

3. Research Center Project (in English)

Host institution	Kyoto University
Head of host institution	Hiroshi Matsumoto, PhD
Research center	Institute for Integrated Cell-Material Sciences (iCeMS)
Center director	Norio Nakatsuji, PhD
Chief center-project officer(in October 2007)	Norio Nakatsuji, Ph. D. Director, Institute for Frontier Medical Sciences, Kyoto University
Project summary	<p>• Briefly describe the general plan of the project.</p> <p><u>1. Original research objectives in 2007 and progress to date</u></p> <p>This proposal is a response to the government initiative to found world-premier research institutes to explore <i>interdisciplinary fields</i>, which will be placed within the <i>global career-development flow</i> of young scientists. We will accumulate a <i>critical mass of leading scientists for the symbiotic integration of material and cell sciences</i> (focusing on stem cells), based on the notion that <i>the fundamental understanding and control of molecular complexes in the meso-scale of 10-100 nm is critical for creating the science and technology of the next generation.</i> Namely, the science directions of this Institute were conceived based on the two key concepts: MESO-SPACE and STEM CELLS. For the fundamental understanding and application of the mesoscopic molecular events occurring throughout the science world, cross-disciplinary approaches are essential.</p> <p>For its first five years, the iCeMS has achieved outstanding results in stem cell biology, cell biology, chemistry, materials science, and physics, resulting in 464 papers, 59 of which in leading journals with an impact factor (IF) of 10 or more.</p> <p>Most notably: 1) Reprogramming and iPS cell research with papers in <i>Nature</i>, <i>Cell</i>, etc and 2) Functional porous materials research with 7 papers in <i>Nature</i> journals, 11 in <i>Angew Chem Int Ed</i> (IF: 11.8, the highest impact factor in the field except review journals), etc.</p> <p>Key multidisciplinary publications include: 1) new probes and control of stem cells with chemical compounds (<i>Angew Chem Int Ed</i> 2011, <i>JACS</i> 2009), and 2) real-time visualization and investigation of bio-functional molecules with DNA-origami engineering and AFM (<i>Nature Nanotechnology</i> 2011, <i>Angew Chem Int Ed</i> 2010).</p> <p><u>2. Clarified research objectives and plan for the next five years</u></p> <p>Previously, the iCeMS' key concepts have been criticized as being too broad and too ambiguous. This was mainly due to persistent emphasis of the term "meso" to describe the iCeMS' research domains, apparently giving the impression that this was the main direction of all of the research taking place at the iCeMS.</p> <p>We wish to clarify that the iCeMS' goal, as indicated by its name, is <u>to create new cross-disciplinary fields through the integration of cell and material sciences</u> with a focus on <i>stem cell science and technology</i> and <i>mesoscopic science and technology</i>, bringing about innovations in medicine, pharmaceuticals, the environment, and industry.</p> <p>Also, the interim evaluation report states that "Scientific results are outstanding, at least in iPS cell research, functional porous structures, new</p>

probes and control of stem cells. However, there are still a few visible interacting studies between cells and materials.”

It is therefore our aim to employ a variety of strategies to further accelerate the integration of cells and materials. These strategies are described in the following chapters of this proposal.

3. Organizational reform

a. Overview

The center is managed as a **future-model-institute** at Kyoto University and in Japan, including the creation of new **iCeMS Kyoto Fellow** (independent junior PI) positions. The institute is free from many binding rules of the Japanese university archetype, and flexible rules are employed. It has minimal hierarchical layers. English is used on all occasions, including in written documents. Major decisions are made by the center director with the aid of the Executive Board of the institute, consisting of the director, the deputy director, the chair of the Board of PIs, and the administrative director. The director reports directly to the university president and the Executive Board of Kyoto University.

One satellite laboratory has been established at Gifu University, where the first-class synthetic glycosylation chemistry lab of Prof. Makoto Kiso is located. This laboratory will continue to function as an iCeMS satellite.

Thirteen collaboration partners around the globe help accelerate the flow of researchers and also advance this multi-disciplinary research field. From FY2012, we will enter a second phase in which it will be necessary to reach higher benchmarks in areas such as joint research paper publication in high quality journals, and more frequent long-term exchanges of young researchers. In order to attain these goals, we will prioritize and weight the allocation of personnel and financial resources to partner institutions.

b. Unique support of administration by research groups

The Science Communication Group (SCG), established in 2007, continues to implement numerous outreach efforts such as science cafés, hands-on stem cell classrooms, hands-on exhibitions at science festivals hosted by the Cabinet Office, and lectures for middle and high school students.

The Innovation Management Group (IMG): forging alliances in academia, industry, government, and with overseas institutions. Established in FY 2009, the IMG continues to handle cross-sector and overseas linkages both as a subject of academic study, as well as putting theory into practice by undertaking the management of the institute’s external relations.

c. A variety of other organizational reforms

The iCeMS has realized a variety of other reforms as shown below and will continue further to become a truly international research hub.

1) Environment to interact across boundaries

- Shared labs and open offices
- Weekly joint lab meetings
- 43 cross-disciplinary seminars held at PI meetings
- Annual retreats: 80 (2009), 121 (2010), 152 (2011) participants
- Cross-disciplinary journal club on cell-material integration and mesoscopic sciences

2) Incentives to encourage collaboration across boundaries

- iCeMS exploratory cross-disciplinary grants supported:
 - 13 (2009), 29 (2010), 41 (2011) joint projects within iCeMS
 - 19 (2010), 15 (2011) joint projects with other Kyoto Univ departments

3) Internationalization

- English is the official language
- High ratio of overseas researchers (30% or more)

- High ratio of bilingual administrative staff (50% or more)
- Overseas researchers support office

4. Collaboration with the Center for iPS Cell Research and Application (CiRA)

The relationship between iCeMS and CiRA has been one of the important issues at Program Committee meetings in terms of organizational differentiation of the two institutions. After a variety of discussions, the relationship of the two institutions is as follows:

- The CiRA was officially established on April 1, 2010, enabling it to freely develop clinical applications while maintaining its basic research arm within the iCeMS. Namely, Prof **Yamanaka** continues his basic research on iPS cells as one of the iCeMS PIs while concurrently managing the CiRA as its director. Overall, the iCeMS and the CiRA collaborate closely as sister institutes.
- At present, there are six Yamanaka Lab researchers affiliated with the iCeMS. They are simultaneously employed as adjunct researchers at the CiRA. Of four research divisions at the CiRA, the Division of Reprogramming Science includes these six iCeMS researchers (together with five others fully employed by the CiRA). Their dual affiliations are differentiated in that their iCeMS work is related to the integration of cell and material sciences.

5. Launch of a new scientific journal

The **Royal Society of Chemistry** and the iCeMS jointly launched a new journal *Biomaterials Science* in 2012, and set up the Asia Pacific Editorial Office at the iCeMS. The official journal tag line: “***Biomaterials Science*** is an international, high impact journal bringing together the molecular and **mesoscopic** interactions of biomaterials and their applications.”

This is an important step forward to leading the global development of the iCeMS' central scope.

