

2. Summary of Proposal

(Compile in English within 3 pages.)

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| Host institution | Kyoto University |
| Head of host institution | Hiroshi Matsumoto, Ph. D. President of Kyoto University |
| Research center | Institute for Integrated Cell-Material Sciences |
| Center director | Norio Nakatsuji, Ph. D. |
| Chief center-project officer (in October 2007) | Norio Nakatsuji, Ph. D. Director, Institute for Frontier Medical Sciences, Kyoto University |
| Project summary | <p>1. Original research objectives in 2007 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></p> <p>2. Clarified research objectives and plan for the next 5 years The iCeMS aims to create new cross-disciplinary fields through the integration of cell and material sciences 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>3. Organizational reform</p> <ol style="list-style-type: none"> 1) Swift decision-making enabled by the Director's strong leadership and the Executive Board's counsel 2) One satellite laboratory established at Gifu University 3) Thirteen collaboration partners around the world 4) iCeMS Kyoto Fellow (junior PI) positions created 5) The Science Communication Group (SCG), serving as a working laboratory for broadening communication among scientists and with the public 6) The Innovation Management Group (IMG), forging alliances in academia, industry, government, and with overseas institutions 7) Ideal environment to interact across boundaries <ol style="list-style-type: none"> 1. Shared labs and open offices promoting collaboration 2. Center for Meso-Bio Single Molecule Imaging (CeMI) established 3. 43 cross-disciplinary seminars held at PI meetings 4. Retreats for all iCeMS researchers held annually 5. Cross-disciplinary journal club on cell-mat. integration & mesoscopic sci. 8) Incentives to encourage interaction across boundaries <ol style="list-style-type: none"> 1. iCeMS exploratory cross-disciplinary grants available both for joint projects within iCeMS and for research with other Kyoto University departments 9) Internationalization <ol style="list-style-type: none"> 1. English as the official language 2. High percentage of overseas researchers (more than 30%) 3. High percentage of bilingual administrative staff (more than 50%) 4. Overseas Researchers Support Office established <p>4. Center for iPS Cell Research and Application (CiRA) collaboration Prof. Shinya 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.</p> <p>5. Launch of a new scientific journal The Royal Society of Chemistry (RSC) and the iCeMS jointly launched <i>Biomaterials Science</i> in 2012. The official description: "<i>Biomaterials Science is an international, high impact journal bringing together the molecular and mesoscopic interactions of biomaterials and their applications.</i>"</p> <p>6. Post-WPI Plans A 2011 Kyoto University strategic plan, approved by President Hiroshi Matsumoto, states that "<i>the university should strongly promote multi-disciplinary studies by establishing hubs for such research.</i>" In this context, the iCeMS will act as a role model for future planning and reforms at the university level.</p> |

