Self-Evaluation Report for Interim Evaluation
World Premier International Research Center Initiative (WPI)

Host Institution	Kyoto University	Host Institution Head	Hiroshi Matsumoto
Research Center	Institute for Integrated Cell-Material Sciences (iCeMS)	Center Director	Norio Nakatsuji

Report Abstract

1. Science level (conversion rate throughout this report: JPY100 = US$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: 1) Reprogramming and iPS cell research by the **Yamanaka** Lab with papers in *Nature*, *Cell*, etc and 2) Functional porous materials research by the **Kitagawa** Lab 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.

Key multidisciplinary publications include: 1) new probes and control of stem cells with chemical compounds by the **Uesugi** Lab (*Angew Chem Int Ed* 2011, *JACS* 2009), and 2) real-time visualization and investigation of bio-functional molecules with DNA-origami engineering and AFM by the **Sugiyama** Lab (*Nature Nanotechnology* 2011, *Angew Chem Int Ed* 2010).

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).

Obtained major grants [**Grantee**, JPY million/year] include: Cabinet Office's FIRST program for iPS cell research and application [Prof **Yamanaka**, 1,200], next-gen FIRST program [Profs **Harada**, **Kengaku**, **Sengoku**, **Ueno** and **Uesugi,** 55 each], Ministry of Economy, Trade and Industry's NEDO programs for porous materials R&D [Prof **Kitagawa**, 500], magnetic nanoparticles R&D [Prof **Takano**, 180], stem cells R&D [Prof **Nakatsuji**, 420].

2. Interdisciplinary research activities

The institute's objective is "***to create new cross-disciplinary fields through the integration of cell and material sciences***." Its key concepts have been redefined as *stem cell technologies* and *mesoscopic sciences*.

35 interdisciplinary collaborative projects are underway. **25** have produced concrete results, **9** of which are in the process of manuscript preparation, submitted, or accepted for publication. In particular: Stem cell probes [**Uesugi**, **Yamanaka**, **Nakatsuji**, **Ueda** Labs], Control of reprogramming genes by synthesized chemical compounds [**Sugiyama**, **Yamanaka** (Prof **Yamada**) Labs], Cardiomyocyte differentiation from ES/iPS cells by chemical compounds [**Nakatsuji**, **Uesugi**, **Yamamoto** Labs], and Molecular dynamics imaging on cell membranes [**Kusumi**, **Kiso**, **Ueda**, **Kalay** Labs and **CeMI**].

Original and innovative cross-disciplinary collaboration integrating functional smart materials with living cells including stem cells are now underway via collaboration among the **Kitagawa**, **Imahori**, **Takano**, **Kiso**, **Chen**, **Kusumi**, **Ueda**, **Harada**, **Heuser**, **Kengaku**, and **Nakatsuji** Labs.

The iCeMS has started multiple incentives for cross-disciplinary collaboration, such as new researcher posts, start-up funds, and lab space specifically for multidisciplinary joint projects. Also, half-day workshops for planning and accelerating such projects have been held on a monthly basis.

3. Globalization of the institution

Strategic hiring to provide a truly international environment:

- Overseas researchers account for **31**% (**54** out of **174** total).
- Prof **John Heuser** (named an NAS Member in May 2011) is increasing his time to be spent at the iCeMS from 20% to **50%**, starting April 2011.
- **3** out of **5** iCeMS Kyoto Fellows (junior PIs) are from overseas, which brings the ratio of the foreign PIs and equivalent to **26%** (6 out of 23).
- Strong support for overseas researchers: 1) Overseas Researchers Support Office established; 2) workshops on obtaining grants held in English.
- **53%** of administrators are bilingual; all-English work practices established.

Circulating the world's best minds:
- **9** iCeMS International Symposia held to date.
- **4** joint symposia have been held by the iCeMS and its partner institutions, such as the UCLA-CNSI and the NCBS-inStem (another joint symposium with Heidelberg University scheduled for July 2011).
- **10** young researchers were sent to world-class institutions via the iCeMS-JSPS Overseas Visit Program for Young Researchers.

Fostering global partnerships (notable progress):
UCLA California NanoSystems Institute (CNSI):
- Memorandum of understanding (MoU) signed in March 2010.
- Joint research projects on porous materials, biomaterials, and drug delivery are well underway, with work starting on cancer stem cells.
- **2** co-authored papers published (*Angew Chem Int Ed* 2011, *Small* 2010).

National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem) in Bangalore, India:
- Based on an MoU, satellite labs established at both the iCeMS and the NCBS-inStem, enabling long term researcher exchanges and collaboration.

University of Edinburgh MRC Centre for Regenerative Medicine (CRM):
- MoU signed in March 2011; joint symposium scheduled in July 2011.

Heidelberg University:
- Joint symposium entitled "Crossing Boundaries: Stem Cells, Materials, and Mesoscopic Sciences" taking place in Heidelberg in July 2011.

Raising global visibility:
- Advertisements placed in *Nature* and *Science*, as well as in program books at large-scale conferences, such as the International Society for Stem Cell Research (ISSCR) and the American Chemical Society (ACS).
- Statistical analysis of the iCeMS website reveals:
  - **247,000** site views in 30 months (**8,200** views per month), **76% above** the average of science-related, similar-scale websites
  - **11%** of visitors from **130 overseas countries**

- The iCeMS hosted a booth, showcasing the institute's research areas and scope, at the 2011 AAAS annual meeting in Washington DC.
- The university has raised the iCeMS' profile in its organizational structure, as well as on the university website.

4. Organizational reform

Management:
- Kyoto University re-established the Center for iPS Cell Research and Application (CiRA) in 2010 as a university institute. CiRA Director **Shinya Yamanaka** remains an iCeMS professor, and iPS cell basic research continues to be conducted at the iCeMS, the two closely collaborating as sister institutes. **5** joint projects underway, with published results by an **Inoue**, **Uesugi**, **Nakatsuji** joint project (*J Biomol Screen* 2011).
- Leadership of the iCeMS Director is supported by the Executive Board, enabling remarkably swift decision-making.
- The university's strong support enables the iCeMS to: 1) employ researchers with increased flexibility in salary scale and retirement age, 2) effectively allocate all indirect costs, and 3) cover personnel costs for 5 PIs and 8 administrative employees with the university's budget.

Facilities and research environment:
- The Center for Meso-Bio Single-Molecule Imaging (CeMI) was established in March 2009, and is open for collaboration with global scientists.
- All labs and offices are shared in a newly-completed 3,000 m^2 research building; and all key equipment is shared and accessible to all groups.

Public outreach and engagement:
- The Science Communication Group (SCG), led by Adj Assoc Prof **Kazuto Kato**, has implemented numerous outreach efforts such as science cafés, hands-on stem cell classrooms, a hands-on exhibition at a science festival hosted by the Cabinet Office, and lectures for middle and high schools.
- Press releases distributed worldwide via the AAAS' news wire service.
- Media coverage: **1,500** times (print media, TV, web), **78** from overseas.

Industry-government-academia collaboration:
- The Innovation Management Group (IMG), led by Assoc Prof **Shintaro Sengoku**, manages cross-sector and overseas linkages as both a subject of academic study as well as in practice in the field.
- Nonprofit organization *Kyoto SMI* (Smart Materials & Innovation) founded to quickly deliver the outcomes of scientific research to industry and society.

1. Summary of Center Project

<Initial plan>

We will accumulate a critical mass of leading scientists for the symbiotic integration of material and cell sciences (focusing on mouse and monkey pluripotent 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. We will achieve this goal by taking cross-disciplinary approaches, with the following inter-related targets. For basic science:

1) New Chemistry/Physics of Meso-Space 2) Cellular meso-biophysics; and 3) Stem-cell-differentiation meso-engineering. We will contribute to human wellness by developing A) environmentally-friendly chemical reaction systems, by developing new methods of material conversion (chemical reaction), separation, and storage B) drug-synthesis/controlled-release microvessels working in the body, and C) regenerative medicine based on regulated cell-material complexes.

<Current status>

1. Clarifying the iCeMS' mission

In FY 2009 the iCeMS was ordered by the WPI Program Committee and the site visit team to redefine its research mission as follows:

- Reappraisal of the basic concepts: *meso-scale control* and *integration of cell-material science*; and
- Rewriting the mission statement and roadmap of the center.

As a result, extensive thought was given to 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. The following summarizes how the institute's key concepts have evolved over the past four years:

- October 2007: (1) *New chemistry/physics of meso-space*, (2) *Cellular meso-biophysics*, and (3) *Stem-cell control meso-engineering*.

Criticized at FY 2008 Site Visit and Program Committee as being too broad, lacking a clear sense of what is actually to be studied.

- January 2009: (1) *Meso-control of stem cell systems*, and (2) *Meso-control of functional architectures*.

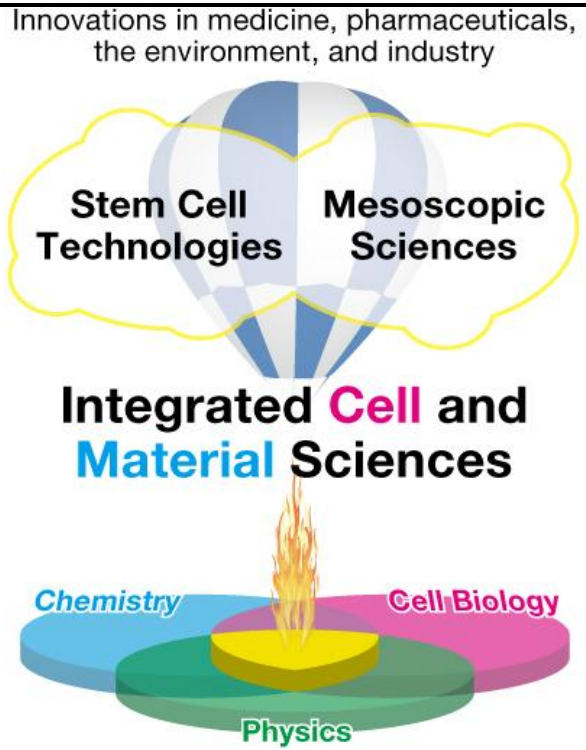
Criticized at FY 2009 Site Visit and Program Committee for vagueness of the "meso" concept, which is not especially well understood by biologists.

- October 2010: (1) *Stem Cells*, and (2) *Soft functional architectures*.

The PD and PO advised that (2) is difficult to understand, and recommended that the Advisory Committee be consulted for advice.

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." See "Appendix 1-1: Report of the Advisory committee FY2010" for details.) ➢ February 2011: (1) *Stem cell technologies*, and (2) *Mesoscopic sciences*. 2. Redefined research objectives As described above, the iCeMS' key concepts have been criticized as being 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 Institute for Integrated Cell-Material Sciences, is **to create new cross-disciplinary fields through the integration of cell and material sciences**. Investigating the control mechanisms of multimolecular structures within cells on the one hand, and artificial materials on the other, as well as bringing about the fusion of the two, the iCeMS is pioneering the development of *stem cell technologies* and *mesoscopic sciences*. These are anticipated to lead to innovations in medicine, pharmaceuticals, the environment, and industry.



Stem Cell Technologies Research includes:

- Reprogramming with chemical compounds for iPS cell derivation;
- Chemical probes for stem cell research;
- Control of ES/iPS cell growth and differentiation with chemicals and materials; and
- Creation and applications of stem cell-derived model cells in medicine and drug discovery.

Mesoscopic Sciences Research includes:

- Imaging and probing of meso-complexes in cells;
- Production of functional mesoscopic materials;
- Integration of mesoscopic materials and living cells; and
- Modeling, simulation, and physics theories of mesoscopic events in materials and living cells.

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.

*Reference: Yoseph Imry, *Introduction to Mesoscopic Physics*, Oxford University Press (1st ed 1997, 2nd ed 2002)

3. Top scientists conducting cross-disciplinary research at the highest level
[**Note**: up-to-date scientific progress is reported in Section 2, below]

3a. High research standards

- A total of **464** papers published under the iCeMS' name:

  a) **59** papers published in leading journals with an **impact factor of 10 or more**, including *Nature* journals (except *Nature Chemistry* and *Nature Communications*), *Science*, *Cell*, *Angewandte Chemie, International Edition*, and *Developmental Cell*.

  b) **6** more papers published in other *Nature* journals (*Nature Chemistry* and *Nature Communications*) with no impact factors so far available.

- Obtained major grants [**Grantee**, JPY million/year] include:

  a) Cabinet Office's Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST) for iPS cell research and application [Prof **Yamanaka**, 1,200]

  b) Cabinet Office's Funding Program for Next Generation World-Leading Researchers (FIRST2) program [Profs **Harada**, **Kengaku**, **Sengoku**, **Ueno** and **Uesugi**, 55 each on average]

  c) Ministry of Economy, Trade and Industry's New Energy and Industrial Technology Development Organization (NEDO) programs for:
  - porous materials R&D [Prof **Kitagawa**, 500]
  - magnetic nanoparticles R&D [Prof **Takano**, 180]
  - stem cells R&D [Prof **Nakatsuji**, 420]

- Receipt of numerous, notable academic awards, in particular:

  a) Profs **Heuser** and **Yamanaka**: National Academy of Sciences (USA) membership (May 2011).
  b) Prof **Kusumi**: Elected to the American Society for Cell Biology (ASCB) Council (2010).
  c) Profs **Kitagawa** and **Yamanaka**: Thomson Reuters Citation Laureates (2010).
  d) Prof **Yamanaka**: Albert Lasker Basic Medical Research Award (2009).
  e) Prof **Kitagawa**: Humboldt Research Award (2008).

  See "6. Criteria and methods used to evaluate center's global standing" for more details.

3b. Actively crossing disciplines

- In October 2009, **28** collaborative interdisciplinary PI research projects were selected, and since then their progress has been closely monitored by the Director. Later, **7** new collaborative projects were added. At present, **25** projects have progressed significantly, one of which has been published (*Angew Chem Int Edit*, 2011) and **8** are in the final stage and being prepared for publication.

- Active leadership by a special task force, led by deputy director **Susumu Kitagawa**, on strategic cross-disciplinary research: (a) 7 meetings held by the task force to spearhead integration of cell and material sciences; (b) **10** top-priority projects selected for focused support; (c) planning for further utilization of a Cross-Disciplinary Journal Club.

- Annual iCeMS retreats for all research staff
  a) **2009:** Kyoto Prefectural Seminar House (**74** attended, **39** posters presented)
  b) **2010:** Awaji Yumebutai International Conference Center (**115** attended, **74** posters presented); featured highly stimulating presentations by researchers who had participated in JSPS-sponsored overseas visit programs.

- **43** Cross-disciplinary seminars conducted as a core element of regular

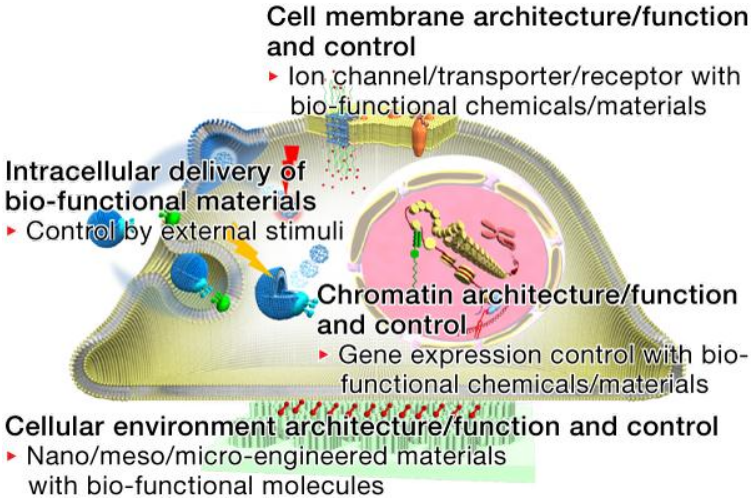
PI meetings.

- iCeMS Exploratory Grants for Junior Investigators promote cross-disciplinary research among young iCeMS scientists. Selected so far: **13** projects (2009), **29** projects (2010), **41** projects (2011).

- Extension of exploratory cross-disciplinary research grants to Kyoto University scientists outside of the iCeMS. So far selected: **19** projects from **12** university departments (2010). A call for proposal submission is now underway for FY 2011.

- Two review papers on mesoscopic sciences (by Dr **Kalay** and Prof **Ueda**) have been accepted for publication.

3c. Conceptual diagram of redefined areas and subjects of research, giving important cross-disciplinary examples of mesoscopic architectures and functions in living cells and their control with chemicals and materials:



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

Major developments in the relationship between the iCeMS and the Kyoto University Center for iPS Cell Research and Application (CiRA) include:

- In FY 2007, the iCeMS Director swiftly implemented his decision to create the Center for iPS Cell Research and Application under the auspices of the iCeMS, marking a major advance in the effort to apply human stem cell research to the field of regenerative medicine.

- Reflecting progress in the field as well as answering public expectations, clinical applications for regenerative medicine were added to the CiRA's mission on top of basic research. This change necessitated restructuring of the iCeMS-CiRA relationship because this new application-oriented mission extended the CiRA's research areas beyond the basic research scope of the WPI Program.

- Thanks to the strong leadership of Kyoto University's president as well as the iCeMS Director, working together to consolidate opinions on all levels, the process was started to make the CiRA a new institute within the university while simultaneously making a correspondingly high priority budget request to the Ministry of Education, Culture, Sports, Science and Technology (MEXT).

- A new 12,000 m^2 CiRA research building was completed on the Kyoto University Hospital Campus in February 2010, conveniently located for collaborative clinical research with the hospital.

- The resulting new institute 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.

Specific areas of joint research (and relevant faculty) include:

- Differentiation of ES/iPS cells using synthetic chemical compounds (**Nakatsuji**, **Uesugi**, iCeMS Kyoto Fellow and CiRA PI **Yamamoto**)

- Development of small molecules as stem cell probes and as synthetic cell adhesion factors (**Uesugi**, iCeMS PI and CiRA Director **Yamanaka, Ueda**, **Nakatsuji**)

- Control of reprogramming gene expression using synthetic

transcription factors (**Sugiyama**, iCeMS Prof and CiRA PI **Yamada**, **Nakatsuji**)

- Single-molecule imaging study of muscle cells differentiated from mouse iPS cells, with normal and dystrophin-deficient genotypes (**Kusumi**, CiRA Deputy Director **Nakahata**)

- Small molecule tools and chemical libraries produced by the **Uesugi** group have been used extensively in CiRA's research as a part of collaborations with the **Yamanaka**, **Sakurai**, **Inoue**, and **Osafune** labs, aiding their clinically relevant investigations. The results of one of these collaborations, with the **Inoue**, **Uesugi** and **Nakatsuji** Labs, has recently been published (*Journal of Biomolecular Screening* 2011).

Recent examples of iCeMS-CiRA organizational cooperation include:

- **7** faculty members, including Prof **Shinya Yamanaka**, Prof **Yasuhiro Yamada**, and Asst Prof **Takuya Yamamoto** (appointed as one of the four original iCeMS Kyoto Fellows) are employed at the iCeMS while continuing to conduct basic research on iPS cells.

- Consolidation of overseas networking efforts, led by iCeMS Assoc Prof **Shintaro Sengoku**, head of the iCeMS Innovation Management group, and CiRA Assoc Prof **Tetsuya Ishii**, head of the CiRA Research Management Office.

- Consolidation of cooperative research efforts, led by iCeMS Prof **Motonari Uesugi** and CiRA Prof **Yasuhiro Yamada**.

- Consolidation of ES/iPS cell culture quality control management systems with cooperation and collaboration between the **Nakatsuji** and relevant **CiRA** Groups.

- Participation of CiRA researchers in iCeMS Seminars (eg Prof **Yamanaka** and many others attended an iCeMS Seminar by **Sir John Gurdon** of the University of Cambridge).

