# Summary of Proposal

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| Host institution | Nagoya University |
| Chief entire-project officer (Head of host institution) | Dr. Michinari Hamaguchi, President of Nagoya University |
| Chief center-project officer | Dr. Kenichiro Itami<br>Professor, Department of Chemistry, Graduate School of Science, Nagoya University |
| Center director | Dr. Kenichiro Itami<br>Professor, Department of Chemistry, Graduate School of Science, Nagoya University |
| Center name | Institute of Transformative Bio-Molecules (ITbM) |
| Project Summary | Our goal is to develop innovative functional molecules that make a marked change in the form and nature of biological science and technology by taking full advantage of the cutting-edge molecular synthesis expertise of our chemistry principal investigators (PIs) and intense interactions with our leading plant/animal biology PIs. Through this interaction, which is fundamental to the Center, transformative bio-molecules will be synthesized that can (1) **enhance biotic productivity and quality** and (2) **realize innovative bio-imaging**. To ensure the advancement of these projects, we will (3) **develop catalysts that enable incredibly efficient synthesis and molecule activation on demand**. The ultimate goal is to have a positive impact on global issues such as food production. Our team of PIs is an innovative mix of chemists and biologists from Japan and abroad. A Co-PI system, and an efficient administration with English will ensure that international members will have significant involvement in the project. |
| Mission statement and/or Center identity | The mission of the Center is to develop diverse functional molecules that afford innovative impact on the operating principle of the biological systems. To accomplish this, we will harness our synthetic abilities based on molecule-activation chemistry (see below). We seek to effect a paradigm shift in science by creating a new field of research that aims to implement programmed chemical transformations in vivo for precisely controlling the production of bio-functional molecules of requisite structures and their functional expressions. The identity of this Center resides in the development of brand new synthetic bio-molecules that will affect this goal. To accomplish this, we will enlist the best synthetic chemists and plant and animal biologists worldwide. |
| Target research field | Target research field: **Molecule-Activation Chemistry for Advanced Systems Biology** (This is an area in which Nagoya University has significant international competitive advantages: synthetic chemistry, molecular catalysis, systems biology, plant science, peptide science, live-cell imaging.)<br><br>The interface of chemistry and molecular biology has already resulted in important new research fields of significant scientific impact, such as chemical biology and medicinal chemistry. We plan to bring this to a new level by exploiting newly developed molecule-activation chemistry* partnered with fundamental biological systems of plants and animals. This research endeavor will have significant impacts in the closely related fields of chemical biology and medicinal chemistry, but most importantly, on areas that are of urgent global importance including world food production, medical care, and bioenergy.<br><br>*__Molecule-Activation Chemistry__: The synthetic chemistry that enables the activation and direct transformation of stable, simple molecules into useful, complex structures. This methodology can rapidly convert biologically active “lead” molecules into more selective and active derivatives.<br>**Systems Biology**: The biology to unveil the pivotal mechanism of how organisms function as a system. The discovery of key molecules operating biological systems at an individual organism level is crucial. |
| Research objectives | (1) To develop molecules that precisely control biotic function and production. Specifically, we will target (a) molecules that dramatically enhance plant growth based on the discovery of new signal transduction pathway of plant hormone auxin, (b) molecules that regulate season-sensing systems and reproduction in animals, and (c) molecules that can overcome species barriers in plant breeding to produce novel crops.<br>(2) To develop innovative bio-imaging molecules and related photoelectronic molecular technologies that enable the visualization of biological phenomena at will. For instance, we will design and synthesize new fluorescent molecules that feature high luminance, low molecular weight, and controlled labeling properties.<br><br>Meanwhile, we will propel the development of small-molecule catalysts for achieving ideal chemical synthesis, which can also be used for the selective activation and |

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| | transformation of bio-molecules in vivo, in order to provide a viable method for realizing the two main objectives. Through these endeavors, we will create “transformative bio-molecules” that will dramatically change the way of research in chemistry, biology, and other related fields. Most importantly, we will make these molecules readily available for all the researchers in the world to expand the global impact of the Center. |
| Outline of management | The Center will take number of measures to remove the barriers that hinder interdisciplinary research and internationalization thereby triggering a fundamental transformation of existing academic systems.<br>(1) The Center Director will have the authority to make the final decisions over the appointment of personnel, the Center budget, and research priorities etc.<br>(2) A rigorous evaluation of researchers will be made by the Evaluation Committees, and the results will be reflected in the salaries of researchers.<br>(3) We will establish an effective and efficient administration with English-speaking staff for accelerating the true internationalization of the Center as well as the fusion of different research fields. This includes a talented administrative director with a strong background of scientific research.<br>(4) We will introduce a **Co-PI system**, whereby bright young scientists are paired with overseas PIs to facilitate the research activities of the eminent foreign PIs in the Center. This will increase the worldwide visibility of the Center, facilitate research in Japan under the direction of overseas PIs and also help train the young researchers (Co-PIs) to be the scientific leaders of the next generation.<br>(5) An **international promotion unit** will be developed. This unit will play the crucial role of providing researchers worldwide with access to the transformative bio-molecules developed at Nagoya. This will include negotiating issues with regard to intellectual property, accessibility of the molecules and technologies, and also the distribution and scale up of any molecules discovered at the Center.<br>(6) We will support promising results that emerge from other researchers in Nagoya University. We will also make a strong commitment to nurture the next-generation of researchers through a productive cooperation with Nagoya University Program for Leading Graduate Schools and Global 30 International Programs. |
| Researchers and other center staffs, satellites, partner institutions | Number of Principal Investigators (number of foreign researchers) 15 (5)<br>Total number of researchers (number of foreign researchers) 70 (35)<br>Total number of people at the “core” of the Center 130<br>as of March, 2016<br>**Principal Investigators (PIs):** Kenichiro ITAMI, Tetsuya HIGASHIYAMA, Jeffrey W. BODE, Cathleen M. CRUDDEN*, Stephan IRLE, Toshinori KINOSHITA, Takashi OOI, Keiko TORII*, Shigehiro YAMAGUCHI, Takashi YOSHIMURA<br>*10 PIs in total (we will hire additional 5 PIs), average age 43*<br>*underlined names represent PIs from abroad; asterisks represent female PIs*<br>**Cooperating Institutes:** Queen’s University (Canada), University of Washington (USA), Eidgenössische Technische Hochschule, Zürich (Switzerland). These institutes are considered to be gateways to our Center and the PI who holds a position in the institute will engage in active collaboration directly and through research exchanges.<br>**Co-PI System:** Overseas PIs are talented research stars in the world and will have double affiliations. We will introduce a system of Co-Principal Investigators (Co-PIs) to: (1) ensure close contact and continuity in the research maintained; and (2) mentor leading young researchers. Co-PIs will be based at Nagoya, but chosen and guided by the foreign PIs for actively managing their research groups in the Center. Co-PIs will be considered for promotion to full PI status when their research potential is realized. |
| Administrative director | Dr. Yoshihito Watanabe (Trustee, Vice-President, Nagoya University) |
| Outline of research environment | (1) We will establish a **Mix-Lab system**, where international young researchers from different fields will work together in order to accelerate multidisciplinary advances through informal discussions on a daily basis.<br>(2) All postdoctoral researchers and students will be supervised by two PIs from different fields (**Co-supervising system**) in order to accelerate collaboration and nurture the next generation of cutting-edge research, unrestricted by the bounds of traditional disciplines.<br>(3) In order to ensure that excellent foreign PIs and Co-PIs will spend significant time at Nagoya, we will provide the following: (a) a team that is responsible for assisting them in applications for competitive domestic (Japanese) research funds; (b) opportunities for partners/spouses to hold positions in the University based on their skill sets (**Dual Career Support**); and (c) adequate information on education opportunities for the children of foreign PIs who may join them during their time at Nagoya. Through these mechanisms, we expect foreign PIs to base a significant portion of their activities at Nagoya, and we aim to attract a certain percentage of researchers permanently to Nagoya. |

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<tr><td></td><td>(4) Each new researcher will be provided sufficient research space and start-up funds.<br>(5) We will locate the world's most advanced equipment and facilities in a single space at Nagoya University, staffed with expert equipment managers such that it is fully accessible for promoting research, international collaboration, and discovery.<br>(6) We will engage in high-profile recruitment campaigns to attract highly qualified postdoctoral researchers using web sites with a global appeal describing current efforts of the Institute, University, and the international appeal of Nagoya City.</td></tr>
<tr><td>Outline of indicators for evaluating a center's global standing</td><td>Three aspects are important for the global standing of the Center:<br>1) research quality and impact, 2) breakthroughs resulting from the inter-disciplinary research activities, and 3) human resources development as an international institute.<br>The following is a selection of data for the current 10 PIs, which clearly indicate that we have a group of outstanding individuals.<br>Numbers of paper in Science, Nature, and Nature sister journals: 15<br>Numbers of paper in high-impact journals (impact factor >9): 253<br>Numbers of keynote/plenary/invited lectures (last 4 years): >500<br>Selected awards, honors, and prestigious positions:<br>German Innovation Award (Itami), Novartis-MIT Lectureship Award (Itami), Vice President of International Association of Sexual Plant Reproduction Research (Higashiyama), President of Canadian Society for Chemistry (Crudden), IBM Japan Science Prize (Ooi), EJ Corey Award (Bode), Society of Biology Fellow (Yoshimura), Tokyo Techno Forum 21 Gold Medal (Yamaguchi), JSPS Prize (Torii, Yoshimura, Ooi, Higashiyama), Elected Fellow of AAAS, HHMI Investigator (Torii)</td></tr>
<tr><td>Securing research funding</td><td>The PIs of this Center have received competitive research funding such as ERATO, CREST, NEXT Program, ALCA, and a Grant-in-Aid for Scientific Research on Innovative Areas (the average of FY 2007-2011 is 7.7 million USD / year). Thus, we are confident that similar or even greater amounts of funds will be obtained in future.</td></tr>
<tr><td>Exploiting the results of previously-initiated center-building efforts</td><td>None: However, we will exploit the results of following past and current projects.<br>Chemistry Global COE program (JSPS), Biology Global COE program (JSPS), Research and Education Funding for Inter-University Research Project (MEXT), Japanese-German Graduate Externship (JSPS/DFG), Program for Leading Graduate Schools (JSPS). Re-Inventing Japan Project – Campus Asia Program (JSPS), Japan Advanced Plant Science Research Network, Live Imaging Center (MEXT).</td></tr>
<tr><td>Appropriations plan<br><br>(Exchange Rate: JPY/USD=80)</td><td>
<table>
<tr><td>FY</td><td>2012</td><td>2013</td><td>2014</td><td>2015</td><td>2016</td><td>2017</td><td>2018</td><td>2019</td><td>2020</td><td>2021</td><td>Total<br>($ millions )</td></tr>
<tr><td>WPI grant</td><td>4.61</td><td>7.76</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>82.37</td></tr>
<tr><td>Funding for previously-initiated center-building efforts</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Total</td><td>4.61</td><td>7.76</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>8.75</td><td>82.37</td></tr>
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</td></tr>
<tr><td>Summary of host institution's commitment</td><td>Nagoya University (hereinafter referred to as "NU") aims to conduct world-class research and internationalization based on the Academic Charter and the Hamaguchi Plan. In accord with these declarations, NU will treat the Center with special rules enabling the Center to most easily achieve its goals, thus playing a key role in the academic mission of NU. If this proposal is successful, NU will amend its Midterm Plans and Research Promotion and Strategy Plans specifically with regard to the WPI and the Center. The major ways in which NU is supporting this Center are given below.<br>Perpetuation of the Center: NU has agreed to sustain the Center's pioneering research activities after the WPI-grant period ends. In order to do so, NU will allocate the Center as part of the Institute of Advanced Research, which has been established as an institute independent from the other departments and research centers at NU.<br>System Reform: The University rules will be revised to: give executive authority to the Center Director to make top-down decisions on the important matters of the Center; enable the Center to be independent in the execution of its budget; and allow the Center to develop its own personnel policies and management, such as allowing double affiliation and introducing performance-based salaries. NU will assign a member of their Board of Trustees/Vice-President as the Administrative Director to help accelerate the system reform in not only the Center but also the entire university.<br>Provision of Building Space: NU will provide 6,000 $m^2$ of building space to establish the Center. To further promote the WPI-catalyzed interdisciplinary research, NU is planning to build a new building within the context of NU's strategy for research system reform. NU will also offer living accommodations for foreign PIs and collaborators.<br>Financial and Personnel Assistance: NU will continue to cover the equivalent amount of the salaries of researchers at the Center who already hold posts at NU. NU will assign 7 associate professors, who will assist in teaching at the departmental level, and to maintain high-level education. NU will provide opportunities for partners/spouses of foreign PIs to hold positions in NU (Dual Career Support).</td></tr>
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Note: Supplemental documents in PPT format may be attached to make the summary of the center project easier to understand (up to 10 pages, in English).