6. Beyond WPI-iCeMS

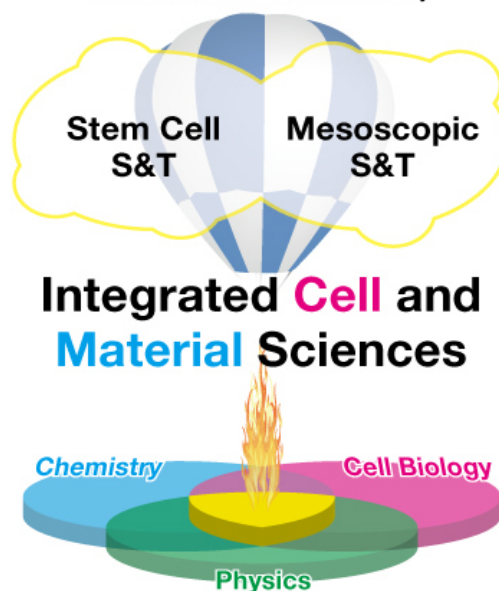
Given present economic uncertainties in Japan, at a minimum any plans for a new research organization at Kyoto University must be leading-edge and multidisciplinary, with a future-oriented research vision and solid financial footing based on funding from competitive sources. To date, the iCeMS has succeeded in establishing a new research field based on the integration of the cell and material sciences, as well as in securing substantial sources of external funding. If able to continue this progress toward scientific as well as financial self-standing over the next five years, based in large part on continued strong scientific output, the path toward establishment as a new organization will be assured. Such a new "global multidisciplinary research hub" may retain the integrated cell-material sciences at its core, while progressively incorporating new fields of research. This hub will be supported by the internationally- and human resources-oriented spirit of strategic management brought to maturity at the iCeMS. Kyoto University, for its part, will lend full support over the next five years to efforts to establish such an expanded organization for international multidisciplinary research based on the founding principles of the WPI program. Additionally, as part of ongoing educational and research organization reform efforts, the university anticipates that the iCeMS will serve as a role model in the creation of new world-leading scientific research institutions (refer to the attached “Host Institution’s Commitment”).

Major changes from the initial project plan:

Previously, the iCeMS' key concepts have been criticized as being too broad and too ambiguous. As a result, extensive thought has been given to

	<p>the way in which the “meso” concept could be worked into new key concepts that could best illustrate the research taking place at the iCeMS. <u>The following summarizes how the institute’s key concepts have evolved over the past four years in response to comments from the Working Group, Program Committee, and Advisory Board.</u></p> <ul style="list-style-type: none"> ➤ <u>October 2007</u>: (1) <i>New chemistry/physics of meso-space</i>, (2) <i>Cellular meso-biophysics</i>, and (3) <i>Stem-cell control meso-engineering</i>. <p>Criticized at FY 2008 Site Visit and Program Committee as being too broad, lacking a clear sense of what is actually to be studied.</p> <ul style="list-style-type: none"> ➤ <u>January 2009</u>: (1) <i>Meso-control of stem cell systems</i>, and (2) <i>Meso-control of functional architectures</i>. <p>Criticized at FY 2009 Site Visit and Program Committee for vagueness of the “meso” concept, which is not especially well understood by biologists. WPI Program Committee ordered iCeMS the following two points.</p> <ul style="list-style-type: none"> • Reappraisal of the basic concepts: <i>meso-scale control</i> and <i>integration of cell-material science</i>; and • Rewriting the mission statement and roadmap of the center. <ul style="list-style-type: none"> ➤ <u>October 2010</u>: (1) <i>Stem Cells</i>, and (2) <i>Soft functional architectures</i>. <p>The PD and PO advised that (2) is difficult to understand, and recommended that the Advisory Committee be consulted for advice.</p> <p>The Advisory Committee later agreed on the point concerning (2), adding that: the concept of “meso-scale control” continues to be difficult for cell biologists to grasp; the primary focus of the institute should remain on “integration of cell and materials science”; and the “meso” theme is central to the iCeMS’ goal because it is in this realm that materials turn into life. (“It is on these mesoscopic length scales that matter becomes capable of the complexity involved in generating a living system.”)</p> <ul style="list-style-type: none"> ➤ <u>February 2011</u>: (1) <i>Stem cell technologies</i>, and (2) <i>Mesosopic sciences</i>. <p>Working group claims at 2011 Site Visit that the present iCeMS missions seem to be too technology-oriented. Of course, science and technology are two indispensable vehicles to promote research.</p> <ul style="list-style-type: none"> ➤ <u>September 2011</u>: (1) <i>Stem cell science and technology</i>, and (2) <i>Mesosopic science and technology</i>.
<p>Mission statement and/or center’s identity</p>	<ul style="list-style-type: none"> • Briefly and clearly describe the mission statement and/or the project’s identity as WPI center. <p>The iCeMS’ mission is to <u>create new cross-disciplinary fields through the integration of cell and material sciences</u> with a focus on <i>stem cell science and technology</i> and <i>mesoscopic science and technology</i>, bringing about innovations in medicine, pharmaceuticals, the environment, and industry.</p>

Innovations in medicine, pharmaceuticals,
the environment, and industry



Mesoscopic domains lie between 1 nm and 1 μm , a realm where materials become life, and life inspires materials. Physicists explore this domain using “mesoscopic physics”. We seek to expand this research area by developing “mesoscopic sciences”, a truly interdisciplinary study including physics, chemistry, and biology.

(1) Research fields

1. Research fields and key concepts

- Describe in simple words and phrases within one line the research field of the project.

Integrated Cell-Material Sciences

This cross-disciplinary field is based on Cell Science and Material Science (in the broad meaning of Material Science, including Physics, Chemistry, and the narrower meaning of Material Science).

Key concepts:

- Stem cell science and technology
- Mesoscopic science and technology

2. Relevant research fields

- Choose relevant fields from among ①—⑦ below, specifying the interdisciplinary field(s) that the project addresses.
①Biosciences, ②Chemistry, ③Material sciences, ④Electronics engineering and information sciences,
⑤Precision and mechanical engineering, ⑥Physics, ⑦Mathematics

Biosciences, Chemistry, Material sciences, and Physics

3. Importance of the proposed research

- Describe the importance of the proposed research, including domestic and international R&D trends in the field and Japan's advantages.

The founding concept of the Institute for Integrated Cell-Material Sciences (iCeMS) is the **integration of cell biology and material sciences (chemistry/physics)**, two prominent fields that are strongly represented at Kyoto University. Their integration provides the potential for a wide variety of research. Among those, we have focused our efforts to date on two important areas: (A) *stem cell science and technology* and (B) *mesoscopic science and technology*. Our current work in these two areas has produced ground-breaking, internationally recognized results, and our institute has already become a leader in these fields.

A. Stem cell science and technology

The iCeMS seeks to develop truly cross-disciplinary research fields by integrating cell biology, chemistry, material science, and physics to capture the potential power of mesoscopic

architectures and functions of living cells and functional materials, in order to apply these to stem cell research. Thus we aim to create and advance stem cell science and technology based on a multidisciplinary fusion of cell-material sciences.

Cells in living organisms have acquired marvelous mechanisms to control cell growth, differentiation, and functions through the course of evolution. We investigate and utilize such mechanisms and functions to control stem cells. In particular, we focus on pluripotent stem cells, such as embryonic stem (ES) and induced pluripotent stem (iPS) cells, because of their great potential in proliferation and differentiation, and thereby harness their unlimited possibility for application in biomedical and pharmaceutical fields. We put emphasis on cross-disciplinary research, because novel approaches to stem cell research will ultimately realize great potential by applying cell-material integration-derived control strategies to ES/iPS cells, resulting in unprecedented abilities to shape the course of stem cell technology development.

B. Mesoscopic science and technology

Mesoscopic cell architectures and functions: For advancing the aim of the iCeMS, i.e., integrative studies of cell biology and material sciences and technological innovation based on such cross-disciplinary studies, we now focus on two cellular mesoscopic functional architectures/systems: (1) cellular membrane systems, with a special emphasis on the domain structures of the plasma membrane, and (2) chromatin and gene regulation systems. These systems have been selected because (a) they can be key sites for the initial binding/actions of various materials and molecules we are now developing and (b) they are likely to be important paradigms for studying the formation and function of macromolecular assemblies or meso-scale functional complexes, made both naturally (by cells) and artificially.

Smart materials for mesoscopic functions and applications: One important aim of the iCeMS is to establish a symbiotic integration of spatial architectures and chemical and/or physical functions, hence, to develop materials with controllable and flexible performance responsive to target environments and to apply them to biological systems. These environments range in size from the aggregates of molecules or ions in the nano domain up to the space inside biological cells (micrometer domain). We are aware that truly interesting events, which are challenging to understand and control, tend to occur in this complex mesoscopic space, in the size range between 1 nm and 1 μm . To date, we have created and studied a variety of new porous coordination polymers, magnetic nanoparticles, DNA tiled assemblies, and hybridized carbons, porous proteins, and supramolecular materials.