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| Mission statement and/or center's identity | 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. |
| Research fields | In addition to having established the study of cell-material integration , the iCeMS also promotes study in the emerging field of mesoscopic science, which is gradually gaining interest in academia, industry, and government: for example, the new RSC-iCeMS journal <i>Biomaterials Science</i> focuses on mesoscopic science; and the United States Department of Energy (DOE) has asked its advisory committee to identify mesoscale science directions most promising to advance the DOE's mission. |
| Research objectives | The main research objective is the integration of cell and material sciences . Examples include: A. Stem cell science and technology 1. Reprogramming with chemical compounds for iPS cell derivation 2. Chemical probes for stem cell research 3. Control of ES/iPS cell growth and differentiation with chemicals/materials 4. Creation and applications of stem cell-derived model cells for cell biology, medical research and drug discovery B. Mesoscopic science and technology 1. Imaging and probing for mesoscopic complexes in the cell 2. Production of functional materials performing in the mesoscopic domain 3. Integration of living cells and functional materials performing in the mesoscopic domain 4. Modeling/simulation/physics theories of mesoscopic events in living cells |
| Outline of management | <p><u>1. Composition of administrative staff</u></p> <p>1) The Administrative Director possesses a wealth of experience in research, management, and international academic exchange; a total of 34 talented administrative staff (in 8 sections) has been hired. 2) More than 50% of the staff is English-Japanese bilingual. 3) The iCeMS administration is strongly supported by two unique research groups, the SCG and the IMG (see project summary 3.5)&6)).</p> <p><u>2. Decision-making system</u></p> <p>1) The Executive Board, consisting of the director, deputy director, chair of the Board of PIs, and administrative director, deliberates on high-ranking personnel issues and other key decisions of the institute. This enables notably swift decision making by the iCeMS Director, incorporating thorough deliberation with the Executive Board. 2) The Board of PIs hosts seminars by job applicants, and deliberates on iCeMS planning matters. 3) The Strategic Task Force for Cross-Disciplinary Research provides strong institutional support to cross-disciplinary research projects. 4) The Advisory Committee, consisting of 10 distinguished outside researchers (7 non-Japanese) provides the institute with unbiased and expert feedback.</p> <p><u>3. Allocation of authority between the Institute and the host institution</u> The host institution is responsible for overall governance and rule-making, while the center director determines policies that are specific to the institute. The host institution and center director will continue to share authority as they consult closely and constantly on the future direction of the institute.</p> |
| Researchers and other center staffs, satellites, partner institutions | <p><u>1. Personnel</u> (as of 2012.3.31): 1) 18 Principal Investigators (including four overseas and two female researchers, and one located at a satellite location) 2) 179 Investigators (including 60 overseas and 47 female investigators) 3) 289 personnel including administrative and other staff</p> <p><u>2. Satellite:</u> Faculty of Applied Biological Sciences, Gifu University. Prof. Kiso is a PI of the iCeMS as well as of Gifu University.</p> <p><u>3. Partner institutions:</u> The iCeMS has 13 partner institutions. 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, we intend to achieve even more substantial collaborations.</p> |

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| | For this purpose, prioritized and weighted personnel and budget planning will be undertaken, as seen in the NCBS partnership. | | | | | | |
| Administrative director | Shinji Tomita, Ph. D. | | | | | | |
| Outline of research environment | <ol style="list-style-type: none"> 1) Kyoto University provides Complex 1 and Complex 2 research buildings with office and lab space totaling 11,000m² creating a research environment suitable for a first-class research institute. 2) A policy of open offices and shared laboratories has been implemented to promote interdisciplinary research. 3) CeMI was established to enable the wide use of state-of-the-art imaging equipment for collaborative research. 4) A highly-skilled and ample administrative staff helps minimize the administrative burden on researchers. 5) The official language is English, for both research and administration. 6) An Overseas Researchers Support Office has been established. 7) Startup funds for researchers from other institutions will be guaranteed by the Institute and Kyoto University. In addition, startup small grants to initiate cross-disciplinary collaboration are provided to junior faculty and postdocs. 8) An overseas visit program for young researchers is supported by the JSPS. 9) International symposia at both domestic and overseas venues, promoting the integration of the cell and material sciences, are held at least twice a year, inviting leading scientists from around the globe. 10) Annual research staff retreats, Cross-Disciplinary Seminars, the Cross-Disciplinary Journal Club, and other mechanisms accelerate the fusion of differing disciplines. | | | | | | |
| Outline of indicators for evaluating a center's global standing | <p>The following five criteria have been adopted since the iCeMS' foundation:</p> <ol style="list-style-type: none"> 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 investigators, 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? <p>Additionally, the Innovation Management Group (IMG) is developing quantitative means of evaluating the institute's global standing, in strict adherence to academic principles.</p> | | | | | | |
| Securing research funding | External funding in the form of Grants-in-Aid in Scientific Research and large grants from NEDO and Next Generation FIRST have been secured. Total external funds, including financial support by the host organization for personnel and facilities, are 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. | | | | | | |
| Appropriations plan (Exchange Rate: JPY/USD=80) | FY | 2012 | 2013 | 2014 | 2015 | 2016 | Total |
| | Cost (\$ millions) | 16.68 | 16.68 | 16.68 | 16.68 | 16.68 | 83.4 |
| Summary of host institution's commitment | <ol style="list-style-type: none"> 1) Kyoto University covers all indirect costs associated with competitive grants obtained by the center's researchers. 2) The university provides five positions and expenses for principal investigator-class personnel. 3) Nine full-time administrative staff and necessary personnel expenses are provided. (Ongoing discussions related to the overall university administrative reform may lead to numerous improvements). 4) The University will continue to provide a high-quality research environment. 5) The university recognizes the iCeMS as being a role model for university institutions in the future. Beyond WPI-iCeMS, the knowledge and experience of the Institute will be part of a process defining a future reformed and revitalized Kyoto University. | | | | | | |

