
   Exchange of researchers and administrative staff, research collaboration, joint symposium, exchange of information

3. Counterpart of an Agreement: Medical Bioconvergence Research Center, Seoul National University
   Name of an Agreement:
   General Memorandum for Academic Cooperation and Exchange between Medical Bioconvergence Research Center, Seoul National University, Korea and Institute for Integrated Cell- Material Sciences, Kyoto University, Japan
   Dates of an Agreement: 29 March, 2011-28 March 2016 (included in the university-level agreement after March 29, 2016)
   Summary of an Agreement:
   Exchange of researchers and students, research collaboration, joint symposium, exchange of information

4. Counterpart of an Agreement: Center for Regenerative Medicine, University of Edinburgh
   Name of an Agreement:
   Memorandum of Understanding between the University Court of the University of Edinburgh (MRC- Centre for Regenerative Medicine) and the Institute for Integrated Cell- Material Sciences (iCeMS), Kyoto University
   Dates of an Agreement: 30 March, 2011-29 March 2016 (included in the university-level agreement after March 30, 2016)
   Summary of an Agreement:
   Exchange of researchers, administrative staff and students, research collaboration, joint symposium, exchange of information

5. Counterpart of an Agreement: Moscow Institute of Physics and Technology (MIPT)
   Name of an Agreement:
   General Memorandum for Academic Cooperation and Exchange between Moscow Institute of

Physics and Technology, Russia, and the Institute for Integrated Cell- Material Sciences, Kyoto University, Japan
Dates of an Agreement: 31 March, 2011-30 March, 2016
Summary of an Agreement:
Exchange of researchers and students, research collaboration, joint symposium, exchange of information

6. Counterpart of an Agreement: Jawaharal Nehru Center for Advanced Scientific Research
Name of an Agreement:
Memorandum of Understanding on Academic Exchanges between Jawaharal Nehru Center for Advanced Scientific Research (JNCASR), India, and the Institute for Integrated Cell- Material Sciences (iCeMS), Kyoto University, Japan
Dates of an Agreement: 18 April, 2011
Summary of an Agreement: Exchange of researchers, research collaboration, joint symposium, exchange of information

7. Counterpart of an Agreement: Division of Advanced Materials Science, Pohang University of Science and Technology
Name of an Agreement:
General Memorandum for Academic Cooperation and Exchange between Division of Advanced Materials Science, Pohang University of Science and Technology, Korea, and Institute for Integrated Cell-Material Sciences, Kyoto University, Japan
Dates of an Agreement: 16 November, 2011
Summary of an Agreement:
Exchange of researchers and students, research collaboration, joint symposium, exchange of information

8. Counterpart of an Agreement: Center for Regenerative Medicine, National Institute of Health
Name of an Agreement:
General Memorandum for Academic Cooperation and Exchange between the NIH Center for Regenerative Medicine, National Institutes of Health, USA and the Institute for Inetgrated Cell-Material Sciences, Kyoto University, Japan
Dates of an Agreement: 21 November, 2011
Summary of an Agreement:
Exchange of researchers and students, research collaboration, joint symposium, exchange of information

9. Counterpart of an Agreement: Tsinghua University - Peking University Center for Life Sciences (CLS)
Name of an Agreement:
General Memorandum for Academic Cooperation and Exchange Between the Center for Life Sciences, China and the Institute for Integrated Cell-Material Sciences, Kyoto University, Japan
Dates of an Agreement: 20 April, 2012
Summary of an Agreement:
Exchange of researchers and students, research collaboration, joint symposium, exchange of information

10. Counterpart of an Agreement: Welcome Trust Centre for Stem Cell Research, University of Cambridge
Name of an Agreement:
(University Level Agreement) General Memorandum for Academic Cooperation and Exchange Between the University of Cambridge (the United Kingdom) and Kyoto University (Japan)
Dates of an Agreement: 5 August, 1997
Summary of an Agreement:

Exchange of researchers, administrative staff and students, research collaboration, joint symposium, exchange of information

11. Counterpart of an Agreement: Heidelberg University
    Name of an Agreement:
    (University Level Agreement) Rahmenvereinbarung Uber Wissenschaftliche Zusammenarbeit Und Den Austausch Zwishen DER Ruprecht-Karls-Universitat Heidelberg (Bundesrepublik Deutschland) Und Der Universitat Kyoto (Japan)
    Dates of an Agreement: 11 October 1990
    Summary of an Agreement:
    Exchange of researchers and students, research collaboration, joint symposium, exchange of information

12. Counterpart of an Agreement: Max Planck Institute of Molecular Cell Biology and Genetics
    Name of an Agreement: (Official MOU has not been concluded yet)
    Dates of an Agreement:
    Summary of an Agreement:
    Exchange of researchers and students, research collaboration, exchange of information

13. Counterpart of an Agreement: Center for Basic and Applied Membrane Sciences, Purdue University
    Name of an Agreement: (Official MOU has not been concluded yet)
    Dates of an Agreement:
    Summary of an Agreement:
    Exchange of researchers and students, research collaboration, exchange of information

14. Counterpart of an Agreement: Stem Cells Australia, the University of Melbourne
    Name of an Agreement:
    (University Level Agreement) Memorandum of Understanding as Between Kyoto University, Japan and the University of Melbourne, Australia
    Dates of an Agreement: 14 September, 2009
    Summary of an Agreement:
    Exchange of researchers and students, research collaboration, exchange of information

15. Counterpart of an Agreement: Vidyasirimedhi Institute of Science and Technology
    Name of an Agreement:
    Memorandum Of Understanding Between The Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University and the Executive Council of Vidyasirimedhi Institute of Science and Technology (VISTEC), Thailand
    Dates of an Agreement: 29 February 2016
    Summary of an Agreement:
    Exchange of researchers, administrative staff and students, research collaboration, joint symposium, exchange of information

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Appedex 4-6. Holding International Research Meetings

* For each fiscal year, indicate the number of international research conferences or symposiums held and give up to two examples of the most representative ones using the table below.

Date	Meeting title and Place held	Number of participants
February 20-22, 2008	1st iCeMS International Symposium /The 11th Membrane Research Forum Held at: Hotel Fujita Kyoto	136
June 22-27, 2008	2nd iCeMS International Symposium/The 8th International Conference on Excitonic Processes in Condensed Matter Held at: The Clock Tower, Kyoto University	191
January 27-29, 2009	3rd iCeMS International Symposium: Symposium on the MESO CONTROL of the cells, by the cells, for the cells -- featuring transportsomes Held at: Hotel Fujita Kyoto	173
May 27-29, 2009	4th iCeMS International Symposium: “Integrated Physical/Chemical Biologyof the Cell: from Genes to Membrane Systems” Held at: Hotel Fujita Kyoto	205
July 27-28, 2009	5th iCeMS International Symposium: Meso-Control of Functional Architectures “Biomaterials at the Interface of Chemistry, Physics, and Biology” Held at: The Clock Tower, Kyoto University	146
January 27-29, 2010	6th iCeMS International Symposium/ The Thirteenth Membrane Research Forum Held at: Hotel Fujita Kyoto	210
June 14, 2010	Kitagawa-iCeMS/ERATO (JST)–Yaghi CNSI Joint Symposium: Framework materials in the future: PCPs meet COFs & MOF Held at: UCLA, California	62
June 24, 2010	7th International Symposium: Emerging Approaches and Applications in Developmental Biology: Taking the Next Step Held at: The Clock Tower, Kyoto University	146
November 9-11, 2010	8th iCeMS International Symposium: Meso-Control of Functional Architectures Held at: Shiran Kaikan, Kyoto University	250
December 2-3, 2010	9th iCeMS International Symposium: Mesoscale Control and Engineering of Self-Organized and Excitable Systems in Biology and Chemistry Held at: iCeMS, Kyoto University	85
December 17, 2010	NCBS-inStem/iCeMS joint symposium Held at: iCeMS, Kyoto University	40
July 21-23, 2011	10th iCeMS International Symposium: “Crossing Boundaries: Stem Cells, Materials and Mesoscopic Sciences” Held at: Heidelberg University, Germany	296

Date	Meeting title and Place held	Number of participants
July 25, 2011	MRC-CRM and iCeMS Joint Symposium: “Next Generation Stem Cells: Tools and Technologies Symposium” Held at: Edinburgh University, UK	150
December 6, 2011	11th iCeMS International Symposium: “Chemical Control of Cells” Held at: Shiran Kaikan, Kyoto University	152
April 20-22, 2012	iCeMS-CLS Joint Symposium: Crossing Boundaries: Stem Cells, Materials, Mesoscopic Sciences and Beyond Held at: Peking University, China	236
November 8-9, 2012	12th iCeMS International Symposium/6th Annual Symposium on Nanobiotechnology “Kyoto Cell-Material Integration” Held at: Shiran Kaikan, Kyoto University	142
March 7-8, 2013	UK-Japan Workshop on Stem Cells "Building a Better Environment for Application" Held at: iCeMS, Kyoto University	49
March 18–19, 2013	13th iCeMS International Symposium/RSC-iCeMS Joint International Symposium “Cell-Material Integration and Biomaterials Science” Held at: Shiran Kaikan, Kyoto University	157
June 6-9, 2013	14th iCeMS International Symposium/CNRS-4WPI: 10th Japan-France Workshop on Nanomaterials Held at: iCeMS, Kyoto University	81
October 10-11, 2013	15th iCeMS International Symposium: UK-Japan Workshop on “Organic-Inorganic Framework Materials” Held at: iCeMS, Kyoto University	82
June 12-13, 2014	The 16th iCeMS International Symposium “Light Control in Cell Biology” Held at: iCeMS, Kyoto University	115
September 28 –October 1, 2014	The 17th iCeMS International Symposium“MOF2014: 4th International Conference on Metal Organic Frameworks and Open Framework Compounds” Held at: Kobe International Conference Center	705
March 2-4, 2015	The 18th iCeMS International Symposium “The 15th International Membrane Research Forum” Held at: iCeMS, Kyoto University	163
September 23-26, 2015	The 19th iCeMS International Symposium “Hierarchical Dynamics in Soft Materials and Biological Matter” Held at: Masukawa Hall and Graduate School of Science Bldg. No.6, Kyoto University	168
January 25, 2016	University of Bordeaux-Kyoto University Mini-Symposium on Biomolecular Science Held at: iCeMS, Kyoto University	46
March 21-22, 2016	The 20th iCeMS International Symposium “The 15th International Membrane Research Forum” Held at: Peterhouse, Cambridge	34