4. Importance of the proposed field in the context of worldwide R&D trends

- Describe the importance of the proposed research, including domestic and international R&D trends in the field and Japan's advantages.

a. Worldwide R&D trends and the iCeMS' scope

Interdisciplinary research fields bringing the material and biological sciences together with a unified perspective are being conceived around the globe. A popular effort along these lines has been the integration of nanotechnology and molecular biological sciences, including Bio-X at Stanford University, the California NanoSystems Institute (CNSI) at UCLA, and the Bionanotechnology Interdisciplinary Research Centre at Oxford University.

In the course of conducting R&D in nanotechnology and nanobiology/molecular biology, researchers started becoming aware that interesting events, which are challenging to understand and control, tend to occur in the more complex world of mesoscopic space. Non-linear, weakly-cooperative events, which present challenging problems and seeds for the technology of tomorrow, take place in this mesoscopic domain. Therefore, the interest of researchers in physics and chemistry in mesoscopic interactions is on the rise.

In the biological field, interest in molecular complexes as basic units of key functions is rising. However, very little cross-disciplinary research has been done for discovering the underlying physical and chemical principles for the formation and function of these mesoscopic molecular complexes.

- If centers in similar fields already exist in Japan or overseas, please list them.

b. Research at the iCeMS' partner institutions

We have chosen world-wide famous research institutions which are relevant to the iCeMS' research fields as iCeMS partner institutions. Many of the iCeMS' partner institutions share our interest in

exploring this cross-disciplinary field bridging the cell and material sciences.

- **Biology-based** approaches to such an integration are employed at:
 - MRC Centre for Regenerative Medicine (CRM), The University of Edinburgh
 - National Centre for Biological Sciences (NCBS), India
 - Institute for Stem Cell Biology and Regenerative Medicine (inStem), India
 - Medicinal Bioconvergence Research Center (Biocon), Seoul National University, Korea
- **Materials science-based** approaches for multidisciplinary research are employed at:
 - California NanoSystems Institute (CNSI), UCLA, USA
 - Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, India
 - Division of Advanced Materials Science, Pohang University of Science and Technology (POSTECH AMS), Korea

All the above-mentioned institutions are oriented either toward biology or toward materials science and none pursue the fully-fledged integration of both research areas. The iCeMS is unique in that it is fully committed to cross-disciplinary research with cell-material integration at its core.

c. Emerging interest in mesoscopic science at the US Department of Energy (DOE):

- [Feb. 2011] DOE asked its Basic Energy Science Advisory Committee to identify mesoscale science directions most promising to advance DOE's mission.
- [Mar. and Aug. 2011] BESAC meetings held; Comments include:
 - "The study could encourage a national discussion of mesoscale science to the level comparable during the initial formulation of the [Clinton] National Nanotechnology Initiative a decade ago."
 - "Mesoscale is the study of the biological world from the nanoscale range to our macroscale world."
 - "Mesoscale science could generate a renaissance in American manufacturing."
 - "Mesoscale science enables us to understand better and synthesize materials with desired properties."

(2) Research objectives

- Describe in a clear and easy-to-understand manner the research objectives that the project seeks to achieve by the end of the grant period. In describing the objectives, the following should be articulated in an easily understandable manner: What new domains are expected to be pioneered by fusing the target fields. In the process, what world-level scientific issues are sought to be resolved. What is the expected impact of the scientific advances to be achieved on society in the future.

1. Original goals in 2007

We will accumulate a *critical mass of leading scientists for **the symbiotic integration of material and cell sciences*** (focusing on **stem cells**), based on the notion that **the fundamental understanding and control of molecular complexes in the meso-scale of 10–100 nm is critical for creating the science and technology of the next generation**. Namely, the science directions of this Institute were conceived based on the two key concepts: MESO-SPACE and STEM CELLS. For the fundamental understanding and application of the mesoscopic molecular events occurring throughout the science world, cross-disciplinary approaches are essential. Our inter-related targets for the next 10 years in brief:

- Creating smart microporous materials
- Developing environment- and human-friendly chemistry as well as energy-efficient technologies to capture and convert various gases
- Obtaining physical perspectives of cellular functions through single-molecule nanotechnology methods and terahertz optics
- Advancing stem-cell differentiation meso-engineering
- Creating drug synthesis-controlled release microvessels that could work in animal bodies
- Developing methods and technologies to control stem cells (e.g., ES and iPS cells)

2. Clarified goals in 2012

As described earlier, the iCeMS' key concepts previously have been criticized as being too broad and too ambiguous. This is mainly due to persistent emphasis of the term "meso" to describe the iCeMS' research domains, apparently giving the impression that it is the main direction of all of the research taking place at the iCeMS.

We wish to clarify that the iCeMS' goal, as indicated by its name, is **to create new cross-disciplinary**

fields through the integration of cell and material sciences, with a focus on *stem cell science and technology* and *mesoscopic science and technology*. These scientific endeavors will bring about innovations in medicine, pharmaceuticals, the environment, and industry.

The overall objectives continue to be **the integration of cell and material sciences**, focusing on (A) *stem cell science and technology* and (B) *mesoscopic science and technology*. To identify more specific research goals for the coming years, PIs and young investigators have held informal, intensive strategic planning meetings almost every month (each for 4 hours) to consider research results to date and formulate new ideas. These meetings identified four representative specific aims in stem cell science and technology and four in mesoscopic science and technology.

Please note that these categorized aims often overlap with each other: innovative mesoscopic research of living cells may generate or inspire new applications in stem cell biology and technology.

A. Stem cell science and technology

A-1. Reprogramming with chemical compounds for iPS cell derivation

- Control of gene expression by synthesized chemical transcription factors, and chemical reprogramming

A-2. Chemical probes for stem cell research

- Small molecule tools for stem cell research/applications

A-3. Control of ES/iPS cell growth and differentiation with chemicals and materials

- Chemical inducers for cardiomyocyte etc. differentiation from ES/iPS cells
- Functionalized nanofibers and other materials for stem cell growth and control

A-4. Creation and applications of stem cell-derived model cells for cell biology, medical research and drug discovery

- Neurodegenerative etc. disease model creation and investigation
- Cardiac etc. tissue models and analyses using stem cell-derived cardiomyocytes etc. using nanofibers and light-sensitive functional materials
- Visualization and analyses of the dynamics of cell behavior using novel chemical compounds

B. Mesoscopic science and technology

B-1. Imaging and probing for mesoscopic complexes in the cell

- Investigating the effects of mesoscopic compartments on kinetics of bimolecular reactions in the plasma membrane, and cell membrane single molecule imaging using synthesized probes
- Novel probes (such as diamond particles) for investigating cell architecture dynamics
- Terahertz (THz) microscopy of living tissues and cells for functional imaging
- Single molecule observation studying the functions and dynamics of transporters on the cell membrane

B-2. Production of functional materials performing in the mesoscopic domain

- Development of new carriers for targeted drug delivery using carbon nanotubes and liposomes functionalized by peptides and glyco-coating
- Synthesis of magnetic nanoparticles and fabrication of their functional assembly
- Development of hybrid functional mesoscopic molecules using proteins and inorganic compounds

B-3. Integration of living cells and functional materials performing in the mesoscopic domain

- Functional porous materials and charge separation molecules, which are made bio-compatible and water-soluble by glycans, to elucidate and control cellular functions
- Development of light-harvesting functional materials for photoregulation of cell functions
- Development of nanofibers combined with porous coordination polymers (PCPs) for spatial and temporal control of release of bioactive small molecules such as nitric oxide (NO), which can be used for cell physiology research

B-4. Modeling, simulation, and physics theories of mesoscopic events in living cells

- Mesoscopic theory of cellular function and supramolecular chemistry

(3) Management

1. Center director

- Provide the name of the center director, his/her age (as of 1 April 2012), specialties, and brief career profile (within 5 lines).