3. Research Center Project (in English)

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| 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

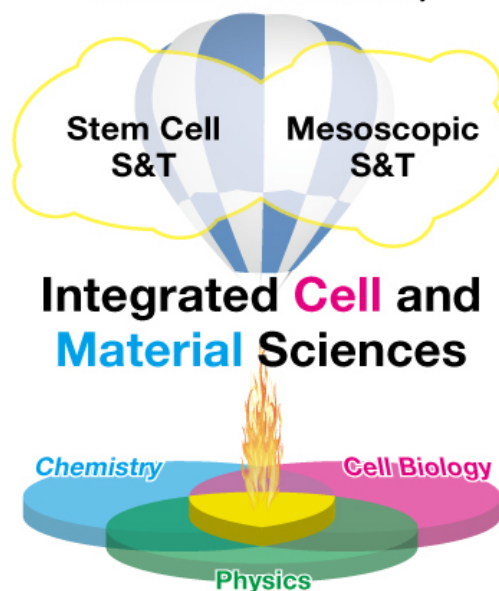
Given present economic uncertainties in Japan, at a minimum any plans for a new research organization at Kyoto University must be leading-edge and multidisciplinary, with a future-oriented research vision and solid financial footing based on funding from competitive sources. To date, the iCeMS has succeeded 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

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| | <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.

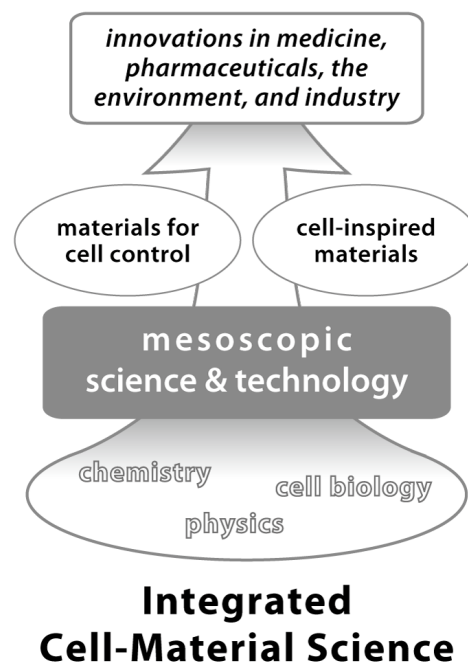
6) The institute has hired a special, senior faculty member with extensive and proven experience bridging academia, industry, and government to secure large-scale sources of external funding.

Vision Statement

Susumu Kitagawa
iCeMS Director-Designate

I. Vision for an Integrated Cell-Material Science

All cellular processes can ultimately be comprehended as chemical events, and such a chemical understanding of cells should allow us to mimic cellular processes using chemical materials. Our institute seeks to illuminate precisely such a *chemical basis of cells*, creating compounds to control processes in cells such as stem cells (*materials for cell control*) in addition to sparking cellular processes to create chemical materials (*cell-inspired materials*). Combining Kyoto University's established strength in cell biology, chemistry, and physics to delve deeply into the mesoscale world lying at the boundary of materials and life, we are making a concerted effort, through interdisciplinary research, to ultimately create a new research field of **integrated cell-material science**.