# Research Center Project

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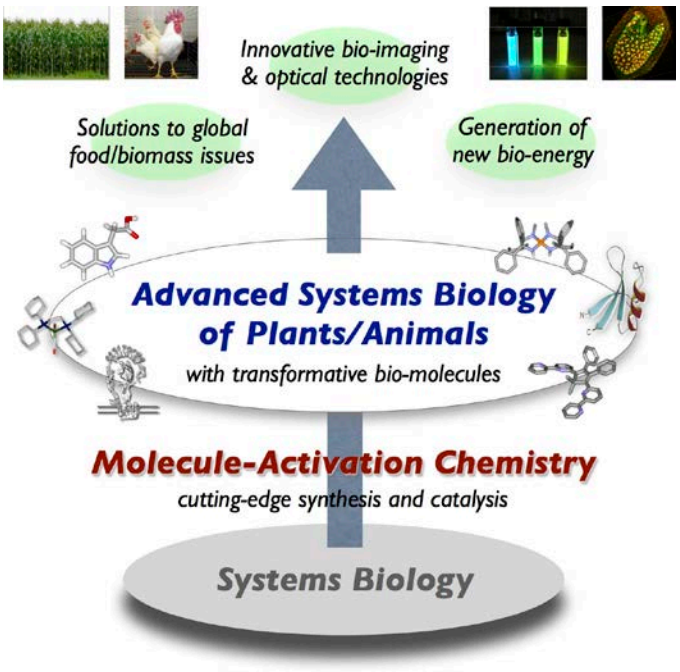
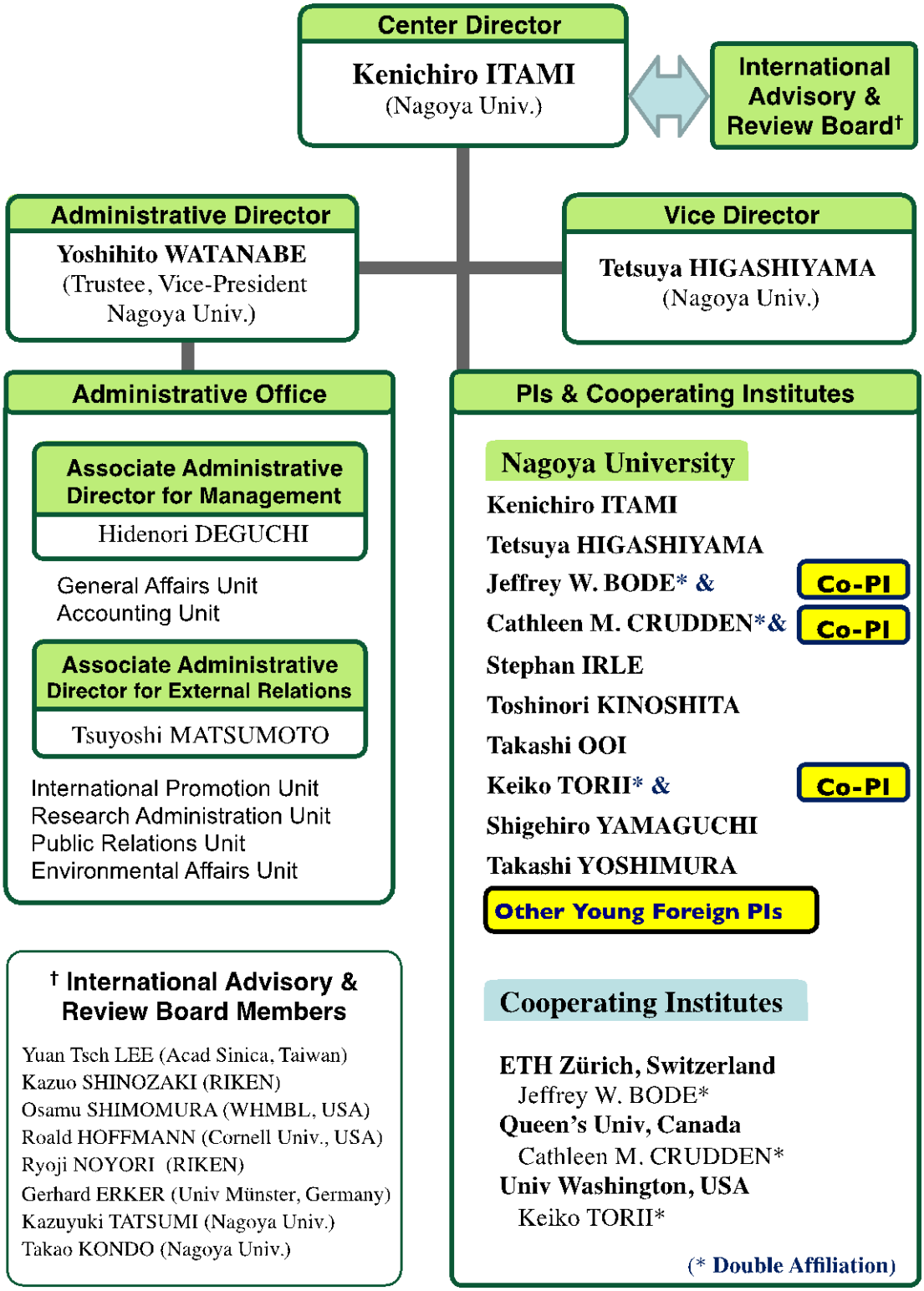
| Host institution | Nagoya University |
| Chief entire-project officer (Head of host institution) | Dr. Michinari Hamaguchi, President of Nagoya University |
| Chief center-project officer | Dr. Kenichiro Itami<br>Professor, Department of Chemistry, Graduate School of Science, Nagoya University |
| Center director | Dr. Kenichiro Itami<br>Professor, Department of Chemistry, Graduate School of Science, Nagoya University |
| Center name | Institute of Transformative Bio-Molecules (ITbM) |
| Project summary | **Our purpose** is to establish a world-leading molecular research institute whose focus will be the design and synthesis of molecules for the discovery, visualization, and manipulation of biological systems.<br>**Our goal** is to develop **"transformative bio-molecules"**, innovative functional molecules that make a marked change in the form and nature of biological science and technology.<br>**Our unique approach** is to apply our **cutting-edge synthesis** (molecule-activation chemistry), with the support of molecular design and computational chemistry, to synthesize key molecules to explore **advanced systems biology in plants and animals**. This is an unprecedented endeavor and the first such research institute in the world.<br>**The identity of the Center** is its capability to synthesize completely new bio-functional molecules with carefully designed functions.<br>**Our ten-year campaign** will culminate in a wealth of **synthetic bio-molecules** that will be key to solving urgent problems at the interface of chemistry and biology. Innovations in food/biomass production, optical technologies, and generation of new bio-energy can be imagined as our dream.<br>  |

# Organization



***Core Members of the Center***

The Center will start with 10 Principal Investigators (PIs), including 3 international researchers, and one Administrative Director. These founding members will then hire post-doctoral researchers, research assistants, administrative staff, and secretaries. At the end of FY 2012, the total number of these core members of the Center will be 50. At the end of FY 2015, the Center will have grown to 15 PIs, 55 other researchers, 40 research support staff and 20 administrative staff (total: 130 core members).

***Principal Investigators and Researchers in Nagoya University***

The seven world-class PIs selected from Nagoya University all have proven abilities to make major contributions to the objectives of this Center and the flexibility to integrate the accumulated wisdom of diverse disciplines. The large proportion of talented young PIs included in this proposal will help ensure the long-term vitality of the WPI Center and mentoring of the next-generation of researchers in this field.

As we look to the future, we also recognize that our proposal builds on a strong background of research at Nagoya University in chemistry and biology. Amongst many others, we are honored to recognize the achievements of our faculty and alumni including four Nobel laureates. Many leading researchers from Nagoya University are working in these fields and already have “seeds” of Transformative Bio-Molecules in their research programs. The promising results that emerge from them will be supported by our Center.

***Overseas PIs and Co-PI System***

PIs from overseas cooperating institutes include eminent international chemists and biologists. These PIs will have double affiliation with Nagoya University and their home institutions, and they will actively transmit information and provide significant opportunities for other foreign researchers to participate in the Center. Their present host institutions will be designated as Cooperating Institutes, which are regarded as major gateways to our Center.

It is important to note that the three overseas PIs, Bode, Crudden, and Torii already have strong collaborative relationships with Nagoya PIs and have agreed to spend a considerable amount of their time at the Center. In addition to their roles as collaborators, these PIs already have strong ties to Japan, in particular to Nagoya University. For example, Crudden was a visiting RCMS Professor in 2006 spending 3 months in Nagoya as part of a collaboration with Itami, gave a graduate course at Nagoya and was a speaker at the 2006 International GCOE Conference in Nagoya. She has also held a GCOE visiting professorship at Kyoto University (2011) and carried out part of her PhD at Osaka University with Professor Shinji Murai. Bode was selected from the organic chemistry community of Nagoya University as the prestigious Hirata Memorial Lecturer in 2010 and has maintained strong ties to Japan since his postdoctoral fellowship at Tokyo Institute of Technology in the group of Prof. Keisuke Suzuki. Torii has given leading-edge seminars to graduate students of Nagoya University annually for the last four years. Torii is also cooperating with our Program for Leading Graduate Schools (JSPS).

We consider this double affiliation strategy to be a considerable strength of our proposal, even if double-affiliated PIs will not be physically present full time at the Center. To ensure close contact and continuity in research, we will support the hiring of Co-Principal Investigators (Co-PIs). Co-PIs will be based at the Center in Nagoya, but chosen and guided by double-affiliated PIs. Co-PIs will be considered for promotion to full PI status when their research potential is realized.

***Cooperating Institutes (Overseas Gateways)***

The research activity of the Center will be further augmented through effective collaboration with three foreign institutions in Canada, USA, and Switzerland:

**Queen's University, Canada;**

**University of Washington, USA;**

**Eidgenössische Technische Hochschule (ETH) Zürich, Switzerland;**

WPI researchers including members of the International Promotion Unit will frequently visit these institutes as basecamps opening up overseas opportunities.

***Young Foreign PIs***

Young talented foreign researchers will be recruited from overseas as PIs in our Center. To attract top scientists to Nagoya, we will provide a fully English-language environment, a support team to assist in writing Japanese domestic grants, the world's most advanced equipment and facilities staffed with expert equipment managers, double career support for spouses of PIs and information on international education for children of PIs. Through these mechanisms, we expect foreign PIs to spend significant amounts of time at Nagoya, and we aim to attract a certain percentage of researchers permanently to Nagoya.

***International Promotion Unit***

This unit will play the crucial role of providing researchers worldwide with access to the transformative bio-molecules developed at Nagoya. This will include negotiating issues with regard to intellectual property, accessibility of the molecules and technologies, and also the distribution and scale up of any molecules discovered at the Center.

***Public Relations Unit***

This unit is responsible for the coordination of all public presentations, lectures and seminars. This unit coordinates and ensures the smooth running of this program and publicizes the outcome of our research through press releases.