- Participation of **8** members from the CiRA, including **4 CiRA PIs**, at the 2010 iCeMS Retreat.

- Participation of CiRA Senior Lecturer **Keisuke Okita** in the July 2011 Heidelberg-Kyoto Joint Symposium, co-organized by the iCeMS.

- Joint planning and hosting of iCeMS/CiRA stem cell classroom events for high school students and their teachers (for details, see "8. Other important measures taken to create a world premier international research center").

- Adding to the iCeMS-CiRA collaboration detailed above, the following researchers have joined the staff to strengthen the key role that iPS/stem cell-related basic research plays within the iCeMS: Prof **Takashi Shinohara** of the university's Graduate School of Medicine joined the adjunct faculty and strengthened stem cell research with his study of germ cell lineage stem cells; and Prof **Mitinori Saitou**, also an adjunct professor, brought his expertise in fate determination and differentiation mechanisms of stem cells in early embryos. Also, Prof **Azim Surani**, a world leading scientist in the germ/stem cell lineage and epigenetic reprogramming research and a professor at the University of Cambridge's Gurdon Institute, took up a visiting professor post at the iCeMS.

5. Research environment

A new 3,000 m^2 research building was completed in FY 2010. All large scale shared equipment have been installed to provide researchers with an excellent research environment, including the iCeMS Center for Meso-Bio Single-Molecule Imaging (CeMI). For details, see "5-1) Environment in which researchers can devote themselves to their research."

Owing to limited space as well as building restrictions imposed by the Kyoto city government, these complexes are separated but within walking distance of each other. To overcome this issue, the iCeMS has implemented a number of measures aimed at bringing researchers together, including monthly meetings of PIs and on strategic cross-disciplinary research, the Cross-Disciplinary Journal Club, annual retreats, and a variety of seminars and other events usually held at the iCeMS main building.

In addition, video conferencing systems have been deployed throughout

the institute to link Kyoto with satellite labs and overseas partner institutions, enabling researchers on both sites to naturally interact with each other during meetings and joint events.

6. Globalization of the institution

Strategic hiring to provide a truly international environment:

- Overseas researchers account for **31**% (**54** out of **174** total).
- Prof **John Heuser** (named an NAS Member in May 2011) is increasing his time to be spent at the iCeMS from 20% to **50**%, starting April 2011.
- **3** out of **5** iCeMS Kyoto Fellows (junior PIs) are from overseas, which brings the ratio of the foreign PIs and equivalent to **26**% (6 out of 23).
- Strong support for overseas researchers: 1) Overseas Researchers Support Office established; 2) workshops on obtaining grants held in English.
- **53**% of administrators are bilingual; all-English work practices established.

Circulating the world's best minds:

- **9** iCeMS International Symposia held to date.
- **4** joint symposia have been held by the iCeMS and its partner institutions, such as the UCLA-CNSI and the NCBS-inStem (another joint symposium with Heidelberg University scheduled for July 2011).
- **10** young researchers were sent to world-class institutions via the iCeMS-JSPS Overseas Visit Program for Young Researchers.

Fostering global partnerships (notable progress):

UCLA California NanoSystems Institute (CNSI):

- Memorandum of understanding (MoU) signed in March 2010.
- Joint research projects on porous materials, biomaterials STM/AFM, and drug delivery are well underway, with work starting on cancer stem cells.
- **2** co-authored papers published in *Angew Chem Int Ed* (2011) and *Small* (2010).
- A seminar on global visibility meant for both scientists and administrators held by CNSI Director for International Partnership at the iCeMS

National Centre for Biological Sciences (NCBS) and the Institute for Stem

Cell Biology and Regenerative Medicine (inStem) in Bangalore:
- Based on the MoU, satellite labs established at both the iCeMS and the NCBS-inStem, enabling long term researcher exchanges and collaboration.

University of Edinburgh MRC Centre for Regenerative Medicine (CRM):
- MoU signed in March 2011; joint symposium scheduled in July 2011.

Heidelberg University:
- Joint symposium entitled "Crossing Boundaries: Stem Cells, Materials, and Mesoscopic Sciences" taking place in Heidelberg in July 2011.
- A Wiley journal planning to publish a special issue featuring the above symposium in early 2012.

Additionally:
- MoUs newly signed with the Medicinal Bioconvergence Research Center at Seoul National University and with the Moscow Institute of Physics and Technology, and set to be signed in April 2011 with the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR).
- MoUs currently being negotiated with Peking University and Tsinghua University.

Raising global visibility:
- Advertisements placed in *Nature* and *Science*, as well as in program books at large-scale conferences, such as the International Society for Stem Cell Research (ISSCR) and the American Chemical Society (ACS).
- The university has raised the iCeMS' profile in its organizational structure, as well as on the university website.
- Statistical analysis of the iCeMS website reveals:
  - **247,000** site views in 30 months (**8,200** views per month), **76% above** the average of science-related, similar-scale websites
  - **11%** of visitors from **130 overseas countries**
- The iCeMS hosted a booth, showcasing the institute's research areas and scope, at the 2011 AAAS annual meeting in Washington DC.

For more details, see:
- "4. Researchers and center staffs, satellites, partner institutions";
- "5. Summary of center's research environment (particularly 5-3, 5-4, 5-7)"; and
- "6. Criteria and methods used to evaluate center's global standing".

7. Preparing for the period after WPI project funding ends

- Previously in a miscellaneous category, the iCeMS has succeeded in being repositioned higher within the university's organizational structure as well as on the university website, now highlighted prominently as a "World Premier International Research Center".

- 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.

- 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.

<Future prospects>

Leading edge research (for details, see "2-3. Future Policy and Concrete Plans")

- Advancing basic stem cell research, contributing to medicine and drug discovery
- Advancing mesoscopic materials science, contributing to environmental and industrial technologies
- Advancing novel research fields aiming to **integrate stem cell research and cell biology with chemistry and material sciences**
- Building on ever closer ties with the CiRA
- Establishment of a multidisciplinary stem cell and integrated cell-material research network for all of Kyoto University, including among its members the iCeMS, the CiRA, the Institute for Frontier Medical Sciences, the university hospital, and the Graduate Schools of Agriculture, Biostudies, Medicine, Science, and Pharmaceutical Sciences

Cross-disciplinary research (for details, see "2-3. Future Policy and Concrete Plans")

- 35 cross-disciplinary research projects identified and progressing
- Spearheading integration of cell and material sciences with a special task force, enthusiastically attended by PIs and young researchers alike
- Selection of particularly promising projects for focused support
- Plans to further utilize the Cross-Disciplinary Journal Club on multidisciplinary cell-material research and mesoscopic sciences, taking a lead role in global scientific interactions in the field

- Taking the lead in supporting cross-disciplinary research conducted by young researchers of other university departments and beyond
- Advancement of basic mesoscopic science research and the publication of relevant review articles

Internationalization

- Expanding ties with the UCLA, particularly in the field of cancer stem cells
- Strengthening joint satellite laboratories with the NCBS-inStem in Bangalore, India
- Expanding contacts with the MRC-CRM in Edinburgh, Scotland
- Co-organizing a joint symposium planned for July 2011 based on an MoU between Kyoto University and Heidelberg University
- Exploring the possibility of expanding ties with universities and research institutes in China, South Korea, Egypt, and Russia
- Increasing global visibility through: (a) international press release distribution services; (b) placement of timely advertisements in leading journals; (c) full use of social media such as *Twitter.*
- Accelerating the field of chemical biology in East Asia, with Prof **Uesugi** coordinating a JSPS-sponsored joint effort with South Korea, China, and Singapore (the JSPS Asian CORE Program "Asian Chemical Biology")

Institutional Reform

- Expanded internationally-oriented administrative reform (structurally and in content)
- Knowledge-sharing of strategic reform with institutions beyond the iCeMS in order to promote the structure and philosophies of the institute past the period of WPI program funding

2. Center's Research Activities

2-1. Initial plan

<Research fields>
An interdisciplinary research field, spanning Biosciences, Chemistry, Material Sciences, and Physics (selected from the provided list of fields). The scientific direction of this proposed Institute was conceived based on two key concepts. They are meso-space and stem cells.

<Research objectives>
(1) Meso-space is the space of 10-100 nm. Between the two well-walked lands of bulk- and nano-spaces, there is the vast unexplored field of meso-space. However, we can find fledgling developments there in various branches of science. The cooperative structural changes of porous coordination polymers present good examples. Many key functions of the cell, such as transcription (mRNA synthesis using a DNA template) and signaling, are achieved by large molecular complexes of 10-100 nm, rather than simple bimolecular collisions. In this Institute, we will develop a fundamental understanding and control of the key molecular (weakly cooperative) interactions occurring in the meso-space, throughout cellular, chemical, physical, and materials sciences. By taking interdisciplinary approaches, we will establish a unified view of the molecular interactions in the meso-space in all of these fields, and will develop a variety of unprecedented technologies based on the meso-scale interactions.

(2) Mouse and monkey pluripotent stem cells will be used as an important paradigm of the cell throughout the research in this Institute. A unified cellular paradigm is critical for fostering the collaborative research by investigators with various backgrounds. This would enable the application to regenerative medicine using human embryonic stem (ES) cells. Kyoto University has been known worldwide for its excellence in both material and cell sciences. Physics and chemistry-related departments have produced four Nobel Laureates, and the times cited for Chemistry of Kyoto University was fourth in the world and first in Japan in 2006. Its Institute for Frontier Medical Sciences is a strong world leader in pluripotent stem cell research. Many faculty members of Kyoto University are active leaders in the forefront of such scientific integration, and thus will enable a critical mass of researchers to establish an ideal research

environment.

2-2 Research results to date

2-2-1 Center's research activities and results

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 emerging areas: (A.) *stem cell technologies* and (B.) *mesoscopic sciences*. 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. Below, we summarize the major outcomes of our recent research, including individual studies by our PIs, inspired by the goals of the iCeMS, and multidisciplinary collaborations newly initiated within the iCeMS. Although each major outcome is listed under one of the two research areas, some of the research is relevant to both stem cells and mesoscopic sciences.

A. Stem cell technologies

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 technologies 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 mesoscopic control strategies to ES/iPS cells, resulting in unprecedented abilities to shape the course of stem cell technology development.

A-1. Reprogramming and iPSC derivation

The **Yamanaka** Lab is the world pioneer in iPS cell research and has provided the basis for a number of collaborations at the iCeMS. Prof **Yamanaka** continues to serve as an iCeMS PI, while also acting as the director of the applications-oriented Center for iPS Cell Research and Application (CiRA). The two institutes are carrying out many collaborative projects as sister institutes of Kyoto University.

The **Yamanaka** Lab first established pluripotent stem cells derived from human adult dermal fibroblast culture by using four transcription factors. These reprogrammed cells, termed induced Pluripotent Stem (iPS) cells, have great potential in basic research and application in regenerative medicine and disease modeling because of their characteristics as pluripotent stem cells such as human ES cells (*Cell* 2007). Lately, the group has reported the generation of mouse iPS cells from embryonic fibroblasts without viral vectors. The iPS cells without evidence of plasmid integration was created and they contributed to adult chimeras. The production of virus-free iPS cells addresses a critical safety concern for potential use of iPS cells in regenerative medicine (*Science* 2008). More recently, they succeeded to increase the efficiency of the integration-free human iPSC lines (*Nature Methods* 2011).

iPSCs was first generated with retroviruses of Oct3/4, Sox2, Klf4 and c-Myc. Reactivation of the c-Myc retrovirus, however, increases tumor generation in the chimera mice. To overcome this issue, they modified the protocol and successfully generated iPSCs without c-Myc. Mice derived from Myc(-) iPS cells did not show the tumor formation (*Nature Biotechnology* 2008).

The **Yamanaka** Lab demonstrated that culturing with hypoxic conditions enhance the efficiency of iPS cell generation using retroviruses or non-viral vectors

such as expression plasmids or the piggyBac transposition system. They hope understanding the basis of this hypoxic enhancement will contribute to efficient iPSC generation with no genetic modification (*Cell Stem Cell* 2009).

Suppression of p53 was shown to promote human iPS cell generation. They reported 34 p53-regulated genes that are common in mouse and human fibroblasts. Functional analyses demonstrate that the p53-p21 pathway serves as a barrier not only in tumorigenicity, but also in iPS cell generation (*Nature* 2009).

A-2. Chemical/material probes and functional factors for stem cell research

The **Uesugi** Lab has been attempting to provide chemical solutions in basic science and clinical application of human stem cells or related cells and distributing chemical tools to other groups in the iCeMS and the CiRA.

Small molecule probes have made significant contributions to biomedical research. However, many cellular components remain to be explored by small molecule probes. The **Uesugi** Lab has now discovered the first fluorescent probe specific for surfaces of mitochondria, an organelle proposed to be important in the maintenance of self-renewal and pluripotency of stem cells (*Angew Chem Int Ed* 2011). Interestingly, this molecule is converted to be fluorescent inside cells.

The **Uesugi** Lab discovered a small molecule that turns off genes responsible for making fat in cells and animals (*Chemistry & Biology* 2009). The molecule named "fatostatin" binds to a protein called SCAP, and inhibits the activation of SREBP transcription factor. Mice treated with fatostatin do not get fat, even with excessive food consumption. These results attracted attention from the public and were reported broadly in national and international newspapers, including all of the major Japanese newspapers.

The **Uesugi** Lab discovered a small molecule that boosts the attachment and growth of human cells (*Chemistry & Biology* 2009). This molecule represents the first non-peptidic molecule that induces physiologically relevant, normal cell adhesion and may be useful for basic science and clinical application of human stem cells or related cells. The molecule named "adhesamine" targets selective cell-surface glycosaminoglycans, especially heparan sulfate. Adhesamine has been licensed out and is now commercially available for a range of applications.

A-3. Differentiation of stem cells into important cell lineages

The **Nakatsuji** Lab has been continuing research on pluripotent stem cell lines, such as human ES/iPS cell lines, and also closely related mammalian germline. They are focusing on differentiation of human ES/iPS cells into cardiomyocytes and central nervous system for research and application.

The first differentiation step to mesoderm and endoderm, separated from ectoderm lineage, occurs at gastrulation stage in mammalian embryos. At this crucial step, Wnt/β-catenin signaling is playing important roles. Thus, the **Nakatsuji** Lab created transgenic hESC line, in which Wnt/β-catenin signaling can be switched ON/OFF, to investigate molecular mechanism for differentiation onto mesoderm and endoderm lineages, such as cardiomyocytes (*Development* 2008). They have been working extensively on not only initial differentiation from hES/iPS cells, but also maturation of cardiomyocytes for application in drug safety assay (*Stem Cell Research* 2010). Another focus is neuronal differentiation for creation of neurodegenerative disease model cells such as Alzheimer's, ALS and Huntington's by introduction of mutated genes into hES/iPSC lines, followed by differentiation into relevant specific neurons or glia (*PLoS ONE* 2009).

The **Nakatsuji** Lab has been also working on molecular mechanisms for differentiation and genetic integrity involved in the germline cell lineage. Mammalian germline cells, which produce oocytes and sperm, contain unique molecular complexes named "nuage" in their cytoplasm, but their function is still not clear. They have been investigating gene function of the complex components by creating gene knockout mouse strains of the Tudor family genes (*Developmental Cell* 2009). They published another work on the related nuage component: MITOPLD is a mitochondrial protein essential for nuage formation and piRNA biogenesis in the mouse germline (*Developmental Cell* 2011).

A-4. Genetic engineering of stem cells and creation of model cells for research and application

Genetic modification of human ES/iPS cell lines has unique difficulty due to their sensitivity to various stresses and strong silencing effects to transgenes integrated into chromatin. The **Nakatsuji** Lab has been advancing various novel methods to produce transgenic hES/iPS cell lines for many purposes such as creation of neurodegenerative disease model cells. One example is to create a highly efficient method for homologous recombination by using improved virus vectors (*Proc Nat Acad Sci USA* 2008). Another example is to integrate Cre/loxP-driven exchange gene cassette at the HPRT locus with homologous recombination to allow reliable and robust expression of transgenes (*Nucleic Acids Research* 2010).

A-5. Investigation of differentiated cell function and multidisciplinary approaches

Elucidation of molecular and biophysical mechanisms of cell function and its regulation is another important aspect of multidisciplinary research in iCeMS. The **Agladze** Lab has been working on biophysical aspects of the control mechanisms of cardiomyocyte cells and tissue function. The unpinning of spiral waves by the application of high-frequency wave trains was studied in cultured cardiac myocytes, as a model for low voltage defibrillation. Successful unpinning was observed when the frequency of the paced waves exceeded a critical level. The unpinning process was analyzed by a numerical simulation with a model of cardiac tissue (*Physical Review E* 2008). Also, the unpinning of a spiral wave from an anatomic obstacle by the application of a single stimulus near the core of the rotating wave was studied experimentally in a cell culture of cardiomyocyte monolayers as well as by computer simulations. (*Physical Review E* 2009).

The **Kengaku** Lab has been working on molecular and spatial/physical control of neuron migration and pattern formation in the brain. Sonic hedgehog is an important signal molecule regulating various biological responses through gene activation. They identified a novel Sonic hedgehog pathway directly regulating actin cytoskeleton independent of gene activation. The novel Sonic hedgehog pathway is involved in shaping dendritic spines, which are actin-rich protrusions receiving synaptic inputs from other neurons (*Molecular and Cellular Neuroscience* 2010). Also, type I lissenchephaly (LIS1) regulates intracellular transport and its mutation is a major cause for the neurological disorder LIS1. The **Kengaku** Lab and others showed that inhibition of calpain protected LIS1 from degradation and rescued cell death and neuronal migration defects in Lis1(+/-) mutant mice. These results imply potential therapeutic application of calpain inhibitors for lissencephaly. Inhibition of calpain increases LIS1 expression and partially rescues in vivo phenotypes in a mouse model of lissencephaly (*Nature Medicine* 2009).

The **Chen** Lab is providing nano/meso/micro-engineered physical substrate and scaffolds to combine with many cell types to produce novel tools and platform for investigation of cell and tissue functions. They has found a simple way to observe 3-dimensional morphology at a nanoscale level of adherent cells using a new technique called reversed cell imprinting. With an atomic force microscope, they can now have both top and bottom views of cells cultured on different substrates (*Lab on a Chip* 2010).

B. Mesoscopic sciences

B-1. Mesoscopic cell architectures and functions

For advancing the aim of the iCeMS, ie, 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) 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.

The central imaging laboratory established within iCeMS in March 2009, the **Ce**nter for **M**eso-Bio Single-Molecule **I**maging (**CeMI**), is playing a key role in advancing this study. The core scientists include Profs **Harada**, **Heuser**, **Kusumi**, and **Tanaka** and iCeMS Kyoto Fellow Dr **Carlton**, as well as Scientific

Administrator (Senior Lecturer) Dr **Fujiwara**. The CeMI focuses on single-molecule imaging and terahertz microscopy both conducted in living cells, and is developing instruments and methodologies leading the world in these important areas. Together with Prof **Heuser**'s electron microscopy laboratory and Dr **Carlton**'s 3D optical microscopy laboratory, the iCeMS is uniquely equipped with these newly developed imaging technologies. These technologies are now also being used by the groups studying stem cells and material-cell interactions.

B-1-1. Cytoskeleton-induced domains and the interaction between the cytoskeleton and the plasma membrane: the **CeMI**, **Heuser**, and **Kusumi** Labs have continued extensive investigations on the models of molecular dynamics in the plasma membrane, including dynamic entrapment model, simple-Brownian diffusion model, and the model of hop diffusion in the partitioned plasma membrane, and found that the most basic architecture of the plasma membrane is provided by its partitioning by the actin-based membrane skeleton (*Biophysical Journal* 2008). For conducting this research, the microscope station to perform the world-fastest single fluorescent-molecule imaging (a 100-microsecond resolution) has been developed. The **Heuser** Lab established a quantitative method for determining the mesh size of cortical actin filaments on the inner surface of the plasma membrane (*Methods in Molecular Biology* 2010).