Efforts to explain cell functions using chemistry are not new. *Biochemistry*, for instance, uses proteins as a starting point in attempting this at a molecular level, and *molecular biology*, while also focused on molecules, takes a DNA-based approach. And in their own ways, both methods have yielded significant innovations in pharmaceuticals and biotechnology.

Meanwhile, *cell biology* has also seen substantial success by considering the cell as a whole, most notably in research related to embryonic stem (ES) cells and induced pluripotent stem (iPS) cells, in turn beginning to make an impact on the biomedical industry.

Our institute seeks a middle ground: between the large, whole-cell approach of cell biology, and the small, protein and DNA approaches of biochemistry and molecular biology. We call this the *mesoscopic* realm, lying between a few tens and a few hundreds of nanometers, on the border between materials and living matter. Investigating this boundary region, we strive to explain the material-chemical basis of cells' living functions, ultimately using materials to create facsimiles of these mechanisms.

A study of the melded boundary between cells and materials based on a fusion of cell biology, chemistry, and physics is our goal. We seek to be the best in the world, with the fruits of our international, interdisciplinary labors bringing nourishment and fresh ideas to research in industries as diverse as medicine and the environment.

Our efforts focus on examination of the following two questions.

(1) Can we describe mesoscopic cellular processes in terms of chemistry?

Cells sustain life through properties of self-assembly and cooperative interactions among nearly countless chemical materials, moving ceaselessly in space and time. Broadening our scope beyond the narrow confines of nanoscale molecular interactions, we find it necessary to take a wider, mesoscopic view of molecular complexes. To accomplish this, we are pursuing the development of advanced imaging technologies and modeling, and physical and chemical technologies to dissect complex cellular events. We plan to focus on the following three areas:

- **Gene Expression Control in Stem Cells.** Changes in the chromatin structure (essentially, the genetic code) of stem cells come about as a result of complex space-time movements of myriad proteins and

nucleic acids. We strive to understand the chemical basis of this dynamic control.

- **Organized Functions on the Cell Membrane.** Not merely a boundary wall, the cell membrane serves as a host environment for the intricate assembly and cooperation of proteins, lipids, and glycans. We seek to explain the chemical basis of these organized functions.
- **Energy Storage in Cells.** As water is stored in dams, energy is stored in intricate structures within cells, via the ion density difference across the cell membrane and in meso-domains of concentrated proteins and lipids. This stored energy is in turn used to create compounds and deliver signals necessary to sustain life. We aim to decipher the chemical basis of these energy storage and conversion mechanisms.

(2) Can we reproduce mesoscopic cellular structures with materials, and manipulate them?

Renowned physicist Richard P. Feynman once wrote: “What I cannot create, I do not understand.” In other words, only in the process of creation can we achieve true understanding.

In this spirit, our institute aims to replicate mesoscopic cellular functions with designer materials. This should be possible once a full understanding of such cellular processes (as described above) has been achieved. We therefore simultaneously advance analysis and synthesis, applying the resulting higher level of knowledge to further research, such as in the proposed creation of chemical materials related to the three focal areas of study:

- with **Gene Expression Control in Stem Cells**, materials capable of manipulating gene expression resulting from cell reprogramming or differentiation;
- with **Organized Functions on the Cell Membrane**, compounds to mimic and replicate the complex, cooperative processes on and inside the cell membrane; and
- with **Energy Storage in Cells**, learning from the beauty of how living creatures store energy, materials capable of transporting and storing ions or molecules, or transforming carbon dioxide and nitrogen gas into energy-storage molecules.

II. Vision for the Institute’s Research and Management

(1) Strengthening cell science

In response to WPI Program Committee and Site Visit Working Group remarks questioning the strength of the institute’s cell science team, we are taking measures to strengthen the lineup of researchers, such as with the potential inclusion of world-renowned Kyoto University scientists **Ryoichiro Kageyama** (Institute for Virus Research) and **Mitinori Saitou** (Graduate School of Medicine).