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Appedex 5-1. Host Institution's Commitment

1. Contributions from host institution

(1) Fund, Personnel

* Regarding "Fund" entry, describe with reference to the items in the Progress Report (Jisseki-hokoku-sho) based on Article 12 of the Grant Guidelines (Kofu-yoko).
* Don't include competitive funding obtained by researchers (used as research project funding)
* Under "Personnel", enter the number of full-time administrative staff within the parenthesis.

(2007-2012)

<Fund> **(million yen)**

Fiscal Year	2007	2008	2009	2010	2011	2012
Personnel	76	230	255	217	213	209
- Faculty members (including researchers)	52	164	148	152	142	139
Full-time	52	121	113	144	116	113
Concurrent	0	43	35	8	26	26
Postdocs	0	0	0	0	0	0
RA ect.	0	0	0	0	0	0
Research support staffs	0	2	16	6	6	5
Administrative staffs	24	64	91	59	65	65
Project activities	41	317	790	296	60	39
Travel	0	1	11	30	22	15
Equipment	65	370	1,525	68	8	21
Research projects	45	34	88	188	39	44
Total	227	952	2,669	799	342	328

<Personnel> **(person)**

Fiscal Year	2007	2008	2009	2010	2011	2012
Personnel	16	27	34	24	25	26
- Faculty members (including researchers)	8	18	17	12	13	15
Full-time	7	9	11	11	11	11
Concurrent	1	9	6	1	2	4
Postdocs	0	0	0	0	0	0
RA etc.	0	0	0	0	0	0
Research support staffs	0	1	10	3	3	3
Administrative staffs	8<8>	8<8>	7<7>	9<9>	9<9>	8<8>

(2013-2016)					
<Fund>					**(million yen)**
Fiscal Year	**2013**	**2014**	**2015**	**2016**	**Total**
Personnel	238	221	209	258	2126
- Faculty members (including researchers)	158	138	158	168	1419 0 0
Full-time	137	118	135	141	1190
Concurrent	21	20	23	27	229
Postdocs	0	0	0	0	0
RA ect.	0	0	0	0	0
Research support staffs	3	0	0	0	38 0
Administrative staffs	77	83	51	90	669 0
Project activities	97	141	52	162	1995
Travel	11	11	14	20	135
Equipment	86	85	0	30	2258
Research projects	39	48	92	59	676
Total	471	506	367	529	7190
<Personnel>					**(person)**
Fiscal Year	**2013**	**2014**	**2015**	**2016**	**Total**
Personnel	25	24	24	24	249
- Faculty members (including researchers)	16	16	16	16	147
Full-time	11	10	10	10	101
Concurrent	5	6	6	6	46
Postdocs	0	0	0	0	0
RA etc.	0	0	0	0	0
Research support staffs	1	0	0	0	21
Administrative staffs	8<8>	8<8>	8<8>	8<8>	81<81>

(2) Provision of land and/or building(s), lab space, etc.

1) Kyoto University provides a high-quality research environment with a total area of about 11,000 m^2 including exclusive-use facilities with fully equipped infrastructure.
2) Kyoto University built a new, iCeMS dedicated use research building with 3,000m^2 in 2010.

2. System under which the center's director is able to make substantive personnel and budget allocation decisions

(a) Strong directorship authorized

Except university overall management matters and appointment of the iCeMS Director, all of the top-down decision making is carried out by the Director.

The iCeMS director, for example, has authority over personnel affairs and salaries for program-specific research center faculty and researchers, as well as award amounts for an "iCeMS Incentive" program and the structure of the institute's internal organization.

The host institution, meanwhile, is responsible for the appointment of the iCeMS Director, the role of the institute within the university, the overall hiring structure for program-specific faculty and researchers, and the rules governing the awarding of incentives.

(b) Dense communication channel

A close relationship exists between the iCeMS and Kyoto University, with the center director frequently discussing important matters with the university president and the executive vice president for research.

(c) Membership of deans meeting

The director is a regular member of the university's Deans and Directors Meeting, the highest deliberative board of Kyoto University. This membership helps to raise the iCeMS' profile.

(d) Indirect costs

As a necessary financial measure for the center's operation, the university fully provides indirect costs associated with competitive grants to iCeMS.

(e) Personnel support

The university provides five positions and expenses for principal investigator-class personnel. For the administration, the university provides eight full-time administrative staff and necessary personnel expenses in order to establish an independent administrative organization.

(f) Financial support

Financial support by action plan until FY2013 (Total: JPY 709 million)

3. Support for the center director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments

(a) Support for researcher transfers to iCeMS

Six iCeMS PIs have been affiliated with departments where they had held positions prior to joining the institute. This dual affiliation system has allowed these PIs to continue taking part in a portion of these departments' research and graduate education programs, as well as allowing graduate students in these departments to participate in research taking place at the institute. In the case of moving faculty posts (primary affiliation) to iCeMS, some compensation money is specially allocated to the original departments.

(b) Support for faculty staff to participate in other departments

There are faculty members who are employed specifically by WPI iCeMS and not affiliated with other departments. One of their biggest problems is not being able to supervise graduate course students and participate in education. If approved by the departments, these faculty members will be allowed to do so as adjunct professors while concurrently doing research in iCeMS. This dual affiliation system contributes towards promoting collaborative, multidisciplinary research with other departments as well. Two PIs (Profs Kengaku and Harada) and one PI (Prof Motomu Tanaka) have dual affiliations with Graduate School of Biostudies and Graduate School of Science, respectively.

4. Revamping host institution's internal systems to allow introducing of new management methods

(e.g., English-language environment, merit-based pay, cross appointment, top-down decision making unfettered by conventional modes of operation)

(a) Establishing Kyoto University International Strategy (Approved on September 2013)

As globalization continues to advance at a rapid pace, Kyoto University has launched The **2x by 2020 Initiative** as its new international strategy to promote the further development of the university as a world-class institution of higher learning, and consolidate our global position as a World Premier University (WPU). 2x by 2020 is the slogan of the new International Strategy by which Kyoto University aims to double its international indices in research, education and international service by the year 2020.

(b) Kyoto University Global Academy (Approved on September 2013)

Global Academy is designed as one of the Kyoto University International Strategies to be a suite of innovative education and research programs and initiatives that seek to instill international competence in our students from the undergraduate level and expand our international cooperative research undertakings.

Kyoto University Global Academy covers a wide area from education to research, ranging from "Institute for Liberal Arts and Sciences" to foster practical international communication skills of young students to "International Center for Emerging Sciences" under which the present iCeMS will be designed to be one of its main institutes.

(c) Establishment of new educational organizations (started in April, 2013)

With the aim to cultivate global leaders and strengthen the university's level of education, the Graduate School of Advanced Integrated Studies in Human Survivability (Shishu-Kan) and the Institute for Liberal Arts and Studies were established in April, 2013.

In the Institute for Liberal Arts and Studies, more than one hundred of overseas faculty are employed as tenured staff to teach classes in English. These overseas faculty have dual-appointments with other graduate schools and research institutes where they are partially engaged in research. 10 bilingual administration staff are already allocated to graduate schools and institutes.

(d) Establishment of a new system for faculty management (approved on February, 2014)

All faculty members have traditionally had primary affiliations with a single educational or research organization, such as a graduate school or research institute. However, the inflexibility of this system has been the cause of delays, hampering efforts to establish new educational and research organizations or rebuild existing ones.

In order to overcome these difficulties, a new Faculty Management Organization is being implemented to act as the primary affiliation for all university teaching and research staff, from which they will be appointed as necessary to one or more department, research center, etc. All faculty will be expected to participate fully in undergraduate teaching. Peer evaluation and other personnel matters (including those related to organizational reforms) will be decided by designated committees within the new system.

This new faculty system will enable the post-WPI institute to dynamically bring top-level researchers together from across the university for the purposes of pursuing collaborative work and to discover new fields of endeavor.

(e) Reappointment of tenured positions (approved on July 2013)

150 reappointed tenured positions are to be established at the president's discretion over the course of 8 years starting in 2014, to be assigned strategically according to the achievements and future potential of applicable university organizations. After WPI finishes, iCeMS is requested to acquire some of these

positions competitively.

(f) Establishing cross appointment scheme and merit-based salary system (approved on March 2014)

Researchers can be employed by multiple organizations including Kyoto University, other universities and companies. In this scheme collaboration between the Kyoto University and industries will be further promoted. Merit-based annual salary-system will be partially introduced.