***Environmental Affairs Unit***

This unit is mandated to ensure the protection of the environment and conservation of biodiversity, balanced with development and distribution of unnatural bio-molecules and novel crops. This unit is also responsible for the "safe" development of new functional molecules.

***International Advisory & Review Board, and Administration***

An International Advisory & Review Board has already been put in place, which will support our research. The Center will establish an effective and efficient administration staffed by talented individuals with a good command of English, as well as a global outlook and vision. In addition, resources will be allocated to hire a substantial number of technical staff in order to minimize the extra demands on the time of researchers, freeing them to concentrate on their core research activities.

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| Mission statement and/or Center identity | The mission of the Center is to develop diverse functional molecules that afford innovative impact on the operation of biological systems. To accomplish this, we will harness our synthetic abilities based on molecule-activation chemistry (see below). We seek to cause a paradigm shift in science by creating a new field of research that aims at implementing programmed chemical transformations in vivo for precisely controlling the production of biofunctional molecules of requisite structures and their functional expressions. The identity of this Center resides in the development of brand new bio-molecules that will affect this goal. To accomplish this, we will enlist the best synthetic chemists and plant and animal biologists worldwide. |

(1) Target research field

## Molecule-Activation Chemistry for Advanced Systems Biology

To establish this new interdisciplinary field, Nagoya University has significant international competitive advantages in the requisite basic research fields such as synthetic chemistry, molecular catalysis, systems biology, plant science, peptide science, and live-cell imaging.

**Molecule-Activation Chemistry**: The synthetic chemistry that enables the activation and direct transformation of stable, simple molecules into useful, complex structures. This methodology can rapidly convert biologically active “lead” molecules into more selective and active derivatives.

**Systems Biology**: The biology to unveil the pivotal mechanism of how organisms function as a system. The discovery of key molecules operating biological systems at an individual organism level is crucial. Our systems biology is not simply comprehensive biology based on high-throughput data.

**This project is closely related with the interdisciplinary fields of chemistry and biology, which include chemical biology, medicinal and agricultural chemistry, and bio-imaging technology research.**

The interface of chemistry and molecular biology has already resulted in important new research fields of significant scientific impact, such as chemical biology and medicinal chemistry. We plan to bring this to a new level by exploiting newly discovered molecule-activation chemistry and focusing on fundamental biological systems of plants and animals, aiming to develop transformative bio-molecules. This research endeavor will result in a considerable ripple effect not only in the closely related fields of chemical biology and medicinal chemistry, but also on many other areas that face important and urgent problems calling for sustainable solutions, such as environment, food, medical care, and bioenergy.

It should also be noted that significant ethical and safety concerns related to human health, biodiversity and the environment have been raised around genetically modified organisms. Thus, demand for chemical or biochemical-derived molecules that specifically control identified biological mechanisms is rapidly rising in medical and agricultural fields as an alternative to gene-manipulation. The need for such molecules is especially pressing in the plant science field, which has a significant potential to contribute to the solution of many global problems. Our center is the first molecular science center wherein desired molecules for plant/animal sciences and technologies can be designed and synthesized by leading-edge chemistry. The importance of the proposed research field is considerably high.

The fields of medicinal chemistry and chemical biology have been established and there are some centers and organizations for these fields. For example, the Broad Institute established by Harvard University and MIT is a big center of biology and medicine including chemical biology. However, no center exists for leading-edge chemistry targeting fundamental biological systems of plants and animals. Thus many Japanese and foreign researchers who want to produce and/or use new bio-molecules will be attracted to our Center.

Nagoya University's place as one of the leading research universities in the world is highlighted by its achievement in producing 4 recent Nobel laureates. Two among them, Ryoji Noyori and Osamu Shimomura were awarded in the field of Chemistry. The legendary Nagoya University professor Yoshimasa Hirata (1915-2000) nurtured both of these two Nobel laureates and many other internationally famous professors. The Hirata spirit continues at Nagoya University in its drive to encourage and foster researchers very early in their careers. Building on the historically strong chemistry at Nagoya University, our strength lies in organic synthesis and catalysis, and our PIs (Itami, Ooi, Yamaguchi) have been recognized as the world's top researchers in this field. Participation of international eminent foreign researchers (Bode, Crudden) together with the structure theorist (Irle) provides remarkable strength in synthetic ability based on molecule-activation chemistry.

Recently, new interdisciplinary research fields have emerged at the interface of chemistry and biology. Our biology PIs (Higashiyama, Kinoshita, Yoshimura, Torii) are also highly visible in the world and are recognized as leading scientists especially in the fields of plant biology, reproduction, systems biology and live cell imaging. The demand for our proposed interdisciplinary research field "Molecule-Activation Chemistry for Advanced Systems Biology" is increasing remarkably and our results will have tremendous impact on modern human society. Our center is internationally appealing as our project is highly original, being the only one of its kind in the world.

All the PIs have excellent records of grantsmanship, receiving large-scale competitive funds (e.g., ERATO, CREST, NEXT Program, ALCA, HHMI-GBMF, a Grant-in-Aid for Scientific Research on Innovative Areas, etc.) and publishing ground-breaking papers. Itami has developed a number of unique and efficient catalysts for carbon-hydrogen (C-H) activation. Yamaguchi has succeeded in the synthesis of a series of new ladder $\pi$-conjugated compounds. Ooi has brought out the inherent ability of tetraaminophosphonium salts in the design of four different asymmetric catalyses. Irle has described carbon nanostructure formation by theoretical computational simulation. Crudden has reported a breakthrough method for the Suzuki-Miyaura cross-coupling that is the number one reaction employed in the pharmaceutical industry. Bode has identified a mechanistically and synthetically unique approach to amide bond formation (KAHA ligation) for protein synthesis. Higashiyama has discovered the long-sought (~140 years) pollen tube attractant essential for plant reproduction. Kinoshita has identified major components of light-induced stomatal opening reported by Darwin in 1898. Torii is well known for groundbreaking work elucidating the key mechanisms for development of stomata. Yoshimura has identified the "springtime hormone" that triggers seasonal reproduction in animals and clarified the signal transduction cascade for animal seasonal reproduction. In accord with these achievements, they have delivered numerous invited lectures and received various high profile prizes.

Although the research activities and accomplishments of Principal Investigators are truly outstanding as described above, their average age is 43. Since the PIs are all energetic and promising young stars, we are confident that we can continue to innovate at the highest international level for the next decade. However, to ensure this strategy, we will continue to attract researchers worldwide, recruit additional excellent foreign young PIs, and make full use of the innovative Mix-Lab, Co-supervising, and Co-PI systems as described below. We will further make a strong commitment to nurture the next-generation of researchers in the area of bio-molecules through a productive cooperation with the Nagoya University Program for Leading Graduate Schools and Global 30 International Programs for the growth of this Center. We seek to cause a paradigm shift in science via this project.

(2) Research objectives

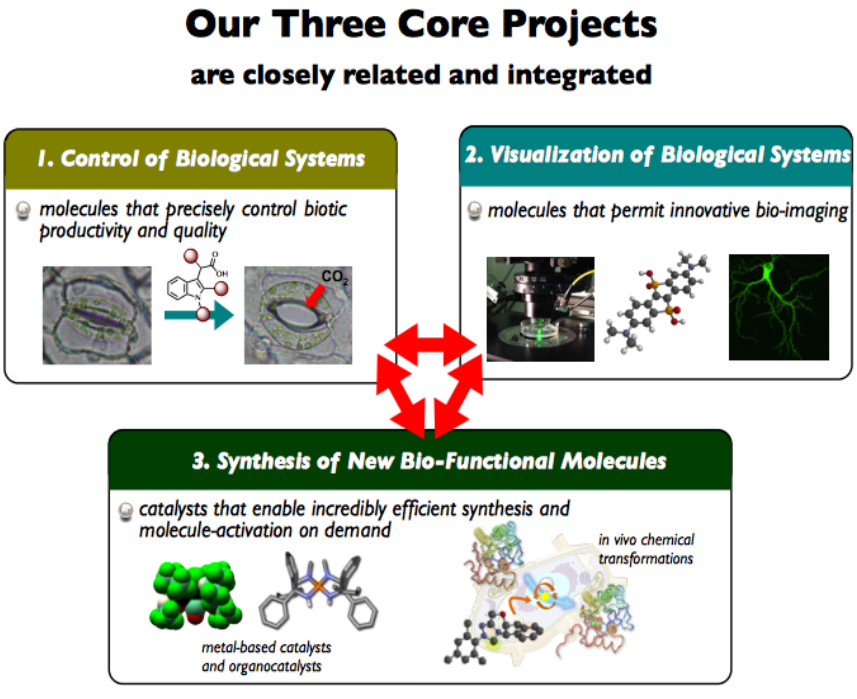
Based on our vision of employing on Molecule-Activation Chemistry for Advanced Systems Biology, we propose the following research consisting of three core projects.

**I) Control of Biological Systems:** *Development of molecules that precisely control biotic productivity and quality*
- (a) Molecules that dramatically enhance plant growth: new approaches for the best known plant hormone, auxin
- (b) Molecules that improve animal reproduction innovatively: controlling seasonality of animals
- (c) Molecules that overcome the genome barrier to produce novel crops

**II) Visualization of Biological Systems:** *Development of molecules that permit innovative bio-imaging*
- (a) Target biological models
- (b) Highly efficient, full-color fluorescent molecules
- (c) Specific conjugation technologies

**III) Synthesis of New Bio-Functional Molecules:** *Development of catalysts that enable incredibly efficient synthesis and molecule-activation on demand*
- (a) Catalysts activating C-H bonds
- (b) Catalysts acting without heavy metals
- (c) Catalysts for protein ligation
- (d) Catalysts for in vivo chemical transformations

Research project (I) aims to precisely control biological systems. We will utilize all the outcomes obtained in this Center to accomplish this objective. Research project (II) aims to visualize biological systems at will. The outcome of this research project (II) will have a significant impact on a wide range of life science-related fields. At the same time, it accelerates research project (I). In research project (III), we will develop small-molecule catalysts for achieving ideal chemical synthesis. This is the core of the Center and provides viable methods for realizing both projects (I) and (II). In addition to these, feedback from projects (I) and (II) further promotes the development of catalysts in project (III). Thus, the three core research projects are closely integrated. Importantly, progress in these core projects will together result in the development of transformative bio-molecules.



**I. Control of Biological Systems:** *Development of molecules that precisely control biotic productivity and quality*

World food prices increased dramatically during the past decade creating a global crisis and causing worldwide political and economical instability. This food crisis stems from unprecedented population growth in developing countries, rising demand for biofuels and farm crop decline due to irregular weather. Food shortages are predicted to become more severe and the food problem is one of the most pressing issues for humankind to resolve in this century. Therefore, innovative improvements in plant and animal production are indispensable. By taking full advantage of our strong backgrounds in plant biology and animal reproduction, we will uncover novel mechanisms for growth and reproduction in plants and animals. Using the knowledge obtained from our achievements and this program, we will develop transformative bio-molecules that precisely control biotic function and production. This research endeavor will have significant impact on food production, biofuel and biomass.

**II. Visualization of Biological Systems:** *Development of molecules that permit innovative bio-imaging*

The discovery of Green Fluorescent Protein (GFP) resulted in a fundamental change in the form and nature of biological science and technology. GFP is the perfect example of a transformative bio-molecule. Various related probes and technologies have been developed by improving GFP and its relatives. However, a bold new direction in bio-imaging molecules is required to open up advanced systems biology. There have been many issues to be solved in this regard, for example, difficulties associated with molecular size, labeling methods, labeling sites of molecules, permeability, wave length of fluorescence, and fluorescence intensity. Integrated chemical and biological technology will overcome these difficulties and lead to the development of transformative bio-molecules for bio-imaging.