(2) Strengthening collaboration with CiRA

Differences between iCeMS’ and CiRA’s scientific approaches and goals, often a point of discussion in years past, are now sufficiently clear: iCeMS incorporates iPSCs into its research combining cells and materials, while CiRA focuses on clinical applications of iPSCs. In this context, six CiRA scientists have iCeMS affiliations, performing basic and multidisciplinary research related to iPSCs in conjunction with iCeMS colleagues. Moreover, **Yasuhiro Yamada** (CiRA PI and iCeMS Professor) and **Takuya Yamamoto** (CiRA PI and iCeMS Kyoto Fellow) both engage in the management of this institute as participants in iCeMS Board of PIs meetings.

(3) Strengthening institute management

Director-designate Susumu Kitagawa is a specialist in materials science. Two deputy directors will be named to support his leadership, one to be a world-leading cell scientist, and the other to be iCeMS Professor **Motonari Uesugi**, a highly-regarded chemical biologist in the United States and Japan with a solid record of uniting cell-material research. The institute’s new leadership team, strong in both international and interdisciplinary contexts, will be well placed to lead iCeMS in this new phase of its unified study crossing the boundaries between cells and materials.

Susumu Kitagawa
October 2012

4. Host Institution's Commitment (in English)

Date

January 25, 2012

To MEXT

Name of host institution

Kyoto University

Name and title of head of host institution

Hiroshi Matsumoto, President

(Signature)



I confirm that the measures described below will be faithfully implemented on behalf of the Institute for Integrated Cell-Material Sciences (iCeMS) as part of the World Premier International Research Center (WPI) Initiative.

<Provision in host institution's mid-to-long-term plan>

- Describe clearly the host institution's mid-to-long-term strategy plan and how the center is positioned within that strategy.

Beginning with the iCeMS' founding in October 2007 and continuing for 10 years, Kyoto University has given and will continue to give the World Premier International Research Center Initiative a position of special prominence. As clearly defined in its mission statement, the university strives to achieve a sustainable society for humanity, in harmonious coexistence with the natural environment, by continually nurturing its world-class research and education programs. Kyoto University strongly believes that having a world-leading research center within the university is an indispensable step toward furthering this mission to achieve ultimate sustainability. Under the strong leadership of the president, the university is vigorously committed to promote the WPI program and to actively take concrete and responsible measures, such as provision of research support systems and allocation of resources, necessary in maintaining such a world-leading research center. In terms of university policy making, a future strategy task force recommendation was submitted to the university's Deans and Directors (March 8, 2011) and the President and Executive Directors enacted a "10 Year Plan for Research and Educational Structural Reform Supporting Kyoto University's Growth" (December 6, 2011). To date, the iCeMS has demonstrated itself to be a proven leader within the university in numerous areas of structural reform in research, including in internationalization, multi-disciplinarity, and focused personnel policies. The university will use the institute as a role model for a highest world-standard scientific research institution, incorporating the iCeMS' extensive body of knowledge and experience into deliberations defining a future reformed and revitalized Kyoto University (for details on 'beyond WPI-iCeMS' refer to (6)).

<Concrete Measures>

- Describe the concrete measures that the host institution will take to satisfy the following requirements.

- (1) How it will support the center's need to secure resources that match or exceed the project grant through such means as competitive grants obtained by researchers participating in the project, in-kind contributions and other forms of assistance by the host institution (including partial payment of salaries, provision of research space), and/or external donations.

To secure resources for center operation and research activities, the university takes the following measures:

- a) Provision of expenses of infrastructure to support the center's operation

As a necessary financial measure for the center's operation, the university provides indirect costs associated with competitive grants obtained by the center's researchers.

Infrastructure costs including building maintenance and utility fees will be allocated from the university budget. Fundamental research grants will be provided as well.