Abolishment of retirement age has been conducted in other institutes such as CiRA and Graduate School of Shishu-Kan and will be expanded to other organizations.

(g) Change of Kyoto University presidential selection scheme (approved on May 2014)

Until now The Kyoto University President is selected via voting by about 3,000 faculty members. Intensive discussions have been done on the presidential election scheme so far. This time the traditional scheme has been slightly modified by the presidential selection committee and its drastic change is left for further discussion.

5. Utilities and other infrastructure support provided by host institution.

(*In addition to listed in the item 1. Contributions from host institution)

6. Support for other types of assistance

(a) Featuring in University publications

Frequent introduction of iCeMS research activities through Kyoto University PR magazines. Given the iCeMS' mandate to fulfill a role as an international research hub, the university supports the institute's international publicity and linkage efforts via measures including the issuance of publications such as pamphlets and press releases.

(b) Exemption from administrative committees

There are a variety of administrative committees with the university in which researchers should participate. iCeMS members are exempted from participating in these routine committees to reduce their administrative burden and allow them to devote time to their research. iCeMS Director has a duty to attend to the university's Deans and Directors Meeting, being exempted from other administrative duties.

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Appedex 5-2. The Host Institution's Mid-term Plan

中期目標・中期計画一覧表

（法人番号　52）　（大学名）　京都大学

中　期　目　標	中　期　計　画
（前文）大学の基本的な目標	
京都大学は、国立大学法人化後 12 年間の取組を踏まえて、創立以来築いてきた自由の学風を継承・発展させつつ多元的な課題の解決に挑戦し、地球社会の調和ある共存に貢献するため、今後６年間に向けた決意として下記の目標を定める。 【研究】 ・未踏の知の領域を開拓してきた本学の伝統を踏まえ、研究の自由と自主を基礎に、高い倫理性を備えた先見的・独創的な研究活動により、次世代をリードする知の創造を行う。 ・総合大学として、研究の多様な発展と統合を図る。 【教育】 ・多様かつ調和のとれた教育体系のもと、対話を根幹とした自学自習を促し、卓越した知の継承と創造的精神の涵養に努める。 ・豊かな教養と人間性を備え、責任を重んじ、地球社会の調和ある共存に貢献し得る、優れた研究能力や高度の専門知識をもつ人材を育成する。 【社会との関係】 ・国民に開かれた大学として、地域をはじめとする国内社会との連携を強め、自由と調和に基づく知を社会に還元する。 ・世界に開かれた大学として、国際交流を深め、地球社会の調和ある共存に貢献する。 【運営】 ・学問の自由な発展に資するため、教育研究組織の自治を尊重しつつ、調和のとれた全学的組織運営を行う。	

（52　京都大学）

2　研究に関する目標	2　研究に関する目標を達成するための措置
本学が創立以来培ってきた自由の学風と、対話を根幹とした自学自習のもと、自主独立と創造の精神を涵養し、多元的な課題の解決に挑戦して、地球社会の調和ある共存に貢献すべく、基盤的研究を重視しつつ、先端的、独創的、学際的研究を推進する。これにより、世界を先導する国際的研究拠点機能を高めるほか、共同利用・共同研究拠点において、異分野融合・新分野創成に向けた取組等を推進する。	
（１）研究水準及び研究の成果等に関する目標	**（１）研究水準及び研究の成果等に関する目標を達成するための措置**
【16】学問の源流を支える基盤的研究を重視するとともに、先端的、独創的、学際的研究を推進して、世界を先導する国際的研究拠点機能を高める。	【20】基盤的研究環境の維持発展や、先端的、独創的、学際的研究の推進に向けて、全学的かつ戦略的なリサーチ・アドミニストレーター（URA）の組織体制を整備し、研究支援事業の強化を行う。
	【21】世界に冠たる研究を行っている世界トップレベル研究拠点（WPI 拠点）を核とした世界トップレベルの国際研究拠点として高等研究院を設置するとともに、iPS 細胞研究の裾野拡大や研究体制の強化に向けた取組の推進など、国際的研究拠点等の支援を行う。
【17】共同利用・共同研究拠点においては、学問領域の特性を生かしつつ、拠点の枠を超えた連携による異分野融合・新分野創成に向けた取組を推進するとともに、海外機関との連携や情報発信力を強化する。	【22】研究連携基盤内の未踏科学研究ユニットを活用し、異分野融合による新たな学術分野の創成を促進する取組を通じて、共同利用・共同研究拠点の運営基盤を確保しつつ組織間の連携強化を図り、研究力強化やグローバル化を推進する。
	【23】共同利用・共同研究拠点において、国際ネットワークを形成して国際共同研究や人材交流を推進するため、柔軟な人事制度や研究環境の整備を行う。また、拠点の活動実態や所属研究者の最新の動向に係る情報発信を国内外に向けて積極的に行う。

World Premier International Research Center Initiative (WPI)

Appedex 5-3. Transition in the Number of Female Researchers

* Enter the number and percentage of female researchers in the top of each space from 2010 to 2015 and the total number of all the researchers in the bottom.

(person)

	FY2010	FY2011	FY2012	FY2013	FY2014	FY2015	Final goal
Researchers	45, 25.9 %	48, 28.7%	41, 22.4%	51, 25.8%	42, 22.1%	37,21.3%	52, 26.0%
	174	167	183	198	190	174	200
Principal investigators	2, 11.1 %	2, 11.1 %	2, 10.5%	2, 1.1%	3, 12.0%	3, 12.0%	2, 10.0%
	18	18	19	18	25	25	20
Other researchers	43, 27.6 %	46, 30.9%	39, 23.8%	49, 27.2%	39, 23.6%	34, 22.8%	50, 27.8%
	156	149	164	180	165	149	180

World Premier International Research Center Initiative (WPI)
Progress Plan (For Final Evaluation)

Host Institution	Kyoto University	Host Institution Head	Juichi Yamagiwa
Research Center	Institute for Integrated Cell-Material Sciences (iCeMS)	Center Director	Susumu Kitagawa

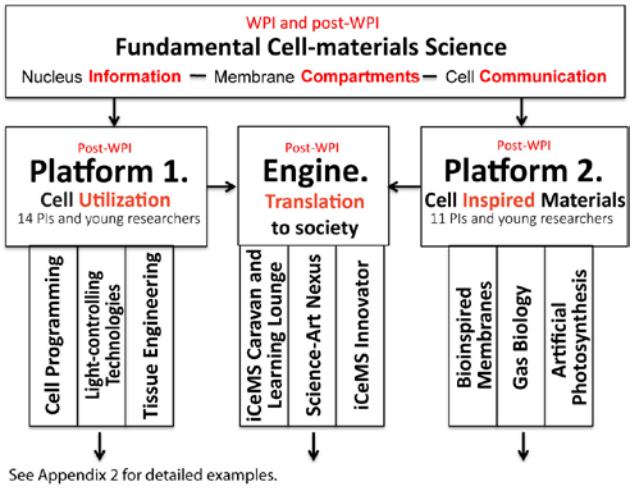
* Write your report **within 6 pages**.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

1. Mid- to Long-term Research Objectives and Strategies Based on the Center's Results during Funded Period

Describe new challenges in the Center's research objectives and plans after the funding period ends. If major adjustments will be made in the Center's operation, such as newly set research themes/objectives or a change in the director, describe the strategic background to the adjustments.

The WPI program at iCeMS was always about creating and spreading the creed of '**Global Awareness, Lateral Thinking, Iconoclastic actions'**. This core ideal of iCeMS must survive in the post-WPI era. iCeMS has been an island of creative free thought in science and administration for the last 10 years, providing a catalyst for innovative change in the rest of Kyoto University's administrative system. As the ocean devours the island by day and replenishes it by night, there is always a dynamic struggle to maintain newborn, fragile, ecosystems. To expand the island that is WPI-iCeMS so its principles are deeply embedded within Kyoto University and indeed throughout the fabric of Japanese Universities, we must continue to preserve this creed.

True integration of cell and material sciences should be bidirectional, making ground-breaking contributions to both cell biology and material sciences. In the first 7 years, iCeMS has focused on utilizing material science technology for cell biology. To accomplish the true integration of cell and material sciences, iCeMS has pursued two antiparallel challenges in the last 3 years: one for material science-enabled cell biology, and the other for cell-inspired material science.



However the common person in the world is not interested in how a heart beats, but instead worries about what can be done if their child's heart stops beating. This is the dichotomy of fundamental and applied science. One cannot overstate the importance of understanding the former to resolve the latter. In educating the world to this key characteristic of iCeMS, we enhance the possibility for future support for the key fundamental research in cell-materials science. It is important to establish a credible, visible, and well-communicated link between the fundamental and applied aspect of smart cell-inspired materials. Importantly the post-WPI phase of iCeMS must accomplish this in order to justify and encourage future sustainable financial support of the institute. We do this through two *platform* concepts of **Utilization** of cells, **Inspiration** to materials and through an *engine* for its **Translation** to society.

● Platform 1. Synthetic paradigms for cell programming and its utilization.