**III. Synthesis of New Bio-Functional Molecules:** *Development of catalysts that enable incredibly efficient synthesis and molecule-activation on demand*

In assembling molecules through forming and breaking chemical bonds, catalysis plays a crucial role and serves as a fundamental core technology to supply requisite molecular entities in diverse scientific disciplines. However, current state-of-the-art catalysis technologies are far from ideal, exhibiting limited ability to activate/convert chemical bonds, limited stability under physiological conditions, limited environmental friendliness, and limited substances and structures that can be created. In this WPI project, we will develop truly innovative molecule-activation catalysts that can revolutionize organic reactions and chemical synthesis. The importance of this research endeavor is obvious not only to accelerate the discovery of transformative bio-molecules but also to provide sustainable chemical processes for making valuable organic compounds indispensable to modern society.

(3) Management

i) Center director

**Dr. Kenichiro Itami** (age: 41)
Professor, Department of Chemistry, Graduate School of Science, Nagoya University
*Specialties*: Organic Synthesis, Catalysis, Pharmaceutical Science, Nanocarbon Chemistry

***Qualifications***
Itami is a world-renowned synthetic chemist with broad vision. His achievements range from organic chemistry, synthetic chemistry, catalysis chemistry, to pharmaceutical science and even to materials science and nanocarbon science. Itami's unique synthetic chemistry research has had a significant influence on many chemistry-related fields. His broad interests and capabilities are critical to the success of this type of interdisciplinary research institute. Itami has also been active in serving the global scientific community, as an organizer and a leader. He has served as editor of high-level international journals, as organizer of international conferences, and as a core member of large-scale international and domestic collaborations. These aspects, together with his research achievements and ongoing activities, demonstrate that Itami is not only a top-caliber researcher, but also exceptionally well qualified as the Center Director. Comments written in the six recommendation letters from eminent scientists from around the world clearly show the capability of Itami.

ii) Administrative director

**Dr. Yoshihito Watanabe** (age: 59)
Professor, Department of Chemistry, Graduate School of Science, Nagoya University;
Trustee and Vice-President of Nagoya University (International Affairs and Public Relations)

***Qualifications***
Watanabe was the project leader of the Global COE Program in Chemistry at Nagoya University for 5 years (2007-2011). Under his leadership, the Program was conducted as a joint project of the entire Nagoya Chemistry Community, i.e., professors and researchers in the Graduate School of Science and the Graduate School of Engineering worked together to run research programs, classes, seminars, and symposia. The GCOE activity received the maximum score during evaluation by the review committee. Watanabe has also been appointed as a Vice-President of the Chemical Society of Japan since 2011 and he is currently engaged in the management of society activities. More importantly, Watanabe has been responsible for the Internationalization Initiatives of Nagoya University including the Global 30 program for more than 3 years. Among his achievements in this mission, he launched International undergraduate and graduate courses, in which all the classes are delivered in English. Currently 5 programs, Physics, Chemistry, Biology, Automotive Engineering, and Social Science for the undergraduate courses and 6 programs, Physics/Mathematics, Chemistry, Biology, Economy, Language, and Medical Science at the graduate level are available. In order to launch the International Courses, he convinced Nagoya University faculty members to conduct all classes related to Global 30 programs in English.

***Important Advantages of Assigning Dr. Yoshihito Watanabe, a Vice President of Nagoya University, as the Administrative Director***

(1) Coordination of host institutes and WPI research centers has been a problematical issue in all WPI programs. Vice President Dr. Watanabe can directly coordinate our Center and Nagoya University.
(2) One of the important aspects of the WPI program is to accelerate system reform in Japanese universities, including their internationalization. The intensive commitment of University trustee Watanabe to this WPI Center is a significant measure to accelerate this system reform in not only our WPI Center but also the entirety of Nagoya University.
(3) His strong expertise in biological chemistry provides significant advantage for the management of our Center according to decisions by the Center Director.
(4) In order to manage his time between the various projects he is involved with, we will assign two "Associate Administrative Directors", who are high-level experts in administrative affairs with a good command of English.

iii) Administrative staff composition

In organizing the administration of the WPI Center, two issues are of paramount importance. The first is to set up an efficient and effective administration, which can assist the researchers in concentrating their efforts on their research activities. The second is to appoint talented staff capable of handling business matters with a global vision. Key appointments are as follows.

1) The Administrative Director should have high business acumen and be a highly skilled manager with a good command of English and a good scientific background. The Administrative Director manages six units of administration: 1) general affairs unit, 2) accounting unit, 3) international promotion unit, 4) research administration unit, 5) public relations unit, and 6) environmental affairs unit, with the support by Associate Administrative Directors. We are fortunate in already having secured the services of Dr. Yoshihito Watanabe in this role.

2) Two Associate Administrative Directors will be appointed. One is for internal affairs (to manage the general affairs unit and the accounting unit) and the other is for external relations (to manage the international promotion unit, the research administration unit, the public relations unit, and the environmental affairs unit). We are fortunate in already having secured the services of Mr. Hidenori Deguchi and Dr. Tsuyoshi Matsumoto as the Associate Administrative Directors.

3) Beneath the Administrative Director and the Associate Administrative Directors, a total of 18 experts will be involved in 6 units: 4 in general affairs unit, 3 in the accounting unit, 3 in the public relations unit, 3 in the research administration unit (including 2 Ph.Ds. to support foreign PIs in their applications for Japanese domestic research grants), 3 in the international promotion unit (including 2 Ph.Ds.), and 2 in the environmental affairs unit. Each unit will have 1 unit chief.

4) A total of 15 bilingual laboratory secretaries will be assigned to assist the Principal Investigators. These secretaries will assist with paper work and matters regarding foreign researchers and students.

iv) Decision-making system

The Center Director will have the authority to make final decisions over the appointments of personnel, the Center budget and research priorities etc.

The Center Director needs to maintain good communications with Administrative Directors and the Principal Investigators in the Center. To this end, we envisage establishing the following councils and committees. In order to ensure sufficient time for the scientific goals of the Center, **the number of meetings will be kept to a minimum.**

1) **Joint Management Council**
*Mission*: To discuss and to propose issues of fundamental importance to the Center
*Members*: The Center Director, the Vice Center Director, the Administrative Director, the Associate Administrative Directors, the President of Nagoya University, the Director-General of Nagoya University, any member of the International Advisory and Review Board, and/or the representatives of Cooperating Institutes may also be invited to join the Council Meeting.

2) **Research Council**
*Mission*: To discuss important issues regarding research projects and other matters
*Members*: The Center Director, the Vice Center Director, the Administrative Director, the Associate Administrative Directors, and Principal Investigators at Nagoya University.

3) **Personnel Committee**
*Mission*: To make the final short list of candidates for new positions
*Members*: The Center Director, the Vice Center Director, the Administrative Director, the Associate Administrative Directors, and 2 members appointed by the Center Director and selected from the Principal Investigators

4) **Budget Committee**
*Mission*: To design a budgetary plan
*Members*: The Center Director, the Vice Center Director, the Administrative Director, the

Associate Administrative Directors, and 2 members appointed by the Center Director selected from the Principal Investigators

5) **Internal Evaluation Committee**
*Mission*: To evaluate research activity within the Center and the Cooperating Institutes, and to prepare reports to the External Evaluation Committee
*Members*: The Center Director, the Vice Center Director, the Administrative Director, the Associate Administrative Directors, and 2 members appointed by the Center Director selected from the Principal Investigators

v) Allocation of authority between the center director and host institution

**The Center Director**
The Center Director will have the authority to make the final decisions over the appointments of personnel, the Center budget, and research priorities etc. For that purpose, Nagoya University has taken the significant step of revising its rules in order to give executive authority to the director to make top-down decisions. Nagoya University will also reform its regulations to allow the Center the prerogative to establish its own system for pay structures, employment periods, and other preferential treatment such as the conferment of appropriate titles for its members including project managers and guest researchers.

**Host Institution (Nagoya University)**
The host institution has the authority and responsibility to allocate some part of the University budget for appropriate financial support of the Center. The host institution has the authority to inspect the management of the Center, and to audit the Center accounts.

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

i) The "core" to be established within the host institution
a) Principal Investigators (full professors, associate professors or other researchers of comparable standing)

| | Numbers | | | |
|---|---|---|---|---|
| | At beginning | | At end of FY 2012 | Final goal (Date: March, 2017) |
| | | Those in existing center-building project | | |
| Researchers from within the host institution | 7 | N/A | 7 | 7 |
| Foreign researchers invited from abroad | 3 | N/A | 3 | 5 |
| Researchers invited from other Japanese institutions | 0 | N/A | 0 | 3 |
| Total principal investigators | 10 | N/A | 10 | 15 |

In addition to the 10 PIs as listed in Appendices 1 and 2, when the Center starts, we plan to hire 3 Co-PIs. Candidates for Co-PIs will be recommended or publicly-advertised by corresponding foreign PIs and reviewed by the Personnel Committee. If these Co-PIs have significantly contributed to our Center after some time, they can apply for the position of full PI. Their application will be considered by the review process comparable to that employed with publicly-advertised PIs.

In addition to the three Co-PIs, we will recruit 5 more PIs. All applications will be completely open, while the specific field might be chosen according the strategy of our Center. Applications will be reviewed by the Personnel Committee. We will hire at least 2 young foreign PIs. To attract prominent young PIs from overseas, we will provide significant internal support for them, including a support team for domestic research applications and dual career support for spouses and partners.

b) Total members

| | Numbers | | | |
|---|---|---|---|---|
| | At beginning | | At end of FY 2012 | Final goal (Date: March, 2017) |
| | | Those in existing center-building project | | |
| Researchers | 20 <5, 25%> [4, 20%] | N/A | 25 <6, 24%> [5, 20%] | 70 <35, 50%> [14 , 20%] |
| Principal investigators | 10 <3, 30%> [2, 20%] | N/A | 10 <3, 30%> [2, 20%] | 15 <5, 33%> [3, 20%] |
| Other researchers | 10 <2, 20%> [2, 20%] | N/A | 15 <3, 20%> [3, 20%] | 55 <30, 55%> [11, 20%] |
| Research support staff | 10 | N/A | 15 | 40 |
| Administrative staff | 10 | N/A | 10 | 20 |
| Total number of people who form the "core" of the research center | 40 | N/A | 50 | 130 |

In addition to the 10 PIs mentioned, when the Center starts we plan to hire 10 additional researchers including Co-PIs and postdoctoral researchers, 10 research support staff including laboratory secretaries, and 10 administrative staff including 1 Administrative Director and 2 Associate Administrative Directors.

By the end of FY 2012, 25 researchers (10 PIs, 3 Co-PIs, 12 postdoctoral researchers), 15 research support staff, and 10 administrative staff will be hired. In 2013, we plan to hire 15 PI and 3 Co-PIs and 36 postdoctoral researchers, 20 research support staff, and 20 administrative staff. Postdoctoral researchers and research support staff will increase approximately by 10 and 5 people per year, respectively. By the end of FY 2016, we expect the total number of people who form the core of the Center to reach 130.

We will collaborate with all Nagoya researchers in related fields in a dynamic fashion. We will also make a strong commitment to nurture the next-generation of researchers through a productive cooperation with the **Nagoya University Program for Leading Graduate Schools** and **Global 30 International Programs**.

ii) Collaboration with other institutions

Satellite institutes are NOT applicable in our WPI Research Center Project.

We will start the Center with overseas PIs—these are young eminent chemists and biologists in the world. Overseas PIs will have double affiliation, and their present host institutions will be treated as Cooperating Institutes to our Center as mentioned in the Project Summary (page 3). We will carry out research in cooperation with these institutions, which will also serve the function of overseas gateways.

In order to facilitate this cooperative research, "Agreements for Academic Exchange and Cooperation" will be concluded by taking advantage of our significant experience with overseas exchanges.