- b) Support in obtaining external funds such as competitive grants

To facilitate the center's researchers obtaining external funds, the university provides various support including opportunities to apply for startup funds. The funds will be used to support young researchers and foreign researchers to pursue research until they obtain their own external funds. The university will also provide researchers with various supports in every aspect of preparing the applications.

c) Support for center management to attract world top-level researchers

1) Provision of personnel expenses

The university provides five positions and expenses for principal investigator-class personnel in order to enable Kyoto University's world-leading researchers to conduct academic research at the center while cooperating with their original departments, as well as to minimize the impact of the absences of top-level researchers on their departments' educational and research activities.

For the administration, the university provides full-time administrative staff and necessary personnel expenses in order to establish an independent administrative organization. **Nine current university administrative staff will be allocated for major functions such as general affairs, planning, finance, research support and facilities.** Administrators with a good command of English will be preferentially selected. Note that, given ongoing discussions related to overall university administrative reform, numerous improvements are under consideration (including consolidation of administrative resources and revision of placement of university administrators).

2) Provision of research space

Aiming to maintain a world-class institute with global visibility, Kyoto University will provide a high-quality research environment with a total area of about 12,000 m² including exclusive-use facilities with fully equipped infrastructure. The iCeMS reached approximately this scale in fiscal 2010 with the completion of Complex 2 (including a new 3,000 m² building). The university intends to pursue further efforts to improve the research environment at the iCeMS.

3) Measures related to internationalization and public relations

Given the iCeMS' mandate to fulfill a role as an international research hub, the university will support the institute's international publicity and linkage efforts via measures including the issuance of publications such as pamphlets and press releases. Previously divided among various research and overseas-related offices, university-level support in this area was consolidated into the Research and International Affairs Division beginning in fiscal 2011.

In addition, the iCeMS will have access to the highest quality university facilities available, such as meeting spaces and halls for use during international symposia and academic conferences, campus libraries, cafeterias, and other common use facilities.

- (2) How it will institute a system under which the center's director is able to make substantive personnel and budget allocation decisions necessary to implementing the center project—a system, which in practice, allows the center director autonomy in making decisions regarding the center's operation.

To ensure autonomy of the center's operation, the university takes the following measures:

a) Flexible management of organization and operation system

An autonomous and independent management system that plays a role equivalent to the faculty will be implemented, to ensure the center's autonomy and the center director's leadership in making decisions regarding the center's overall operation. Decisions on important matters (personnel, budget, etc.) of the center will be made by the center director through discussions with the deputy center director, PI board chair, and administrative director (executive board), who assist and support the center director, in order to ensure appropriate operation. The director's term shall be for five years. Reappointment is possible. A director candidate shall be nominated by the executive board, and appointed by the university president.

At the same time, to enable the university to provide various support and advice promptly, the university president and executive vice-presidents meet the director of the center on a regular basis.

b) Introduction of flexible salary system to allow researchers' easy transfers

The world's leading foreign researchers, Japanese researchers who are highly recognized worldwide, and postdoctoral and other promising young researchers will be assembled at this center. For these researchers, whether from inside or outside the university, Kyoto University will allow applying a new personnel system that can appropriately reflect their achievements. To attract various researchers both from Japan and around the world, the university will accept the center director's request to implement a system of special allowances. The university also introduces a flexible personnel system in which the center director can select a salary system appropriate for each researcher that will assure the maximum flexibility for researchers in

transferring to the center.

- The annual faculty salary system that the university has already introduced (a fixed-term employment contract and an annual salary system based on achievements) will be applied. Hiring beyond the retirement age will be allowed.
- The current salary system will be applied to the researchers while they will be allowed to concurrently remain in the original departments if approved. These systems will promote; (1) intra-university cooperation among researchers, (2) integration of different academic fields, (3) human resource development through their participation in the university's educational activities, (4) effective usage of university facilities, and (5) flexible transfer of researchers within the university.
- Salaries for foreign researchers can be paid in the foreign currency of their home countries upon request.
- For qualified technical and administrative staffers, a special employment contract will be arranged to extend a regular retirement contract.