Norio Nakatsuji, Ph.D. (62), specialist in stem cell biology and developmental biology. Bachelor of Science (1972) and Doctor of Science (1977) from Kyoto University. Various overseas appointments at Umea University in Sweden (1978), MIT (1978), GWU Medical School (1980), MRC in the UK (1983) and in Japan, most notably as Prof. at the Natl. Inst. of Genetics (1991-98) and Kyoto University (from 1999). Director of Kyoto University's Inst. for Frontier Medical Sciences (2003-2007).

2. Administrative director

- Provide the name of the administrative director, his/her age (as of 1 April 2012), and his/her brief career profile(within 5 lines).

Shinji Tomita, Ph.D. (66), specialist in informatics. Bachelor of Engineering (1968) and Doctor of Engineering (1974) from Kyoto University. Assoc. Prof. at Kyoto University (1978-86) and Prof. at Kyushu University (1986-91). Kyoto University Prof. in the Grad. Schools of Engineering (1991-98) and Informatics (1998-2009). Director of the Center for Information and Multimedia Studies (1997-2002) and Dean of the Graduate School of Informatics at Kyoto University (2006-2009).

3. Composition of administrative staff

- Concretely describe how the administrative staff is organized.

a. Overview

The Administrative Director has a wealth of experience in international academic exchange and scientific management. The Deputy Administrative Director is a long-time national university administrator, lending the institute a solid footing in institutional knowledge and guaranteeing smooth relations with university headquarters. The administration consists of 8 sections with support from the university including the placement of new permanent employee positions. This brought the division to a level close to the long term plan outlined at the institute's founding.

b. Composition of the administration

- Total: 34 staff members
- Senior Executives: director and deputy director
- General Affairs (including personnel): manager and 4 staff
- Overseas Affairs and Planning: manager and 4 staff (2 of whom perform the duties of the Overseas Researchers Support Office)
- Research Planning: manager and 2 staff
- International Public Relations: manager and 2 staff (one of whom is a native speaker of English)
- Finance: manager (deputy administrative director) and 4 staff
- Funding Management (including intellectual property rights management): manager and 5 staff
- Facilities and Environment: manager and 2 staff
- IT Support (including data security): manager
- Secretaries to the director: 2 staff

c. iCeMS administration strongly supported by unique and specialized groups

Unique to the iCeMS is the presence of specialized groups supporting the administration in the areas of public relations and competitive funding. These groups are as follows.

1) International Public Relations and Science Communication

In order to meet the WPI program goal of raising the international visibility of the institute, the iCeMS both collects relevant information from domestic and international sources and actively transmits news to a global audience as part of its strategic public relations efforts, while at the same time sponsoring public outreach programs based on science communication theory and practice.

The public relations team brings a wealth of international training and experience to bear upon the mission, and the **Science Communication Group** (SCG), headed by researchers with extensive training in the field, also serves as a working laboratory for broadening the public communication skills of the institute's scientists.

2) Strategic Plans to Acquire Sources of Competitive Funding

As part of a strategy to closely match the fruit of the institute's basic research with the needs of prospective private sector partners, the iCeMS' senior staff includes two specially appointed professors and an associate professor with strong ties to industry, who leads the **Innovation Management Group** (IMG).

The IMG both conducts research on international partnerships, multi-sector ties, and cross-disciplinary research, as well as implements strategies related to these areas, greatly aiding the institute director in his decision-making.

d. Future plans

The administration reached 7 sections in FY 2010. In FY 2012 the Research Planning Section, including science and technology administrators, has been newly established with the aim of securing

larger sources of external funding using strategic methods. Further expansion of efforts to secure sources of external funding, establish ties with other international institutions, and provide support for foreign researchers will likely lead to growth in these areas. Training strategies to enhance planning and implementation skills required in each section will be formulated.

Kyoto University is presently pursuing large scale administrative reform. Much routine administrative work undertaken at individual graduate schools and institutes is envisioned to be eventually performed at a centralized office in order to promote efficiency and smooth operations. More creative functions at graduate schools and institutes related to planning and internationalization, linkages with industry, acquisition of competitive funds, etc. will be strengthened. The iCeMS will also be taking part in this reform effort, in order to streamline the administration, making it truly appropriate for an international research hub.

4. Decision-making system

- Concretely describe the center's decision-making system.

The institute's faculty cooperates to smoothly and rapidly implement the director's decisions via a clear and effective system of committees. The key elements of this system are as follows:

Executive Board

Consisting of the director, deputy director, chair of the Board of PIs (see below), and administrative director, deliberating top personnel and other key decisions of the institute.

Board of PIs

Consisting of all 18 PIs, 5 iCeMS Kyoto Fellows (junior PIs), and 3 special research group leaders (associate professors), conducting job seminars related to the hiring of iCeMS Kyoto Fellows and other faculty, deliberating the awarding of exploratory cross-disciplinary research grants, and planning for seminars, retreats, and international symposia, and discussing other iCeMS planning proposals.

Strategic Task Force for Cross-Disciplinary Research

Led by the institute deputy director and consisting of relevant PIs from varying fields, providing strong institutional support to cross-disciplinary research projects. Younger researchers are also involved and meet monthly targeting specific projects.

Faculty Selection Committee

Established in February 2011 as part of the Executive Board to deliberate recruitment of new faculty and renewal of employment contracts for faculty who have served their full 5 years at the institute. Additional senior scientists are invited from outside the iCeMS to participate in the evaluation process to offer their unbiased and expert opinion.

Advisory Committee

Consisting of 10 distinguished outside researchers (7 non-Japanese) meeting once annually to provide the institute with unbiased and expert feedback.

As envisioned at its founding, the institute's decision making structure works both smoothly and efficiently, and will be retained in its present form.

5. Allocation of authority between the center director and the host institution

- Concretely describe how authority is allocated between the center director and the host institution's side.

The host institution is responsible for overall governance and rule-making, while the center director determines policies that are specific to the institute.

The iCeMS director, for example, has authority over 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 role of the institute within the university, the overall hiring structure for program-specific faculty and researchers (expanded university-wide beginning in 2008), the rules governing the awarding of incentives, and reduction of the administrative burden on researchers.

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.

In addition, the director is a regular member of the university's Deans and Directors Meeting, the highest deliberative board of Kyoto University. This membership helps raise the iCeMS' profile, while exempting the center's faculty from participating in other routine university committees.

Regarding the CiRA, special iCeMS-related rules were applied by Kyoto University at the time of the CiRA's founding in FY 2010.

As described above, the host institution and center director will continue to share authority as they consult closely and constantly on the future direction of the institute.

(4) Researchers and other center staff, satellites, partner institutions

1. The "core" to be established within the host institution

a. Principal Investigators (full professors, associate professors or other researchers of comparable standing)

	Numbers		
	At beginning	At end of FY 2011	Final goal (March 31, 2014)
Researchers from within the host institution	12	11	11
Foreign researchers invited from abroad	0	4	4
Researchers invited from other Japanese institutions	2	3	3
Total principal investigators	14	18	18

- Describe the concrete plan to achieve final staffing goal, including steps and timetables.
- Attach a list of principal investigators using the Appendix. Place an asterisk (*) by names of the investigators considered to be ranked among the world's top researchers. Describe the policy and strategy for inviting the PIs who are to be included after 1 April 2012.

b. Total staff

	Numbers		
	At beginning	At end of FY 2011	Final goal (March 31, 2014)
Researchers	70 <10,15%>	179 <60,34%> [47,27%]	185 <64,35%> [55,30%]
Principal investigators	14 <0,0%>	18 <3,17%> [2,12%]	18 <3,17%> [2,12%]
Other researchers	56 <10,18%>	161 <57,36%> [45,28%]	167 <61,37%> [53,32%]
Research support staff	45	79	81
Administrative staff	27	31	34
Total number of people who form the "core" of the research center	142	289	300

- Enter the total number of people in the columns above. In the "Researchers" column, put the number and percentage of overseas researchers in the < > brackets and the number and percentage of female researchers in the [] brackets.
- Enter matters warranting special mention, such as concrete plans for achieving the Center's goals, established schedules for employing the main researchers, particularly principal investigators.