All living organisms are made up of various types of cells that are differentiated from embryonic stem cells. Cell Biology, globally, received a major injection of momentum with the ground-breaking discovery by one of iCeMS PIs, Shinya Yamanaka that four co-factors could be used to return cells to their pluripotent state. Since then, a new institute, CIRA, which first existed as a iCeMS funded center, is focussed on the clinical applications of iPS cells. Howevert iPS cells is only a small part of cell programming spectra, and major efforts in the fields of cell biology have been made toward understanding the molecular signals regulating cell differentiation and function and those orchestrating the cell-cell interactions in tissues. iCeMS, having pioneered such research

at its most fundamental level, will continue it by developing new materials chemistries and technologies to monitor and control differentiation of stem cells into functional cells and tissues.

iCeMS has already developed a number of seed technologies toward this challenging goal, including SAHA-PIP molecules that regulate specific gene expression, a unique gas-releasing material that activates signaling pathways, and a light illumination technology that permits precise spatiotemporal gene regulation. By combining and fine-tuning these technologies, iCeMS will boldly create chemically defined, effective methods to induce activation and differentiation of stem cells into functional cells, such as germ cells, cardiomyocytes, pancreatic β-cells, and neurons. iCeMS will also pursue the 3-dimensional reconstitution of tissues and organs of desired shape and size by developing novel synthetic assemblies. State-of-the-art development of cell-on-a-chip technology at iCeMS will allow realistic in-vitro early stage prescreening of the interaction between different cellular system and their synthetic programming switches. Special focus will be given to the reconstitution of stratified heart muscle, neural networks in the cortex, and tubular testis. Our approaches may prove useful for regenerating damaged tissues and treating diseases using endogenous dormant stem cells.

- **Platform 2. Breathing, cleansing and transformation through cell-inspired materials**

In particular we take on the cellular function of membrane compartments. Membrane compartments in living cells simultaneously "select" and "condense" molecules. Learning from sequential, integrated functions of cells in capturing, separating, transporting, storing, and transforming molecules. We will use this general Cell-Inspired theme to generate Smart Materials to achieve the equivalent of these membrane functionalities.

Organelles, cells and tissue work concertedly to cleanse or partition and transform. Consider the role of the lung in its interchange of oxygen and carbon dioxide. Or the kidneys that divert dangerous toxins away from the blood stream. There are a host of membrane protein functionalities that far exceed the capability of current synthetic membranes to do such things. To do so, they employ non-passive modes of transport energized by energy-loaded chemicals such as ATP. In this platform, synthetic membranes will be developed that have enhanced capacity, and specificity. We will be developing new materials that have the capacity to mimic the functions of lungs, kidneys, and other cellular systems that process important small molecules including such as carbon dioxide, oxygen, carbon monoxide, nitric oxide. In doing so we will build devices that have application in reducing CO2 in the air, significantly oxygenating the air that feeds car engines, fuel cells or power stations and creating artificial lungs and kidneys and cleaning the water that we drink. Alternatively, by using smart, light activated membrane transporters, we can trigger cellular responses within neuronal or gastrointestinal networks. Notably, whilst cellular membrane systems are capable of separating gases, the photosynthetic system is able to convert CO2 into a dense energetic form (such as glucose). In fact from an environmental point of view, this is far more preferable to the currently proposed methods of carbon capture and storage where CO2 is stored in underground geological formations. Within this platform we develop porous materials that not only concentrate CO2 but enable it transformation to a dense, transportable energetic chemical (such as methanol).

- **Translation Engine. A crucible for creativity.**

Translation is now a key concept in biological and medical sciences, reflecting the connectivity between laboratory and medical practice. However that concept of translation can be more broadly applied to the concept of risk and creativity in fundamental science and its development towards societal need. In Platform 1 and 2 we described some very crucial applications that can only be powered by breakthroughs in fundamental cell-material synergetic science. However, it is equally important to **translatively** educate the world to this activity. As we all know, the best education in creative life is through playfulness. Therefore we will engage our materials for simple yet effective solutions to global problems, and address them to an audience at the local, national and international level. A simple example of this is the iCeMS Garage developed by Dr. Furukawa, a venue for creative brainstorming on goal-oriented projects (for this and other examples see Appendix 1.2). We will continue to develop this environment of creativity and unfettered imagination for how simple adjustments at the fundamental level have striking impacts at the societal level. To make this most effective we will make full collaborations with the media and humanities schools in Kyoto University, inviting where necessary, professors to join iCeMS as adjunct members. There are numerous on-going examples where iCeMS has begun in the last

year, impactful, **translational** programs, where there is now the onset of quantifiable feedback (see examples of platform 3 in Appendix 1.2)

We believe that in coordinating the two platforms so, we will bring WPI-iCeMS to a much higher level of visibility than is often available to fundamental science *only* based research. This in turn will enhance the institute's capability to self-sustain itself in order to develop further broadly impactful fundamental breakthroughs in cell-materials science.

2. Management System of the Research Organization

2-1. Describe the Center's Research Organizational Management System that will Execute the Research Strategy and Plan Described above.

In Appendix 1, list the PIs who will ensure that the Center's project is sustained and advanced after the funding period ends. In Appendix 2, diagram the Center's organizational management system.

We have identified two challenging *platform* areas beyond the individual group's research interests The *engine* system of **translation** of such research, described above, will help to maintain focused, impact-oriented, progress in these platforms. Moreover, funding and personnel sustainability as well as future planning are invaluable to managing such systems effectively.

(a) Strengthen self-sustainability beyond WPI

To formulate a future research strategy and gain large-scale competitive funding, Kyoto University URA (KURA) was established in 2012, subsequently hiring nearly 46 new URAs. Acquisition of external funds will be critical to sustain iCeMS after the WPI program finishes. At present, iCeMS has obtained 1.38 times more funding from external sources compared with that received from the WPI budget. It is concomitant on iCeMS to increase its level of external funding massively to compensate the dramatic funding-gap will occur immediately POST-WPI program. Of course this fund-gap represents a severe challenge to the future identity of WPI-iCeMS. Funds, of any sort, inevitably come with conditions that alter the initial mandate of the WPI program. iCeMS is actively soliciting routes to at least maintaining its administrative sustainability, through institutional sponsorship, without removing the brand-name of WPI for small scale endowments.

Such an ambitious objective will not happen instantly. The essential fact is that WPI-iCeMS has reached science excellence but very poor visibility within an international setting. We are building more visible international links beyond the shores of Japan. For example following a visit by the Princess of Thailand in 2015, iCeMS will receive students in 2016, and a joint symposium with Kyoto University and the princess's flagship institute in Thailand, VISTEC, will occur in 2017. PTT Ltd. who is the chief financiers of VISTEC and Thailand's largest corporation are presently considered an endowed chair at WPI-iCeMS to enhance this relationship further.

Another program in development is the establishment of a satellite laboratory with CNRS, the French National funding federation. This is a major target to enhance the sustainability of funding international researcher in iCeMS. Although JSPS has set the example of accepting research proposal submission in English, this is a relatively minor component of the overall Japanese funding landscape. A singular asset of a WPI-iCeMS CNRS satellite laboratory is the empowerment of European researchers within WPI-iCeMS to apply for competitive European research funds such as ERS starter and advanced grants as well as participation in EU Horizon 2020 grants.

(b) Retaining Youth, Key Personnel and Reorganization of research groups

In the aftermath of the non-extension of the WPI program, there was an unsurprising apprehension for 'whats next'. Especially in the case of the young independent researchers, who came to iCeMS at the later stages of the WPI program. We recognized that these young researchers, who come to iCeMS, accepting the risks associated with non-tenure, are the real disciples of the iCeMS. They deserve the time to prove themselves and to demonstrate the impact of the iCeMS creed of **Globally Awareness, Lateral Thinking, Iconoclastic actions'**. The iCeMS directorate, with assistance from Kyoto University has already secured the immediate future of these researchers at iCeMS till 2020 (see Appendix 1). Thus faculty such as Drs. Hirori, Sugimura, Kamei, Ohtan, Carlton, Hasegawa, Fujishima, Sakaguchi are retained in FY2016. In addition two international researchers, Packwood (formerly of WPI-MANA), and Namasivayam

were engaged to iCeMS. Many of these researchers have received national awards, or prestigious young researcher funds such as the Sakigake program and several of these iCeMS young researchers will be promoted to PIs as Kyoto University prepares their posts.

In order to focus on more goal-oriented research described in 1., we will reorganize existing PIs as shown in Appendix 1. Five of the present PI's will be retired and Profs Kengaku, Kusumi, Ueda, Tanaka(M), Uesugi, Imahori, Kageyama, Saitou, Tanaka(K), Sugiyama will continue their research activities as senior PI's. We will employ world-renowned professors within Kyoto University as adjunct PIs (Prof Eisuke Nishida (Graduate School of Life Science), Prof Ryu Abe (Graduate School of Engineering). Moreover in FY2016, we have already invited applications for two world-renowned researchers as PIs with tenure position in the fields of chemical biology and cell biology. Finally, to actuate the third platform of **Translation**, it is important to invite as adjunct, professors from the school of arts and humanities such as Prof. Naoko Tosa who contributes an alternative way to generate an appreciation for the significant impact of cell materials science to the wider society.

(c) Quantum leaps to the future by Incubating Risk in Discovery and Development.

There is a significant chasm in the translation of fundamental cell-materials research; this occurs at the level between a fundamental observation and its development towards utilization. Traditionally risk averse, Japanese University-led Entrepreneurship culture is low and this tends to reduce the pathways to out-of-the-box, or serendipitous discoveries or even the development of early stage promising research. Whilst the obvious solution is a healthy IP and licensing activity, it is notable that a significant portion of University IP, across Japan, fails beyond the initial application stage. Even if successful to the PCT stage, its licensing by industry; the vehicle to reach society; is scarce. The common critique is that the fundamental work is too 'early-stage'. We are currently developing a broad program that will require the stake-holdership of various parties including the Kansai business community, local government and tech transfer offices of various, as well as the support of MEXT and METI to help incubate such early stage discoveries in cell materials science.