The **Ueda** (*Journal of Biological Chemistry 2011*) and **Kengaku** Labs (*Molecular and Cellular Neuroscience* 2010) independently found two new pathways for actin reorganization (WAVE2-PKA and a novel Sonic hedgehog pathway), leading to membrane protrusion and dendritic spine formation, respectively. These studies are performed also in the context of studying the dynamic control of cell shape and motility in the developing brain, clarifying the biomedical importance of these findings.

The **Hiiragi** Lab previously found that the assembly of many surface glycoproteins in the cleavage furrow, where actin bundles form, is essential for cytokinesis (*Genesis* 2008), and has now obtained data suggesting that the reorganization of actin-based membrane skeleton is involved in the assembly of cell surface proteins.

B-1-2. Raft-domain organization and function in the plasma membrane: Some of ATP-binding cassette (ABC) proteins, such as ABCA1, transport cholesterol rapidly in an ATP-dependent manner and might be involved in raft-domain formation. The **Ueda** Lab found that the interaction of ABCA1 and the HDL precursor apolipoprotein A-I (apoA-I) is essential for HDL formation (*Journal of Biological Chemistry* 2009). Furthermore, they found that ABCA1 works as both a lipid transporter and a receptor for apoA-I (*Journal of Lipid Research* 2009).

The **NCBS-inStem Satellite** (Assoc Prof **Ken Suzuki**), **CeMI**, and **Kusumi** Labs have clarified the mechanisms by which the raft-based lipid interactions and more specific protein-protein interactions cooperatively work for signal transduction of GPI-anchored receptors. In steady-state cells, GPI-anchored receptors continually form transient homo-dimers by ectodomain protein interactions, stabilized by raft-based lipid interactions (~200 ms). Upon ligation, they form stable dimers or greater oligomers, triggering intracellular signaling.

They also found that GPI-anchored proteins diffuse even faster than their transmembrane counterparts, disproving the conventional notion that GPI-anchored proteins are entrapped within stable raft domains (*Biophysical Journal* 2008). The **Kusumi** Lab revealed that GPI-anchored proteins and lipids cannot be immobilized by conventional chemical fixation, and established a method for fixing GPI-anchored proteins for immunostaining studies (*Nature Methods* 2011).

B-1-3. Protein-complex domains made of membrane-associated and integral membrane proteins: In many important signaling pathways, protein complexes involving three and (many) more molecules formed in/on the plasma membrane have been found, and these entail the smallest domains considered here. Many diseases that are induced by the failure in forming such complexes have now been described extensively, which provide another good reason for including these complexes as research targets.

The **CeMI** and **Kusumi** Labs developed a new single fluorescent-molecule imaging method, termed "super quantitation", and determined the dynamic monomer-dimer equilibrium in the plasma membrane, first time ever for any membrane molecules, using the N-formyl peptide receptor, a chemoattractant GPCR, in live cells as an important paradigm (*Journal of Cell Biology* 2011). The **Ueda** Lab found that ABCA1 directly binds to a nuclear receptor, LXR, causing

both transcriptional and post-translational responses, modulating cholesterol efflux (*Journal of Biological Chemistry* 2008).

B-1-4. Specialized membrane domains and 3D dynamics between the plasma membrane and intracellular membranes: The **Heuser** Lab made a discovery that supports a new role for caveolae as a physiological membrane reservoir that quickly accommodates sudden and acute mechanical stresses (*Cell* 2011). The **Kengaku** Lab previously showed that brain-specific protein DNER is selectively transported to dendrites, and now they demonstrated that polarized DNER localization is maintained by rapid clearance of mis-targeted DNER in the axon by endocytosis (*Journal of Neurochemistry* 2010).

B-1-5. Gene regulation systems: For the basic understanding of the stem cell (de)differentiation, we have started investigations of how chromosomes are reorganized at the time of (de)differentiation and how the small chemical compounds that induce (de)differentiation enhance/suppress specific transcription. These studies are now at the fledgling stages, but they are important targets of the iCeMS. The **Carlton** Lab initiated observing specific chromosomes in living cells using 3D deconvolution fluorescence microscopy they developed. The **Harada** Lab is developing a single-molecule imaging method for the observation of specific mRNAs in living cells (*Nucleic Acids Research* 2011) and various processes related to gene transcription (presently *in vitro*).

B-1-6. Development of new imaging methods: Near-field terahertz microscopy and its application to living cells and tissues. The **Tanaka** Lab has succeeded in greatly reducing the signal acquisition time and improving the spatial resolution. Within the next five years, we anticipate that this microscopy will be useful for imaging water interaction with cell surfaces, tissues, and intracellular structures. Such observation has already been achieved by terahertz spectroscopy (*Physical Review Letters* 2011) and will be expanded to microscopy.

B-2. Smart materials for mesoscopic functions and applications

Our aim of this project is to establish a symbiotic integration of spatial architectures and chemicals 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 intermolecular or interatomic distances of the pores of materials (0.1–10 nm) up to the space inside biological cells (100 nm). We are aware that truly interesting events, which are challenging to understand and control, tend to occur in the more complex world of mesospace, in the size range of 10 to 100 nm. To date we have obtained a variety of new porous coordination polymers, magnetic nanoparticles, DNA tiled assemblies, and hybridized carbons, porous proteins, and supramolecular materials.

B-2-1. Design and synthesis of porous coordination polymers (PCPs) for smart functions and applications: the **Kitagawa** Lab focuses on a porous solid material possessing integrated attributes of both crystallinity and flexibility, providing capability of gas capture/release and separation, electronic and optical properties, ion transport capability in meso-domain. Their geometric and/or electronic structures are so flexible as to respond external stimuli of temperature, pressure, light, and electric field.

Prof **Kitagawa** has developed new porous materials that give an opportunity to find novel phenomena based on molecular coagulation, molecular stress, and activation of molecules. He focuses on the concept of the cooperative integration of 'softness' and 'regularity' in porous materials, so-called soft porous crystals, with dynamic frameworks that are able to respond to external stimuli such as light, electric fields or the presence of particular species. These materials show potential applications not only for living cells but also for green sustainable materials. This new class of materials are defined and overviewed with perspectives as a review article with respect to phase transitions as collective phenomena in the mesoscopic domain (10–100 nm) (*Nature Chemistry* 2009).

The **Kitagawa** Lab synthesized a PCP with a switchable pore surface that can be highly activated by photo-irradiation and applicable to on-demand trapping of gaseous molecules such as harmful carbon monoxide (*Nature Materials* 2010). They designed a new molecular decoding system utilizing a structural entanglement of a PCP to detect a single target molecule of benzene derivatives in a vapor form with a corresponding luminescent readout (*Nature Communications* 2011). The other is a new mechanism to capture O_2 and NO selectively among various gases. The **Kitagawa** Lab has succeeded in

separating mixture of gases containing a biologically important NO gas utilizing an electron-donating organic linker with the concerted effect of the charge-transfer interaction between the linker and these guests (*Nature Chemistry* 2010). They have noticed that thermal transitions of confined polymers are important for the application of polymers in molecules/ions transport technology and showed that the pore size and surface functionality of PCPs can be tailored to study the transition behavior of confined polymers, providing properties characteristic of a few polymer chains (*Nature Communications* 2010). They proposed a new idea of encapsulation of a proton-carrier molecule—imidazole in PCPs for the creation of a hybridized proton conductor under anhydrous conditions for high-temperature, providing an anhydrous proton-conductive materials operating at temperatures above 100°C (*Nature Materials* 2009). There are many other potential applications of PCPs in the nanometer-micrometer range, especially in biological systems, where the target environments are biological cells with sizes around 1–2 μm, and in electronics, where the devices should be fixed on substrates with ordered structures at nanometer scale. For the application of PCPs in the nanometer-micrometer regime, the hybridization of each function into a single particle is essential, creating so-called *'single particle devices'*. They present a new technique for the rapid preparation of porous coordination polymer nanocrystals (*Nature Chemistry* 2010).

B-2-2. Carbon nanotubes and other functional molecules: the **Imahori** Lab focuses on artificial photosynthetic and solar energy conversion materials, which are applied to cell biology and medicine, and will exploit novel cell engineering and therapy by light. Dye-sensitized solar cells have attracted much attention relevant to global environmental issues. One of them is carbon nanotubes chemically modified with a number of porphyrins, which have been investigated as materials for organic solar cells. The light-harvesting carbon nanotubes exhibited enhanced conversion of light to heat, indicating their utilization for photothermal cancer therapy because cancer tissues are generally more sensitive to heat than normal tissues.

The **Imahori** Lab has found that large π-aromatic molecules, such as porphyrins, are important classes of potential sensitizers for highly efficient dye-sensitized solar cells. The achievement has been summarized in a review article (*Accounts of Chemical Research* 2009). In order to enhance electrical communication between the grains and to modulate the arrangements within the grains, Imahori has succeeded in synthesis of a hierarchical self-assembly of donor-acceptor linked molecules with molecular wires for efficient photocurrent generation (*Angew Chem Int Ed* 2011). The **Imahori** and **Takano** Labs have developed an external stimuli-responsive azobenzene polymers for dispersion of carbon nanotubes and subsequent designated patterning of the carbon nanotube-based electrodes (*Chemical Communications* 2010). Vertical arrangement of donor-acceptor arrays on an electrode is essential to attain efficient photocurrent generation in bulk heterojunction solar cells. The **Imahori** Lab has developed a novel strategy for constructing such architecture on an electrode and realized supramolecular donor-acceptor heterojunctions by vectorial stepwise assembly of porphyrins and coordination-Bonded fullerene arrays for photocurrent generation (*Journal of the American Chemical Society* 2009).

B-2-3. Hybrid nano/meso-materials: the **Ueno** and **Kitagawa** Labs are developing protein assemblies which can serve as porous materials with high bio-compatibility toward control of cell functions. In particular, protein crystals and protein tubes are the appropriate candidates for these purposes because we can display multifunctionality on/in them. They have demonstrated the availability of their designed protein crystals and tubes as the molecular scaffolds.

The **Ueno**, **Kitagawa** and **Tanaka** Labs succeeded in obtaining an artificial photo-induced electron transfer system by accumulating redox cofactors in a myoglobin crystal (*Angew Chem Int Ed* 2011). Collaboration research was done by Drs **Ueno** and **Kitagawa** and a collaboration partner institute**, CNSI, UCLA.** They succeeded in synthesizing a robust bio-nanotube consisting of the β-helical tubular component proteins of bacteriophage T4. AFM experiments collaborated with Prof **Gimzewski** (**CNSI**) indicate that it has a well-defined nano-scale length of 10 nm as a result of head-to-head dimerization of b-helices. Surprisingly, the tube assembly has high thermal stability, and tolerance to organic solvents as well as a wide pH stability range (*Small* 2010). **Takano** Lab is trying to power up nano-sized magnets to be used for bio- and medical-sciences. They propose the utilization of ferromagnets like α-Fe and α"-Fe16N2 having magnetizations of more than 2.5 times than conventional ferrimagnets like Fe3O4 and γ-Fe2O3 (*Chemistry of Materials* 2011), preparing the stable and easily handled 6 nm-sized particles (*Physical Review B* 2008) and fixing the orientated nanoparticles on Si Substrates (*Applied Physics Express* 2009).

Another category of their research is solid state chemistry on oxides containing economical and functional 3D transition metal elements like iron and manganese, which will contribute to sustainable ecological economic developments of human life (*Nature Chemistry* 2009).

B-2-4. Delivery devices for cell functional control and therapy: This project has been carried out as collaboration among the **Murakami**, **Hashida**, **Imahori**, **Kiso**, and **Takano** Labs.

The **Murakami**, **Hashida**, and **Imahori** Labs have developed a facile method for the size control of HDL within the mesoscale (*Molecular BioSystems* 2010). Meso-scale drug carriers are known to accumulate at tumor tissues and inflammatory sites. According to this method, HDL was enlarged by loading of various drugs including anticancer and anti-inflammatory drug when simply prepared with increased amount of phospholipid. The **Murakami** and **Hashida** Labs developed a cell-penetrating HDL for intracellular delivery of functional molecules including drugs and external stimuli-responsive nanomaterials (*Nanomedicine* (London) 2010). They prepared novel molecular devices using carbon nanotubes functionalized by peptide (The **Hashida** and **Imahori** Labs, *Japan Patent Application No 2011-68972*). The **Hashida** and **Kiso** Labs has demonstrated that liposomes modified with various sugar moieties such as galactose, mannose, fucose, and mannose 6-phosphate, showed selective delivery to cells with receptors corresponding to each sugar (*Journal of Controlled Release* 2011, *Pharmaceutical Research* 2011, *Biomaterials* 2010, *Molecular Pharmaceutics* 2011). The **Murakami**, **Imahori** and **Hashida** Labs has developed molecular devices for cell tracing with multifunctional quantum dots or gene transfection (*Journal of Controlled Release* 2008, *Molecular Therapy* 2011).

B-2-5. DNA origami and tile for molecular tools and bio-function study: DNA origami techniques allow to build nano- and meso-sized structures with great precision. The **Endo** and **Sugiyama** Labs succeeded in creating a programmable molecular transport system, the workings of which can be observed in real time. Controlled motion at the nanoscale was achieved using Watson–Crick base-pairing to direct the assembly and operation of this transport system consisting of a track, a motor and fuel, all made from DNA. This innovative system opens up a wide range of possible applications like the construction of synthetic ribosomes to perform autonomous multi-step synthesis (*Nature Nanotechnology* 2011).

The **Endo** and **Sugiyama** Labs have designed a new DNA frame nanostructure with two structurally fixed types of double-strand DNAs to control the methylation reaction and by simulating the enzymatic reaction have demonstrated the role of DNA flexibility on an enzymatic modification. This method can be extended to various enzymatic phenomena for understanding the epigenetic code (*J Am Chem Soc* 2010); the **Sugiyama** Lab has successfully investigated the dynamics of the formation and disruption of G-quadruplexes with real-time observation of the changes in the DNA nanostructure. (*J Am Chem Soc* 2010); and the **Endo** and **Sugiyama** Labs have created tension-controlled dsDNA substrates in a designed DNA nanoscale scaffold called "DNA Nanochip" and disclosed the importance of DNA-strand relaxation in allowing double helix bending during the enzymatic reaction. (*Angew Chem Int Ed* 2010, *Angew Chem Int Ed* 2011).

2-2-2 Research Achievements

A. Refereed papers (published or accepted for publication)
Total: **464**

FY 2007-2008	101	FY 2009	163	FY 2010	200

B. Invited lectures, plenary addresses (etc.) at international conferences and international research meetings
Total: **351**

FY 2007-2008	121	FY 2009	97	FY 2010	133

C. General lectures at international conferences
Total: **93** oral, **317** poster

FY 2007-2008	oral	poster	FY 2009	oral	poster	FY 2010	oral	poster

	16	58		14	98		63	161

D. Invited lectures at domestic scientific societies and research meetings
Total: **402**

FY 2007-2008	188	FY 2009	112	FY 2010	102

E. General lectures at domestic scientific societies and research meetings
Total: **417** oral, **290** poster

FY 2007-2008	oral	poster	FY 2009	oral	poster	FY 2010	oral	poster
	149	96		131	94		137	100

F. Books (e.g., scientific, specialized volumes)
Total volumes: **83**

FY 2007-2008	28	FY 2009	24	FY 2010	31

G. Industrial property rights
Total: **0** registered, **105** being processed

FY 2007-2008	registered	processed	FY 2009	registered	processed	FY 2010	registered	processed
	0	40		0	33		0	32

H. Major awards received (including those formally announced)
Total: **78**

FY 2007-2008	30	FY 2009	17	FY 2010	31

2-3 Future Policy and Concrete Plans

<Research fields>

Our research will continue to focus on the **integration of cell biology and material sciences (chemistry/physics)**, with the goals of achieving ground-breaking scientific discoveries and developing innovative technologies in the stem cell and mesoscopic sciences and technologies. When the iCeMS was founded, the research team of each PI made individual efforts to achieve these goals, inspired by the iCeMS' multidisciplinary environment. Recent research activities are increasingly driven by close collaborations among PIs with expertise in different fields. This highly promising trend will continue to be strongly promoted.

<Research objectives>

The overall objectives continue to be achievement of ground-breaking scientific discoveries and development of innovative technologies in two fields: (A.) *stem cell technologies* and (B.) *mesoscopic sciences*. To identify more specific research goals for the coming years, PIs and young investigators 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 technologies and four representative specific aims in mesoscopic sciences and technologies. We would like to note that these categorized aims often overlap each other: innovative mesoscopic research of living cells may generate or inspire new applications in stem cell biology and technology.

A. Stem cell technologies
A-1. Reprogramming with chemical compounds for iPS cell derivation
A-2. Chemical tools for stem cell research
A-3. Control of ES/iPS cell growth and differentiation with chemicals and materials
A-4. Creation and applications of stem cell-derived model cells for cell biology, medical research and drug discovery

B. Mesoscopic sciences
B-1. Imaging and probing meso-complexes in the cell
B-2. Production of functional mesoscopic materials
B-3. Integration of mesoscopic materials and living cells
B-4. Modeling, simulation, and physics theories of mesoscopic events in materials and living cells

Multidisciplinary collaborations among our PIs will enable us to succeed in these specific research goals, which would be difficult to conduct without such diverse expertise. Below are representative collaborative research projects that are ongoing, some of which include brief research summaries.

A. Stem cell technologies

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

- Control of gene expression by synthesized chemical transcription factors, and chemical reprogramming [**Sugiyama**, **Yamanaka** (Yamada) Labs]**:**

A-2. Chemical probes for stem cell research

- Small molecule tools for stem cell research/applications [**Uesugi**, **Yamanaka**, **Ueda**, **Nakatsuji**, **Sugiyama** Labs]:

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

- Chemical inducers for cardiomyocyte differentiation from ES/iPS cells [**Nakatsuji**, **Uesugi**, **Yamamoto** Labs]:
- Functionized nanofibers and other materials for stem cell growth and manipulation [**Chen**, **Nakatsuji**, **Takano** Labs]

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

- Neurodegenerative disease model creation and investigation [**Nakatsuji**, **Heuser** Labs, **CeMI**]
- Cardiac tissue models and anisotropy analysis using stem cell-derived cardiomyocytes on nanofibers and light-sensitive functional materials [**Agladze**, **Nakatsuji**, **Chen** Labs]
- Visualization and analysis of the dynamics of dendritic arborization using novel chemical compounds [**Kengaku**, **Uesugi** Labs]

B. Mesoscopic sciences

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

- Investigating the effects of meso-scale compartments on kinetics of bimolecular reactions in the plasma membrane, and cell membrane single molecule imaging using synthesized glycan probes [**Kusumi**, **Kiso**, **Kalay** Labs, **CeMI**]:

- Novel probes (diamond particle) for investigating cell architecture dynamics [**Harada**, **Shirakawa**, **Nakatsuji** Labs]:
- Terahertz (THz) microscopy of living tissue and stem cells for functional imaging [**Tanaka**, **Kusumi**, **Harada**, **Nakatsuji**, **Hiiragi** Labs]
- Single molecule observation of ABCA1 to study function and dynamics of transporters on the cell membrane [**Ueda**, **Kusumi** Labs]

B-2. Production of functional mesoscopic materials

- Development of new carriers for targeted drug delivery using carbon nanotubes and lipsomes functionalized by peptides and gyco-coating [**Murakami**, **Hashida**, **Imahori**, **Kiso**, **Takano** Labs]:
- Synthesis magnetic nanoparticles and fabrication of their functional assemblies [**Takano**, **Sugiyama**, **Kitagawa** (Ueno) Labs]
- Development of hybrid functional mesoscopic molecules using proteins and inorganic materials [**Ueno**, **Kitagawa**, **Takano** Labs]

B-3. Integration of mesoscopic materials and living cells

- Development of light-harvesting functional materials for phototherapy and photoregulation of cell functions [**Murakami, Imahori, Heuser, Hashida, Kengaku, Nakatsuji** Labs]:

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

- Mesoscopic theory of cellular function and supramolecular chemistry **[Kalay, Kusumi, Kitagawa, Nakatsuji** Labs**]:**

< Major changes >
There is no major change in the research fields and objectives. However, we have clarified and refined our research fields and objectives, by confirming that integration of the cell and material sciences is the main field of the iCeMS. The concept and terminology of "meso-" has been clarified as described in "1. Summary of Center Project" of this report. The meso-concept is well-established in the field of physics (mesoscopic physics), and we are aiming to expand the mesoscopic sciences to include cell biology and life sciences, which will be achieved by crossing the borders between materials and living cells.