2. Collaboration with other institutions

- If the "core" forms linkages with other institutions, domestic and/or foreign, by establishing satellite functions, Provide the name of the partner institution(s), and describe the role of the satellite functions, personnel composition and structure, and collaborative framework between the host institution and the said partner institutions (e.g., contracts to be concluded, scheme for resource transfer).
- If some of the principal investigators will be stationed at satellites, attach a list of these principal investigators and the name of their satellite organizations using the Appendix.

- If the “core” forms organic linkages with other institutions, domestic and/or foreign, without establishing satellite functions, provide the names of the partner institutions and describe their roles and linkages within the center project.

a. Satellites

Faculty of Applied Biological Sciences, Gifu University

One satellite laboratory was established at Gifu University in 2008. As an iCeMS PI, Prof. Makoto Kiso collaborates and interacts in the area of glycol-technology and its application to cell biology based on an agreement between Kyoto University and Gifu University.

b. Partner institutions

The Institute has formed linkages with the following high-level institutions, based on two overall objectives. The first aim is to enhance the academic exchange and traffic of researchers, including postdoctoral and graduate students, with these partners. This point is extremely important in order to position the institute in the global flow of young researcher career paths. The aim has been to launch this project rapidly and smoothly, with partnerships giving this process a head-start. The second objective is to enhance the scientific output at the institute and at partner Institutions by complementing each other’s research efforts.

1) Partner institutions established at the iCeMS’ founding

The iCeMS’ partner institutions in 2007 were as follows. Memoranda of Understanding (MoUs) have been exchanged with some of these institutions.

- Wellcome Trust Centre for Stem Cell Research and its sister institute, Wellcome/Gurdon Institute, Cambridge University
- National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem), Bangalore, India (MoU exchanged on April 28, 2010)
- Max Planck Institute for Molecular Cell Biology and Genetics (MPI-CBG)
- California NanoSystems Institute, UCLA (MoU exchanged on March 15, 2010)
- Center for Basic and Applied Membrane Sciences, Purdue University
- The Center for Developmental Biology, RIKEN
- Bionanotechnology Interdisciplinary Research Centre (BIRC), the University of Oxford

Of the above institutions, the partnership with BIRC ended in FY2010 due to the close of this time-limited organization.

2) Partner institutions at present and in the near future

In addition to the above institutions, we have extended or will extend our partnership to other seven institutions as listed below:

- MRC Centre for Regenerative Medicine (CRM), The University of Edinburgh (MoU exchanged on March 30, 2011)
- Moscow Institute of Physics and Technology (MIPT) (MoU exchanged on March 31, 2011)
- Medicinal Bioconvergence Research Center (Biocon), Seoul National University (MoU exchanged on March 29, 2011)
- Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR) (MoU exchanged on April 18, 2011)
- Collaborative Research Center SFB 873 of the University of Heidelberg
- NIH Center for Regenerative Medicine, National Institutes of Health (NIH CRM) (MoU exchanged on November 21, 2011)
- Division of Advanced Materials Science, Pohang University of Science and Technology (POSTECH AMS) (MoU exchanged on November 16, 2011)

3) Future plans

All partners have played important roles particularly in the initiation phase (first five years), assisting the iCeMS to establish itself quickly as a global organization and helping increase the institute’s name recognition.

From the start of the second phase in FY2012, the iCeMS intends to achieve even more substantial collaborations through such measures as joint research paper publication in highly ranked journals, and more frequent and longer-term exchanges of young researchers. In order to attain this goal, the iCeMS will prioritize and weight the allocation of personnel and budgets to partner institutions in accordance to their relevance to the iCeMS’ research, host institution policies related to internationalization, and so forth.

One example of this priority-based planning is seen in the NCBS partnership. The iCeMS satellite lab

in Bangalore on Stem Cell research and Single Molecule Imaging has been set up in the NCBS's new building, which will be completed in Spring 2012. A Senior Lecturer for Stem Cell research and an Assoc. Prof. for Single Molecule Imaging conduct research activities at the iCeMS' satellite lab in Bangalore as group leaders. Their primary appointments are as faculty members of the iCeMS, while also being appointed as visiting Associate and Assistant Professors of the NCBS from April 17, 2011. Several younger researchers will join the laboratory. Research space, facilities, as well as research funds are being provided by NCBS-inStem.

(5) Research Environment

- Concretely describe measures to be taken to satisfy each of the requirements outlined below, including steps and timetables.

1. Provide an environment in which researchers can devote themselves exclusively to their research, by exempting them from other duties and providing them with adequate staff support to handle paperwork and other administrative functions.

The Executive Board (consisting of the center director, the deputy center-director, the chairman of the board of PIs, and the administrative director) undertakes all of the administrative matters under the leadership of the center director. The administration consists of eight sections: General Affairs, Finance, Funding Management, Facilities and Environment, International Public Relations, Overseas Affairs and Planning, Research Planning, and IT Support. All administrative sections have staff who are able to communicate fluently in English. Investigators are exempt from most administrative duties. Board of PIs meetings ("PI meetings") focuses only on matters directly related to research activities. Each lab is staffed with an English-speaking secretary.

As of FY2012, the following specific areas of support continue to relax the administrative burden on researchers, allowing them to further focus their creativity on research:

- 1) With the hiring a former Kyoto University Graduate School of Informatics dean as its Administrative Director, the institute gained a scientist and a manager with impeccable credentials in guiding international scientific exchange and extensive experience in bringing together researchers from varying fields and disciplines.
- 2) The institute's effort to assist researchers includes a dedicated administrative staff of 34 (more than half of whom are English speakers) as well as a research support staff of 79.
- 3) The Overseas Researchers Support Office works to assist foreign researchers in adjusting to life in Kyoto, helping them quickly begin making real contributions to the scientific life of the institute. This office will be further strengthened with the possible addition of staff experienced in this area.
- 4) International public relations efforts, supported by the Science Communication Group (SCG), are described in 3, iii, c (iCeMS administration strongly supported by unique and specialized groups).
- 5) Strategic planning supported by the Innovation Management Group (IMG) in the acquisition of sources of competitive funding is described in 3, iii, c (iCeMS administration strongly supported by unique and specialized groups).
- 6) Collaboration among academia, industry, and government is being accelerated by identifying new research projects with potential for applications beyond academic research. For this purpose, nonprofit organization (Kyoto Smart Materials & Innovation, SMI) has been established by the IMG together with several iCeMS researchers.
- 7) The institute employs a unified database system which can be utilized for the creation of various documents. This reduces the need for repetitive information collection.
- 8) In line with improved administrative and research support, improvements are planned for the management and maintenance of large, shared research equipment.
- 9) In preparing important documents such as annual progress reports and presentations for the WPI Program Committee, administrative staff makes significant contributions, from proposing drafts to English proofreading.
- 10) Institute researchers are exempt from routine university administrative duties.

2. Provide startup research funding as necessary to ensure that top-caliber researchers invited to the center do not upon arrival lose momentum in vigorously pursuing their work out of concern over the need to apply immediately for competitive grants.

- 1) Startup funds have been provided to new PIs (including iCeMS Kyoto Fellows) arriving at the

Institute at a level of 3 to 10 million yen per year for two years, covering small equipment and supplies, in addition to the normal support for PIs. Remodeled laboratory space and basic lab equipment are also provided. If necessary, additional high-value equipment has also been provided for the specific needs of new researchers.

2) Small startup grants to initiate cross-disciplinary collaboration are provided to junior faculty and postdocs as part of the “iCeMS Exploratory Grants for Junior Investigators” program, and separately, “Cross-Disciplinary Exploratory Grants” have been made available to researchers of other departments of the university to start collaborations with iCeMS researchers. Exploratory cross-disciplinary research has been strengthened, with a rigorous evaluation system in place. Increased collaboration with young researchers in other Kyoto University departments and institutes is being actively pursued.

3) Support for the iCeMS Kyoto Fellows will be extended.

3. As a rule, fill postdoctoral positions through open international solicitations.

Each institute laboratory consists of a PI, non-tenured junior faculty members, and postdoctoral fellows. These positions are globally advertised in all possible venues, such as including advertisements in Nature and Science.