Historically iCeMS has an excellent track history for encouraging the translation from fundamentals to society. ReproCELL Inc was established through the entrepreneurship of Prof Nakatsuji and is listed in the 2014 JASDAQ Stock Exchange. Support for nurturing entrepreneur startups such as ReproCELL should be strengthened (refer to 2-6 of Progress Report). The spirit of entrepreneurship is continued at iCeMS through the activities of young researchers such as Hasegawa, Kamei and Sivaniah with direct interactions through licensing with start-up ventures. In the latter case, Prof. Sivaniah approaches the last year of a JST START program incubated within iCeMS to develop a membrane filtration start-up company in 2017.

2-2. Initiatives and Plans that will Impel System Reforms

Describe the Center's action plan that embodies the basic policies of the National University Reform Plan or Independent Administrative Agency Reform Plan, and the Center's plan and strategies that lead to host institution reforms either directly or via ripple effects (also to other institutions, if applicable). Describe also the Center's strategies for fostering and securing the next generation of researchers (e.g., introduction of tenure tracks), and the system for enhancing the Center's organizational management, such as the implementation/verification PDCA system.

(a) Center's action plan that embodies the national policies for research institutions

As described in the Progress Report, iCeMS has undertaken a variety of system reforms in terms of internationalization, research support and open collaboration with industries and management. Most of them are in anticipation of system reforms suggested by the MEXT **National University Reform Plan**. But iCeMS has to continue to promote further system reforms within iCeMS and broaden their reach to the rest of the university.

i. University-wide network for internationalization

Due to an overhaul in Kyoto University's administration reforms, iCeMS International Affairs and Planning Section has become a valuable resource to support and accelerate internationalization of the Graduate School of Advanced Integrated Studies in Human Survivability (*Shishu-Kan*) and the Foundation for Liberal Arts Studies, established in FY2013. In order to disseminate iCeMS wealth of experience in internationalization, far beyond iCeMS, to other graduate schools and institutions, we will establish a university-wide network which connects administration staff responsible for internationalization distributed individually to other graduate schools and institutes.

Moreover many of the international researchers who joined iCeMS during its ten year period are being incorporated into the broader University network and even promoted within the system. Prof. Sivaniah, who recently received promotion, also joins the Department of Molecular engineering as an associated faculty. He would be the 1st foreign full professor associated with Kyoto University's School of Chemistry in 40 years. Continued appointments such as those of Dr. Carlton and Dr. Wang, and new appointments such Dr. Namasivayam and Dr. Packwood, who was appointed as a tenured junior faculty demonstrates iCeMS and Kyoto University's continued commitment to internationalization.

ii. More merit-based personnel and salary system

A merit-based system has been employed since iCeMS was founded, yet special monetary incentives have only been offered to executive-level positions. As a first step towards providing an incentive for young researchers, the iCeMS Director Award for a Distinguished Researcher was established in FY 2013, which rewarded recipients with an additional bonus of JPY 300,000. Notably, the merit-based system should be modified on the basis of research outcomes. Recent winners include Dr. Kamei, Dr. Hirori and Dr. Furukawa, all of whom have either published at the highest levels, or won prestigious national awards. Naturally, all such recipients will continue at iCeMS, in positions of independent researchers till 2020.

(b) iCeMS plans and strategies that lead to host institution reforms either directly or via ripple effects (also to other institutions, if applicable).

As described in Appendix 5 (1-4) of the Progress Report, Kyoto University is making great efforts to embody the **National University Reform Plan**, a policy for independent administrative reforms. Since 2013 there are a variety of university reform initiatives planned swiftly under the leadership of Kyoto University President, including the establishment of a Kyoto University International Strategy, new educational organizations, new faculty management systems, cross appointment schemes, and culminating in establishing of the Institute for Advanced Study in 2016.

The framework for these initiatives has been laid out but will require several years to solidify. iCeMS has been at the forefront and served as the testbed for these system reforms. In fact, the new paradigm created by iCeMS has been highly evaluated and strongly influenced plans for Kyoto University reforms. (For details, refer to 5-2 and 5-3 of Progress Report). iCeMS will continue to make a great contribution to realizing these goals by advanced action plans given above (2-2(a)).

(c) iCeMS strategies for fostering and securing the next generation of researchers

Moreover, iCeMS has made a remarkable effort in FY2015 to retain the presence of nearly 10 young, potentially world-class, young researchers at iCeMS till 2020, in an environment where they would otherwise be snapped up by other institutes. Many of these came on the iCeMS Kyoto Fellows program, an initiative innovated by iCeMS several years ago and since copied across the WPI spectrum. By providing them with this vital breathing space within the supportive environment of iCeMS, it is expected these researchers will mature to fulfill their potential. These young researchers have been afforded significant start-up funding during the WPI period. Additionally efforts are made to link these young researchers to teaching opportunities within the university so that, time permitting, they can accrue the necessary experience for a future academic career.

3. Center's Position within Host Institution and Measures to Provide It Resources

Describe the Center's future plans with regard to the following points after the funding period ends.

3-1. From a Mid- to Long-term Perspective, the Position of the Center within the Organization of the Host Institution

Describe where the Center will be placed within the host institution's overall organizational strategy under the leadership of the institution's president. In Appendix 3, diagram the Center's position within the organization of the host institution, and describe that positioning using excerpts from the institution's mid- to long-term plan. If the plan has not been established yet, describe the consideration being given to the Center's positioning.

(a) Establishing the Institute for Advanced Study

The incumbent President of Kyoto University, Juichi Yamagiwa formulated the *WINDOW* concept as a vision for the future. IAS is directly cited within WINDOW's 2nd Strategic Priority 2-2 of

being *'International and Innovative'* as follows. "*We will establish a World Premier International Research Center (WPI Research Center) as a hub of front-line research at Kyoto University. Through the center, tentatively named the Kyoto University Institute for Advanced Study we aim to facilitate the advancement of cutting-edge research that capitalizes on Kyoto University's particular strengths, cultivate the next generation of research professionals, and circulate outstanding research talent both within Japan and overseas*". The Institute for Advanced Research (IAS) was officially established on April 2016 following university wide consultation to ensure acceptance of the principles of IAS in the future. In FY2016, IAS sits in a parallel capacity to iCeMS and is establishing its administrative system. iCeMS will join on April 2017 as the main institute of IAS.

(b) A future blueprint of Kyoto University reforms affecting the iCeMS beyond WPI

In order to attain the aims of the university's second mid-term goal period, a variety of university-wide reforms of education and research have been undertaken. The following two items will strongly affect the iCeMS beyond WPI program (For details refer to Appendix 4, Strategy and action plan for allocating personnel and space).

1. Establishment of a new system for faculty management (start on April, 2016)

A new Faculty Management Organization is being implemented to act as the primary affiliation for all university teaching and research staff, from which they will be appointed as necessary to one or more departments, research centers, etc. This new faculty system will enable the post-WPI institute to dynamically bring top-level researchers together from across the university for the purpose of pursuing collaborative work and to discover new fields of endeavor.

2. Reappointment of tenured positions (approved on July 2013)

150 reappointed tenured positions are to be established at the president's discretion over the course of 8 years starting in 2014, to be assigned strategically according to the achievements and future potential of applicable university organizations. After WPI finishes, iCeMS is competitively applying for some of these positions.

3-2. Host Institution Action Plan for Sustaining and Advancing the Center as a World Premier International Research Center (e.g., positioning, financial resources)

Support by the host institution after WPI funding ends:

1. As a necessary financial measure for the iCeMS' operation, the university provides indirect costs associated with competitive grants to iCeMS.

2. The university provides five positions and expenses for principal investigator-class personnel; moreover the university provides eight full-time administrative staff and necessary personnel expenses in order to establish an independent administrative organization. As indicated earlier, there is a constant dynamic between the 'old and established' system of administration in Kyoto University and the 'new and ground-breaking' systems introduced by WPI-iCeMS. Efforts to maintain these new systems are crucial to preserving the ambition of the WPI program. Kyoto University will guarantee the independence of WPI-iCeMS within IAS to administrate its internal affairs, its research strategy and its brand development.

3. The university will provide 10 positions for tenure track researchers and 5 oversea researchers with tenure position within the coming 5 years. At present the university already allocated 6 tenure-track researchers and 2 overseas researchers, which iCeMS has swiftly filled. This is in recognition of the inevitable vulnerable state that these elite young researchers are at. iCeMS can best sustain itself through the enthusiasm, energy, and imagination of its youth. Therefore iCeMS has already begun to retain the best of this talent before they are snatched by disparate universities and their collective enthusiasm for the iCeMS philosophy is dissipated.

4. Aiming to maintain a world-class institute with global visibility, the university provides a high-quality research environment with a total area of about 11,000 square meter including exclusive-use facilities with a fully equipped infrastructure. Moreover the university will support expenses such as administrative personnel cost and maintenance cost for large-scale equipment.