3. Management

<Initial plan>	<Efforts to date and current state>
1) Composition of administrative staff An Administrative Director and a Deputy-Director, together with an administrative staff (approximately 27 people) will be hired. One of the Directors should have impeccable experience in international scientific collaboration matters, whereas the other should know how administrative business is carried out in a Japanese national university, thus complementing each other. Six administrative sections will be created, to be in charge of General Affairs (including Personnel and Public Relations), Planning and Industry Liaison, Finance, Research Support and Intellectual Property, Facilities (Physical Plant), and Research Ethics and Safety. All sections will have at least two staff members who are fluent in English.	1) Composition of the administrative staff Notable points of progress in FY 2007 At the time of its founding, the iCeMS' administrative division consisted of 19 people, including a former Kyoto University research promotion division director as its head and a long-time national university administrator as its deputy-chief, lending the new institute a solid footing in institutional knowledge and guaranteeing smooth relations with university headquarters. Remaining staff were divided into three areas: senior administrators, general affairs (including planning and public relations), and finance (including intellectual property management). Notable points of progress in FY 2008

For the qualifications of such administrative leaders, firstly, she/he needs to be familiar with university administrative matters, including those of Kyoto University, and to be able to plan and create new directions in the administration of this new Institute. On the other hand, she/he must have impeccable experience in international scientific collaboration matters. An especially close connection with the administrative headquarters of Kyoto University will be strongly required during the initial establishment of the center. Thus, the Director of Research Promotion of the Kyoto University Administration Bureau will be designated as the Administrative Director, and the Deputy Director will be recruited from a younger member of the career staff of JSPS (Japan Society for Promotion of Science) overseas center in Europe, for the above-mentioned necessity.	International Public Relations office established. As part of the founding of the CiRA within the iCeMS, 10 personnel led by a second deputy-administrative chief joined the organization, forming the CiRA Support Office. <u>Notable points of progress in FY 2009</u> A new Administrative Director was appointed, bringing a wealth of experience in international academic exchange and scientific management. The Overseas Researchers Support Office (ORSO) was established. Along with a substantial increase in research personnel, the iCeMS administrative division, including the CiRA Support Office, increased to 41 members. <u>Notable points of progress in FY 2010</u> Along with the CiRA's reestablishment as a sibling institute to the iCeMS, its support office staff were redeployed to the new CiRA. At the iCeMS, new sections were established to oversee international affairs and funding management, bringing the administrative division to 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. A new office for IT support and data security was also established, led by a computer science researcher. This manager administers IT infrastructure development and content creation, as well as strategic IT planning aiming to increase the institute's visibility abroad. <u>Present composition of the administration: 30 total</u> **Senior Executives**: Director and Deputy Director **General Affairs**: Manager and 4 staff members **Overseas Affairs and Planning**: Manager and 3 staff members (2 of whom perform the duties of the Overseas Researchers Support Office) **International Public Relations**: Manager and 2 staff members (one of whom is a native speaker of English) **Finance**: Manager (senior administrator) and 4 staff members

	Funding Management (including intellectual property rights management): Manager and 4 staff members **Facilities and Environment**: Manager and 2 staff members **IT Support**: Manager **Secretaries to director**: 2 staff members
2) Decision-making system The Director is responsible for all aspects of running the Institute, with the aid of the Deputy Director as well as the Administrative Director. A Steering Committee, which advises the Director, will consist of both scientists and non-scientists from within and outside Kyoto University, and will gather twice a year regularly, and accordingly upon the Director's request. The Core Committee Meeting of the Principal Investigators will provide scientific advice.	2) Decision-making system As illustrated in the attached organization chart (Appendix 7), the institute's faculty cooperate 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: <u>Executive Board</u> 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. <u>Board of PIs</u> Consisting of all 18 PIs, 5 iCeMS Kyoto Fellows (junior PIs), and 2 special research group leaders (associate professors), conducting 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. <u>Strategic Task Force for Cross-Disciplinary Research</u> 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. <u>Faculty Selection Committee</u> Established in February 2011 as part of the Executive Board to deliberate the renewal of employment contracts for faculty who have served their full 5 years at the institute. <u>Advisory Committee</u> Consisting of 9 distinguished outside researchers (6 non-Japanese) meeting once annually to provide the institute with unbiased feedback.

3) Allocation of authority between center director and host institution In the organizational structure of Kyoto University, this Institute will occupy a special position, freed from many binding rules of the classical Japanese university archetype, to present a future-model of a highly authorized research institute not only to Kyoto University but also throughout Japan and to the world. For this purpose, flexible rules of a new paradigm, as for the relationships with the university headquarters, the salary levels and deserved special bonuses, and the reduced duties in various committees and undergraduate education, will be created. These rules will be applied as a basis and model for the foundation of other research institutes within Kyoto University in the future. The Director will report directly to the President of Kyoto University and the Member of Executive Board in charge of research, but the Institute will basically be run autonomously.	3) Allocation of authority between center director and host institution The host institution is responsible for overall governance and rule-making, while the center director determines pay levels etc 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 to 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. 4) Other key developments <u>International public relations and science communication</u> 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, likewise 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. <u>Strategic plans to acquire sources of competitive funding</u> 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 an associate professor with strong ties to industry, acting as head of the Innovation Management Group (IMG). This group's members both conduct research on international partnerships, multi-sector ties, and cross-disciplinary research, as well as implement strategies related to these areas, greatly aiding the institute director in his decision-making.

< Future policy and concrete plans >

1) Composition of the administrative staff

As described above, the administration reached 8 sections in FY 2010. 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.

2) Decision-making system

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

3) Allocation of authority between center director and host institution

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 center staffs, satellites, partner institutions

4-1. Number of researchers in the "core" established within the host institution

All members

	Goal set in proposal	Results at end of FY 2008	Results at end of FY 2009	Results at end of FY 2010	Final goal (Date: March 31, 2012)
Researchers	171 <52, 31%>	90 <16, 18%>[15, 17%]	151 <46, 31%>[43, 29%]	174 <54, 31%>[45, 26%]	180 <59, 33%> [50, 28%]
Principal investigators	21 <5, 24%>	17 <2, 12%>[2, 12%]	18 <3, 17%>[2, 12%]	18 <3, 17%>[2, 12%]	18 <3, 17%> [2, 12%]
Other researchers	150 <48, 32%>	73 <14, 20%>[13, 18%]	133 <43, 33%>[41, 31%]	156 <51, 33%>[43, 28%]	162 <56, 35%> [48, 30%]
Research support staffs	59	43	64	70	75
Administrative staffs	29	19	28	30	32
Total	259	152	243	274	287

Other matters of special mention

- The iCeMS Kyoto Fellow positions have been established in an attempt to recruit young, promising researchers capable of leading their own teams as junior principle investigators. Fellows are given priority over lab space and startup funds to pursue collaborative, cross-disciplinary research projects. A total of **five** Fellows including **three from overseas** have been selected, which brings the overseas principle investigators ratio to **26%** (six out of 23) from **17%** (three out of 18), the figure reported above as of the end of FY 2010.

- John Heuser, an internationally recognized authority on electric microscopy, will be hired at the 50% effort level (previously 20%) from FY 2011.

- Career paths from the iCeMS to prominent institutions

Program Specific Researcher (WPI), 1 April 2008-31 December 2008:	Full-time Researcher, Japan Biological Informatics Consortium (Japan)
Program Specific Researcher (WPI), 1 March 2008-31 May 2009:	Researcher, Japan Science and Technology Agency (Japan)
Program Specific Researcher (WPI), 1 April 2008-30 June 2009:	Assistant Professor, Indian Institute of Technology (India)
Program Specific Researcher (WPI), 1 April 2009-31 March 2010:	Researcher, Japan Foundation for Neuroscience and Mental Health (Japan)

Program Specific Researcher (WPI), 1 April 2009-31 March 2010:	Assistant Professor, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University (Japan)
Program Specific Researcher (WPI), 1 April 2010-11 June 2010:	The Institute of Science and Industrial Research, Osaka University (Japan)
Program Specific Assistant Professor, 1 July 2009-30 September 2010:	Senior Scientist, Petrochemical Research Institute of Petrochina (China)
Program Specific Researcher (WPI), 1 March 2009-31 December 2010:	Postdoctoral Fellow, Ecole Nationale Superieure de Tecniques Avancees (France)
Program Specific Researcher (Industry-Government-Academia Collaboration), 6 October 2009-28 February 2011:	Research Scientist, Samsung Advanced Institute of Technology (Korea)
JSPS Postdoctoral Fellow, 30 November 2008-31 October 2010:	Research Fellow, National University of Singapore (Singapore)

4-2. Satellites and partner institutions

<Initial plan>	<Collaboration to date>
i) Satellites <u>Institution (1)</u> <u>Faculty of Applied Biological Sciences, Gifu University</u> -Role Collaboration and instruction between glycol-technology and stem cell biology -Personnel composition and structure A PI -Collaborative framework In relation to the chemical reaction between: - cells and cells - cells and air quality	i) Satellites <u>Institution (1)</u> <u>Faculty of Applied Biological Sciences, Gifu University</u> -Role Collaboration and interaction between glycol-technology and stem cell biology -Personnel composition and structure Prof **Makoto Kiso**, Assoc Prof **Hiromune Ando** -Collaborative framework Collaborative research and exchanges of scientists, research idea and materials In FY 2009, 260 m^2 of new laboratory space were added, augmenting Gifu University's role as a satellite facility. In collaboration with the **Kusumi** Lab, the **Kiso** Lab has been first to develop ganglioside probes for dynamic and functional analysis of lipid rafts using single molecule tracking. In collaboration with the **Hashida** Lab, the **Kiso** Lab has succeeded in the creation of highly liver-specific glyco-coated liposomes as drug carriers.

	The **Kiso** Lab had established new methods to synthesize bioactive or autoimmune disease-relevant gangliosides, thereby succeeding in the first total syntheses of X1, LLG-3 and GalNAc-GD1a. -Research outcome 1. Establishment of novel methods for glycan synthesis 2. Development of glycan mimic which regulates immune suppressing system (collaboration with the Tsubata Lab at Tokyo Medical and Dental University) 3. Development of sialidase inhibitor (collaboration with the Suzuki Lab at Chubu University) 4. Development of ganglioside probes as raft markers (collaboration with the Kusumi Lab) 5. Development of novel DDS utilizing cell-specific glycan receptors in active targeting of drug carrier (collaboration with the Hashida Lab) -Research Papers 1. "Design, Synthesis, and Structure-Affinity Relationships of Novel Series of Sialosides as CD22-Specific Inhibitors," Hajaj H. M. Abdui-Allah, Taichi Tainanaka, Jie Yu, Lu Zhuoyuan, Magesh Sadagopan, Takahiro Adachi; Takeshi Tslibata, Soerge Kelm, Hideharu Ishida, Makoto Kiso, *Journal of Medicinal Chemistry* (2008) 2. "Ganglioside GQ1b: Efficient Total Synthesis and the Expansion to Synthetic Derivatives To Elucidate Its Biological Roles," Akihiro Imamura, Hiromune Ando, Hideharu Ishida, Makoto Kiso, *Journal of Organic Chemistry* (2009) 3. "The total synthesis of neurogenic ganglioside LLG-3 isolated from the starfish Linckia laevigata," Hideki Tamai, Hiromune Ando, Hide-Nori Tanaka, Ritsuko Hosoda-Yabe, Tomio Yabe, Hideharu Ishida, Makoto Kiso, *Angew Chem Int Ed* (2011)

ii) Partner institutions Institution (1) Bionanotechnology Interdisciplinary Research Centre, the University of Oxford -Role Collaborative research on DNA-based nano-meso technology -Personnel composition and structure Prof John Ryan -Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students	ii) Partner institutions Institution (1) Bionanotechnology Interdisciplinary Research Centre, the University of Oxford -Role 2007: Collaborative research on the structure-function of G-protein-coupled receptors. The initial target of the research has shifted due to changes in research direction of the main collaborators at Oxford University. 2008: Collaborative research on the structure-function of G-protein-coupled receptors. -Personnel composition and structure Profs **John Ryan, Anthony Watts, Dustin Molloy,** and **Simon Davis** -Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students. Profs **Yoshie Harada** and **Akihiro Kusumi** of the iCeMS have conducted collaborative studies with Profs **Anthony Watts** and **John Ryan** of the Oxford University. In 2008, Prof **Kusumi** was invited to a scientific symposium on Nanobiotechnology held at Oxford University. Collaborative research has been carried out by Profs **Simon Davis** and **Kusumi** on the project of first entirely quantitative analysis of dynamic equilibrium of monomers and dimers of membrane molecules. Because the Bionanotechnology Interdisciplinary Research Centre at the University of Oxford was a time-limited organization, and its financial support period ended in 2009, this partnership was terminated. However, collaborative research projects will continue at the level of individual researchers. In December 2010, Prof **Ryan** was invited to deliver a talk at the Ninth iCeMS International Symposium. In March 2011, Prof **Davis** visited the iCeMS for research discussions on the dynamic formation of meso-scale molecular complexes and molecular

	interactions for signal transduction in the plasma membrane. In addition, he gave a lecture on this subject in the context of T-cell receptor signaling. Based on these exchanges, a new collaborative study has been launched on how the membrane-spanning phosphatase CD45 interacts with meso-scale signal-transduction complexes. The plan includes sending an iCeMS researcher to Oxford in September-October in 2011 and accepting an Oxford researcher early next year for a few months, for joint collaborative experiments. -Research Papers 1. "Full characterization of GPCR monomerdimer dynamic equilibrium by single molecule imaging," Rinshi S. Kasai, Kenichi G. N. Suzuki, Eric R. Prossnitz, Ikuko Koyama-Honda, Chieko Nakada, Takahiro K. Fujiwara, Akihiro Kusumi, *Journal of Cell Biology* (2011) (Prof Simon Davis was not included as an author, but was acknowledged.)
Institution (2) Wellcome Trust Centre for Stem Cell Research, The University of Cambridge -Role Research collaboration in interdisciplinary stem cell biology studies -Personnel composition and structure -Collaborative framework Joint research and academic interaction including the professors, postdocs and graduate students visiting one another	Institution (2) Wellcome Trust Centre for Stem Cell Research and its sister institute, Wellcome/Gurdon Institute, Cambridge University -Role Research collaboration in interdisciplinary stem cell biology studies -Personnel composition and structure Profs **Fiona Watt, Austin Smith, Azim Surani** -Collaborative framework Joint research and academic interaction including the professors, postdocs and graduate students visiting one another A strong connection has existed between the Wellcome Trust Centre for Stem Cell Research and the iCeMS since the iCeMS' founding. Prof **Fiona Watt** delivered an inauguration lecture at the iCeMS Opening Ceremony on February 19, 2008. Prof **Watt** has been a member of the iCeMS Advisory Committee since FY 2008, and has continued to offer the institute valuable advice on stem-cell research. She was invited for a talk at the Eighth iCeMS International Symposium on November 11, 2010.

	In FY 2009, Prof **Azim Surani** became an iCeMS visiting professor; collaboration with Prof **Surani** will contribute to the iCeMS' progress toward assembling the world's strongest network of researchers in the biological functions and mechanisms of reprogramming and pluripotency. On November 26, 2010, Prof **John Gurdon** visited iCeMS to deliver a seminar on reprogramming of cell nuclei in eggs and oocytes. The seminar attracted over 100 iCeMS, CiRA, and other university department participants. Prof **Surani** was invited to an international symposium during November 22–24, 2010 in Japan (Prof **Norio Nakatsuji** was one of the organizers). They discussed about the latest situation and future trends of the stem cell and reprogramming research.
Institution(3) National Centre for Biological Sciences (NCBS), Bangalore, India -Role Collaborative research on membrane meso-domains -Personnel composition and structure Profs Satyajit Mayor and K. VijayRaghavan -Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students. Co-sponsoring meetings and symposia.	Institution (3) National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem), Bangalore, India -Role Collaborative research on stem-cell sciences, single-imaging technologies, and membrane meso-domains -Personnel composition and structure Profs **Satyajit Mayor** (Academic Dean), **Madan Rao**, and **K VijayRaghavan** (director of the NCBS) and **S Ramaswamy** (Dean of inStem) -Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students; co-sponsoring meetings and symposia; collaborative research jointly conducted by the iCeMS and NCBS satellite labs Prof **Akihiro Kusumi** of the iCeMS has been conducting collaborative research with Profs **Satyajit Mayor** and **K VijayRaghavan** of the NCBS. The NCBS co-sponsored the Sixth International Symposium of the iCeMS, January 27–29, 2010. Profs **Mayor** and **Madan Rao** of the NCBS were both invited to speak at this symposium. A visit by Prof **Kusumi** to the NCBS and inStem was made on December 2

	and 3, 2009 and in terms of expanding the collaboration front toward stem cell research, discussions were also held with Profs **S Ramaswamy** and **Jyotsna Dhawan**, Deans of inStem. The NCBS and the iCeMS signed a memorandum of understanding (MoU) on April 28, 2010. Prof **Norio Nakatsuji** and iCeMS' senior faculty visited the NCBS and inStem in August, 2010 and participated in a joint symposium. To promote further long term collaboration, the NCBS and the iCeMS agreed to establish mutual satellite laboratories. The NCBS-inStem Satellite at the iCeMS opened on December 17, 2010. In commemoration, an opening ceremony and the second NCBS-inStem/iCeMS joint symposium was held at the iCeMS. At the same time, Prof **VijayRahavan** conferred honorary NCBS-inStem visiting professorships on Profs **Nakatsuji** and **Kusumi**. -Research outcome 1. A paper reporting the result of the collaborative research on the method for fixing raft-associated molecules for immunostaining has been published in *Nature Methods* (2010). 2. The **Kusumi** Lab is in the process of writing a paper describing diffusion and its regulation of raft-associated molecules in the plasma membrane. -Research paper 1. "Membrane molecules mobile even after chemical fixation," Kenji A. K. Tanaka, Kenichi G. N. Suzuki, Yuki M. Shirai, Shusaku T. Shibutani, Manami S. H. Miyahara, Hisae Tsuboi, Miyako Yahara, Akihiko Yoshimura, Satyajit Mayor, Takahiro K. Fujiwara, Akihiro Kusumi, *Nature Methods* (2010)
Institution(4) Max Planck Institute for Molecular Cell Biology and Genetics -Role Collaborative research on vesicular-transport meso-complexes -Personnel composition and structure Prof Kai Simons -Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students	Institution (4) Max Planck Institute for Molecular Cell Biology and Genetics (MPI-CBG) -Role Collaborative research on vesicular-transport meso-complexes -Personnel composition and structure Profs **Kai Simons**, **Wieland Huttner**, **Mario Zerial**, and **Jonathan Jones** are the key scientists of collaboration at the MPI-CBG, to be joined by many more in the future