*For example, our host departments of graduate school of science have directed the following programs: JSPS/DFG Japanese-German Graduate Externship ~ International Research Training Groups (IRTG), "Complex Functional Systems in Chemistry"* ***(FY2005-2011)****, JSPS, Re-Inventing Japan Project – Campus Asia Program, "Cutting Edge Science and Technology in Chemistry and Materials ~ A Cooperative Asian Education Gateway for a Sustainable Society"* ***(FY2011-2015)****, two G-COE programs for chemistry and biology* ***(FY2007-2011)****, JSPS Institutional Program for Younger Researcher Overseas Visits* ***(FY2009-2012)****, JSPS, Strategic Young Researcher*

*Overseas Visits Program for Accelerating Brain Circulation, "Innovative Molecular Catalysis and Novel Functional Materials"* ***(FY2011-2014)***,.

In order to facilitate the collaboration between the Center and the Cooperating Institutes, meetings will be organized on a regular basis, and the exchange of graduate students and researchers will be promoted.

**Cooperating Institutes:**

**Queen's University, Canada**

**University of Washington, USA**

**ETH Zurich, Switzerland**

( 5 ) Research Environment

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

**Mix-Lab System**

To realize truly cross-disciplinary research projects and to nurture the next generation researchers in this field, we will create special laboratories we refer to as **"Mix-Labs"**. Rather than doing research in a small laboratory consisting of one research group, we will ask young researchers of different fields to work together in a large laboratory (**Mix-Lab**). We strongly believe that this working style will not only accelerate the mixing/merging of people, ideas, equipment, and research, but also help nurture a new generation unrestricted by the bounds of traditional disciplines.

An efficient administration run by talented staff will be introduced to free Principal Investigators from administrative duties.

**Co-supervising system**

To reinforce the value of the Mix-Lab concept, all postdoctoral researchers and students will be supervised by two PIs from different fields for accelerating collaboration and nurturing the next generation of cutting-edge research, unrestricted by the bounds of traditional disciplines.

In order to recruit excellent PIs and Co-PIs, we will provide the following [***see (5)-viii for details***]: (a) **a team** that is responsible for supporting their applications for competitive domestic (Japanese) research funds; (b) opportunities for partners/spouses to hold positions in the University on the basis of proper evaluation (**Dual Career Support**); and (c) adequate **information on education opportunities** for the children of foreign PIs who may join them during their time at Nagoya. Through these mechanisms, we expect foreign PIs to spend significant amounts of time at Nagoya.

We will locate the world's most advanced equipment and facilities in a single space at Nagoya University, staffed with expert equipment managers such that it is fully accessible for promoting research, international collaboration, and discovery. A substantial body of postdoctoral researchers and technical assistants will be hired to ensure smooth operation of analytical instruments etc.

In order to reduce the educational and administrative burden of Principal Investigators, the University will furnish the original faculty of Principal Investigators with additional staff (a total of 7 associate professors).

A total of 15 bilingual secretaries will be assigned to the Principal Investigators in 2013 to help the Investigators cope with their paper work and any matters regarding foreign researchers and students in the groups.

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

Provide each of the new researchers with research space and start-up funds with an average value of 125,000 USD. If necessary, the start-up money will be increased for top-caliber researchers by using a discretionary budget allocated to the Center Director.

Furnish the new researchers with full access to instruments in the Center.

Except for the start-up funds, all of the following costs are covered by our Center: lab spaces fee of 200-300 $m^2$, utility costs including electricity and water fees, employment costs of two postdoctoral researches, one secretary, and one technical staff.

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

We will engage in high-profile recruitment campaigns to attract highly qualified postdoctoral researchers using web sites with global appeal describing the current efforts of the Center, University, and Nagoya City for internationalization.

Keep channels open to world premier chemists and biologists, and solicit their recommendations for suitable candidates as post-doctoral researchers.

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

The research groups of the Principal Investigators are international in outlook, and have excellent track records in inviting foreign researchers as visiting professors, post-doctoral researchers, and exchange students. English is routinely used in their research groups.

Not only our WPI Center but also all of Nagoya University is internationalized as Nagoya University has started the Global 30 International program to accept foreign undergraduate and graduate students (all classes and experimental courses are taught in English). The G30 students are also in the laboratory of the Principal Investigators.

The Administration Director is fluent in English, and the projected administrative staff will also have high English skills.

v. Adopt a rigorous system for evaluating research and a system of merit-based compensation. (For example, institute a merit-based annual salary system)

A rigorous evaluation of researchers will be made by an external evaluation committee, with the assistance of the International Advisory and Review Board.

The annual salary of researchers hired from outside the host institute will be adjusted based on the evaluation. There will also be a merit-based fringe benefit system for internal hires.

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

**Nagoya University will provide 6,000 $m^2$ of research space for the Center.**

The Science and Agricultural Building and Science South Building are regarded as the premier global facilities, and 3,000 $m^2$ of the building space will be allocated to the WPI Research Center. These two buildings, which are directly connected, were built in 2011 to accelerate the collaboration of science and agriculture research within Nagoya University. **A brand-new live-cell imaging center space of 300 $m^2$**, which was originally part of our GCOE program and will be further developed by our WPI program, is also in the Science South building. **A teatime space of 70 $m^2$** will also be placed in the Science and Agricultural Building to facilitate communication among members of our WPI Center.

Nagoya University will provide additional laboratory space of 3,000 $m^2$ for the Center including the Institute for Advanced Research (1,500 $m^2$). Two large rooms (each 500 $m^2$ room) will be used for the **Mix-Lab** [as described in (5)-i, the research environment section]. In total, 500 $m^2$ will be assigned for the administration office space including rooms for the 6 administrative units, a Center Director room, and meeting rooms.

To further promote the WPI-catalyzed interdisciplinary research and a number of related activities, Nagoya University is planning to build a new building within the context of University's strategy for research system reform.

Nagoya University will provide financial support for maintaining the research environment at a world-class level including the enforcement of appropriate safety measures.

Nagoya University is very well equipped with top-level major instruments necessary for our WPI research. The quality and number of these instruments rivals the best institutions in the world.

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

A large-scale international research conference will be organized each year, primarily at Nagoya University.

A limited number of international workshops of a small-to-medium size will be organized each year.

For the first year of the Center, the 1st international research conference is scheduled at the end of FY2012 in March 2013.

In Japanese universities, such international meetings are usually managed mainly by researchers, including administrative matters. However in our WPI Center, the Administrative Office directed by the Administrative Director and Associate Administrative Directors will manage meetings according to the decision of the subject, candidates of invited speakers, and schedule of each meeting by PIs, in order to avoid further encroachment on researcher's time.

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

As our foreign Principal Investigators are truly world-leading scientists, we are confident that they can maintain their excellent funding profiles in the future. However, there are special challenges to carrying out research in Japan for foreign PIs, in particular access to information only in Japanese, when they seek competitive funding in Japan. We wish to strongly encourage PIs and Co-PIs to become actively involved in the procurement of external funding from Japanese sources, therefore, the Center will provide **a support team**, which will collect Japanese information and translate application documents (Japanese to English and English to Japanese). The team in the research administration unit includes two Ph.D. administrators from chemistry and biology fields.

To facilitate both domestic and international research collaboration by our foreign Principal Investigators, the Center and Nagoya University will establish a more efficient and flexible administrative structure to process travel expenses and acceptance of outside researchers.

The Center and Nagoya University will provide opportunities for partners/spouses to hold positions in the University on the basis of proper evaluation (**Dual Career Support**).

Nagoya University will give priority to the principal and collaborative researchers in assigning university accommodations. In addition, the WPI Center will collect and provide information on international education opportunities, which are increasingly developed in Nagoya City, for the children of overseas researchers.

Nagoya University established a nursery in its campus (as a part of the program to support female employees and researchers), and it will accept the children of foreign researchers at the Center.

Nagoya University is very well equipped with top-level major instruments necessary for our WPI research. The quality and number of these instruments rivals the best institutions in the world. We

will hire some expert operators and computer programmers for these facilities, which includes 5 postdoctoral researchers. They will strongly support the leading-edge research by the foreign PIs and other researchers.

Nagoya University has grasped the opportunity offered by being selected to host numerous Global-Centers of Excellence and the Global-30 program both to accelerate globalization of its campus and to promote high-level international research. In addition, we have implemented the mid- and long-term mutual exchange of doctoral students and young faculty members, as exemplified by the very successful “International Research Training Group (IRTG)” Program with the University of Münster (FY2005-2011). This program was followed by another Strategic Young Researcher Overseas Visits Program for Accelerating Brain Circulation, “Innovative Molecular Catalysis and Novel Functional Materials” (FY2011-2014). The Center will take full advantage of these international programs to ensure active international research activities.

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

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

The global standing of the Center depends firstly on the performance of the individual researchers, and we will use a set of quantitative metrics combined with more qualitative methods to assess the performance of individual researchers and their contributions to the Center. We consider there are three aspects important to the global standing of the WPI:

1) **research quality and impact**, 2) **breakthrough from the interdisciplinary research activities**, and 3) **human resources development**.

ii) Results of current assessment made using said criteria and methods

1) Publishing our work in top journals is essentially required. The number of papers published in top journals will be counted for evaluation. A selection of such data for our PIs clearly indicates we have a group of outstanding individuals that together will give our Center a very high global profile.

***Total number of papers published in top journals by the 10 PIs:***

| *Journals** | *Number of Papers* |
|---|---|
| Nature | 9 |
| Science | 3 |
| Nature sister journals | 3 |
| Proceedings of the National Academy of Sciences of the USA | 9 |
| Journal of the American Chemical Society | 114 |
| Angewandte Chemie-International Edition | 69 |
| Nano Letters | 2 |
| Advanced Materials | 1 |
| ACS Nano | 5 |
| Chemical Science | 9 |
| Accounts of Chemical Research | 3 |
| Chemical Reviews | 2 |
| Coordination Chemistry Reviews | 1 |
| Genes & Development | 3 |
| Developmental Cell | 1 |
| EMBO Journal | 2 |
| Current Biology | 4 |
| Plant Cell | 6 |
| Annual Review of Plant Biology | 1 |
| Current Opinion in Plant Biology | 5 |
| International Review of Cytology | 1 |
| Total | 253 |

* Representative top journals (Impact Factors >9) are listed. Colored background indicates fields of journals as red for general journals, blue for chemistry journals, and green for biology journals.

Highly cited work is clearly an indication of high quality research and a significant impact. Citations

can be quantified by bibliometrics such as total citations, citations per paper, and h-index.

***Total number of papers cited more than 80 times (10 PIs): 86***

These types of bibliometrics will be gathered for the researchers and used in evaluation throughout the life of the Center. Two more important indicators of research quality and impact are success in obtaining external funding and the number of invited lectures at international conferences and these will also be monitored.

***Total number of keynote/plenary/invited lectures by 10 PIs in the last 4 years: >500***

With the concentration of research talent and resources at the Center, in the longer term we envisage some of our members to be rewarded with significant international prizes in the fields related to the mission of this Center. The number of such prizes will be a good indication of the Center's impact on the wider scientific community. Honors and prestigious positions will also be monitored for the same reason.