World Premier International Research Center Initiative (WPI)

Appendix 2. Diagram of Center Management System

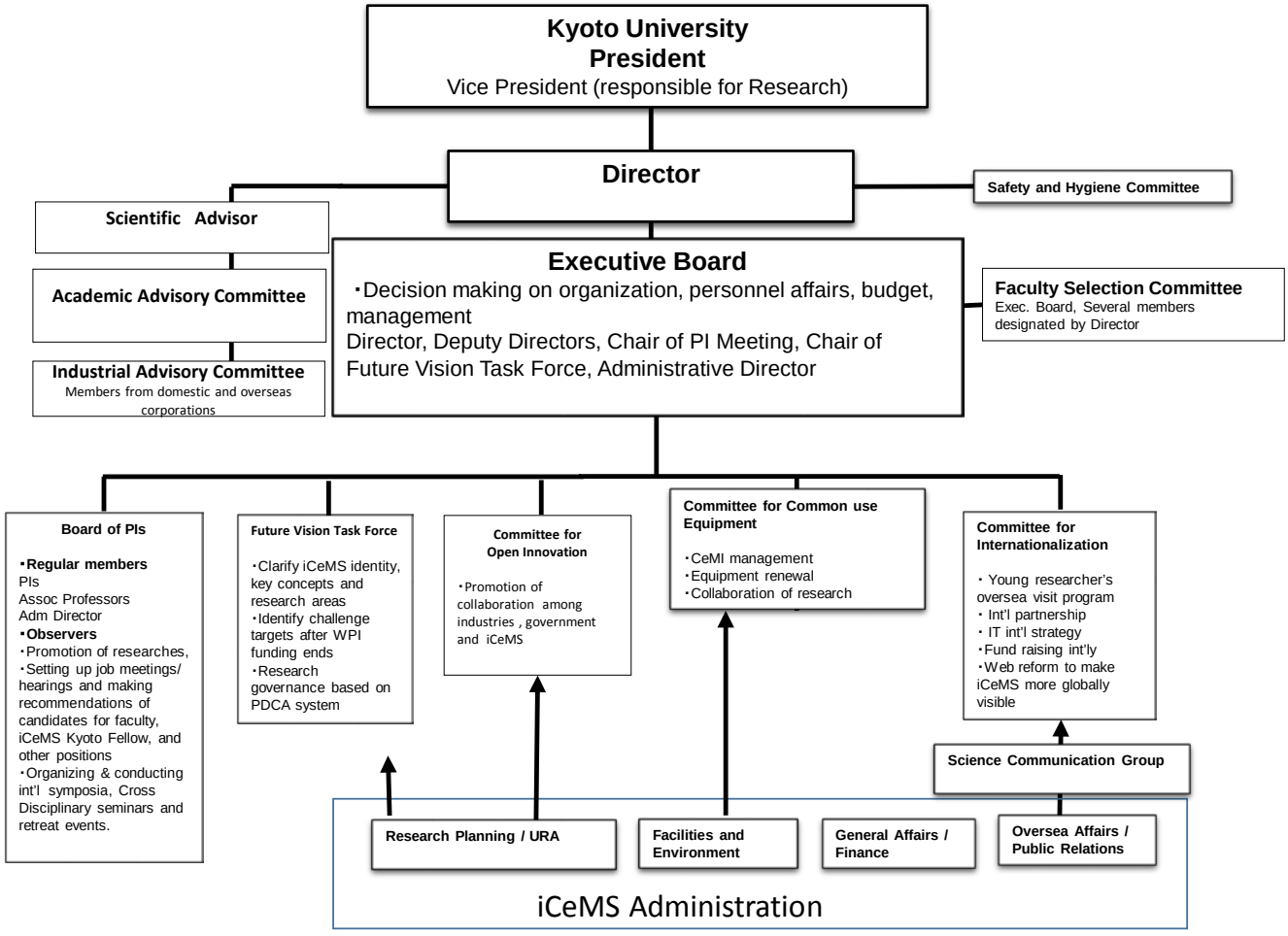
1. Executive board

The board consists of the Director, two Deputy Directors, Chair of PI Meeting ,Chair of Future Vision Task Force and Admin Director. Meetings are held twice a month, and the Director makes top-down decisions on matters related to personnel affairs, budget and other management issues.

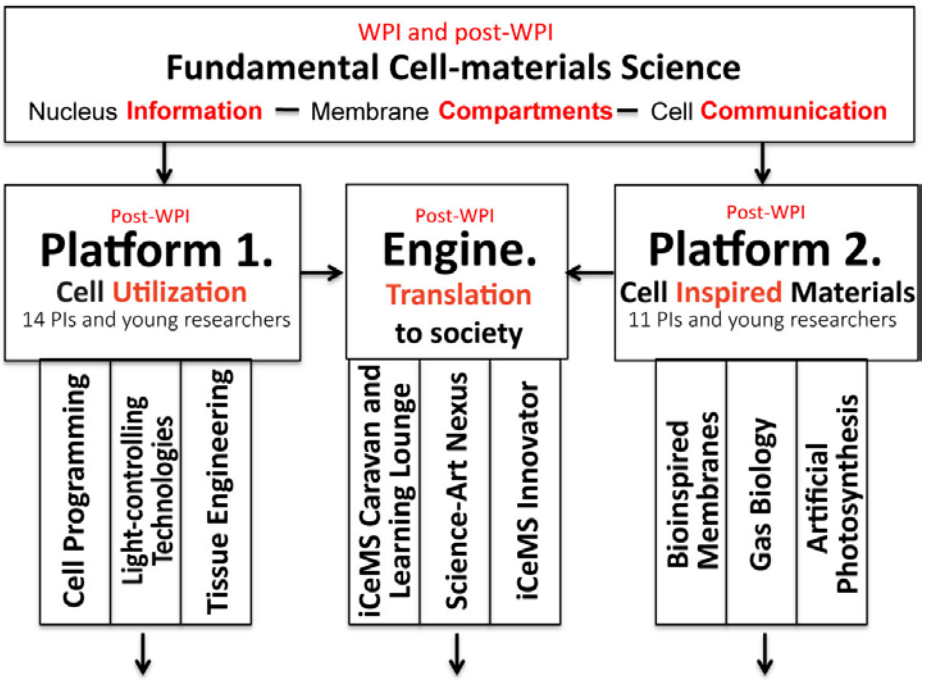
2. Board of PIs

The board consists of PIs and Associate Professors. PI meetings are held monthly to share important management information with the Executive board and to set up job seminars and make recommendations of candidates for faculty and other positions.

3. Committee for research governance



4. Distribution of researchers for future activity platforms



Examples **of Platform 1.**

Cell Programming. iCeMS has already developed a number of seed technologies toward this challenging goal, including SAHA-PIP molecules that regulate specific gene expression, a unique gas-releasing material that activates signaling pathways, and a light illumination technology that permits precise spatiotemporal gene regulation. By combining and fine-tuning these technologies, iCeMS will boldly create chemically defined, effective methods to induce activation and differentiation of stem cells into functional cells, such as germ cells, cardiomyocytes, pancreatic β-cells, and neurons.

Light-controlling Technologies. Rapid advances of light microscopy and light-switchable technologies have revolutionized the way of monitoring and affecting cell behaviors. For example, iCeMS boasts some of the best facilities in the world to carry such research out, including the world's fastest camera operating at the single protein length scale. iCeMS will pursue effective schemes for gene expression control by light-inducible transcription, cell excitability control by charge-separation molecules, and therapeutic application of MOF to intestinal diseases by controlling smooth muscle contraction.

Tissue Engineering. iCeMS will also pursue the 3-dimensional reconstitution of tissues and organs of desired shape and size by developing novel synthetic assemblies. State-of-the-art development of cell-on-a-chip technology at iCeMS will allow realistic in-vitro early stage prescreening of the interaction between different cellular system and their synthetic programming switches. Special focus will be given to the reconstitution of stratified heart muscle, neural networks in the cortex, and tubular testis. Our approaches may prove useful for regenerating damaged tissues and treating diseases using endogenous dormant stem cells.

Examples of **Platform 2.**

Bioinspired Membranes. Synthetic membranes tend to be passive materials, often with randomly distributed pores of an uncontrolled architecture. Biological membranes are anything but this, and have functionality and architectures that generate specificity and higher levels of efficiency. This comes at a cost of stability, within a narrow space of operating parameters. In this area, we seek to create the best of both worlds, combining longevity of synthetic chemistry with the evolved architecture of proteinaceous membrane pores for application in fields as diverse as carbon capture, clean water, and artificial organs.

Gas-Biology. Nitric oxide or carbon monoxide, known to be toxic, has been recently recognized to be significant signaling molecules and related to several important diseases. The current biological approaches activate and inhibit enzymatic activities for gas production but have a lack of spatiotemporal control. We will develop cell-inspired porous materials that produce these gas molecules by physical stimuli such as light, magnetic fields, and ultrasounds and that control signaling pathways, in particular, towards applications in gastrointestinal diseases, and cardiovascular disorders.

Artificial Photosynthesis. Plants fix carbon dioxide with the aid of sunlight. In this process, carbon dioxide is effectively captured and reduced to useful carbon sources for the production of amino acids or sugars. Biological system efficiently implements these sequential reactions by taking advantages of membranes that isolate and orchestrate distinct chemical reactions (light harvesting, energy transfer and chemical reduction). Here we utilize porous materials as artificial compartmentalization not only to effectively capture carbon dioxide but also to realize such sequential and controlled chemical reactions. The artificial carbon fixation will contribute to the environmental issue, for instance, the decrease of carbon dioxides as well as energy related issues such as a production of new carbon materials from air (alchemy of air).