- (3) The support it will provide to the center director in coordinating with other departments within the host institution when recruiting researchers for the center, while giving reasonable regard to the educational and research activities of those departments.

The university takes the following measures with regard to educational and research activities within the university:

a) Support for researcher transfers to the center

To support researchers on their smooth and flexible intra-university transfer to the center, principal investigator-class personnel positions will be provided so that the impacts on current educational and research activities, and administrative works will be minimized.

b) Support in relation to education and research activities

If approved by their original departments, researchers will be allowed to keep their research in part and education concurrently in their original departments. This will facilitate their participation in educational activities and their shared use of research facilities, equipment, and materials. This will, in turn, contribute toward more active research activities.

To support the center's women researchers, the university provides effective assistance for and consultations on their research, child/nursing care, and daily lives.

c) Support for foreign researchers

To support foreign researchers and their families, the university provides job applicants with a handbook that explains immigration procedures, housing, the health-care system, and other daily life information. An experienced foreign mentor will be assigned for a period of time immediately after the researcher's arrival in Japan.

To support schooling for researchers' children, a system will be established to provide pre-Kindergarten through high school education in cooperation with schools in Kyoto Prefecture.

- (4) Its flexibility in applying, revising, or supplementing the host institution's internal systems as needed for the center to effectively implement new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation.

The university will accept necessary system revisions for implementation of new management methods unfettered by conventional modes of operation. Specifically, the university establishes an autonomous and independent management structure that serves a role equivalent to that performed by existing faculty-run management. Important issues (personnel, budget, etc.) will be discussed and decided by the center director, deputy director, PI board chair, and administrative director, in order to ensure prompt and appropriate administrative actions. The center director makes decisions on the following substantive matters necessary to promote this program:

- Matters related to recruitment of foreign and Japanese researchers, and postdoctoral and other young researchers
- Matters related to progress of research programs and evaluation of researchers' achievements
- Matters related to adoption/modification of the center's research programs
- Matters related to allocation and implementation of a budget for supporting research and operational activities of the center

- Matters related to management of research space in the center

For matters that require revision of the university regulations, the executive vice-president of the university in charge will provide specific consultation, and necessary administrative procedures will be handled by the head office administration in coordination with the center administration.

For administration, the university will provide several administrative personnel and necessary personnel costs while ensuring autonomy in administration. External personnel with a good command of English will also be recruited.

- (5) Its accommodation of the center's infrastructural requirements (for facilities, e.g., laboratory space; equipment; land, etc.).

Support for infrastructure requirements

Aiming to maintain a world-class institute with global visibility, Kyoto University will provide a high-quality research environment with a total area of about 12,000 m² including exclusive-use facilities with fully equipped infrastructure. The iCeMS reached approximately this scale in fiscal 2010 with the completion of Complex 2 (including a new 3,000 m² building). The university intends to pursue further efforts to improve the research environment at the iCeMS.

- (6) Other types of assistance it will provide to give maximum support to the center in achieving its concepts and objectives and becoming a world premier international research center in both name and deed.

1) 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.

2) Proactive support related to the establishment of a world class research institute

Kyoto University has been characterized, since its foundation in 1897, by an "academic atmosphere of freedom"; one that values originality and independence rather than the mere accumulation of knowledge. Located in the historic city of Kyoto, the university has developed research on diverse fields with profound originality in this unique "academic atmosphere of freedom".

Based on this historical background, it is defined in its mission statement (declared in 2001) that the ultimate goal of the university is to contribute to future sustainable human societies, featured by harmonious coexistence within human and ecological communities on this planet. This goal can be achieved by bringing forth the outstanding research and education programs in conformance with high ethical standards, and by generating world-class knowledge. We strongly believe that the best research in the world is created in the environment where the academic freedom and autonomy in research are highly valued, and in this regard, Kyoto University is one of the best places to establish a world premier international research center to lead the world's research.