Furthermore, to make this Institute an attractive place for the young and brightest to develop their careers, special iCeMS Kyoto Fellow positions have been established. These Fellows are independent PIs, and given the titles of Assistant Professor or Research Associate, with an annual salary of 7–10 million yen and startup funds of 3–10 million yen, ensuring suitable support for a first position as a laboratory head for five years. The fellows have access to all of the research instruments within the Institute. They are asked to identify a mentor among the institute’s PIs, who can give advice about various aspects of research and research life, while maintaining the independence of the Fellow position. This career phase, being the first independent position, is the best period to make ambitious scientific efforts based on fresh and original ideas. After the head-start at this institute, they are expected to take off for further international scientific careers (or further promoted at Kyoto University). Such a process will help lead our Institute to becoming a prominent hub in global scientific careers.

4. Establish English as the primary language for work-related communication, and appoint administrative personnel who can facilitate the use of English in the work process.

The official language is English within the Institute, in all official meetings and documents, including email announcements. At present, each lab has an English/Japanese bilingual secretary on staff. 19 of the 34 administrative staff (55%) are bilingual.

From FY2012:

- The greater than 50% English-Japanese bilingual staff level will be maintained.
- Incentives will be offered to encourage staff members to receive training and acquire certifications, further raising English ability as appropriate for a WPI institute and also as a means of boosting staff morale.

5. Adopt a rigorous system for evaluating research and a system of merit-based compensation. (For example, institute a merit-based annual salary system primarily for researchers from outside the host institution. As a basic rule, the salaries of researchers who were already employed at the host institution prior to the centers’ establishment are to be paid by the host institution.)

Rigorous, objective evaluations are conducted by the Executive Board, with final evaluations given by the center director. The salaries of the investigators transferred within Kyoto University are paid directly by Kyoto University, according to its rules. Merit-based compensation, in the form of a bonus, also exists (awarded up to 300,000 yen per month). In parallel, a totally merit-based annual salary system is instituted for researchers joining the institute from outside the host institution.

The director-led Executive Board annually evaluates faculty members on their research activities and decides on the awarding of incentives.

The iCeMS employs researchers on the basis of a five-year employment scheme. From FY2012 there will be many researchers whose employment terms will expire and hope to renew their terms. The iCeMS has already clarified a renewal process and evaluation points such as excellence in research, relevance to the iCeMS’ interdisciplinary goals, the number of publications in high quality journals, etc.

6. Provide equipment and facilities, including laboratory space, appropriate to a top world-level research center.

The host institution, Kyoto University, fulfilled the basic need for equipment and facilities during the initial phase of this institute. For further equipment support, Kyoto University provides a budget in the form of a center director's discretionary fund. From this, startup funds have been provided to each new PI transferred to the institute at a level of 3–10 million yen per year for two years, covering small equipment and supplies, in addition to the normal support for PIs. Remodeled laboratory space and basic lab equipment are also provided. If necessary, additional high-value equipment has also been provided for the specific needs of new researchers.

Many laboratories are shared by different groups, avoiding traditional layouts (in which different research groups are separated by walls) to facilitate spontaneous stimulation and to encourage interactions among different groups on a daily basis. This layout also easily accommodates the groups led by the iCeMS Kyoto Fellows.

Sufficient numbers of rooms have been set aside for seminars, meetings, tea times, and happy hour gatherings, and lounges within the Institute and the neighboring buildings and gardens are available.

a. Facilities

Including refurbishments made during FY 2009–10 and in particular the completion of a new 3,000 m² research building in FY2010, lab and office space in Complexes 1 and 2 have reached a total of approximately 11,000 m². This is close to the figure envisioned at the time of the institute's founding.

b. Equipment

1) A large variety of state-of-the-art equipment have been installed, such as a Single Fluorescent-Molecule Imaging Station, Nuclear Magnetic Resonance Spectroscopy Advance III 500 US Plus, 3D Nanometer Scale Raman Microspectroscopy Nanofiner 3D, etc.

Rules for use and relevant manuals for key pieces of large, shared equipment listed above have been enacted, and cooperative use of this equipment is already contributing to the institute's scientific progress.

2) The Center for Meso-Bio Single-Molecule Imaging (CeMI) is the iCeMS' imaging innovation center for cellular mesoscopic science. Its key missions are to develop new, powerful technologies for imaging the restless nano- to meso-scale biomolecular complexes in living cells, at the spatiotemporal resolutions of functioning single molecules, and to make these technologies available quickly to the scientific community worldwide for the further advancement of cellular mesoscopic science.

c. IT Infrastructure

1) Computer networks interconnecting research groups encourage interaction among researchers, while maintaining high standards of safety and security.

2) Computer network infrastructure is centrally administered by the IT Support Office, reducing the IT burden on researchers.

3) A Cross-Disciplinary Journal Club has been established on the institute's website, consisting of a databank of scientific papers that are particularly inspiring and useful in sparking ideas for new iCeMS-related joint research projects.

7. Hold international research conferences or symposiums regularly (at least once a year) to bring the world's leading researchers together at the center.

a. International symposia

For the past five years, the iCeMS has held eleven International symposia.

International symposia in future are planned as follows.

- Two or more international symposia are held annually.
- Joint symposia, sponsored with partner institutions, are held annually at overseas venues.

b. Seminars

The iCeMS has held numerous seminars, featuring leading scientists from overseas and attracting wide participation from numerous other university departments and institutes.

8. Other measures to ensure that top-caliber researchers from around the world can comfortably devote themselves to their research in a competitive international environment, if any.

- 1) Annual researcher retreats have been held to promote interdisciplinary interaction, reaffirm the director's mission for the iCeMS, and as a means for all research staff to exchange ideas.
 - 2009: Kyoto Prefectural Seminar House (74 attended, 39 posters presented)
 - 2010: Awaji Yumebutai International Conference Center (115 attended, 74 posters presented); featured a highly stimulating presentation by researchers who had participated in JSPS-sponsored overseas visit programs
 - 2011: Yoshino Chikurin-in, Nara (152 attended, 97 posters presented); featured a plenary lecture by Prof. Toshio Yanagida of Osaka University's WPI center
- 2) Cross-Disciplinary Journal Club established on the iCeMS website
 - Prof. Nakatsuji initiated the establishment of the Cross-Disciplinary Journal Club on the institute's website, consisting of a databank of scientific papers that are particularly inspiring and useful in sparking ideas for new joint research projects. Prof. Nakatsuji has been actively posting relevant newly published papers to the database, so far accumulating more than 500 original and review articles. This resource also aids the growth of a broad community of scientists who are interested in the integration of cell-material sciences and mesoscopic sciences.
 - Ever greater efforts are underway to encourage the fusion of different disciplines via retreats, Cross-Disciplinary Seminars, the Cross-Disciplinary Journal Club, and other mechanisms.

(6) Indicators for evaluating a center's global standing

- Describe concretely the following points.

1. Criteria and methods to be used for evaluating the center's global standing in the subject field

The following points are particularly important in evaluating the center's global standing:

- 1) Has each investigator conducted high-level research impacting the field?
- 2) Have individual investigators originally from different disciplines worked collaboratively to produce significant results?
- 3) Has the administration properly supported the researchers, in a manner suitable for a premier international research center?
- 4) Has the institute become recognized by researchers worldwide as an excellent place for young investigators to establish their careers?
- 5) Has the institute sufficiently promoted interaction with researchers from other Asian countries?

Additionally, the Innovation Management Group (IMG) is developing quantitative means of evaluating the institute's global standing, in strict adherence to academic principles. These methods, outlined below, replace previous evaluative practices, which were based on individual discussions and were hence largely qualitative.

- Evaluation of the level of achievement of research projects
- Evaluation of the status of internal collaboration projects among PI groups

The IMG also conducts an empirical study combining bibliometric analyses with researcher questionnaires, aiming to identify key success factors to reinforce management of cross-disciplinary research projects at the institutional and individual levels.