***Awards, honors, and prestigious positions:***

**Itami**

2012 Fellow of the Royal Society of Chemistry, UK
2012 German Innovation Award "Gottfried Wagener Prize 2012"
2012 Novartis-MIT Lectureship Award
2011 ACP Lectureship Award, China
2011 ACP Lectureship Award, Malaysia
2011 Nozoe Memorial Award for Young Organic Chemists
2008 Merck-Banyu Lectureship Award
2007 Banyu Young Chemist Award
2006 Minister Award for Distinguished Young Scientists
2005 Mitsui Chemicals Catalysis Science Award of Encouragement
2005 The Chemical Society of Japan Award for Young Chemists
2004 Thieme Journals Award
2000 Nissan Chemical Industries Award in Synthetic Organic Chemistry

**Higashiyama**

**Vice President of International Association of Sexual Plant Reproduction Research**

2010 JSPS Prize
2009 Hirase Awards, The Japan Society of Plant Morphology
2007 Botanical Society Awards (for Technical Development), Botanical Society of Japan
2000 Botanical Society Awards for Young Scientists, Botanical Society of Japan
1999 Inoue Research Aid for Young Scientists
1999 Young Scientist Awards, The Japan Society of Plant Morphology

**Bode**

2011 Elias J. Corey Award for Outstanding Original Contribution (ACS)
2010 Hirata Memorial Lectureship and Gold Medal, Nagoya University
2009 Novartis Lectureship Award
2008 Discover Magazine, Best Brains in Science List, "Top 20 under 40"
2008 Arthur C. Cope Scholar Award (American Chemical Society)
2008 Roche Excellence in Chemistry Award
2007 Alfred P. Sloan Foundation Fellowship
2007 Bristol-Myers-Squibb Unrestricted Grant in Organic Chemistry
2007 Society of Synthetic Organic Chemistry, Japan (SSOCJ) Lectureship Award
2006 David and Lucille Packard Foundation Fellowship
2006 Eli Lilly Grantee Award
2006 MIT Technology Review TR35: Top 35 Innovators Under 35
2006 AstraZeneca Excellence in Chemistry Award
2006 Research Corporation Cottrell Scholars Award
2006 Beckman Young Investigator Award
2006 Amgen Young Investigator Award
2006 UC Regent's Junior Faculty Fellowship
2004 National Science Foundation CAREER Award
2003 Camille and Henry Dreyfus New Faculty Award
2001–2003 Japan Society for the Promotion of Science Postdoctoral Fellowship
1996–1999 National Science Foundation Predoctoral Fellowship

1996 William Crews McGavock Award, Trinity University

**Crudden**

**President of Canadian Society for Chemistry**

2012 Global Centers of Excellence Visiting Professorship, Kyoto University
2008 Merck and Company Academic Development Award
2007 Visiting Professorship, Catalan Government
2006 RCMS Professorship, Nagoya
2006 Johnson and Johnson Focused Giving Award
1998 International Union of Pure and Applied Chemistry Travel Award
1997 Research and Innovation Award

**Irle**

**Advisor to the International Atomic Energy Agency (IAEA)**
**Core member in the "Theoretical & Computational Chemistry Initiative" (TCCI)**

**Kinoshita**

2007 Minister Award for Distinguished Young Scientists
2003 The Japan Society of Plant Physiology Award for Young Scientist
1998 Inoue Foundation Award for Young Scientist

**Ooi**

2011 IBM Japan Science Prize
2010 JSPS Prize
2008 ACP Lectureship Award, Taiwan
2006 Thieme Journals Award
1999 Chemical Society of Japan Award for Young Chemists
1997 Chugai Pharmaceutical Award in Synthetic Organic Chemistry

**Torii**

**Elected Fellow of AAAS**
**Howard Hughes Medical Institute and Gordon and Betty Moore Foundation Investigator (first and only Japanese woman investigator in HHMI)**
**Featured Scientist, SCIENCE Magazine/L'Oréal Women in Science Booklet "Remarkable Women in Science"**

2010 University of Washington Undergraduate Research Mentor Award
2008 JSPS Prize
2006 SJWS Prize, Society for the Japanese Women Scientists

**Yamaguchi**

2009 DIC Award from Synthetic Organic Chemistry, Japan
2008 NISTEP Nice Step Researcher
2008 Nozoe Award for Young Scientist
2007 Tokyo Techno Forum 21 Gold Medal
2006 ACP Lectureship Award, Taiwan
2005 Young Scientist Award from the Minister of Education, Culture, Sports, Science and Technology
2002 The Chemical Society of Japan Award for Distinguished Young Chemists
1999 Young Scientist Award of the Silicon Chemical Society of Japan
1997 Chisso Award in Synthetic Organic Chemistry, Japan

**Yoshimura**

**Society of Biology Fellow,**

2010 Hoffenberg International Medal, Society for Endocrinology
2009 JSPS Prize
2009 Japanese Society of Animal Science Prize
2009 Shizume Lecture, Japan Thyroid Association
2005 Japan Prize of Agricultural Science for Young Scientist from the Foundation of Agricultural Sciences of Japan
2004 Young Scientist Award from the Japanese Society for Chronobiology

2) Breakthroughs from the interdisciplinary research activities will be monitored and evaluated by number of joint papers by PIs from chemistry and biology fields. Grants and patents resulting from collaboration of PIs from chemistry and biology fields will be also monitored.

We have already begun some interdisciplinary collaborations, which are expected to be published in the initial phase of our WPI program.

3) The development of human resources is key to the future development and global standing of

the Center. To evaluate our progress, we will use indicators such as the career paths and academic success of former researchers of the Center and the flow of visitors to and from other international institutions. Six Japanese PIs from Nagoya University have been involved in many international exchange programs and already have good track records of exchanging researchers. In the last three years alone, they have welcomed ***75*** foreign visitors and arranged for ***85*** students and researchers to be sent abroad.

The number of student awards garnered will be also monitored as an important evidence of nurturing the next-generation. For example, the prospective Center Director Itami has produced a number of talented young chemists who have been recognized in the community. The following are representative previous and current students.

**Shuichi Yanagisawa**: Winner of 1st JSPS Ikushi Prize in 2011. *The top award for graduate students in Japan from all areas. He was the only chemistry graduate student selected.*

**Kirika Ueda**: Winner of L'Oréal-UNESCO Young Woman Scientist Award in 2011. *The top award for female graduate students. She was the only chemistry graduate student selected.*

**Debashis Mandal**: One of three winners of Reaxys PhD Prize in 2012. *Selected from 350 chemistry graduate students throughout the world.*

Our focus on quantitative measurements of achievements reflects a worldwide trend in the evaluation of research. However, we are also aware that some aspects of research cannot be easily quantified. The importance of truly original contributions may not be recognized immediately and citation numbers may not directly reflect the quality of research. In using research metrics to assess the performance of individual researchers, it is important to take into account their age and career stage. In addition, because our Center will consist of researchers from diverse fields, we will also be conscious of the ways in which these metrics may be influenced by different research styles and conventions in different fields.

We will, therefore, establish an Internal Evaluation Committee consisting of directors, PIs administrative directors to evaluate research activity within the Center. These results will be used together with the recommendations of the International Advisory and Review Board to carry out a rigorous evaluation of the Center and PIs by an external evaluation committee.

iii) Goals to be achieved through the project (at time of interim and final evaluations)

Our ten-year WPI project will be consisting of two phases with the following emphases and goals.

**Phase 1** (FY2012-2016, 4.5 years)

- Development of key synthetic bio-molecules and molecular functions.
- Establishing truly effective and productive ways to conduct interdisciplinary research.
- Establishing a new building to further promote the WPI-catalyzed interdisciplinary research.
- Creating strong ties with overseas/domestic cooperating institutes, centers, and companies.
- Increasing internationalization at Nagoya University by the establishment of an English-based research environment and administrative offices, and by putting in place measures to attract and retain talented foreign researchers.
- Establishing a system to support young, talented researchers to focus on research.
- Introducing a performance-based salary system.

**Phase 2** (FY2017-2021, 5 years)

- Development of truly innovative synthetic bio-molecules (transformative bio-molecules).
- Providing researchers worldwide with access to the transformative bio-molecules developed at Nagoya (International Promotion Unit).
- Accelerating WPI-catalyzed system reform of Nagoya University.
- Establishing mechanisms to ensure the continuous growth and perpetuation of the Institute of Transformative Bio-Molecules.
- Establishing the reputation as a world-leading molecular research institute, which can design and synthesize brand new molecules for the discovery, visualization, and manipulation of

biological systems.

(7) Securing research funding

i) Past record

The total amount of research funds secured by the Principal Investigators. Only the funds acquired through external competitive funding are counted.

| | | | |
|---|---|---|---|
| FY 2007 | 3,808,779 | USD | |
| FY 2008 | 5,391,104 | USD | |
| FY 2009 | 4,142,444 | USD | |
| FY 2010 | 9,613,810 | USD | |
| FY 2011 | 15,605,005 | USD | |
| Ave | **7,712,228** | USD | (JPY/USD=80) |

ii) Prospects after establishment of the center

Prospects for securing resources for each fiscal year (full-year basis)

- Salaries of Principal Investigators who hold posts at Nagoya University, Administrative staff and new hired additional researchers
  1.4 million USD / year

- Partial support to the costs of utility, maintenance and renovation of laboratory and office space, provided by Nagoya University
  0.8 million USD / year

- Competitive funding based on the past record by PIs
  7.7 million USD / year (the average of FY 2007-2011)

**Sum:** **9.9 million USD / year**

* At least the following amount of funding (Japanese grants) has been already acquired by PIs: the total amount of **5.5 million** USD / year for the first (FY 2012) and the second (FY 2013) years, and the total amount of **4.0 million** USD / year for the third (FY 2014) and the fourth (FY 2015) years.

(8) Exploiting the results of previously-initiated center-building efforts (when applicable)

**Not Applicable**

However, we will exploit the results of following past and current projects:

(1) Chemistry Global COE program (JSPS)
"Elucidation and Design of Materials and Molecular Functions"
Yoshihito WATANABE, FY 2007 – 2011

(2) Biology Global COE program (JSPS)
"Advanced Systems-Biology: Designing the Biological Function"
Takao KONDO, FY 2007 – 2011

(3) Program for Leading Graduate Schools (JSPS)
"Integrative Graduate Education and Research Program in Green Natural Sciences"
Kunio AWAGA, FY 2011 – 2017

(4) Research and Education Funding for Inter-University Research Project (MEXT)
"Integrated Research on Chemical Synthesis"
Kazuyuki TATSUMI, FY 2010 – 2016

(5) Japanese-German Graduate Externship (JSPS/DFG)
International Research Training Groups (IRTG), "Complex Functional Systems in Chemistry"
Kazuyuki TATSUMI, FY 2005 – 2011

(6) Re-Inventing Japan Project – Campus Asia Program (JSPS)
"Cutting Edge Science and Technology in Chemistry and Materials ~ A Cooperative Asian Education Gateway for a Sustainable Society"
Takahiro SEKI, FY 2011 – 2015

(7) Leading-edge Research Infrastructure Program (MEXT)
"Japan Advanced Plant Science Research Network; Research Center of Live Imaging (Nagoya University) "
Tetsuya HIGASHIYAMA (Representative of Nagoya University), FY 2011– 2012

Others

Nagoya University has committed to sustain the Center's pioneering research activities after the WPI-grant period ends. In order to accomplish this, Nagoya University will include the Center as part of the Institute of Advanced Research, which has been established as an institute independent from the other departments and research centers at Nagoya University. The activities, which should be continued even after project funding ends, include the strong ties that we plan to create between the overseas PIs as well as the international cooperating institutes. During this WPI project, Nagoya University will accelerate system reform of the university to ensure that the Institute of Transformative Bio-molecules is maintained. The activity of the International Promotion Unit of our Center will also be continued.

The ripple effects of our WPI program and the molecules we will develop will be multidirectional and unlimited. The potential impact of our program could reach almost every conceivable area of science and technology, but we envisage it will also influence the organization of many different research institutes: set new standards not only for the achievements of research but also in the way in which it is conducted. The issues we highlighted for establishing the framework of this WPI Center (multidisciplinary interaction, excellence in research with a high international profile, an outstanding research environment, nurturing of young scientists, and laying firm foundations for future growth) are all essential for building world-class research institutes.

Nagoya University has recently launched the Graduate School of Pharmaceutical Science in cooperation with Graduate Schools of Science, Bioagricultural Sciences, Engineering, and Medicine. The central area of Japan, represented by Nagoya City, is very famous as the industrial center of Japan. The establishment of the Graduate School of Pharmaceutical Science in Nagoya University was based on strong demand from industrial community. The achievements of our WPI Center will be directly applied through the activities of Nagoya University and Nagoya City. Thus profound ripple effects are expected not only in Nagoya University but also in other research institutions in central Japan.

To establish a truly top world-level research center, the commitment of the host institution is essential. In particular, setting up an efficient and effective administration is crucial. The benefits to the research goals of the Center through assisting the researchers to concentrate on their core research activities cannot be overestimated. In addition, appointing talented individuals, who are capable of handling administration with a global view, is also an essential ingredient to establishing a truly world premier research center.