5. Examples of Translation Engines.

iCeMS Innovation Incubator. iCeMS Garage is an initiative within the iCeMS Innovation Incubator where young undergraduates are mentored within iCeMS to come up with genius ideas, under the simple rule that there are no rules. Interested students are challenged to develop a novel concept, with brainstorming support of iCeMS PIs. They are then encouraged to evolve and evaluate their concept, with a weekly review from experts in materials, biology, physics and chemistry. Moreover they are pushed to build bridges for other contributions in Kyoto such as design or business advice. Such ideas resonate with the public awareness of common realities and connects such awareness to creative approaches to designed science and technology.

iCeMS Caravan. iCeMS Caravan is a collective effort by young iCeMS researchers to spread an awareness of their research efforts beyond the normal reaches of scientific PR. For example, a group of young PIs and researchers, led by Dr. Katsuda of the Uesugi laboratory went in April 2016 to the remote island of Goto in the west of Japan to explain “the mechanism (karakuri) of study” emerged from their interdisciplinary research approaches and to motivate young students in high-schools to aware what the background of study is. The visit is entirely funded by sponsorship, and has received coverage from the local Nagasaki NHK affiliate, with hopes of the program being distributed nationwide. The program has already resulted in small donations to the iCeMS fund, reflecting the start of iCeMS strategy to generate a nationwide grass-roots support for iCeMS long-term sustainability.

iCeMS Learning Lounge. iCeMS developed a ground breaking lecture series, which requires researchers to explain their science at a level that the non-specialist, intelligent but non-scientific research can understand. These presentations, filmed with assistance from the media school, are available online as part of Kyoto University’s open courseware and have received international viewership. Such promotion will be a key component of realizing the global visibility required to support iCeMS’s long term independence.

iCeMS Art-Science Nexus. "One in Every Home" series, a project managed by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) marks its tenth anniversary since its first release of posters to raise public engagement of science, and also to increase their understanding and literacy of science and technology. "I hope children who see this poster will grow up to be scientists, and develop new medicines for incurable diseases" said Prof. Uesugi. Naoko Tosa, a professor for Media Studies "[this poster] can possibly change the outlook of those who dislike chemistry like me."

World Premier International Research Center Initiative (WPI)

Appendix 3. Position of the Center within Host Institution

* Diagram the Center's position within the organization of the host institution, and describe that positioning using excerpts from the institution's mid- to long-term plan. If the plan has not been established yet, describe the consideration being given to the Center's positioning.

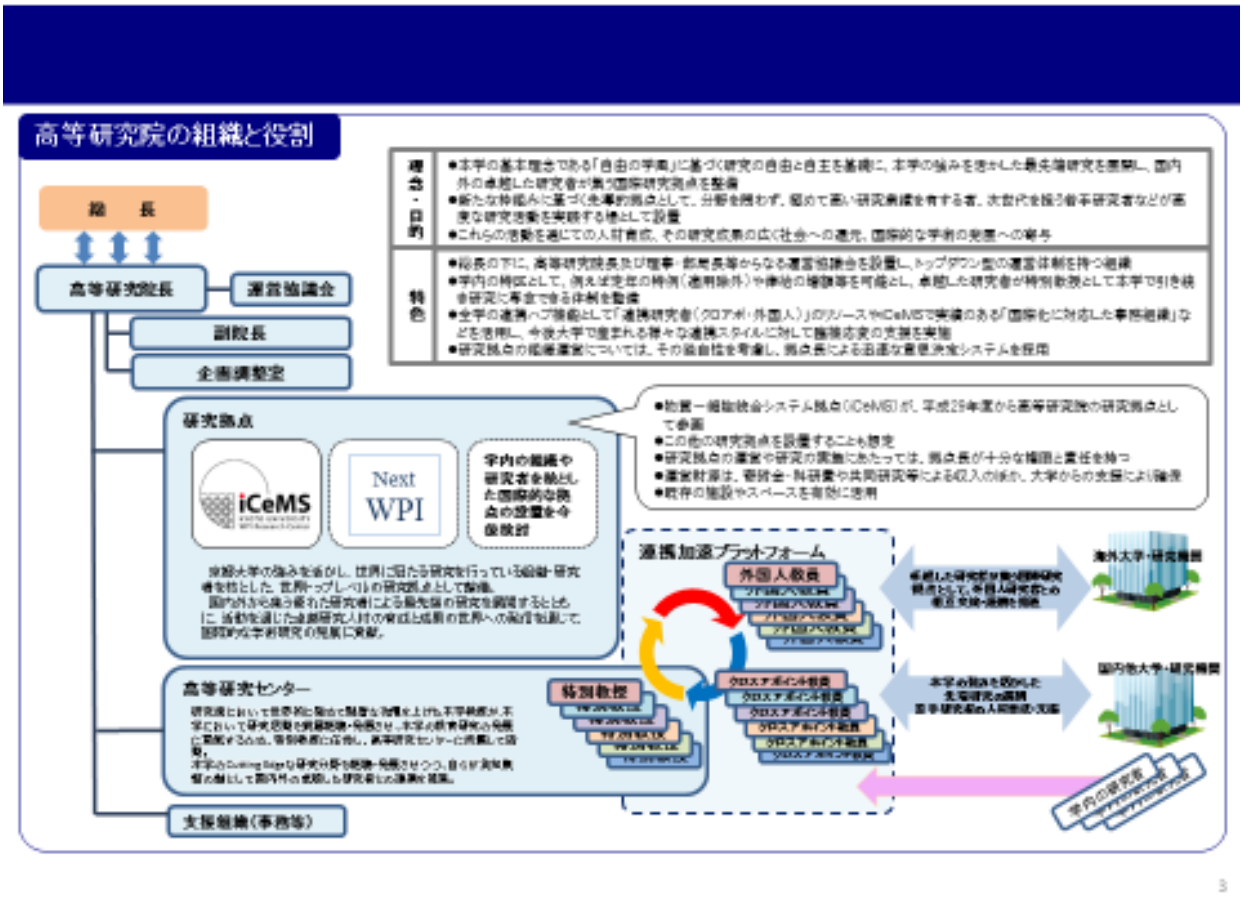
(a) Establishment of Institute for Advanced Study

Kyoto University stated a new institution called Institute for Advanced Research (IAS) on April 2016. The management principles of the IAS are as follows:

- Serve as a global center of excellence where world-renowned scholars can join for collaborative research
- Act as a global hub to promote world-class research and investigate proto-sciences
- Provide an environment where select, talented Kyoto University scientists can devote time to their research interests and where young, promising researchers are nurtured
- Exist under the university president's leadership in order to act as a sustainable testbed for implementing university reforms and to apply them university-wide

The iCeMS will join the IAS on April 2017 as the main institute of the new center after WPI funding ends.

Some parts of the documents distributed at press release on March 8 2016 to announce the establishment of IAS are shown below.



(b) Support by the host institution after WPI funding ends

To secure resources for iCeMS' operation and research activities, Kyoto University is taking the following measures:

1. As a necessary financial measure for the iCeMS' operation, the university fully provides indirect costs associated with competitive grants to iCeMS.
2. The university provides five positions and expenses for principal investigator-class personnel.
3. For the administration, the university provides eight full-time administrative staff and necessary personnel expenses in order to establish an independent administrative organization.
4. The university will provide 10 Posdoc's (tenure track researchers) and 5 oversea researchers with tenure position within the coming 5 years. At present the university has already allocated 6 Posdoc's and 2 oversea researchers.
5. Aiming to maintain a world-class institute with global visibility, the university provides a high-quality research environment with a total area of about 11,000 m^2 including exclusive-use facilities with a fully equipped infrastructure.
6. The university will support expenses such as administrative personnel cost and maintenance cost for large-scale equipment.

These supports were clearly stated by the President at Program Committee Meeting held October 16, 2015. The slide used by the President is shown below.

KU support after WPI funding ends

JPN 1 million

	Funding	Current Budget at iCeMS	Starting Budget for iCeMS after WPI Funding ends	
			Matsumoto plan	Yamagiwa plan
Operational budget	WPI funding	1,304	0	0
	University support breakdown	1,260	→1,683	→2,043
		breakdown	breakdown	breakdown
	• Kyoto U tenured positions	(5 ppl) 72	(5 ppl) 75	(5 ppl) 75
	• Kyoto U adjunct faculty	(7 ppl) 80	(30 ppl) 350	(30 ppl) 350
	• Young researchers	0	0	(10 ppl) 100
	• Overseas researchers	0	0	(5ppl) 100
	• Administrative staff	(8 ppl) 67	(8 ppl) 70	(8 ppl) 70
	• Others	26	*246	*246
	• Indirect funds	208	160	320
	• Building depreciation	124	99	99
	• Land price (3,227m^2)	683	683	683
	Competitive direct fund	1,516	1,761	1,761
	Budge grand total	4,080	3,444	3,804

Researchers	Numbers			
		146	→ 91	→ 106

*Others: administrative fees (50); facility maintenance fees (108); utility fees (26); miscellaneous (62)

World Premier International Research Center Initiative (WPI)

Appendix 4. Resource Allocation Plan for Sustaining and Advancing the WPI Center

Annual Plans (FY 2017 – FY 2021)

<Fund > **(million Yen)**

Fiscal Year	29	30	31	32	33
- WPI grant	- (※)	- (※)	- (※)	- (※)	- (※)
- Funding from host institution	1,721.6	1,801.9	1,882.3	1,962.7	2,043.0
(details)					
Personnel	620.0	653.7	707.5	763.3	821.0
Project activities	924.7	959.1	970.2	982.2	994.9
Travel	4.3	7.5	10.7	13.8	17.1
Equipment	84.6	91.6	99.9	105.4	108.0
Other research projects	88.0	90.0	94.0	98.0	102.0
Costs of Satellites	0	0	0	0	0
- Funding from external sources	1,565.0	1,614.0	1,663.0	1,712.0	1,761.0
Total	3,286.6	3,415.9	3,545.3	3,674.7	3,804.0

<Personnel> **(person)**

Fiscal Year	2017	2018	2019	2020	2021
- Personnel resources from host institution	**189**	**190**	**192**	**194**	**196**
- Faculty members (including researchers)	**49**	**50**	**52**	**52**	**56**
Full-time	19	20	22	24	26
Concurrent	30	30	30	30	30
- Postdocs	50	50	50	50	50
- RA etc.	0	0	0	0	0
- Research support staffs	70	70	70	70	70
- Administrative staffs	**20**	**20**	**20**	**20**	**20**

(*) Do not include expected grant.