List of Principal Investigators

- If the number of principal investigators exceeds 10, add columns as appropriate.
- Place an asterisk(*) by the name of the investigators who are considered to be ranked among the world's top researchers.
- Give age as of 1 April 2012.
- For investigators who cannot participate in the center project from 1 April 2012, indicate the time that their participation will start in the "Notes" column.

| Name | Age | Current affiliation (organization, department) and specialties | Academic degree | Notes |
|-----------------------|-----|---|-----------------|-------|
| ① Norio Nakatsuji* | 62 | Kyoto University, Institute for Integrated Cell-Material Sciences Stem-Cell Biology, Developmental Biology | Ph.D | |
| ② Susumu Kitagawa* | 60 | Kyoto University, Institute for Integrated Cell-Material Sciences Coordination Chemistry, Biological Inorganic Chemistry, Biomaterial Science | Ph.D | |
| ③ Motonari Uesugi* | 45 | Kyoto University, Institute for Integrated Cell-Material Sciences Chemical Biology | Ph.D | |
| ④ Konstantin Agladze* | 56 | Kyoto University, Institute for Integrated Cell-Material Sciences Biophysics, Non-linear science | Ph.D | |
| ⑤ Yong Chen* | 55 | Kyoto University, Institute for Integrated Cell-Material Sciences (Ecole Normale Supérieure, Centre National de Recherche Scientifique) Nano-biotechnology | Ph.D | |
| ⑥ Yoshie Harada* | 52 | Kyoto University, Institute for Integrated Cell-Material Sciences Single-molecule physiology | Ph. D | |
| ⑦ Mitsuru Hashida* | 60 | Kyoto University, Institute for Integrated Cell-Material Sciences (Kyoto University, Graduate School of Pharmaceutical Sciences) Biopharmaceuticals | Ph.D | |
| ⑧ John Heuser* | 69 | Kyoto University, Institute for Integrated Cell-Material Sciences (Washington University, School of Medicine) Biophysics, Cell Biology | M.D. & Ph.D | |
| ⑨ Takashi Hiiragi* | 44 | Kyoto University, Institute for Integrated Cell-Material Sciences (Max-Planck Institute for Molecular Biomedicine, Mammalian Development Laboratory) Developmental Biology | M.D. & Ph.D | |

(Appendix)

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|---|-------------------|----|--|-------------|--|
| ⑩ | Hiroshi Imahori* | 50 | Kyoto University, Institute for Integrated Cell-Material Sciences Photochemistry | Ph.D | |
| ⑪ | Mineko Kengaku* | 45 | Kyoto University, Institute for Integrated Cell-Material Sciences Developmental Neurobiology, Cell Biology | Ph.D | |
| ⑫ | Makoto Kiso* | 64 | Kyoto University, Institute for Integrated Cell-Material Sciences (Gifu University, Department of Applied Bio-organic Chemistry) Glycotechnology | Ph.D | |
| ⑬ | Akihiro Kusumi* | 59 | Kyoto University, Institute for Integrated Cell-Material Sciences Single-Molecule Cell Biophysics | Ph.D | |
| ⑭ | Hiroshi Sugiyama* | 55 | Kyoto University, Institute for Integrated Cell-Material Sciences (Kyoto University, Graduate School of Science) Chemical Biology | Ph.D | |
| ⑮ | Koichiro Tanaka* | 49 | Kyoto University, Institute for Integrated Cell-Material Sciences Terahertz Optical Science | Ph.D | |
| ⑯ | Kazumitsu Ueda* | 58 | Kyoto University, Institute for Integrated Cell-Material Sciences Cellular Biochemistry | Ph. D | |
| ⑰ | Shinya Yamanaka* | 49 | Kyoto University, Institute for Integrated Cell-Material Sciences Stem Cell Biology, Developmental Engineering | M.D. & Ph.D | |