	-Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students Collaborative research has been carried out by Profs **Kai Simons** and **Wieland Huttner** of the MPI-CBG and Prof **Akihiro Kusumi** of the iCeMS. The MPI-CBG and the iCeMS have encouraged PhD students of each institute to do postdoctoral research at the other institute. Prof **Kusumi** visited MPI-CBG between November 10 and 12, 2008, and discussed collaborative directions covering many overlapping areas of iCeMS and MPI-CBG. In February 2009, a delegation from the iCeMS consisting of its PIs and administrators visited MPI-CBG to have a discussion with MPI-CBG members. Between August 30 and September 1, 2009, Prof **Kai Simons** of the MPI-CBG and Prof **Kusumi** of the iCeMS met and held discussions on the occasion of the EMBO (European Molecular Biology Organization) conference held in Amsterdam.
Institution(5) California NanoSystems Institute, UCLA -Role While PCPs (PCP: porous coordination polymer) are mainly constructed by coordination bonds, zeolites are dominated by ionic bonds and activated carbon by covalent bonds. The advantage of the latter chemical bond types is stability against thermal and mechanical stimuli, which is important for industrial applications. Therefore, Kitagawa PI's and Yaghi's groups develop synthetic methods of new materials, which are characterized by covalent organic frameworks with porous crystalline forms constructed solely from light elements (H, B, C, N, and O), and discover new type of functions including sensing, trapping, and conversion of molecules as catalysts, which perform even in biological environment. -Personnel composition and structure Yaghi and coworkers will continue to create these materials while Kitagawa and coworkers plan to explore the functions of such novel porous compounds.	Institution(5) California NanoSystems Institute, UCLA -Role Collaborative research on development of new porous materials, biomaterials STM and AFM, drug delivery and cancer stem cell -Personnel composition and structure Prof **Omar Yaghi** (porous materials), Prof **James Gimzewski** (biomaterials STM and AFM), Prof **Fuyuhiko Tamanoi** (drug delivery, cancer stem cell) -Collaborative framework The iCeMS has been promoting active collaboration with the CNSI. Research groups of Profs **Susumu Kitagawa** and **Omar Yaghi** on porous materials, Assoc Prof **Takafumi Ueno** and Prof **James Gimzewski** on biomaterials STM and AFM, and Prof **Mitsuru Hashida**, Prof **Hiroshi Imahori** and Asst Prof **Tatsuya Murakami** and Prof **Fuyuhiko Tamanoi** on drug delivery

Both leaders will allocate at least one postdoctoral fellow to this project. -Collaborative framework New PCPs will be prepared in Yaghi's group, CNSI while the function is designed and the materials are prepared by Kitagawa's group. Kitagawa PI hires at least one post doctoral fellow for the purpose. They keep the further close and enduring relationship by an internet communication and organize a on-site meetig in either Kyoto or Los Angels in every year.	has been conducting collaborative research. On June 4 and 5, 2009, Assoc Prof **Ueno** presented his research in a seminar at the CNSI, and later Prof **Tamanoi** visited the iCeMS and gave a presentation in a seminar on August 26, 2009. A Memorandum of Understanding (MoU) was exchanged on March 16, 2010. Prof **Norio Nakatsuji** and other iCeMS' senior faculty visited the CNSI to attend a signing ceremony. Both institutions further strengthened their collaborative research as well as administrative cooperation as described below. Profs **Kitagawa** and **Yaghi** held a Joint Symposium on Framework Materials in the Future on June 14, 2010. Profs **Yong Chen** and **Hiroshi Sugiyama**, Asst Prof **Murakami** joined the 4th Annual Symposium on Nanobiotechnology initiated by the CNSI at Ludwig-Maximilians University in Munich, Germany from October 5–7, 2010. Asst Prof **Murakami** and Dr **Satoshi Abe** visited the CNSI to conduct collaborative research activities supported by the iCeMS-JSPS Overseas Visit Program for Young Researchers. Based on discussions between Profs **Kusumi** and **Tamanoi**, the iCeMS and the CNSI discussed collaborative research regarding cancer stem cells in December, 2010. Asst Prof **Ken-ichiro Kamei** was assigned as the development leader of iCeMS–CNSI collaboration. Dr **David Lundberg** (CNSI Director for International Partnership) visited the iCeMS and delivered a lecture regarding global visibility to Kyoto University administrators on December 6, 2010. - Research paper 1. "Construction of Robust Bio-nanotube by Controlled Self-assembly of Component Proteins of Bacteriophege T4," Norihiko Yokoi, Hiroshi Inaba, Makoto Terauchi, Adam Z. Stieg, Nusrat J. M. Sanghamitra, Tomomi Koshiyama, Katsuhide Yutani, Shuji Kanamaru, Fumio Arisaka, Tatsuo Hikage, Atsuo Suzuki, Takashi Yamane, James K. Gimzewski, Yoshihito Watanabe, Susumu Kitagawa, Takafumi Ueno, *Small* (2010) (selected as an inside cover picture)

	2. "Delivery of Intact Transcription Factor Using Self-Assembled Supramolecular Nanoparticles," Yang, Liu, Hao Wang, Ken-ichiro Kamei, Ming Yan, Kuan-Ju Chen, Qinghua Yuan, Linqi Shi, Yunfeng Lu, Hsian-Rong Tseng, *Angew Chem Int Ed* (2011)
Institution(6) Membrane Center, Purdue University - Role Collaborative research of on-chip membrane technology -Personnel composition and structure Prof Ken Ritchie -Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students	Institution (6) Center for Basic and Applied Membrane Sciences, Purdue University -Role Collaborative research of on-chip membrane technology -Personnel composition and structure Prof **Ken Ritchie** -Collaborative framework Academic exchanges of ideas, samples, PIs, postdocs, and graduate students Collaborative research has been carried out between Purdue University and the iCeMS. The iCeMS mainly contributed to this collaboration by using single-molecule detection techniques and by applying the technologies for regulating embryonic as well as induced pluripotent stem cells. Purdue University has pursued nano-meso technological aspects as well as the theoretical framework of research in meso-scale phenomena. This collaborative research aims at developing methods for artificially creating and manipulating membranes and membrane molecules. Prof **Ken Ritchie** participated in the Third iCeMS International Symposium on January 27–28, 2009 and the Sixth iCeMS International Symposium January 27–29, 2010. Prof **John Heuser** of the iCeMS and Prof **Ritchie** of Purdue University discussed the hop diffusion of membrane molecules in the plasma membrane, and started collaborative research efforts by combining the approaches of using electron microscopy (Prof **Heuser**) and single-molecule tracking (Prof **Ritchie**). CeMI Scientific Manager Sen Lec **Takahiro Fujiwara** and Prof **Akihiro Kusumi** collaborated with Prof **Ritchie** of Purdue University to develop a new analysis method for single-molecule trajectories obtained in the plasma

	membrane. This method was incorporated in a submitted manuscript.
Institution(7) The Center for Developmental Biology, RIKEN - Role Research collaboration between developmental biology and stem cell biology -Personnel composition and structure -Collaborative framework Joint research and academic interaction among the professors, postdocs and graduate students	Institution (7) The Center for Developmental Biology, RIKEN -Role Research collaboration between developmental biology and stem cell biology -Personnel composition and structure Center Director **Masatoshi Takeichi**, Team Leader **Masayo Takahashi**, and other CDB members involved in the national network of iPS cell research -Collaborative framework Joint research and academic interaction among the professors, postdocs and graduate students Research collaborations, such as a joint research and an academic interaction, have been conducted since Dr **Masatoshi Takeichi** of RIKEN was invited to iCeMS to deliver inauguration lectures. In FY 2008, workshops were organized to promote iPS cell research in cooperation with the CDB, RIKEN. The CiRA has been engaged in research exchange as one of four centers selected for the MEXT's "Project for Realization of Regenerative Medicine" along with the CDB. Dr **Takeichi** was a guest lecturer at the 4th iCeMS International Symposium May 27–29, 2009, in addition to continuing in his role as a member of the iCeMS Advisory Committee. -Research Papers 1."Conditional knockdown of Nanog induces apoptotic cell death in mouse migrating primordial germ cells," Shinpei Yamaguchi, Kazuki Kurimoto, Yukihiro Yabuta, Hiroyuki Sasaki, Norio Nakatsuji, Mitinori Saitou, Takashi Tada, *Development* (2009) 2. "Generation of retinal cells from mouse and human induced pluripotent stem cells," Yasuhiko Hirami, Fumitaka Osakada, Kazutoshi Takahashi, Keisuke Okita, Shinya Yamanaka, Hanako Ikeda, Nagahisa Yoshimura,

Masayo Takahashi, *Neuroscience Letters* (2009)

3. "Genome-wide DNA methylation profile of tissue-dependent and differentially methylated regions (T-DMRs) residing in mouse pluripotent stem cells," Shinya Sato, Shintaro Yagi, Yoshikazu Arai, Keiji Hirabayashi, Naoko Hattori, Misa Iwatani, Keisuke Okita, Jun Ohgane, Satoshi Tanaka, Teruhiko Wakayama, Shinya Yamanaka, Kunio Shiota, *Genes to Cells* (2010)

4. "Regulatory Impacts on Stem Cell Research in Japan," Masahiro Kawakami, Douglas Sipp, Kazuto Kato, *Cell Stem Cell* (2010)

Institution (8)
MRC Centre for Regenerative Medicine (CRM), The University of Edinburgh

-Role
Initiating collaborative research on stem-cell and biotechnology

-Personnel composition and structure
Prof Sir **Ian Wilmut**, Prof **Charles ffrench-Constant**, Dr **Gordon McLean**

-Collaborative framework
Academic exchanges of ideas, samples, PIs, postdocs, and graduate students. Co-sponsoring meetings and symposia. Joint collaborative research programs. Sharing of scientific information and materials.

Prof Sir **Ian Wilmut**, Prof Charles ffrench-Constant, and Dr. **Gordon McLean** presented their research at the iCeMS seminar on January 26, 2010. They met Prof **Norio Nakatsuji** and Adj Assoc Prof **Kazuto Kato** and later with CiRA Director Prof **Shinya Yamanaka** and Deputy Director Prof **Tatsutoshi Nakahata** to exchange opinions.

Assoc Prof **Shintaro Sengoku** and Dr **Hiroyuki Kodama** visited the University of Edinburgh to discuss collaboration in May and November, 2010. A delegation of Scottish Development International (SDI) visited the iCeMS on September 13, 2010 to discuss a memorandum of understanding with CRM and other institutional collaboration.

Nonprofit organization Kyoto SMI held a multi-sector seminar on February 28, 2011 in Tokyo, featuring presentations by iCeMS faculty. Edinburgh

	BioQuarter Commercialisation Director **Mike Capaldi** also delivered a presentation. MRC-CRM and iCeMS exchanged a memorandum of understanding (MoU) on March 30, 2011. <u>Institution (9)</u> <u>Moscow Institute of Physics and Technology (MIPT)</u> -Role Collaborative research on Material Science and Biophysics -Personnel composition and structure Dean, Prof **M Trunin**, Prof **L Yaguzhinsky**, Senior Researchers **N Ossina** and **K Motovilov**, Engineer **A Egorov**, Graduate Students **I Erofeev**, **L Eroshenko** and **A Mishin.** -Collaborative framework Academic exchange of ideas, samples, PIs, postdocs, and graduate students In November 2010, Prof **Konstantin Agladze** was chosen to organize a modern biophysics laboratory in the research-educational Center of Bionanophysics, managed by the Dean of Department of General and Applied Physics at the MIPT as Invited Leading Scientist. He acquired Russian government grants through December 31, 2012 to support the project. Beginning in Februrary 2011, the iCeMS has accepted a graduate student from the MIPT, as part of efforts expected to promote mutual exchange of researchers between Japan and Russia. Prof **Agladze** visited MIPT in February, gave a lecture for graduate students and junior researchers and also made two presentations of the project: at the Annual Assembly of professors and researchers of the MIPT and at the Scientific Managing Committee of the MIPT. In these presentations he discussed future collaborative research. In the collaboration, the MIPT focuses on fundamental physical principles and theoretical study and the iCeMS carries out advanced experimental study. Thus, both institutes complement each other well.

	A Memorandum of Understanding (MoU) was exchanged on March 31, 2011. <u>Institution (10)</u> <u>Medicinal Bioconvergence Research Center (Biocon), Seoul National University</u> -Role International, interdisciplinary collaborative research for discovery and design of new types of bioactive synthetic molecules -Personnel composition and structure Prof **Sunghoon Kim**, Director -Collaborative framework Biocon is a research-oriented international institution that was recently established on the main campus of Seoul National University in Korea. The overall goal of the institute is to facilitate drug discovery through integration and innovation of related sciences and technologies. Prof **Motonari Uesugi** of the iCeMS and Prof **Sunghoon Kim** have been initiating collaborative research projects for discovery and design of ground-breaking bioactive synthetic molecules for a range of biomedical applications. In 2011, the JSPS Asian CORE Program "Asian Chemical Biology" was awarded to the iCeMS, and Prof **Uesugi** serves as the Japanese coordinator of the program. In this 5-year international program, Seoul National University's Biocon plays a key role as a partner institute. The program members at the iCeMS, Profs **Uesugi**, **Hiroshi Sugiyama**, **Yoshie Harada**, and Sen Lec **Dongju Jung**, will exchange ideas, research resources, researchers, and graduate students with faculty members at Biocon to facilitate mutually beneficial research activities. The iCeMS and Biocon also co-organize chemical biology meetings in South East Asian cities (Hanoi, Manila, Bangkok, and Kuala Lumpur) to recruit the brightest international graduate students from top universities in South East Asia. These interactions are expected to foster interdisciplinary research and internationalization both at the iCeMS and at Biocon. A memorandum of understanding (MoU) was exchanged on March 29, 2011.

<Future Policy and Concrete Plans>

i) Satellites

Institution (1)
Faculty of Applied Biological Sciences, Gifu University

- The iCeMS will continue to foster active collaboration.

Institution (2)
National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem), Bangalore, India

-Role
Stem Cell research and Single Molecule Imaging

-Personnel composition and structure
Assoc Prof **Kenichi Suzuki**, Sen Lec **Kouichi Hasegawa**

-Collaborative framework
The iCeMS satellite lab in Bangalore on single-imaging technologies and stem-cell research will be set up in the NCBS's new building, which will be completed in Autumn 2011. Inauguration at Bangalore to be held on April 17, 2011.

- Sen Lec **Kouichi Hasegawa** for Stem Cell research and Assoc Prof **Kenichi Suzuki** for Single Molecule Imaging will conduct research activities at iCeMS satellite lab in Bangalore as group leader. Drs **Hasegawa** and **Suzuki** will be faculty members of Kyoto University as primary appointment, and to be appointed as visiting appointment of NCBS on April 17, 2011, holding the positions at the iCeMS. Several younger researchers will join the laboratory.

- Laboratory space, facilities as well as research funds will be provided by NCBS-inStem.

ii) Partner institutions

Institution (1)
Bionanotechnology Interdisciplinary Research Centre, the University of Oxford

- As stated above, the Bionanotechnology Interdisciplinary Research Centre at the University of Oxford was a time-limited organization till 2009. Therefore, this partnership was terminated. However, since collaborative research projects are continuing at the level of individual researchers, a new partnership might be formed with another Oxford institution, if a broader collaborative platform becomes useful.

Institution (2)
Wellcome Trust Centre for Stem Cell Research and its sister institute, Wellcome/Gurdon Institute, Cambridge University

- The iCeMS will continue to foster active collaboration.

- Prof **Fiona Watt** has been a member of the iCeMS Advisory Committee since FY 2008, and has continued to offer the institute valuable advice on stem-cell research.

- Prof **Azim Surani** continues to be an iCeMS visiting professor since FY 2009; collaboration with Prof **Surani** will contribute to the iCeMS' progress toward assembling the world's strongest network of researchers in the biological functions and mechanisms of reprogramming and pluripotency.

- Prof **Austin Smith** will be invited to the Heidelberg-Kyoto Joint Symposium to be held in July, 2011, to deliver a keynote lecture.

Institution (3)
National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem), Bangalore, India

- The iCeMS will continue to foster active collaboration.

- At NCBS-inStem, two iCeMS satellite labs (on single-imaging technologies and stem-cell research) are planned to open on April 17, 2011 in the NCBS's new building. Two faculty members of the iCeMS (an associate professor and a senior lecturer) are to be jointly appointed as NCBS faculty members on April 17, 2011, and scheduled to be sent to the satellite at NCBS.

Institution (4)
Max Planck Institute for Molecular Cell Biology and Genetics (MPI-CBG)

- The iCeMS will continue to foster active collaboration.

- Prof **Kai Simons** will visit iCeMS and deliver a seminar during June, 2011. Profs **Simons**, **John Heuser**, and **Akihiro Kusumi**, Assoc. Prof **Ken Suzuki**, and CeMI Scientific Manager Sen Lec **Takahiro Fujiwara** will discuss collaborative plans during his visit.

Institution(5)
California NanoSystems Institute, UCLA

- The iCeMS will continue to foster active collaboration.

- The iCeMS will participate in the 5th Annual Symposium on Nanobiotechnology initiated by CNSI, iCeMS and other institutions at Yonsei University in Seoul, Korea in November, 2011.

Institution (6)
Center for Basic and Applied Membrane Sciences, Purdue University

- The iCeMS will continue to foster active collaboration.

Institution (7)
The Center for Developmental Biology, RIKEN

- The iCeMS will continue to foster active collaboration.
- Dr **Masatoshi Takeichi** continues in his role as a member of the iCeMS Advisory Committee.
- The iCeMS and RIKEN will continue to be involved in the national network of iPS cell research.

Institution (8)
MRC Centre for Regenerative Medicine (CRM), The University of Edinburgh

- The iCeMS will continue to foster active collaboration.
- A joint symposium will take place 25 July, 2011 in Edinburgh.

Institution (9)
Moscow Institute of Physics and Technology (MIPT)

- The iCeMS will continue to foster active collaboration.

Institution (10)
Medicinal Bioconvergence Research Center (Biocon), Seoul National University

- The iCeMS will continue to foster active collaboration.
- Through the JSPS Asian CORE Program "Asian Chemical Biology", the iCeMS and Biocon also co-organize chemical biology meetings in South East Asian cities to recruit brightest international graduate students from top universities in South East Asia. These interactions are expected to foster interdisciplinary research and internationalization both in iCeMS and Biocon.

Institution (11)
Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR)

-Role
Collaborative research on Cell and Material sciences, especially on Porous Coordination Polymer and Stem-cell sciences

-Personnel composition and structure
Prof **CNR Rao**, Prof **MRS Rao**, Prof **Maneesha Inamda**r, Dr **Tapas Kumar Maji**

-Collaborative framework
JNCASR is a multidisciplinary research institute covering broad areas ranging from Materials to Genetics. Prof **C N R Rao**, former Director of JNCASR is also consulting science and technology adviser of Indian Prime Minister.

- Assoc Prof **Ryotaro Matsuda** and Dr **Tapas Maji** have been conducting collaborative research. Prof **Susumu Kitagawa**, Assoc Prof **Matsuda** and Dr **Maji** published research paper in 2009.

- Prof Nakatsuji and Dr **Kouichi Hasegawa** will closely collaborate with Prof **Maneesha Inamdar**, who is also adjunct professor for inStem, to set-up and manage satellite laboratories in inStem, Bangalore.

- Prof **Norio Nakatsuji** and the iCeMS delegation visited JNCASR in August, 2010. Prof **Nakatsuji** and Prof **M R S Rao** discussed further collaboration and a Memorandum of Understanding (MoU).

- JNCASR is conducting leading cutting-edge research on materials in India, at the same time is promoting cell biology. The iCeMS and JNCASR have a common goal regarding cross-disciplinary research in the same area.

- It is quite significant to promote collaborative research with three institutions NCBS, inStem and JNCASR in Bangalore area. It enables to promote interdisciplinary research between material and stem cell biology, accelerating ongoing joint research, discovering new areas for prospective collaborative work.