- When entering amounts, round down numbers to the first decimal.
- When funding is stated in a range between two amounts, explain the reason for the lower and upper amounts and fluctuations between them.

< Measures to be implemented from FY 2017>

- Strategy and action plan for allocating personnel (posts) , space, and others measures required for the Centers' Progress.

- Strategy and action plan for acquiring external funding

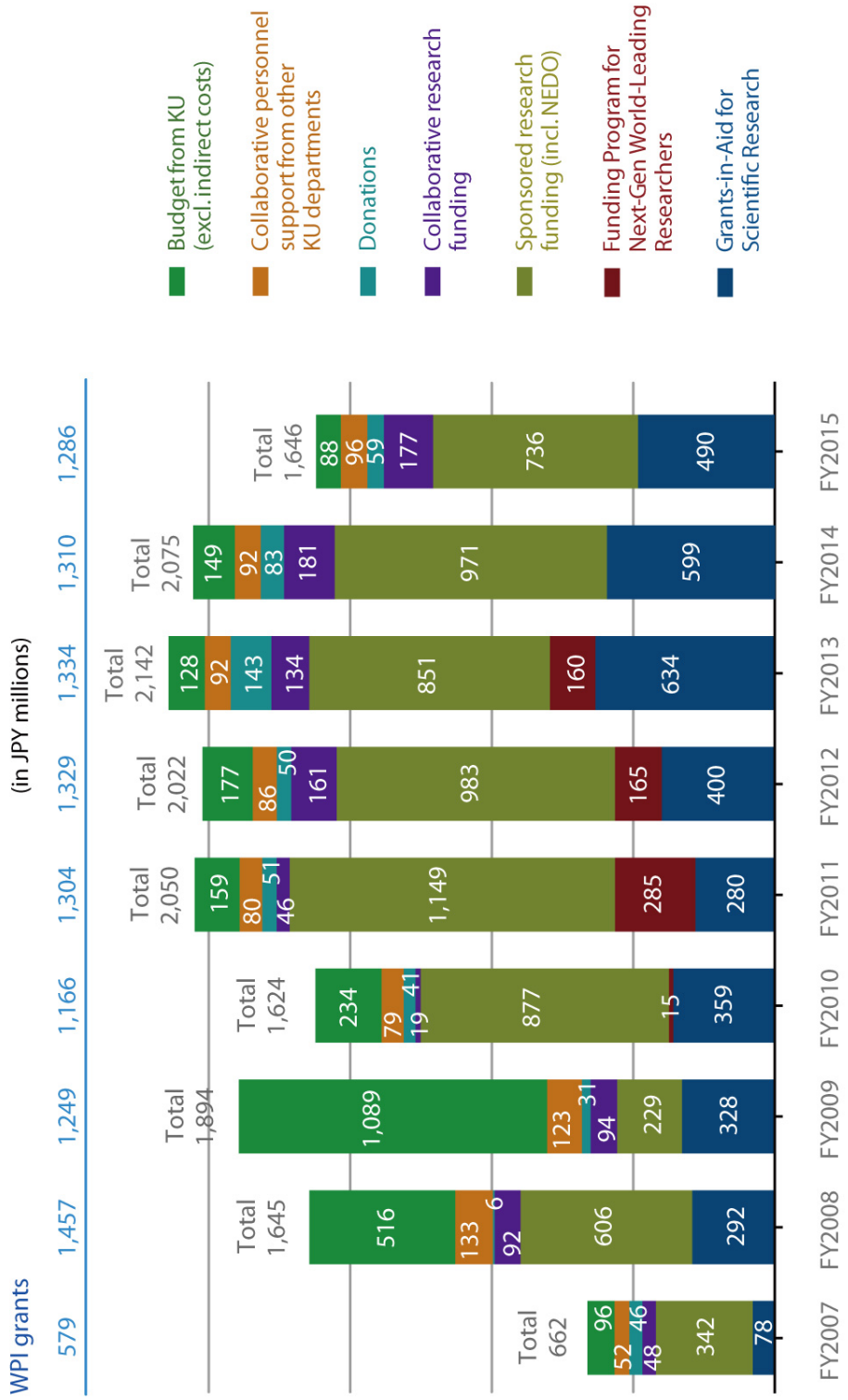
Kyoto University URA (KURA) was established in FY2012 and now consists of 46 members including four senior level managers. KURA will support iCeMS as follows:

1. Acquisition of external funds

As shown in Fig A4-1, iCeMS acquired 1.38 times more funding from external sources compared with that from WPI for the past three years. However, this amount is still insufficient for iCeMS sustainability because indirect funds, used freely as part of iCeMS general budget, are needed. The indirect fund was about JPY 300 million/years compared with the direct fund JPY 2,000 million. Indirect funds are used for hiring researchers (such as proto-scientists) marginally related to main research fields performed by the direct funds and for supporting basic infrastructure such as administration support. In order to further raise the overall budget amount, KURA will support iCeMS in cooperation with the Research Panning Section and Industrial Advisory Board. Acquisition of external funds from overseas is now considered. One examples are coordination with CNRS-UMI and and VISTEC in Thailand.

Fig. A4-1 Acquisition of external funds

Finance



2. Acquisition of patents and collaboration with industries

Fig. A4-2 Acquisition of patents

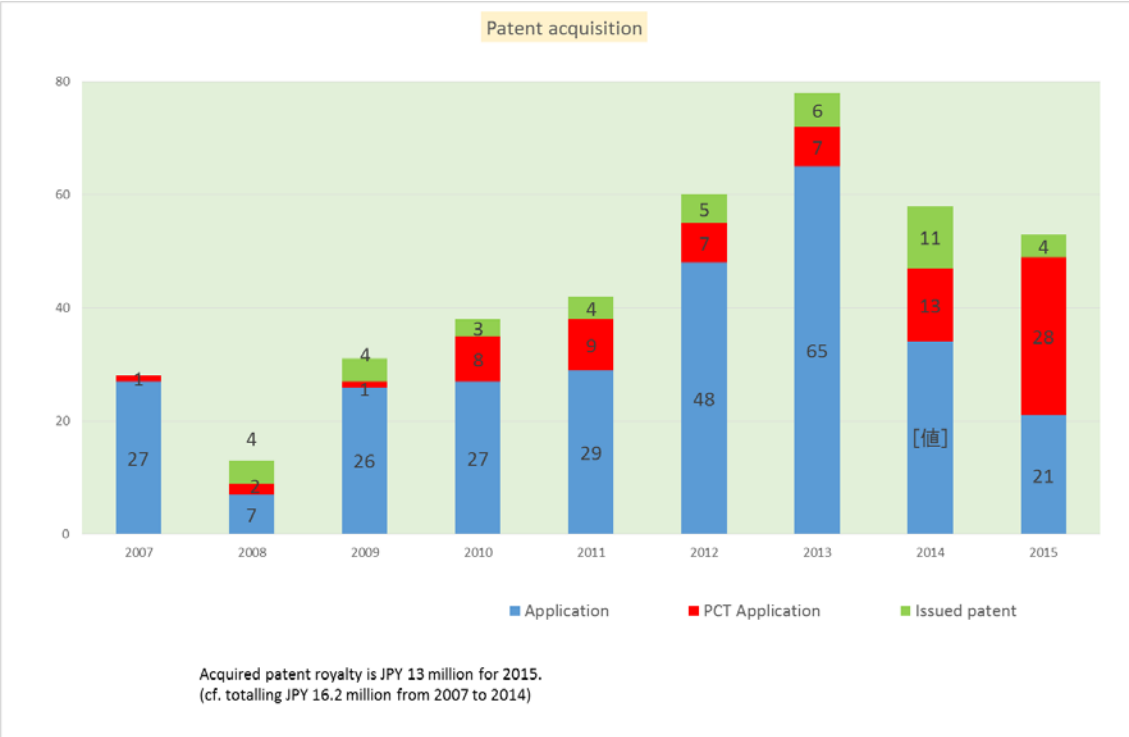


Fig. A4-2 shows the present status of patent acquisition at iCeMS. Patent applications have been submitted, but acquired patent royalty is relatively low (totaling JPY 29.2 million from 2007 to 2015). KURA will support the issuance of patents and acquirement of patent royalties.