2. Results of current assessment made using said criteria and methods

a. Individual researcher accomplishments

- 1) The iCeMS continues to achieve outstanding results in stem cell biology, cell biology, chemistry, materials science, and physics, resulting in **464** papers, **59** of which in leading journals with an impact factor (IF) of 10 or more.

Most notably: i) Reprogramming and iPS cell research with papers in *Nature*, *Cell*, etc and ii) Functional porous materials research with **7** papers in *Nature* journals, **11** in *Angew Chem Int Ed* (IF: 11.8, the highest impact factor in the field except review journals), etc.

- 2) Numerous honors and awards include: National Academy of Sciences membership (Profs **Heuser**

and **Yamanaka**, May 2011), Thomson Reuters Citation Laureates (Profs **Kitagawa** and **Yamanaka**, 2010), Lasker Award (Prof **Yamanaka**, 2009), and Humboldt Award (Prof **Kitagawa**, 2008).

- 3) Major grants obtained include: Cabinet Office's FIRST program for iPS cell research and application, next-gen FIRST program (5 proposals accepted), Ministry of Economy, Trade and Industry's NEDO programs (3 proposals accepted) for porous material R&D, magnetic nanoparticle R&D, and stem cell R&D.

b. Accomplishments by researchers working jointly

- 1) Key multidisciplinary publications include: 1) new probes and control of stem cells with chemical compounds (*Angew Chem Int Ed* 2011, *JACS* 2009), and 2) real-time visualization and investigation of bio-functional molecules with DNA-origami engineering and AFM (*Nature Nanotechnology* 2011, *Angew Chem Int Ed* 2010).
- 2) So far, 13 out of 464 iCeMS papers published since October 2007 are collaborative works by two or more iCeMS groups.
- 3) At present, 38 interdisciplinary projects (out of these, 10 are ranked as top-priority) are in progress. The institute is continuing to make efforts to publish interdisciplinary research outcomes in high quality journals, as strongly recommended in center evaluations.

c. Level of internationally-competitive administration and support

- 1) Each lab has an English/Japanese bilingual secretary on staff. Additionally, 19 of the 34 administrative staff (55%) are bilingual.
- 2) In addition to the standard use of English in all PI meetings and at official institute events, administrative announcements to researchers are written in English.
- 3) The Overseas Researchers Support Office assists the increasing number of foreign researchers with visas, housing, and other issues related to life in Japan.
- 4) Owing in large part to academic input from the Innovation Management Group and operational support by the Overseas Affairs and Planning section, the iCeMS has made substantive progress in joint scientific activities with its partners overseas, such as the UCLA-CNSI, NCBS-inStem, and Heidelberg University.

d. Degree to which the center is a part of global personnel movement

- 1) The implementation of a roadmap for faculty recruitment has raised the number of foreign researchers to 60 (34% of the total) as of March 31, 2012.
- 2) An international effort to recruit young, promising researchers for iCeMS Kyoto Fellow positions attracted over 30 applicants in FY2009 and 33 applicants in FY2010, three of whom were selected from overseas for a total of five fellows.
- 3) In order to accelerate internationalization and cross-disciplinary research at the institute, 17 researcher positions were created exclusively for foreign researchers and for multi-group collaboration under the director's initiative, as part of a continuing effort.
- 4) 105 and 107 prominent researchers from overseas visited the iCeMS in FY2010 and 2009, respectively.
- 5) The iCeMS-JSPS Overseas Visit Program for Young Researchers has been implemented since FY2010 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 the iCeMS' role as an international hub for researchers in related fields. A total of 20 researchers thus far have earned opportunities to visit world-class institutions, opening the door to further international collaborations and careers.

e. Degree to which exchange is taking place with researchers throughout Asia

- 1) Extensive academic and personnel exchange is taking place between the iCeMS and the National Centre for Biological Sciences (NCBS) in Bangalore, India. The NCBS satellite lab at the iCeMS is in operation and researcher exchange is taking place.
- 2) The iCeMS signed a memorandum of understanding for academic exchange with the Seoul National University Medicinal Bioconvergence Research Center to accelerate the JSPS Asian

Core Program "Asian Chemical Biology."

- 3) The iCeMS signed a memorandum of understanding for academic exchange with the Division of Advanced Materials Science, Pohang University of Science and Technology.
- 4) The iCeMS and the Center for Life Sciences jointly established by Peking University and Tsinghua University will hold an international symposium in 2012, marking the start of research collaboration.

3. Goals to be achieved through the project (at time of final evaluation)

(Final Report)

- 1) Establishing the novel research field of Integrated Cell-Material Sciences.
- 2) Contributing to human wellness and society in the areas of medicine, pharmaceuticals, the environment and industry.
- 3) Providing a new model for running a world premier institute in a Japanese academic environment, and revolutionizing traditional Japanese academic practices. The institute should be recognized not only as a world renowned institution where Japanese scientists carry out high-level research, but also as a place where the best and brightest young scientists from around the world can develop their careers.
- 4) Creating a flow of young scientists so that researchers once affiliated with this Institution obtain highly regarded positions worldwide.

(7) Securing research funding

1. Future prospects

- Describe the concrete prospects for securing resources that match or exceed the project grant.
- Calculate the total amount of research funding (e.g. competitive funding) based on the percentage of time the researchers devote to research activities at the center vis-à-vis the total time they spend conducting research activities. Be sure the prospects are realistically based on the past record.

External funding in the form of Grants-in-Aid in Scientific Research and large external grants from NEDO and Next Generation FIRST have been secured. As shown below, the total amount of external funds including financial support by the host organization for personnel and facilities is approximately 1.6 billion yen per year for the next several years. A newly established Research Planning Section including science and technology administrators aims to secure larger sources of external funding using strategic methods. These strategies will contribute toward maintaining the iCeMS after its program termination and encouraging young researchers to develop their careers here as well.

2. Projected External funds in FY2012–2016

(Unit: JPY millions)

	FY2012	FY2013	FY2014	FY2015	FY2016	Total
1. Grants-in-Aid for Scientific Research	283	283	283	283	283	1,415
2. Collaborative Research funding	29	29	29	29	29	145
3. Donations	51	51	51	51	51	255
4. Funding Program for Next Generation World-Leading Researchers (FIRST)	192	199	0	0	0	391
5. Sponsored Research Funding (including NEDO)	1,256	1,011	1,011	1,011	552	4,841
6. Support from Host Institution	205	182	196	176	161	920
Total	2,016	1,755	1,570	1,550	1,076	7,967

1, 2, and 3 are based on the figures for FY2011. 4 and 5 are estimates as of FY2011.

The Yamanaka Lab budget is calculated separately as part of the CiRA, and is not included above.

3. Strategies to acquire external funds

- 1) The institute's administration proactively collects information on grants posted on the internet and

notifies researchers, in addition to forwarding information provided by the university.

- 2) A web portal will be launched to provide researchers with easier access to competitive research grant databases.
- 3) All eligible researchers are actively encouraged to participate in large-scale competitive funding programs.
- 4) Information on external research funding sources is provided in English to more effectively assist non-Japanese researchers in the acquisition of funds.
- 5) The institute has hired an expert in obtaining research funding and in cooperation among the private sector, academia, and government, aiming to optimize knowledge in collaboration with associated nonprofit organizations and foundations, thereby aiding in the acquisition of larger amounts of competitive research funds.
- 6) The institute's administration has held, and will continue to hold English-language workshops on these important funds, helping non-Japanese researchers at the institute become familiar with the domestic grant system and providing them with advice on winning approval.

Others

1. Activities and initiatives to be undertaken after project ends

- Describe activities and initiatives to be taken after project funding ends.

a. Original plan in FY2007

After the project period ends, this institute is expected to obtain continued support from Kyoto University, and will probably be expanded for further advancement of the fused field of cell-material sciences. New frontiers of basic science, e.g., the physics and chemistry unique to nano-meso space, cell biophysics, stem-cell differentiation and morphogenesis, will be important areas of intense research.