- A MoU will be exchanged on April 18, 2011.

Institution (12)
Collaborative Research Center SFB 873 of the University of Heidelberg

-Role
Academic exchanges of ideas, samples, PIs, postdocs, and graduate students. Co-sponsoring conferences and symposia regarding researches on stem cell.

-Personnel composition and structure
Prof **Anthony D Ho**, Prof **Thomas W Holstein**

-Collaborative framework
The Conference of Six Japanese-German University Presidents held at University of Heidelberg in Germany, Prof **Norio Nakatsuji** joined. In the working group "Life Sciences Meet Natural Sciences: Crossing the Border", Prof **Nakatsuji** took the chair, and Profs **Nakatsuji** and **Anthony D Ho**, the spokesperson for the Collaborative Research Center SFB873 delivered the lecture. Through the conference, iCeMS and University of Heidelberg started

academic exchange.

- SFB 873 is the collaborative research center which coordinated at the Medical Faculty in Heidelberg, and entitled "Maintenance and Differentiation of Stem Cells in Development and Disease."

- The iCeMS hosted iCeMS-Heidelberg Seminar "Basic and Multidisciplinary Research to Medical Applications" on November 1, 2010. Profs **Ho** and **Thomas W Holstein** delivered presentations. Prof **Nakatsuji** delivered an invited lecture at the international symposium "Stem Cell Research: Opportunities and Risks" on November 20, 2010 at the University of Heidelberg.

- The symposium "Crossing Boundaries: Stem Cells, Materials, and Mesoscopic Sciences" will be held July 21–23, 2011 in Heidelberg, Germany. The iCeMS and the Collaborative Research Center SFB 873 of the University of Heidelberg have jointly organized this conference on cross-disciplinary research work that break through boundaries between life and material sciences. Emphasis will be focused on innovations that will create novel approaches for stem cell technology.

5. Summary of center's research environment

<Initial plan>
1) Environment in which researchers can devote themselves to their research

The Board Committee, consisting of the director, deputy director and administrative director, is to be formed and to be engaged in the general management of the institute. Six administrative sections will be created, to be in charge of General Affairs (including Personnel and Public Relations), Planning and Industry Liaison, Finance, Research Support and Intellectual Property, Facilities (Physical Plant), and Research Ethics and Safety. All sections will have at least two staff members who are fluent in English. Researchers are exempt from administrative tasks. The PI Board is engaged in only research-related tasks. Two secretaries are to be assigned to each PI group.

<Progress to date>
1) Environment in which researchers can devote themselves to their research

a. Including refurbishments made during FY 2009–10 and in particular the completion of a new 3,000 m^2 research building in FY 2010, lab and office space in complexes 1 and 2 reached a total of approximately 11,000 m^2. Together with the installation of key pieces of large, shared equipment, a research environment enabling rapid acceleration of collaborative research has been in large part realized.

b. The Center for Meso-Bio Single-Molecule Imaging (CeMI) was established on March 3, 2009, as the iCeMS' imaging innovation center for cellular meso-science. Its key missions are:

   - to develop new, powerful technologies for imaging the restless nano- to meso-scale universe of 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 meso-science.

	For details of CeMI facilities and equipment, see "6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center" below. c. With the hiring in FY 2009 of a former Kyoto University Graduate School of Informatics dean as its new 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. d. In addition to the Administrative Director, as of FY 2010 the institute's effort to assist researchers included a dedicated administrative staff of 30 (more than half of whom are English speakers) as well as a research support staff of 70. e. Established in FY 2009, the Overseas Researchers Support Office works to assist foreign researchers in adjusting to life in Kyoto, helping them to quickly begin making real contributions to the scientific life of the institute. f. From the time of its founding, the iCeMS has had as one of its world-class research institute principles a reduction of work for its researchers, exempting them from typical university administrative duties. g. 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.
2) Start-up research funding In addition to general support, PIs joining outside of Kyoto University will be provided with annual financial support as a start-up fund ranging from US$300,000 to US$1,000,000 for two years for the purchase of research equipment and other office supplies. Laboratory space will be renovated and equipped with basic research facilities.	<u>2) Startup research funding</u> In FY 2009, four research groups headed by iCeMS PIs recruited from outside the university received startup funding of about JPY 10,000,000 or US$100,000 (US$1 = JPY100) each, in addition to necessary research equipment for each group. An annual budget (including researcher salary) of up to JPY 30,000,000 or US$300,000 (US$1 = JPY100) was allocated to each foreign iCeMS Kyoto Fellow, a newly created independent junior faculty position.

	Most notably, a startup fund equivalent to JPY 100 million or US$1 million (US$1 = JPY100) mainly covering equipment costs for a next generation optics system was provided for Asst Prof **Peter Carlton**, an iCeMS Kyoto Fellow, who was hired to further develop optical microscopy technology used to examine mesoscopic cellular architectures. In addition, iCeMS Kyoto Fellows from abroad have been given priority over lab space at iCeMS Complexes 1 and 2. Startup small grants to initiate cross-disciplinary collaboration are provided to junior faculty and postdocs as the "iCeMS Exploratory Grants for Junior Investigators," and separately, "Cross-Disciplinary Exploratory Grants" have been made available to researchers of other departments of the university to start collaboration with iCeMS researchers.
3) Postdoctoral positions through open international solicitations Researcher posts at the iCeMS are classified into principal investigators, associate professors, assistant professors and post-doctoral fellows. These posts are to be advertised internationally through every possible means such as advertisement on prominent magazines such as "Nature" and "Science."	<u>3) Postdoctoral positions through open international solicitations</u> In addition to regular listings on the iCeMS website, job openings have been advertised both in *Nature* (April 15, 2010 world edition) as well as in *Science* (April 30, 2010 edition), attracting 264 applications in FY 2010.
4) Administrative personnel who can facilitate the use of English in the work process English is to be used as the official language to form English-language administration.	<u>4) Administrative personnel who can facilitate the use of English in the work process</u> Each lab has an English/Japanese bilingual secretary on staff. Additionally, 16 of the 30 administrative staff (53%) are bilingual, including: • an American citizen with public affairs experience in the US Foreign Service, the Washington DC bureau of Nippon Television, and elsewhere, acting as coordinator for international public relations, and • 2 persons with 990 (perfect) TOEIC (Test of English for International Communication) scores, at the highest rank among approximately 100,000 test takers.
5) Rigorous system for evaluating research and system of merit-based compensation Interim evaluations are to be conducted by the external committee chosen	<u>5) Rigorous system for evaluating research and system of merit-based compensation</u> a. Since its founding, the iCeMS has had a university-approved

from home and abroad in 3, 5, 8 and 10 years, and a merit-based pay system is to be employed.	merit-based system in place, where the institute director may decide to award up to 300,000 yen per month based on research progress. b. Advisory Committee meetings, held in FY 2009 and '10, assessed each PI's research progress as well as the overall management and direction of the institute, yielding highly valuable advice.
6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center Laboratories, lounges and equipment suitable for a World Premiere International Research Center are to be prepared In iCeMS research buildings, walls among different research groups are to be removed and many laboratories are to be shared by several research groups, which is expected to encourage the interaction of the different research groups on a daily basis.	6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center a. Facilities In September 2008, the first research building (at iCeMS Complex 2) was completed, with approximately **2,500 m^2** of floor space. The following March, the iCeMS headquarters building (at iCeMS Complex 1) was completed with approximately **5,000 m^2** of floor space. In September 2009, another approximately **500 m^2** of floor space in a building adjacent to the first research building (at iCeMS Complex 2) was added to increase total laboratory space. Subsequently in October 2010, a new building was opened at Complex 2, adding **3,000 m^2** in laboratory and office space. These buildings together perform the following functions: i) **Complex 1**. The iCeMS Main Building houses laboratories as well as a seminar hall and meeting spaces appropriate for the headquarters of an institute. This building additionally acts as a central document and scientific data repository, and focal point for information exchange. It is worth mentioning that the iCeMS Main Building is located at the gateway to the university's main campus and headquarters building, thus situating it in a prime location for acting as a center of personnel and scientific exchanges involving the entire university. ii) **Complexes 1 & 2**. Designed from the ground up to flexibly facilitate the long term, joint efforts of the world's top scientists, as

they advance numerous ground-breaking and cross-disciplinary research projects, these facilities consist predominantly of open offices and shared laboratories equipped with the highest level research instruments.

iii) **Complexes 1 & 2**. Open offices and lounges throughout the institute have been designed to encourage interaction and a natural, free flow of information among researchers from varying backgrounds, in particular scientists from overseas and in the early stages of their careers.

iv) **Complex 2**. Specialized, shared equipment labs, adjacent to shared projects work spaces, are staffed by research managers with the scientific and technical know-how to efficiently assist cross-disciplinary research projects.

Owing to limited space as well as building restrictions imposed by the Kyoto city government, these complexes are separated but within walking distance of each other. To overcome this issue, the iCeMS has implemented a number of measures aimed at bringing researchers together, including monthly meetings of PIs and on strategic cross-disciplinary research, the Cross-Disciplinary Journal Club, annual retreats, and a variety of seminars and other events usually held at the iCeMS main building.

In addition, video conferencing systems have been deployed throughout the institute to link Kyoto with satellite labs and overseas partner institutions, enabling researchers on both sites to naturally interact with each other during meetings and joint events.

b. Equipment

Rules for use and relevant manuals for key pieces of large, shared equipment, acquired during FY 2008–10, have been enacted, and cooperative use of this equipment is already contributing to the institute's scientific progress. The main pieces include:

i) **CeMI facilities**

Equipment name	**Characteristics**

Single Fluorescent-Molecule Imaging Station	Home-built total-internal reflection fluorescene (TIRF) microscope to perform simultaneous three-color single fluorescent-molecule imaging of live cells
Real-Time Terahertz (THz) Near-Field Microscope	Home-built THz near-field microscope with a 10 μm resolution and a 10-Hz image frame rate (best and fastest in the world)
LSM 780/ConnfoCor3, Carl Zeiss	Single-photon/two-photon laser scanning microscope with a module for correlation spectroscopy measurements

ii) **Other large, shared equipment**

Equipment name	**Characteristics**
Nuclear Magnetic Resonance Spectroscopy Advance III 500 US Plus, Bruker Biospin	Fastest, highest performance and most flexible NMR spectrometer on the market
3D Nanometer Scale Raman Microspectroscopy Nanofiner 3D, Tokyo Instruments Inc	Microscopic Raman spectrometer for analysis of molecular vibrations, 600 nm 3D
5Tesla Magnetic Property Measurement Systems, Quantum Design	Apparatus for magnetization measurement
Confocal Laser Scanning Microscope, Olympus Inc	Multiple-color imaging and time-lapse imaging at multiple areas
FACSAria II Special Order Research Products Cell sorter 3-laser 5-color type, Becton Dickinson	Cell sorting using cell morphology or cell components, or fluorescene labels

c. IT Infrastructure

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

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

iii) The iCeMS Web Room, an internal website for fostering information exchange, is being streamlined.

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

7) International research conferences or symposiums held regularly to bring world's leading researchers together

In order to encourage the useful interaction between world top-notch researchers and researchers of the iCeMS, international research symposia are to be held periodically at least twice a year. Themes of these symposia are to be comprehensive as well as concrete.

7) International research conferences or symposia held regularly to bring world-leading researchers together

In addition to international symposia (such as the selection listed below), since its founding in 2007 the iCeMS has held over 70 international seminars, featuring many leading scientists from overseas and attracting wide participation from numerous other university departments and institutes.

FY 2007-2008: **4** meetings

Major examples (meeting title and place held)	Number of participants
2nd iCeMS International Symposium – EXCON '08	Domestic: 140 Overseas: 51
3rd iCeMS International Symposium: Symposium on the MESO CONTROL of the cells, by the cells, for the cells – featuring transportsomes	Domestic: 147 Overseas: 26

FY 2009: **3** meetings

Major examples (meeting title and place held)	Number of participants
4th iCeMS International Symposium: "Integrated Physical/Chemical Biology of the Cell: from Genes to Membrane Systems"	Domestic: 172 Overseas: 33
5th iCeMS International Symposium: "Biomaterials at the interface of chemistry, physics, and biology"	Domestic: 121 Overseas: 25

8) Other measures, if any

FY 2010: **7** meetings

Major examples (meeting title and place held)	Number of participants
8th iCeMS International Symposium: Meso-Control of Functional Architectures	Domestic: 193 Overseas: 57
9th iCeMS International Symposium: Mesoscale Control and Engineering of Self-Organized and Excitable Systems in Biology and	Domestic: 61 Overseas: 25

8) Other measures

a. The **Innovation Management Group** (Assoc Prof **Shintaro Sengoku**): forging alliances in academia, industry, government, and with overseas institutions

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 achievements in FY 2010 include:

i) The IMG conducted an empirical study combining bibliometric analysis and questionnaire to researchers, aiming to identify key success factors to reinforce management of interdisciplinary research projects at the institutional and individual levels.

ii) Together with the university's Graduate Schools of Economics and Management, the IMG sponsored a workshop on academic innovation management focusing on the evaluation and administration of large-scale research projects.

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

iv) Kyoto SMI sponsored a multi-sector seminar in Tokyo on business applications of ES/iPS cells and smart materials. The event attracted approximately 90 attendees.

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

details, please see section 4-2 ("Satellites and partner institutions").

vi) 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.

b. Efforts to promote cross-disciplinary research

i) **2** researcher retreats held.

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

ii) **43** Cross-Disciplinary Seminars held.

iii) 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 useful in sparking ideas for new joint research projects. Prof **Nakatsuji**, among other iCeMS researchers, has been actively posting relevant novel papers to the database, so far accumulating around 500 original and review articles. This resource is also aiming at the growth of a broad community of scientists who are interested in integration of cell-material sciences and also mesoscopic sciences.

<Future Policy and Concrete Plans>

1) Environment in which researchers can devote themselves to their research

a. With the November 2010 completion of the new 3,000 m^2 research building at Complex 2, total floor space at both complexes has now reached 11,000 m^2, close to the figure envisioned at the time of the institute's founding. As this new building also includes extensive open laboratories and office spaces, as well as large pieces of shared-use equipment, cross-disciplinary collaboration is expected to increase as a result. Additional improvements to facilities together with future equipment acquisitions are anticipated to further accelerate this collaboration.

b. In line with improved administrative and research assistance support, improvements are planned for the management and maintenance of large, shared research equipment.

c. Support for researchers from overseas will be further strengthened with the possible addition of staff experienced in this area.

d. Collaboration among academia, industry, and government will be accelerated by identifying additional research projects with potential for applications beyond academic research.

2) Startup research funding

a. Exploratory cross-disciplinary research will be strengthened, with a rigorous evaluation system in place.

b. Increased collaboration with young researchers in other Kyoto University departments and institutes will be actively pursued.

c. Support for the iCeMS Kyoto Fellows will be extended.

3) Postdoctoral positions through open international solicitations

Active solicitations through all possible channels will continue as before.

4) Administrative personnel who can facilitate the use of English in the work process

a. The greater than 50% English-Japanese bilingual staff level will be maintained.

b. Incentives will be offered to encourage staff members to receive training and acquire certifications, further raising English ability as appropriate to a WPI institute and also as a means of boosting staff morale.

5) Rigorous system for evaluating research and system of merit-based compensation

Regular meetings of the Advisory Committee and the strategic task force for cross-disciplinary research will continue as before, along with the director-led Executive Board system of faculty evaluation and its option of awarding incentives (up to 300,000 yen per month).

6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center

See "1) Environment in which researchers can devote themselves to their research" above.

7) International research conferences or symposia held regularly to bring world-leading researchers together

a. As in preceding years, 2 or more international symposia will be held annually.

b. Joint symposia, sponsored with partner institutions, will be held annually.

8) Other plans

a. Further efforts to link academia, industry, and government, led by the Innovation Management Group.

b. Ever greater efforts to encourage the fusion of different disciplines by utilizing retreats, Cross-Disciplinary Seminars, the Cross-Disciplinary Journal Club, and other mechanisms.

6. Criteria and methods used to evaluate center's global standing

<Initial plan>
The iCeMS will form the international evaluation committee to assess whether:
1. researchers are individually achieve world-class research

<Current assessment>

1. Individual researcher accomplishments

See "2-2 Research results to date" for scientific achievements, including key publications.

[Notable awards and honors]

Prof **Shinya Yamanaka**:
- National Academy of Sciences (USA) membership (May 2011)
- Albany Medical Center Prize in Medicine (2011)
- Wolf Foundation Prize in Medicine (2011)
- Thomson Reuters Citation Laureates (2010)
- Balzan Prize (2010)
- Kyoto Prize (2010)
- Imperial and Japan Academy Prizes (2010)
- Albert Lasker Basic Medical Research Award (2009)
- Canada Gairdner Award (2009)
- Massry Prize (2008)
- Shaw Prize in Life Science (2008)
- Robert Koch Prize (2008)

Prof **Susumu Kitagawa**:
- Thomson Reuters Citation Laureates (2010)
- The Chemical Society of Japan Award (2009)
- Humboldt Research Award (2008)

	Prof **Mitsuru Hashida**: • Japanese Society for the Study of Xenobiotics Award (2010) • International Pharmaceutical Federation (FIP) Fellow Award (2010) • Fellow of the Controlled Release Society (CRS) (2010) Prof **Akihiro Kusumi**: • Science and Technology Film & Video Festival Best Research and Development Video Award (2011) • Elected for American Society for Cell Biology (ASCB) Council (2010) Prof **Kazumitsu Ueda**: • Japan Society for Bioscience, Biotechnology, and Agrochemistry (JSBBA) top prize (2010) Prof **Hiroshi Imahori**: • MEXT National Institute of Science and Technology Policy (NISTEP) Prize (2007) • Osaka Science Prize (2007) Prof **John Heuser**: • National Academy of Sciences (USA) membership (May 2011)
2. joint-research between the PIs are making progress	2. Accomplishments by researchers working jointly **See "2-2 Research results to date" for details.** So far, **13** out of 464 iCeMS papers published since October 2007 are **collaborative work by two or more iCeMS groups**. At present, the following **10** top-priority projects are in progress (for details, see "2-3. Future Policy and Concrete Plans"): 1. Control of gene expression by synthesized chemical transcription factors [**Sugiyama**, **Yamanaka** (Yamada), **Uesugi, Nakatsuji** Labs] 2. Small molecule tools for stem cell research/applications [**Uesugi**, **Yamanaka**, **Ueda**, **Nakatsuji**, **Sugiyama** Labs] 3. Chemical inducers for differentiation of ES/iPS cells [**Nakatsuji**, **Uesugi**, **Sugiyama**, **Yamamoto** Labs]

	4. Effects of meso-scale compartments on kinetics of bimolecular reactions in the plasma membrane and cell membrane single molecule imaging using synthesized probes [**Kusumi**, **Kiso**, **Kalay** Labs, **CeMI**] 5. Novel probes (diamond particle) for investigating cell architecture dynamics [**Harada**, **Shirakawa**, **Nakatsuji** Labs] 6. Development of new carriers for targeted drug delivery using carbon nanotubes and lipsomes functionalized by peptides and gyco-coating [**Murakami**, **Hashida**, **Imahori**, **Kiso**, **Takano** Labs] 7. Artificial transporters made by porous materials and charge separation molecules to elucidate and control cellular functions [**Kitagawa**, **Furukawa**, **Imahori**, **Kusumi**, **Ueda**, **Kiso**, **Nakatsuji** Labs] 8. Development of light-harvesting functional materials for phototherapy and photoregulation of cell functions [**Murakami**, **Imahori**, **Heuser**, **Hashida**, **Kengaku**, **Nakatsuji** Labs] 9. Development of nanofibers combined with porous coordination polymers (PCPs) for spatial and temporal control of nitric oxide (NO) or glutamate release, which can be used for neuron and other cell physiology research [**Kitagawa** (Furukawa), **Chen** (Kamei), **Takano**, **Kengaku**, **Nakatsuji** Labs] 10. Mesoscopic theory of cellular function and supramolecular chemistry [**Kalay**, **Kusumi**, **Kitagawa, Nakatsuji** Labs]
3. the administration and support system for researchers are sufficiently functioning as an international center	<u>3. Level of internationally-competitive administration and support</u> • Each lab has an English/Japanese bilingual secretary on staff. Additionally, **16** of the 30 administrative staff (**53%**) are bilingual, including: ➢ an American citizen with public affairs experience in the US Foreign Service, the Washington DC bureau of Nippon Television, and elsewhere, acting as coordinator for international public relations, and ➢ 2 persons with 990 (perfect) TOEIC (Test of English for International

	Communication) scores, at the highest rank among approximately 100,000 test takers. • 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. • The Overseas Researchers Support Office was established in FY 2009 in order to assist the increasing number of foreign researchers with visas, housing, and other issues related to life in Japan. Additionally, a satisfaction survey was conducted in FY 2010 in order to further improve the service. • 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, such as the UCLA-CNSI, NCBS-inStem, the University of Edinburgh MRC-CRM, and Heidelberg University.
4. the center is in the global career flow	<u>4. Degree to which the center is a part of global personnel movement</u> • The implementation of a roadmap for faculty recruitment has raised the number of foreign researchers to **54** (**31%** of the total) as of March 31, 2011. • An international effort to recruit young, promising researchers for the new iCeMS Kyoto Fellow positions attracted over **30** applicants in FY 2009 and **33** applicants in FY 2010, three of whom were selected from overseas for a total of five new fellows. These scientists have established independent research labs on par with the PIs, receiving sufficient work space and startup funds to pursue collaborative, cross-disciplinary research projects. • In order to accelerate internationalization and cross-disciplinary research at the institute, 17 researcher positions were created exclusively for foreign researchers and for multi-groups collaboration under the iCeMS Director's initiative, as part of a continuing effort. • During FY 2009 an iCeMS postdoc was selected for an assistant professorship at the Indian Institute of Technology. Three other postdocs similarly received appointments up to the assistant professor level.