The word "transformative" implies that our molecules will also make a marked change in human society. Thus another important measure is how novel products based on our molecules and resultant new plant species developed by overcoming reproductive barriers are spread and recognized by general public.

# Vision Statement by the Director

*Institute of Transformative Bio-Molecules (ITbM)*

**Kenichiro Itami**

*Institute of Transformative Bio-Molecules (ITbM), Nagoya University*
*Department of Chemistry, Graduate School of Science, Nagoya University*

*November 14, 2012*

## Changing the world with molecules

Molecules are small but essential parts of all life on the planet. Molecules are groups of atoms chemically bound together that behave as a single unit. They are central to the operation of all industries, including pharmaceuticals, agrochemicals, electronic materials, solar cells, displays, petrochemicals, automotive manufacturing, plastics, polymers and many more sectors. It is my strong belief that molecules have the power to change the way we do science and the way we live. A few examples of molecules that have changed the world include penicillin (the first miracle drug, and the beginning of the field of antibiotics), the Haber-Bosch catalyst (necessary for the production of ammonia from nitrogen gas and hydrogen gas, *the* critical step in the synthesis of fertilizer, without which many people would starve), and green fluorescent protein (GFP, the essential imaging tool for bio-related science, that is used to help doctors differentiate cancerous tissue from non-cancerous tissue during surgery). This is a small sampling of cases where a single molecule changed the world. Such innovative molecules are defined as "*transformative molecules*". The focal point of our proposal is to develop *transformative bio-molecules* that will be key to solving urgent problems at the interface of Chemistry and Biology.

Chemists and biologists have the common goal of understanding and manipulating the relationship between molecular structure and function. The placement of atoms relative to one another in a molecule can have a huge impact on the properties and function of a molecule, and understanding and controlling this relationship is one of the key goals of the synthetic chemist. For example, there are two stable forms of $C_2H_6O$. In the first, the two carbons are bound directly to each other, which makes ethanol ($CH_3$-$CH_2$-OH), a liquid boiling at 78 °C, that has intoxicating properties. However, if the oxygen is inserted *between* the two carbons ($CH_3$-O-$CH_3$), the product is methyl ether, which is a gas at room temperature and is a refrigerant or a fuel substitute for propane! Even more remarkably, molecules can have dramatically different properties simply by changing the arrangement of atoms in space, without any other differences in bonding. Such changes are so dramatic in terms of biological interactions, that they can turn medicines into poisons. Thankfully chemists are able to control and manipulate the arrangements of atoms in space, and thus can synthesize molecules such as ethanol or methyl ether at will. This type of control of

structure, and thus properties, is the basis of a considerable amount of chemistry, and is widely exploited by biologists. Even biological systems, which seem highly complex, are typically comprised of macromolecules (large molecules, such as hemoglobin) interacting with simple "small" molecules, (such as oxygen and carbon dioxide), that function in accordance with well defined laws of science and nature.

Other examples of macromolecules that play a significant role in biology include DNA, which is a well-defined orientation of bases and sugars that twists into a double helix. Proteins are carefully arranged sequences of amino acids, whose detailed molecular structure controls the three dimensional shape of the protein and that shape controls function. For example "mis-folding" of protiens, as observed in prions, can cause dramatically different properties of otherwise identical molecules. Thus it is clear that the organization of these biologically relevant macromolecules, which is derived from atomic level structure, is critical for biological function.

Our dream is to take advantage of the dramatic relationship between structure and function and, by marrying state-of-the-art synthetic chemistry with systems biology, develop new ways of creating designer bio-active molecules with targeted properties. These new synthetic paradigms will permit the design and synthesis of bioactive molecules both in a beaker and actually inside living organisms (*ex vivo* and *in vivo*). Most importantly, our ultimate goal is to solve urgent problems in science and technology that have an impact on society.

**The Institute of Transformative Bio-molecules (ITbM)**

The core members (partners) of the Institute have been selected as a logical consequence of the main goals of the Institute. In order to address the next level of collaboration between chemists and biologists that will have a global impact, we have chosen to put plant- and animal-based molecular biologists side-by-side with synthetic chemists. The fundamental problems that will be addressed by this type of collaboration link directly to global issues such as food production and land-use management, which will be of increasing concern as our planet warms and arable land becomes more and more scarce. Most importantly, chemists and molecular plant biologists all speak in a molecular language, with biologists having an understanding of the types of molecules needed to affect a given biological event, and chemists knowing how to make these molecules. With these broad goals in mind, researchers were then chosen for their significant achievements in the field, as described later in this document.

Thus, synthetic chemistry, catalysis chemistry, systems biology, and plant/animal science will be the key components of the Institute. These research foci build on existing strengths at Nagoya University, which will be key to the establishment of the new interdisciplinary molecular institute: The Institute of Transformative Bio-Molecules (ITbM), whose aim is to create cutting-edge science with potentially significant societal impact. The *raison d'être* of ITbM is *to establish a world-leading molecular research institute for designing and synthesizing molecules directed towards the discovery, visualization, and manipulation of biological systems*. The unique approach of ITbM is to apply recent discoveries in molecular activation-transforming catalysis, with the support of molecular design and theoretical

chemistry, to solve fundamental and urgent biological problems and to explore advanced systems biology. This is an unprecedented endeavor and the first such research institute in the world.

In ITbM, we primarily focus on developing key molecules for two major problems in biology; (1) molecules that precisely control biotic function and production, and (2) molecules that realize innovative bio-imaging. To accomplish these projects, we will (3) develop catalysts that enable incredibly efficient synthesis and molecule activation on demand and under a variety of biologically relevant conditions.

The followings are our three core projects, representative subprojects, and target molecules:

**(1) Control of Biological Systems:** *Development of molecules that precisely control biotic productivity and quality*

(a) Molecules that dramatically enhance plant growth [A solution to potential global food/biomass crises]

(b) Molecules that improve animal reproduction innovatively [Directed towards potential global food crises]

(c) Molecules that overcome the genome barriers to produce novel crops [Generation of new bio-energy]

**(2) Visualization of Biological Systems:** *Development of molecules that permit innovative bio-imaging*

(a) Target biological models [Real-time all-molecule live bio-imaging]

(b) Highly efficient, full-color fluorescent molecules [Real-time all-molecule live bio-imaging]

(c) Specific conjugation technologies [Visualization of small molecules]

**(3) Synthesis of New Bio-Functional Molecules:** *Development of catalysts that enable incredibly efficient synthesis and molecule-activation on demand*

(a) Catalysts activating C-H bonds [Direct transformations of bio-molecules]

(b) Catalysts acting without heavy metals [Environmentally benign molecular transformations]

(c) Catalysts for protein ligation [De novo synthesis of bio-macromolecules]

(d) Catalysts for in vivo chemical transformations [New frontiers in chemistry and biology]

The interface of chemistry and molecular biology has already resulted in important new research fields of significant scientific impact, such as chemical biology and medicinal

chemistry, which have in turn led to incredible advances in modern medicine. We plan to bring this to a new level by exploiting newly developed molecule-activation chemistry partnered with fundamental biological systems of plants and animals. This research endeavor will have significant impacts in the closely related fields of chemical biology and medicinal chemistry, but most importantly, on areas that are of urgent global importance including world food production.

The identity of ITbM is its capability to develop completely new bioactive molecules with carefully designed functions. With biologists knowing *what* functions they need in molecules and chemists knowing *how* to install these functions, huge advances are predicted from our Institute. This unique approach will attract the top researchers worldwide and also nurture the next generation of cutting-edge research, unrestricted by the bounds of traditional disciplines.

**Interdisciplinary research is the key**

The importance of interdisciplinary research cannot be overemphasized. It is obvious from the history of science and technology that many significant discoveries emerged at the interface of disciplines. Marshaling the accumulated wisdom of all modern science is critically important to solve urgent global issues such as food production, thereby establishing a sustainable society. In addition to working to understand the best ways to mitigate effects of global environmental change, it is absolutely critical that scientists also develop a plan that permits us to adapt to these changes and, moreover, to provide the new materials, techniques and processes that are needed to develop a sustainable society.

The value of sharing knowledge freely, or learning from others with complementary expertise is inestimable. Catalyst-enabling synthetic chemistry with broad directions has been the focus of the Itami lab since it was first established at Nagoya University. By coordinating a broad multidisciplinary effort to generate new functional molecules useful in the development and understanding of bio-related science and materials science, we have been able to make significant advances in a variety of chemistry-related fields. Many of these advances came from interactions with researchers outside our traditional area of synthetic organic chemistry. For example, our lab has been able to synthesize structurally uniform carbon nanotubes, nanographenes, and small-molecule modulators of enzymes, which were inspired by and initiated by discussions with top researchers outside of organic chemistry.

Thus the direction of the proposed institute, in which synthetic chemistry and systems biology will be married, is a dramatic, but logical leap considering the strength in both of these areas at Nagoya University. Setting up an environment where the best researchers in these disciplines are able to interact frequently and informally is the goal of the current proposal.

**Molecule-activation chemistry for advanced systems biology** – Perfect match and perfect timing

Recent years have seen a remarkable reintegration of chemistry and biology, particularly in the field of medicinal chemistry and chemical biology. However, the synthetic tools that have been applied in the molecule synthesis part of these collaborative efforts are typically still based on "classical" organic reactions manifesting limited efficiency with lengthy sequences and operations. Remarkably, in many cases the reactions employed are many decades old. Given that the molecule-making step is often the bottleneck in such research, overall synthetic efficiency is critical for almost all areas of chemistry and biology.

Methods that can directly activate and transform simple organic molecules under a variety of conditions are clearly the key for streamlining the synthesis of biologically relevant target molecules. Indeed, the quest for such methods has been the driving force behind enormous recent efforts in the synthetic community including in the Itami lab, culminating in a wealth of useful catalytic systems for reactions directly converting simple building blocks into useful molecular entities. For example, the groups of Itami and Crudden have developed efficient and unique catalysts for activating aromatic and heteroaromatic compounds, which are privileged structures in bio-active molecules. The groups of Ooi and Bode have developed catalysts that can activate bio-related molecules such as amino acid derivatives and peptides. By using these sophisticated catalysts, designed in the labs of our PIs, the rapid synthesis of a number of biologically active compounds and pharmaceutically relevant molecules is now possible. In particular, some of the most recent results from the Itami lab on the *discovery of novel potent inhibitors of important enzymes using molecule-activation chemistry* make it clear that a truly efficient catalyst can have a huge impact in biology. With the advent of this exciting field of catalyst-enabling molecule-activation chemistry, the way that chemists plan and execute chemical synthesis is changing. Indeed, a number of pharmaceutical and agricultural companies as well as chemical industries have already started to use catalysts developed in the Itami labs on a daily basis.

In parallel to the progress of catalyst-enabling synthetic chemistry in Nagoya University, our biology groups have made a number of breathtaking discoveries at a rapid pace while exploring extremely important and fundamental biological issues. For example, Higashiyama discovered key molecules in plant reproduction including pollen tube guidance and double fertilization, which are directly involved in crop production and plant breeding. Kinoshita recently uncovered the long-thought mode of action of the plant hormone auxin for plant growth. Torii discovered several peptide molecules that promote plant growth. Yoshimura identified key hormone TSH regulating seasonal reproduction in animals.

Thus recent discoveries by biologists at Nagoya University have clearly demonstrated the impact of individual molecules on biological systems. The next, critical phase of this research is *designing* properties in specific molecules, *synthesizing* them in a truly practical way and *studying or imaging* their actual interactions in the biological system. In order to engineer such breakthroughs, we plan to partner the discoveries of our biologists with technologies developed by our chemistry groups. In particular, the application of the emerging field of catalyst-enabling synthetic chemistry to systems biology research to solve compelling biological issues such as food production problem and bio-imaging is a timely and important goal.