More direct applications derived from this project will start impacting society and human wellness in 10 years, and we will develop strong ties with industry. Such application prospects would generate more funds from the industry, as well as from the Ministry of Industry and Trade and the Ministry of Health and Labor. Quite a few projects are expected to be transferred to the Venture Business Laboratory of Kyoto University and other incubation laboratories, where the university-industry liaison will be developed.

iCeMS Kyoto Fellow awards will also be continued, assuming that these awards turn out to be very successful.

The new administrative rules developed by this institute and Kyoto University headquarters will become important assets for the future development of new research institutes, and the future restructuring of the university's administration. This project proposal has been prepared based on very extensive and intensive discussions with the head of the host institution, Professor Kazuo Oike, President of Kyoto University, together with the Board of Executive Directors of the Kyoto University. We have received their strong support for this proposal, and most graduate schools and other research institutes have also enthusiastically supported it. Therefore, in all of the probability, this institute shall continue to expand as a treasured asset for Kyoto University.

b. Present plan in FY2012

In addition to the foregoing, the following points have been added as of 2012:

- 1) Kyoto University's Committee of Future Planning has proposed that the university "should strongly back up multi-disciplinary studies by established hubs and securing space for such research," which is stated in the "Fostering high-caliber researchers" clause of a future strategy proposal drafted by the designated task force, approved by President Hiroshi Matsumoto. This perfectly matches the iCeMS' objectives, and therefore will help drive its cross-disciplinary efforts.
- 2) The iCeMS accounted for five out of Kyoto University's 36 proposals accepted by the Japanese Cabinet Office's Funding Program for Next Generation World-Leading Researchers. Additionally, over 450 iCeMS-affiliated papers have been published within the past three and a half years, many in leading journals. Thanks to this solid research record at the iCeMS, awareness for a need to continue and expand iCeMS-like organizations is increasing among university board members.
- 3) In July 2011, Kyoto University began internal deliberations regarding comprehensive reform of the

administration, graduate schools, and institutes. It is anticipated that the administration will undergo significant changes in FY2013, with many of the reforms stemming from the iCeMS' experiences related to internationalization and other matters. While consensus-building related to complete the reform of the graduate schools and institutes is expected to take five years or more, the university anticipates that the iCeMS will serve as a role model in the creation of new world-leading scientific research institutions (refer to the attached "Host Institution's Commitment").

- 4) In January 2012 the iCeMS and the Royal Society of Chemistry (RSC) jointly launched a new scientific journal. "Biomaterials Science" will be edited, and published by the London-based RSC beginning in 2013. The iCeMS Director and Prof. Sugiyama will act as one of two chief editors and one of three associate editors respectively. The new peer-reviewed journal will highlight international research bridging cell biology, materials science, chemistry, and physics.
- 5) Evidence is gathering that the concept of mesoscopic sciences, as championed by the iCeMS, is gaining international acceptance. A prime example is the Basic Energy Sciences Advisory Committee (BESAC) of the United States Department of Energy, a key long term policy-making body at the department, which during a series of meetings in 2011 discussed the importance of investing in the field of Meso-Scale Science in order to gain a foothold in this important area of basic science. Further progress is expected in 2012 and beyond, presenting the iCeMS with new opportunities for collaboration with similarly-minded overseas institutions.

2. Expected ripple effects

- Describe expected ripple effects (e.g. how the research center project will have trailblazing components that can be referred to by other departments in the host institution and/or other research institutions when attempting to build their own top world-level research centers) .

The founding of this institute is expected to have a large ripple effect on related scientific fields, as well as the management of the university, departments, and research institutes at Kyoto University and beyond, throughout Japan.

- 1) Although inter- and cross-disciplinary research between biological and non-biological fields has often been emphasized, it has been under-developed in Japan as well as in many other countries. The founding and the success of this institute is raising scientists' interest in research in the cross-disciplinary areas of biosciences, physics, chemistry, and material science. This field is extremely important, and will become more important for basic research and applied research in future. Many other departments are expected to foster research in this area as well.
- 2) The new administrative paradigm created by this center is strongly influencing future plans for Kyoto University's administration. The iCeMS is expected to continue serving as an administrative and management role model for the university in the future.
- 3) Rigorous, objective evaluations and merit-based compensation are expected to have a strong ripple effect on the management of researchers in universities nationwide.
- 4) Aiding young researchers in the development of their careers is a key goal of the institute. This effort, as exemplified by the iCeMS Kyoto Fellow program, gives bright, young researchers a chance to carry out their research independently and to manage a group on their own. These initiatives are expected to have a broad impact on Kyoto University and beyond.
- 5) This institute embodies the concepts of shared laboratory and office space, as well as shared equipment. This design of rooms and buildings is already affecting the design of research buildings elsewhere.

3. Other important measures

- Describe other important measures to be taken in creating a world premier international research center, if any.

a. Scientific integrity

The iCeMS places a strong emphasis on scientific integrity, an area that tends to be overlooked at new institutions exploring the frontiers of science.

For example, as part of a Kyoto University program targeting graduate students across a wide range of disciplines – ranging from the natural sciences to the humanities – the iCeMS has hosted an "Integrity Seminar Series" exploring scientists' integrity and responsibilities to society. The series included a lecture on "Disaster Prevention Policies and Earthquake Prediction Research" in FY 2010.

b. Science Communication Group (SCG)

Working to build stronger mutual relations among researchers in different fields and between scientific communities and society, the Science Communication Group (SCG), has implemented the following programs:

1) iCeMS Cafés

As of January 2012, science-focused public “iCeMS Cafés” have been organized ten times, attracting a total of 300 participants from the community. In addition to featuring talks by prominent iCeMS scientists, the events give opportunities for young iCeMS researchers to interact with the public and develop their own scientific communication skills.

2) iCeMS/CiRA Classrooms: Hands-on with Stem Cells!

The iCeMS and the CiRA have co-hosted numerous hands-on ES and iPS cell research programs for high school students and teachers in recent years, attracting hundreds of enthusiastic participants. Recent events have also investigated Brownian motion, and combined scientific inquiry with performance art. Several of these sessions were aimed at the general public as well as students in school.

3) iCeMS Crosstalks

A young researcher of the iCeMS interviews one of the iCeMS Principal Investigators (PIs) of his/her choice in this online video series. These discussions provide a glimpse into the PIs’ feelings toward research as well as their personal philosophies.

4) iCeMS Connections

At the June 2010 “Science and Technology Festival in Kyoto” hosted by the Japanese Cabinet Office, the SCG and the iCeMS public relations office together organized and exhibited a booth demonstrating the institute’s cutting edge research with hands-on activities. The iCeMS booth alone, part of the WPI pavilion, counted 700 visitor interactions. The same iCeMS/SCG team again hosted a booth at a follow-up event in December 2011.

5) Looking forward

The fact that the iCeMS has a research group dedicated to science communication is particularly notable, as this enables a level and quality of outreach activities that are both effective and sustainable. The iCeMS recognizes that outreach activities are beneficial both to citizens who learn about the present state of science and technology and to researchers who learn how citizens view their work, which will reflect on their future research. The iCeMS will expand present outreach activities more enthusiastically in future.

c. Innovation Management Group (IMG)

Established in FY 2009, the IMG handles cross-sector and overseas linkages both as a subject of academic study, as well as putting theory into practice by undertaking the management of the institute’s external relations. Notable activities include:

1) The IMG conducts empirical studies combining bibliometric analyses and questionnaires to researchers, aiming to identify key success factors to reinforce management of interdisciplinary research projects at the institutional and individual levels.

2) Together with the university’s Graduate Schools of Economics and Management, the IMG sponsors workshops on academic innovation management focusing on the evaluation and administration of large-scale research projects.

3) Nonprofit organization *Kyoto SMI* (Smart Materials & Innovation) was founded to effectively deliver the outcomes of scientific research to industry and society.

4) *Kyoto SMI* has sponsored several well-attended multi-sector seminars in Tokyo on business applications of ES/iPS cells and smart materials.

5) The IMG leads the institute’s overseas partnership efforts, building and strengthening relationships with institutions across the globe.

6) The institute has hired a special, senior faculty member with extensive and proven experience bridging academia, industry, and government to secure large-scale sources of external funding.