	• **105** and **107** prominent researchers from overseas visited the iCeMS in FY 2010 and 2009, respectively. • The iCeMS-JSPS Overseas Visit Program for Young Researchers has been implemented since FY 2010 with aims to 1) provide opportunities for young iCeMS researchers to conduct research at overseas institutes, 2) to strengthen participants' international competitiveness, and 3) to enhance the iCeMS' role as an international hub for researchers in related fields. A total of **10** researchers thus far have earned opportunities to visit world-class institutions, opening the door to further international collaborations and careers.
5. collaboration with researchers from the East and Asia are promoted.	<u>5. Degree to which exchange is taking place with researchers throughout Asia</u> • Extensive academic and personnel exchange is taking place between the iCeMS and the National Centre for Biological Sciences (NCBS) in Bangalore, India. In addition to the key role played by a NCBS graduate who is now a postdoctoral fellow of the iCeMS, the NCBS cosponsored the iCeMS' Sixth International Symposium held January 27–29, 2010. Furthermore, a memorandum of understanding for academic exchange was signed, another joint symposium was held, and the NCBS satellite lab at the iCeMS was established all in FY 2010. Researcher exchange is to start in FY 2011. • Prof **Nakatsuji** is a member of the Scientific Advisory Board of the Australian Stem Cell Centre. In addition, he plays active advisory roles for stem cell research groups at the National Health Research Institute and others in Taiwan. • Four graduate students from the Indian Institute of Technology and the University of Delhi, while taking part in internships in Japan, visited and toured the iCeMS. They expressed interest in returning to Japan for possible postdoctoral training. • 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." See "4-2. Satellites and partner institutions: Institution #10" for details.

<Future Policy and Concrete Plans>

The Innovation Management Group (IMG) will take the lead in developing quantitative means of evaluating the institute's global standing, strictly adhering to academic principles. These methods, outlined below, will replace current evaluative practices, which are based on individual discussions and are hence largely qualitative.

- **Evaluation of the level of achievement of research projects**
  - Observation and monitoring of the number of accepted publications by top journals (as identified by the WPI Program Office and the iCeMS)
  - Observation and monitoring of the number of most highly-cited papers (as defined by Thomson Reuter's ISI Web of Knowledge, Essential Science Indicators)
  - Comparison of the number of citations to existing publications by research field (using Elsevier's SCOPUS database)
  - Other benchmarking methods (eg assessment with Elsevier's SciVal Strata, in planning)

- **Evaluation of the status of internal collaboration projects among PI groups**
  - The number of cross-disciplinary research projects driven by multiple groups
  - The intensity and distribution of paper co-authorship
  - Development and implementation of a "Cross-Disciplinarity Index", a method designed by Assoc Prof **Shintaro Sengoku** and colleagues, as a quantitative and objective measure for each researcher and his/her research outcomes (in cooperation with of the university's graduate schools of economics and management)

Newly developed evaluation methods and results will be presented to and discussed by the iCeMS Executive Board, and subject to a decision on adoption.

The IMG has also been conducting 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.

7. Securing competitive research funding

<Initial plan>	<Secured to date>
● FY2007 The PIs are to obtain JPY1,000 million from external funding sources, and another JPY 1,000 million from the research center's host institute, Kyoto University.	● FY 2007 Researchers at the institute acquired JPY 618 million from competitive research funding sources, and JPY 232 million from Kyoto University.
● FY2008 The PIs are to obtain large amounts of research funds from governmental bodies such as JSPS, JST, and so forth.	● FY 2008 Researchers at the institute acquired JPY 2,098 million from competitive research funding sources, and JPY 1,455 million from Kyoto University.
● FY2009 The PIs are to obtain large amounts of research funds from governmental	● FY 2009 Researchers at the institute acquired JPY 3,100 million in research funds:

bodies such as JSPS, JST, and so forth.

approximately 1,000 million from Grants-in-Aid for Scientific Research, 800 million from the MEXT Project for Realization of Regenerative Medicine, 300 million from the JST-ERATO Kitagawa Integrated Pores Project, 300 million from the JST iPS Cell Project, and 700 million from other competitive research funding sources.

JPY100 = US$1 (Unit: JPY millions)

Grants-in-Aid for Scientific Research	972
MEXT Project for Realization of Regenerative Medicine (Yamanaka)	748
JST-ERATO Kitagawa Integrated Pores Project (S Kitagawa)	277
JST iPS Cell Project (Yamanaka)	347
Other competitive research funding sources	717
Total	**3,061**

In addition to the above, the iCeMS received JPY 2,580 million in government supplementary funding.

● FY2010
The PIs are to obtain large amounts of research funds from governmental bodies such as JSPS, JST, NEDO, and so forth.

● FY 2010
Researchers at the institute acquired JPY 4,600 million in research funds: approximately 500 million from Grants-in-Aid for Scientific Research, 1,200 million from the Cabinet Office's Funding Programs for World-Leading Innovative R&D on Science and Technology and Next Generation World-Leading Researchers, 1,100 million from NEDO projects, 600 million from the MEXT Project for Realization of Regenerative Medicine, 400 million from the JST-ERATO Kitagawa Integrated Pores Project, 300 million from the JST iPS Cell Project, and 500 million from other competitive research funding sources.

JPY100 = US$1 (Unit: JPY millions)

Grants-in-Aid for Scientific Research	465
Funding Program for World-Leading Innovative R&D on Science and Technology (Yamanaka)	1,221
Funding Program for Next Generation World-Leading Researchers (Harada, Kengaku, Sengoku, Ueno, Uesugi) *total (FY 2010-2013): JPY **689** million	15
NEDO project (S Kitagawa 1)	457
NEDO project (S Kitagawa 2)	40
NEDO project (Takano)	183
NEDO project (Nakatsuji)	417
MEXT Project for Realization of Regenerative Medicine	575

(Yamanaka)	
JST-ERATO Kitagawa Integrated Pores Project (S Kitagawa)	410
JST iPS Cell Project (Yamanaka)	350
Other competitive research funding sources	493
Total	**4,626**

In addition to the above, the iCeMS received additional allowances from the Funding Program for World-Leading Innovative R&D on Science and Technology.

<Future Strategy>

- **Overview**

  Objectives are to:
  - Launch a thorough web portal to provide researchers with easier access to competitive research grant databases.
  - Actively encourage all eligible researchers to participate in large-scale competitive funding programs such as the Funding Program for Next Generation World-Leading Researchers (5 applicants from the institute were awarded the grant in FY 2010).
  - Improve English information on external research funding sources to more effectively assist non-Japanese researchers in the acquisition of funds.

- **Contract research funds**
  - 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.

- **Grants-in-Aid for Scientific Research**
  - 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 grant system and providing them with tips for winning approval.

- **Endowment**
  - 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.

8. Other important measures taken to create a world premier international research center	
<Initial plan> - Mentor development program - Scientific integrity and communication program - Program to support foreign/young researchers - Program to recruit and nurture female researchers	<Measures taken to date> <u>1) Scientific integrity and mentoring program</u> **1-a. Integrity Seminar Series** As part of a Kyoto University FY 2010 program targeting graduate students across a wide range of disciplines – ranging from the natural sciences to the humanities – the iCeMS hosted an "Integrity Seminar Series" exploring scientists' integrity and responsibilities to society. The series included the following topics: "A Scientist's Roles and Responsibilities Today" with Prof **Norio Nakatsuji** "Bridging Neuroscience and Society: Telling Facts and Myths Apart" with Osaka University Prof **Ichiro Fujita** "Leprosy's Lessons: the Root Causes of Policies and Public Awareness Dissociated from Scientific Rationality" with Ritsumeikan University Prof **Yoko Matsubara** "Disaster Prevention Policies and Earthquake Prediction Research" with Kansai University Graduate School of Safety Science Dean **Yoshiaki Kawata** **1-b. Reading Club** In addition to hosting seminars, the iCeMS opened a biweekly lunch time reading club aiming to nurture the institute's researchers to develop the highest sense of scientific integrity and social responsibility. In the reading club, iCeMS researchers get together and discuss reading materials relevant to scientific integrity, mentoring, conduct of research, authorship, intellectual property and so forth. Objectives are to provide opportunities to: • broaden researchers' perspective on science, as scientists. • get to know iCeMS researchers from other labs.

	• learn and discuss together in English using quality reading materials. Reading material during FY 2009 was taken from: *On Being a Scientist – A Guide to Responsible Conduct in Research* (National Academy of Sciences and others, USA, 2009). 2) Science Communication Group (SCG) established Working to build stronger mutual relations among researchers in different fields and between scientific communities and society, the Science Communication Group (SCG), led by Adj Assoc Prof **Kazuto Kato**, has implemented the following programs: **2-a. iCeMS Cafés** 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 participants opportunities to interact with young researchers and conduct their own scientific experiments. **2-b. iCeMS/CiRA Classrooms: Hands-on with Stem Cells!** The iCeMS and the CiRA co-hosted hands-on ES and iPS cell research programs for high school students and teachers in 2009 and 2010. On each occasion, 32 students (selected from 200 applicants in 2009 and 90 in 2010) visited Kyoto University to attend the two-day programs, in which they listened to iCeMS researchers' lectures and observed living cells with research-grade microscopes. These programs aim not only to teach students about scientific facts such as the self-renewal potential or pluripotency of ES and iPS cells, but to give them the opportunity to realize that science is based on cumulative knowledge acquired over generations of experimentation and hypothesis testing. **2-c. 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. The series has so far featured: Koh Nagata & Shinya Yamanaka (4,600 views since April 2009) Michiyo Koyanagi & Mineko Kengaku (3,000 views since September 2009) Jeffrey Robens & Koichiro Tanaka (700 views since October 2010) **2-d. 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. See also "Appendix 9: Outreach" for more details.
<Future Policy and Concrete Plans> 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 also places a strong emphasis on scientific integrity, an area that tends to be overlooked at new institutions exploring the frontiers of science. Female researchers account for around 30% of the total count. Support systems will be further strengthened in association with Kyoto University's Center for Women Researchers.	

9. Host institution's commitment

<Initial plan>

1. Provision in host institution's mid-to-long-term plan

Kyoto University distinctively places the "World Premier International Research Center Initiative" as its top priority program in the current (2004 to 2009) and the next (2010 to 2015) mid-term plans. As clearly defined in its mission statement, the university has strived for sustainable human societies, which are featured by harmonious coexistence within human and ecological communities on this planet, by bringing forth its outstanding research and education programs generating world-class knowledge. Kyoto University believes that establishing a world top-level academic research center within the university is an indispensable step to further promote this mission and to achieve the ultimate goal for the sustainable human societies. Under the strong leadership of the president, Kyoto University is vigorously committed to promote this program, and to actively take concrete and responsible measures, such as preparation of research systems and provision of resources, for establishing the world premier international research center to lead the world's research activities.

2. Concrete Measures

(1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc.

To facilitate the center's researchers obtaining external funds, the university provides the various supports including 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.

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.

<Progress to date>

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

Kyoto University's former mid-term (FY 2004–09) strategies related to the iCeMS stated that "special measures will be undertaken to form an organization promoting creation of a new generation of technologies by developing mesoscopic science and stem cell research at the iCeMS, a WPI research center." The current mid-term strategy (FY 2010–15) reinforces this, stating that "cutting-edge research being conducted at the iCeMS shall be supported to develop the institute into a world-class organization."

Kyoto University President Hiroshi Matsumoto, sworn in on October 1, 2008, made the following commitment: "From October 1, 2008, I will be responsible for performing tasks and duties described in Application Form 4, Host Institution's Commitment, signed by former president Kazuo Oike on September 25, 2007."

-Concrete Measures

(1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc.

The university has authorized the iCeMS to mobilize all indirect costs.

The university covers personnel costs for five iCeMS PIs and eight administrative employees.

The university financially supports the research at the iCeMS through its annual action plans.

For administration, the university provides full-time administrative staff and necessary personnel expenses in order to establish an independent administrative organization. Five current university staff members will be allocated for major functions such as general affairs, planning, finance, research support and facilities. University staffers with a good command of English will be preferentially selected. As for the position of vice center director in charge of administration, a director-class personnel from the university will be allocated initially at the time of the center's establishment. This person will soon be replaced by a full-time vice center director, recruited from outside the university, as soon as he/she is appointed.	
(2) System under which the center's director is able to make substantive personnel and budget allocation decisions 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 vice center directors, who assist and support the center director, in order to ensure appropriate operation. 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 variety of	(2) System under which the center's director is able to make substantive personnel and budget allocation decisions Decision-making: The iCeMS' autonomy and the leadership authority of the Director are supported by the Executive Board, consisting of the Director, Deputy Director, Chairman of the Board of PIs, and the Administrative Director. The role of this board is equivalent to that of a faculty board in an academic department. Personnel affairs: • Under an initiative adopted by the university, the iCeMS employs researchers according to a discretionary labor practice with an annualized salary scale that allows the Institute to hire exemplary staff regardless of the retirement age. • The university covers the personnel costs for five iCeMS PIs. • Beginning in FY 2008, administrative employees over the mandatory retirement age have been employed according to a special discretionary hiring mechanism.

salary payment systems. 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 salary system that the university has already introduced (a fixed-term employment contract and an annual salary system based on achievements) will be applied. • 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 will be paid in foreign currency of their home countries, in principle. • For qualified technical and administrative staffers, a special employment contract will be arranged to extend a regular retirement contract. (3) Support for the center director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments 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, five (at least) 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	(3) Support for the center director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments Six iCeMS PIs are affiliated with departments where they had held positions prior to joining the institute. This dual affiliation system has allowed these PIs to continue taking part in a portion of these departments' research and graduate education programs, as well as allowing graduate students in these departments to participate in research taking place at the institute.

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 prepares a handbook that explains immigration procedures, housing, the health-care system and other daily life information at the time of call for positions. Direct assistance by a foreign mentor will also be provided for a period of time immediately after their arrival in Japan. To support education for their children, a system will be established in cooperation with neighboring Doshisha University to provide them with education services at its international junior/senior high school.	
(4) Revamping host institution's internal systems to allow introducing of 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 from conventional modes of operation The university establishes an autonomous and independent management organization that serves a role equivalent to that performed by the existing faculty. Important issues (personnel, budget, etc.) will be discussed and decided by the center director and vice directors, in order to ensure prompt and appropriate administrative actions. However, 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	(4) Revamping host institution's internal systems to allow introducing of new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation Simply put, the host institution is responsible for overall governance and rule-making, while the center director determines pay levels etc 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

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.	the iCeMS 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 to raise the iCeMS' profile, while exempting the center's faculty from participating in other routine university committees.
(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.) a) Provision of research space necessary to conduct the world top level research It is important to establish a "globally acknowledged" center attracting top-class researchers to conduct world leading research. To this end, Kyoto University provides a high-quality research environment with the total area of about 12,000m^2 by ensuring exclusive facilities with fully equipped infrastructure. As well, the center's head office will be located on the university's main campus to make available the university's diverse facilities, including conference halls for international symposiums and other academic meetings, the university hall, library, and cafeteria. - Center's main office space In addition to the head office functions, core facilities for the center's representative functions including research meetings, literature/academic database and information dissemination will be provided. To demonstrate autonomy of the center, a main office will be established and provided as an exclusive facility on the university main campus. - Research project space As the main space for the center's research activities, the university provides	(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.) Same as above "(4) Revamping host institution's internal systems..."

exclusive research facilities for researchers to concentrate on their own research activities. The university also takes special efforts to provide and maintain a state-of-the-art research environment for the individual research, flexibly responding to requirements from each project over its duration. - Space for shared research equipment To enable integrated management and operation of shared research equipment, exclusive space with technical staffers will be set up next to the research project space. - Researchers' communication space that facilitates the exchanges among researchers from different fields In order to develop new interdisciplinary research fields through a fusion of various studies, the university provides researchers in different academic fields and from various countries with space and opportunities to enhance communications. - Accommodation (housing) facilities for researchers Accommodation facilities will be taken care of for researchers coming from domestic and foreign areas. b) Establishment of basic facilities and equipment As a part of the process establishing the necessary research environment, the university sets up basic facilities and equipment that accompany the buildings and that need intensive initial investment along with the center's head office and basic infrastructure.	
(6) Support for other types of assistance As one of the leaders of the world's academic community, Kyoto University firmly determines to take a responsibility in establishing a genuine "world top-level research center" that will serve as one of "the world's leading knowledge centers". The center is expected to function as a top-level research organization since Kyoto University already has outstanding capabilities; 1) to create research environment that attracts world top level researchers, 2) to facilitate intra-university cooperation among world's	(6) Support for other types of assistance The university has given the iCeMS a place of prominence in its regulations regarding organizational structure as well as on the university website.

leading researchers from different fields, 3) to integrate diverse academic fields to promote an interdisciplinary approach, and 4) to contribute to the present and future societies by generating unprecedented knowledge and research findings. Kyoto University is confident that with these essential capabilities, successful performances of the center will be promised. Kyoto University has been characterized, since its foundation in1897, 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, in this regards, Kyoto University is one of the best places to establish the world premier international research center to lead the world's research.	

<Future Policy and Concrete Plans>
-Provision in host institution's mid-to-long-term plan

As mentioned above, the university's current mid-term strategy (FY 2010–15) affirms that it will continue its support for the iCeMS.

-Concrete Measures

(1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc

The aforementioned support is secure through at least 2014, when a new presidential term begins.

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

The current decision making system is to be maintained as it has proven to be both efficient and effective.

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

Current procedures will be maintained.

(4) Revamping host institution's internal systems to allow introducing of new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation

Current procedures will be maintained.

(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.)

Current procedures will be maintained.

(6) Support for other types of assistance

Current procedures will be maintained.

- What the host institution is/will do to support/sustain the operations of the center (include support activities already underway)?

a) Support to raise the iCeMS' recognition and profile: providing opportunities to advertize the iCeMS in various venues, occasions, etc.

b) Previously in a miscellaneous category, the iCeMS has succeeded in being repositioned higher within the university's organizational structure as well as on the university website, now highlighted prominently as a "World Premier International Research Center".

c) 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. This perfectly matches the iCeMS' objectives, and therefore will help drive its cross-disciplinary efforts.

d) The iCeMS accounted for five out of Kyoto University's 36 proposals accepted by the 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 at the iCeMS, awareness for a need to continue and expand iCeMS-like organizations is increasing among university board members.

10. Efforts to improve points indicated as requiring improvement by Program Committee and results of such efforts

-Points specified as needing improvement (as noted in Item 3 "Points that need improvement" in the FY2009 follow-up results)	Efforts to improve them and results
1. Reappraisal of the basic concepts: "Meso-scale control" and integration of cell-material science	1) Reappraisal of the basic concepts: "Meso-scale control" and integration of cell-material science

2. Rewriting of mission statement and roadmap toward the goal of the center	2) Rewriting of mission statement and roadmap toward the goal of the center The above two points were merged as they are closely linked. The following steps were taken in response to the Program Committee's feedback: • 3 comprehensive PI meetings were held to discuss the concept of mesoscopic sciences; • 3 meetings were held with the WPI Program Director and corresponding Program Officer; • Mesoscopic sciences were the main point of discussion at the annual Advisory Committee meeting, resulting in a great deal of useful feedback; and • Close consultations were held with Dr **Mark Haw** of the University of Strathclyde and author of *Middle World* (Macmillan, 2007). As described above, the iCeMS' key concepts have been criticized as being 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 Institute for Integrated Cell-Material Sciences, is **to create new cross-disciplinary fields through the integration of cell and material sciences**. Investigating the control mechanisms of multimolecular structures within cells on the one hand, and artificial materials on the other, as well as bringing about the fusion of the two, the iCeMS is pioneering the development of *stem cell technologies* and *mesoscopic sciences*. These are anticipated to lead to innovations in medicine, pharmaceuticals, the environment, and industry. **Stem Cell Technologies Research includes**: • Reprogramming with chemical compounds for iPS cell derivation; • Chemical probes for stem cell research;

- Control of ES/iPS cell growth and differentiation with chemicals and materials; and
- Creation and applications of stem cell-derived model cells in medicine and drug discovery.

Mesoscopic Sciences Research includes:
- Imaging and probing of meso-complexes in cells;
- Production of functional mesoscopic materials;
- Integration of mesoscopic materials and living cells; and
- Modeling, simulation, and physics theories of mesoscopic events in materials and living cells.

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.

A roadmap toward reaching the goal of the institute — **integration of the cell and material sciences** — includes the following concrete measures (for details refer to 2. "Center's Research Activities"):
- Active promotion of 35 cross-disciplinary research projects;
- In-depth discussions at a special task force on cell-material science integration, including young researchers and senior scientists alike (7 such meetings held in FY 2010);
- Ongoing discussions concerning **10** top-priority cross-disciplinary research projects; and
- Launch of the Cross-Disciplinary Journal Club.

Additionally, efforts are underway to publish review articles on the subject of mesoscopic sciences in leading research journals:

- iCeMS Kyoto Fellow Dr **Kalay** has a paper in press;
- Prof **Ueda** likewise has a paper in press; and
- In addition, possibly two more papers are being co-authored by Profs **Kusumi**, **Kitagawa**, **Nakatsuji** as well as Dr **Mark Haw** of the University of Strathclyde, UK.

3. Fruitful collaboration between iCeMS and CiRA	3) Fruitful collaboration between iCeMS and CiRA Collaboration between the iCeMS and CiRA is taking place on many levels, both scientific and institutional. In this context, overall cooperative research efforts are being coordinated by iCeMS Prof **Uesugi** and CiRA-iCeMS Prof **Yamada**, while iCeMS Assoc Prof **Sengoku** and CiRA Assoc Prof **Ishii** are leading combined overseas outreach efforts. Specific areas of joint research (and relevant faculty) include: • Differentiation of ES/iPS cells using synthetic chemical compounds (**Nakatsuji**, **Uesugi**, iCeMS Kyoto Fellow and CiRA PI **Yamamoto**) • Development of small molecules as stem cell probes and as synthetic cell adhesion factors (**Uesugi**, iCeMS PI and CiRA Director **Yamanaka, Ueda**, **Nakatsuji**) • Control of reprogramming gene expression using synthetic transcription factors (**Sugiyama**, iCeMS Prof and CiRA PI **Yamada**, **Nakatsuji**) • Single-molecule imaging study of muscle cells differentiated from mouse iPS cells, with normal and dystrophin-deficient genotypes (**Kusumi**, CiRA Deputy Director **Nakahata**) • Small molecule tools and chemical libraries produced by the **Uesugi** group have been used extensively in CiRA's research as a part of collaborations with the **Yamanaka**, **Sakurai**, **Inoue**, and **Osafune** labs, aiding their clinically relevant investigations. The results of one of these collaborations, with the **Inoue**, **Uesugi** and **Nakatsuji** Labs, has recently been published (*Journal of Biomolecular Screening* 2011). Recent examples of iCeMS-CiRA organizational cooperation include: • **6** faculty members, including Prof **Shinya Yamanaka**, Prof **Yasuhiro Yamada**, and Asst Prof **Takuya Yamamoto** (appointed as one of the four original iCeMS Kyoto Fellows) are employed at the iCeMS while continuing to conduct basic research on iPS cells.

	• Consolidation of overseas networking efforts, led by iCeMS Assoc Prof **Shintaro Sengoku**, head of the iCeMS Innovation Management group, and CiRA Assoc Prof **Tetsuya Ishii**, head of the CiRA Research Management Office. • Consolidation of cooperative research efforts, led by iCeMS Prof **Motonari Uesugi** and CiRA Prof **Yasuhiro Yamada**. • Consolidation of ES/iPS cell culture quality control management systems with cooperation and collaboration between the **Nakatsuji** and relevant **CiRA** Groups. • Participation of CiRA researchers in iCeMS Seminars (eg Prof **Yamanaka** and many others attended an iCeMS Seminar by **Sir John Gurdon** of the University of Cambridge). • Participation of **8** members from the CiRA, including **4 CiRA PIs**, at the 2010 iCeMS Retreat. • Participation of CiRA Senior Lecturer **Keisuke Okita** in the July 2011 Heidelberg-Kyoto Joint Symposium, co-organized by the iCeMS. • Joint planning and hosting of iCeMS/CiRA stem cell classroom events for high school students and their teachers (for details, see "8. Other important measures taken to create a world premier international research center"). • Adding to the iCeMS-CiRA collaboration detailed above, the following researchers have joined to staff to strengthen the key role that iPS/stem cell-related basic research plays within the iCeMS: Prof **Takashi Shinohara** of the university's Graduate School of Medicine (Kyoto University) joined the adjunct faculty and strengthened stem cell research with his study of germ cell lineage stem cells; and Prof **Mitinori Saitou**, also an adjunct professor, brought his expertise in fate determination and differentiation mechanisms of stem cells in early embryos. Also, Prof **Azim Surani**, a world leading scientist in the germ/stem cell lineage and epigenetic reprogramming research and a professor at Cambridge University's Gurdon Institute, took up a visiting professor post at the iCeMS.

4. Improvement in the leadership of the center director	<u>4) Improvement in the leadership of the center director</u> Prof **Nakatsuji** has actively and assertively led the institute in a number of areas, including: • Charting an overall course for the institute by defining key concepts and research objectives; • Responding rapidly and decisively to requests from the WPI Program Committee and the site visit team; • Taking active part in the institute's overseas outreach efforts, such as with UCLA, NCBS-inStem, and in co-organizing the Heidelberg-Kyoto Symposium; • Determining the **10** high-priority cross-disciplinary research projects, as well as leading efforts to aid young researchers taking part in cross-disciplinary research; • 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 useful in sparking ideas for new joint research projects. Prof **Nakatsuji**, among other iCeMS researchers, has been actively posting relevant novel papers to the database, so far accumulating around 500 original and review articles. This resource is also aiming at the growth of a broad community of scientists who are interested in integration of cell-material sciences and also mesoscopic sciences; and • Taking the lead in ensuring that the institute's facilities and research environment are beneficial to the promotion of scientific endeavors and are truly up to world-class standards.
5. Increasing the center's international recognition	<u>5) Increasing the center's international recognition</u> Efforts to increase the institute's international recognition are proceeding on numerous fronts, scientifically, institutionally, and in print and electronic media. Specific examples of recent international scientific collaboration include:

- **CNSI** at UCLA, an MoU partner, where 3 material science joint research projects are underway and a new project, in cancer stem cells, is being planned;
- **NCBS** in Bangalore, an MoU partner, who have opened a satellite laboratory at the iCeMS (December 2010) and are actively involved in stem cell and imaging research;
- **Heidelberg University**, an MoU partner of Kyoto University, who are co-organizing an international joint symposium in Germany in July 2011; and
- **MRC-CRM** in Edinburg, an MoU partner, jointly pursuing stem cell research.

Examples in print media include:

- A new, significantly more scientifically comprehensive overview brochure (published summer 2010);
- A new, English-language newsletter, *iCeMS Focus* (summer 2010);
- Mailing of the new brochure to editors of leading journals, coauthors of significant papers, and other influential scientists worldwide; and
- Placement of key job notices and international conference announcements in *Nature* and *Science*, as well as advertising in program materials at international scientific meetings, such as at the International Society for Stem Cell Research (ISSCR) and the American Chemical Society (ACS).

Examples in electronic media include:

- Distribution of standard introductory presentation slides to all institute researchers, for use at international conferences;
- Active and substantive reporting of scientific progress on the institute's and the university's websites;
- Worldwide distribution of press releases via the AAAS scientific wire service *EurekAlert!*;
- Statistical analysis of the iCeMS website:
  - **247,000** site views in 30 months (**8,200** views per month), **76% above** the average of science-related, similar-scale websites
  - **11%** of visitors from **130 overseas countries**
- Implementation of social media functionality, enabling the broad redistribution of institute-related information and announcements, via

	Twitter. Other examples include: • The iCeMS hosted a booth, showcasing the institute's research areas and scope, at the 2011 AAAS annual meeting in Washington DC. • The university has raised the iCeMS' profile in its organizational structure, as well as on the university website.

11. Efforts to improve points indicated as requiring improvement in the Project Progress Verification Report and results of such efforts	
-Points specified as needing improvement (extracted from the FY2009 Project Progress Verification Report)	-Efforts to improve them and results Same as "10. Efforts to improve points indicated as requiring improvement by Program Committee and results of such efforts" above.

12. Project Expenditures

FY 2007

(Exchange Rate: JPY/USD=120)

Cost Items	Details	Costs (ten thousand dollars)
Personnel	Center director and Administrative director	11
	Principal investigators (11 of persons):	47
	Other researchers (10 of persons):	10
	Research support staffs (5 of persons):	3
	Administrative staffs (13 of persons):	22
	Total	93
Project activities	Gratuities and honoraria paid to invited principal investigators (0 of persons):	0
	Cost of dispatching scientists (6 of persons):	9
	Research startup cost (3 of persons):	5
	Cost of satellite organizations (1 of satellite organization):	4
	Cost of international symposiums (1 of symposium):	7
	Rental fees for facilities	1
	Cost of consumables	57
	Cost of utilities	1
	Other costs	117
	Total	201
Travel	Domestic travel costs	3
	Overseas travel costs	8

Ten thousand dollars
(Exchange Rate: JPY/USD=120)

WPI grant for FY 2007	566
Costs of establishing and maintaining facilities in FY 2007:	54
Renovating Funai Tetsuro Auditorium & Funai Center etc.	16
Renovating research space in the Center for iPS cell Research and Application	7
Renovating lab space on the 2nd floor of the Institute for Frontier Medical Sciences (38m²)	3
Others	28
Cost of equipment procured in FY 2007:	219
6 confocal laser microscopes	52
2 sets of mass spectrometer	21
A set of nanoliter dispensing system	13
A Sequential plasma spectrometer	9
A set of assessment system of solar battery	8
3 fume hoods	8
Others	108

	Travel and accommodations cost for invited scientists (47 of domestic scientists): (27 of overseas scientists):	8
	Travel cost for scientists on secondment (1 of domestic scientists): (1 of overseas scientists):	1
	Total	20
Equipment	Depreciation of buildings	78
	Depreciation of equipment	120
	Total	198
Other research projects	Projects supported by other government subsidies, etc.	37
	Commissioned research projects, etc.	351
	Grants-in-Aid for Scientific Research, etc.	127
	Total	515
Total		1,027

FY 2008

(Exchange Rate: JPY/USD=120)

Cost Items	Details	Costs (ten thousand dollars)
Personnel	Center director and Administrative director	20
	Principal investigators (no. of persons): 16	133
	Other researchers (no. of persons): 47	217
	Research support staffs (no. of persons): 25	32
	Administrative staffs (no. of persons): 21	83
	Total	485
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons): 0	0
	Cost of dispatching scientists (no. of persons): 17	32
	Research startup cost (no. of persons): 17	108
	Cost of satellite organizations (no. of satellite organizations): 1	42
	Cost of international symposiums (no. of symposiums): 3	1
	Rental fees for facilities	27
	Cost of consumables	144
	Cost of utilities	5
	Other costs	236
	Total	595
Travel	Domestic travel costs	8
	Overseas travel costs	16
	Travel and accommodations cost for invited scientists (no. of domestic scientists): 37 (no. of overseas scientists): 22	7
	Travel cost for scientists on secondment (no. of domestic scientists): 12 (no. of overseas scientists): 2	3
	Total	34
Equipment	Depreciation of buildings	5
	Depreciation of equipment	308
	Total	313
Other research projects	Projects supported by other government subsidies, etc.	11
	Comissioned research projects, etc.	1,717
	Grants-in-Aid for Scientific Research, etc.	322
	Total	2,050
Total		**3,477**

Ten thousand dollars (Exchange Rate: JPY/USD=120)

WPI grant for FY 2008	**1,296**
Costs of establishing and maintaining facilities in FY 2008	**2,480**
Repairing facilities : Research Bldg. No.1 / ProjectLab (Number of facilities: 1 , 2,390 m²) Costs paid:	228
Repairing facilities : West General Research Bldg. (subject to change) (Number of facilities: 1 , 4,800 m²) Costs paid:	733
Establishing new facilities : West General Research Bldg. (subject to change) (Number of facilities: 1 , 12,000 m²) Costs paid:	1,485
Establishing new facilities : iCeMS Research Bldg. (subject to change) (Number of facilities: 1 , 3,000 m²) Costs paid:	13
Others	21
Cost of equipment procured in FY 2008	**845**
Transmission Electron Microscope Number of units: 1 Costs paid:	29
Field Emission Scanning Electron Microscope Number of units: 1 Costs paid:	36
High Performance Liquid Chromatograph Mass Spectrometer Number of units: 1 Costs paid:	21
High-Throughput Sequence Analysis System Number of units: 1 Costs paid:	92
Virtual Slide Imaging System Number of units: 1 Costs paid:	14
Others	653

FY 2009

i) Overall project funding

(Exchange Rate: JPY/USD=100)

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	31
	Principal investigators (no. of persons):16	172
	Other researchers (no. of persons):101	494
	Research support staffs (no. of persons):53	64
	Administrative staffs (no. of persons):27	133
	Total	894
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):	
	Cost of dispatching scientists (no. of persons): 31	111
	Research startup cost (no. of persons): 16	214
	Cost of satellite organizations (no. of satellite organizations): 1	50
	Cost of international symposiums (no. of symposiums): 3	7
	Rental fees for facilities	9
	Cost of consumables	392
	Cost of utilities	5
	Other costs	406
	Total	1,194
Travel	Domestic travel costs	7
	Overseas travel costs	20
	Travel and accommodations cost for invited scientists (no. of domestic scientists):66 (no. of overseas scientists):71	14
	Travel cost for scientists on secondment (no. of domestic scientists):9 (no. of overseas scientists):6	5
	Total	46
Equipment	Depreciation of buildings	318
	Depreciation of equipment	1,606
	Total	1,924
Other research projects	Projects supported by other government subsidies, etc.	79
	Comissioned research projects, etc.	762
	Grants-in-Aid for Scientific Research, etc.	570
	Total	1,411
Total		5,469

Ten thousand dollars (Exchange Rate: JPY/USD=100)

WPI grant for FY 2009	**2,350**
Costs of establishing and maintaining facilities in FY 2009	**3,453**
Establishing new facilities: research building for CiRA (Number of facilities: 1, 12,000m²) Costs paid:	3,016
Establishing new facilities: rsearch building 3 at iCeMS Complex 2 (Number of facilities: 1, 3,000m²) Costs paid:	330
Repairing facilities: rsearch building 2 at iCeMS Complex 2 (Number of facilities: 1, 500m²) Costs paid:	76
Others	31
Cost of equipment procured in FY 2009	**2,486**
Stimulated Emission Depletion Spectral Fluorescence Microscope System, Number of units:1 Costs paid:	138
Two-photon excitation fluorescence inverted microscope Number of units: 1 Costs paid:	135
Transmission Electron Microscope Number of units: 1 Costs paid:	126
High–throughput ultra–high speed sequencing system Number of units: 1 Costs paid:	79
Super-Resolution Imaging Microscopy Number of units: 1 Costs paid:	74
Others	1,934

ii) Costs of Satellites and Partner institutions

(Exchange Rate: JPY/USD=100)

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of persons):	
	Other researchers (no. of persons): 1	
	Research support staffs (no. of persons): 7	
	Administrative staffs (no. of persons):	
	Total	23
Project activities		7
Travel		3
Equipment		17
Other research projects		14
Total		64

FY 2010

i) Overall project funding (Exchange Rate: JPY/USD=100)

Cost Items	Details	Costs (10,000 dollars)
Personnel	Center director and Administrative director	31
	Principal investigators (no. of persons):16	180
	Other researchers (no. of persons):93	476
	Research support staffs (no. of persons):50	72
	Administrative staffs (no. of persons):20	103
	Total	862
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):	0
	Cost of dispatching scientists (no. of persons):48	101
	Research startup cost (no. of persons):20	99
	Cost of satellite organizations (no. of satellite organizations):1	50
	Cost of international symposiums (no. of symposiums):3	4
	Rental fees for facilities	8
	Cost of consumables	100
	Cost of utilities	67
	Other costs	171
	Total	600
Travel	Domestic travel costs	10
	Overseas travel costs	17
	Travel and accommodations cost for invited scientists (no. of domestic scientists):1 (no. of overseas scientists):61	14
	Travel cost for scientists on secondment (no. of domestic scientists):1 (no. of overseas scientists):10	5
	Total	46
Equipment	Depreciation of buildings	95
	Depreciation of equipment	2,047
	Total	2,142
Other research projects	Projects supported by other government subsidies, etc.	91
	Commissioned research projects, etc.	625
	Grants-in-Aid for Scientific Research, etc.	252
	Total	968
Total		**4,618**

Ten thousand dollars

WPI grant	**1,350**
Costs of establishing and maintaining facilities	**716**
Establishing new facilities: Research Building 3 at the iCeMS Complex 2	
Number of facilities: 1 (3,000m²) Costs paid:	671
Others	45
Cost of equipment procured	**133**
Name of equipment: Confocal laser scanning microscope	
Number of units: 1 Costs paid:	15
Others	118

ii) Costs of Satellites and Partner institutions

Cost Items	Details	Costs (10,000 dollars)
Personnel	Principal investigators (no. of persons):	
	Other researchers (no. of persons):2	
	Research support staffs (no. of persons):7	
	Administrative staffs (no. of persons):	
	Total	30
Project activities		8
Travel		1
Equipment		11
Other research projects		30
Total		**80**