Our cutting-edge catalysts will be able to activate and transform “seed” or “lead” biofunctional molecules, discovered by our biology groups, into more selective and more active molecules in a single operation. In addition, this new molecule-making and -manipulating technology will allow us to synthesize rationally designed candidate molecules, provided by our theoretical groups, in a straightforward and rapid manner. Moreover, our molecule-activation catalysts will be applied for the *in vivo* manipulation of biofunctional molecules such that we can employ the existing biochemical machinery for the synthesis of the core structure, and then employ an artificial small-molecule catalyst to decorate and manipulate these products to enhance their activity and control their properties. Finally, in order to understand the action of our molecules in biological systems beyond macroscopic effects, we will use state-of-the-art imaging techniques also developed as part of this program.

**Experiment-theory synergy for rational design**

In addition to the chemistry-biology collaboration, experiment-theory synergy is also essential to fulfill our goal of developing transformative bio-molecules. Although it is clear that our highly efficient catalysts will dramatically accelerate the development and discovery of key bio-functional molecules, the synthesis-testing experiments alone cannot provide a detailed understanding as to how the molecules, empirically shown to be effective, exert bioactivity at an atomic level. Theoretical support is critically needed to rationally design truly effective molecules with high potency and selectivity. As a pioneer in the quantum chemical study of complex systems, Irle will spearhead this task. He recently established quantum chemical molecular dynamics techniques to study transformative processes in materials sciences on realistic timescales. Parameter development is an integral part of his research, and the method itself is now being incorporated in fragmentation and genetic algorithms that will allow the simulation of small bio-molecules with entire proteins under realistic timescales on the basis of accurate quantum chemical potentials.

In addition to the above-mentioned computer-assisted studies, it is also essential to design the next generation of imaging molecules, by taking advantage of the understanding chemists have of structure-function relationships. In this regard, Yamaguchi is indispensable to this Institute. With a strong command of physical organic chemistry, organo-element chemistry, and synthetic chemistry, Yamaguchi has designed and synthesized a large number of structurally unique molecules possessing unusual photophysical and electronic properties. Yamaguchi is an international expert in this field, knowing exactly how to design and synthesize new molecular structures that will display a desired optical property (i.e. fluorescence, luminescence, phosphorescence). Thus, Yamaguchi’s molecular design and Irle’s theoretical methods will play critical roles in the development of highly efficient full-color fluorescent small peptides for new bio-imaging tools. Very recently, the Yamaguchi–Irle–Itami team established an extremely reliable methodological platform for understanding and designing fluorescent molecules. These newly developed methodologies will be an essential element of ITbM.

**Our dream team**

A team of Principal Investigators (PIs) has been assembled to permit us to address these critical issues in Chemistry and Biology. This is the ideal moment to initiate this urgent research, based on predicted global need, and current advances in both synthetic chemistry and systems biology. There is no doubt that with the team we have assembled, great things will happen within the new WPI-funded research environment. The scientific strengths of our PIs and their roles in ITbM are described briefly below.

**Kenichiro Itami** (41) Director of ITbM, Nagoya University

*Organic synthesis, catalysis, molecule activation, pharmaceuticals, organic materials*

In addition to holding the role of director, I will also be one of the PIs in the Institute and thus will actively collaborate with all PIs, playing a key role in synthesizing molecules using our catalysts. My research group has developed a number of unique and highly efficient molecular catalysts for C-H coupling, an ideal approach to rapidly increase molecular complexity in organic synthesis. Our synthesis-oriented catalyst development campaign has provided opportunities for markedly different connection/disconnection strategies in the construction of useful organic molecules, including pharmaceuticals, natural products, and new enzyme inhibitors.

As the Director, I have taken into consideration several important issues that need to be implemented while assembling the team described below: potential for interdisciplinary interactions, excellence in research with a high international profile, ability to nurture young scientists and lay a firm foundation for the continued growth of ITbM. The Institute must be ambitious but maintain realistic goals, we must routinely assess our progress based on real deliverables, and adapt in order to maximize the success of the institute. I will make every effort to fulfill our mission and to ensure that ITbM is ranked the best in the world.

**Tetsuya Higashiyama** (41) Vice-Director of ITbM, Nagoya University

*Plant reproduction, peptides, micro-genomics, cell manipulation, live cell imaging*

Higashiyama is one of the most recognized plant biologists focusing on the identification of key molecules of plant reproduction. In particular, his discovery of the long-sought (~140 years) pollen tube attractant molecule “LURE”, which is essential for plant reproduction, has secured his position as a world-renowned biologist. The identification of LURE peptides provide us with a major breakthrough to study and control pollen tube guidance of flowering plants and to break reproductive barriers. Moreover, he has also made significant technical development of micro-genomics and live cell imaging. Currently, he serves as one of the youngest directors of prestigious ERATO funding program supported by the Japan Science and Technology Agency. He will be involved mainly in the development of molecules that can overcome species barriers as well as innovative bio-imaging tools, collaborating with the groups of Yamaguchi, Irle, Torii, Itami, Ooi, Crudden, and Bode.

**Jeffrey W. Bode** (38) Eidgenössische Technische Hochschule (ETH), Zürich, Switzerland

*Organic synthesis, carbene-catalysis, protein synthesis, bioconjugation, oligomerization*

Bode is a gifted young rising star in synthetic chemistry. The work of Bode is directed towards the chemical synthesis of molecules and conjugates that are currently outside the reach of conventional synthetic methods. He is developing new chemical reactions and catalysts for making molecules of biological importance such as proteins, glycopeptides, sequence and length-controlled polymers, and covalent conjugates of these large structures. Recently, he developed a novel method for the ligation of unprotected protein segments, producing synthetic proteins very efficiently. He is also known as one of the pioneers of an entirely new branch of catalytic asymmetric synthesis, commonly known as "chiral *N*-heterocyclic carbene (NHC) catalysis". His catalysts will be applied in the development of molecules that selectively induce plant growth and molecules that can overcome species barrier. In addition, collaborating with the group of Ooi, he will also be involved in the development of small-molecule catalysts that can activate and transform bio-molecules *in vivo*.

**Cathleen M. Crudden** (46) Queen's University, Canada

*Organometallic catalysis, organo-element catalysis, nanoporous materials*

Crudden centers on the use of catalysis for organic synthesis and materials chemistry. A key focus is the use of boron chemistry to achieve these goals in an efficient and green manner. She will be involved mainly in the development of molecules that selectively induce plant growth as well as in our bio-imaging projects. In addition to her expertise in synthesis and catalysis, Crudden is one of the most visible and capable leaders of the chemistry community in the world. Most notably, she was one of the Canadian organizers for Pacifichem 2010, the largest chemistry conference worldwide, and will continue on as one of two Canadian representatives for 2015. Even more importantly, she is now serving as the President of the Canadian Society for Chemistry. Her visions combined with her enthusiasm and energy are unmatched and essential to ITbM.

**Stephan Irle** (45) Nagoya University

*Quantum chemistry, molecular dynamics, approximate density functional theory*

The central theme of Irle's work is the quantum chemical study of complex systems. On the basis of approximate density functional theory (DFT) techniques, his group can conduct the routine, fully quantum chemical simulation of large molecular systems containing 1000's of atoms on timescales into the 10's of nanoseconds, and thus provide a theoretical means to understand and design efficient chemical synthesis in complex molecular environments and to characterize and create novel molecules for bio-related applications. In this Institute, he will mainly apply his density-functional tight-binding (DFTB) method for the understanding of ligand-protein interactions as well as the rational design of fluorescent molecules for bio-imaging, collaborating with virtually all members.

**Toshinori Kinoshita** (44) Nagoya University

*Plant molecular biology, plant chemical biology, stomata, auxin, plant growth*

Kinoshita has been studying signaling pathways of stomatal opening and closing, and molecular mechanisms of plant cell growth in response to the phytohormone auxin. By using genetic, biochemical, and physiological approaches, he has identified the key components regulating stomatal opening and closing reported by Darwin in 1898. More recently, he reported evidence for the existence of an unidentified auxin receptor responsible for plant growth, which became the basis of one of the core projects in this Institute. He will be involved mainly in the development of molecules that selectively induce plant growth, collaborating with the groups of Itami, Crudden, Ooi, and Torii.

**Takashi Ooi** (47) Nagoya University

*Organic ion pair catalysis, molecular recognition, molecule activation, pharmaceuticals*

Ooi has been creating a bold stream of research on the molecular design of various chiral organic ion pairs and their rational structural modifications for eliciting unique functions as molecular catalysts, providing a solid basis for safe and sustainable supply of useful organic compounds. His accomplishments have had a significant impact on the frontiers of chemistry in terms of developing a fundamental understanding of the relationship between the three-dimensional structure of a chiral organic ion pair and its catalytic and stereocontrolling abilities. He will be involved mainly in the development of molecules that selectively induce plant growth, molecules that improve animal reproduction, and molecules that can overcome species barrier, collaborating with the groups of Kinoshita, Yoshimura, Higashiyama, Bode, and Itami.

**Keiko Torii** (46) University of Washington, USA

*Plant development, cell-cell communication, peptides, receptor kinase, stomata*

Through being selected as an HHMI-GBMF investigator of Howard Hughes Medical Institute, Torii has been recognized as one of “the 15 most innovative plant scientists in the US". Torii has elucidated the molecular and genetic basis of cell-cell communication and dynamics of cellular behaviors that coordinate plant organ morphogenesis and tissue patterning. She has also identified two peptides, EPFL4 and EPFL6, that act as ligands for receptor kinases to promote plant growth. She will be involved mainly in the development of molecules that selectively induce plant growth as well as the bio-imaging project, collaborating with the groups of Higashiyama, Kinoshita, Itami, Yamaguchi, and Irle.

**Shigehiro Yamaguchi** (43) Nagoya University

*Fluorescent molecules, molecular design, physical organic chemistry*

Yamaguchi works on a variety of topics in the general fields of main group chemistry and physical organic chemistry. In particular, emphasis is placed on the development of new functional π-electron materials possessing unusual photophysical and electronic properties. On the basis of the new design concepts emanating from his lab, he is able to exploit the

features of various main group elements as well as the newly developed synthetic methodologies, various types of functional materials have been developed; including the key molecule in commercial organic electroluminescent devises. He will be involved mainly in the development of innovative bio-imaging tools, collaborating with the groups of Higashiyama, Irle, Itami, and Crudden.

**Takashi Yoshimura** (42) Nagoya University

*Biological clock, systems biology, animal production, pharmaceuticals*

Yoshimura's research focuses on the regulatory mechanisms of biological clock and signal transduction pathway regulating seasonal reproduction in vertebrates. The uniqueness of his research lies in the use of non-model animals and the systems biology approach. Most importantly, he has identified a "springtime hormone" that triggers seasonal reproduction and clarified the signal transduction cascade for animal seasonal reproduction. Yoshimura also identified a key gene regulating seasonal reproduction in birds, and later demonstrated that the discovered reproduction mechanism is conserved in seasonal mammalian species. These breakthrough findings became the basis of one of the core projects in ITbM. He will be involved mainly in the development of molecules that improve animal reproduction, collaborating with the groups of Ooi, Bode, Irle, and Itami.

**Nagoya University** – Suitability and support

Nagoya University is the ideal place to establish this new interdisciplinary research institute. This proposal builds not only on the strong tradition of research in chemistry and biology at Nagoya University but also on the free and vibrant academic culture that has traditionally nurtured the creativity of young scientists. This is clearly evidenced in the freedom given to academic stars emanating from Nagoya University, including Osamu Shimomura (Nobel Prize in Chemistry, 2008) and Ryoji Noyori (Nobel Prize in Chemistry, 2001). As evidence of this continuing strategy, Nagoya University is fully supportive of one of its youngest full professors in the University as the leader of this largest research program in Japan.

The enthusiastic support for this initiative offered by Nagoya University is remarkable. For example, Nagoya University has agreed to revise the University rules to give executive authority to the Director such that he may make top-down decisions on the important matters of the Institute; they have agreed to enable the Institute to be independent in the execution of its budget; and will allow the Institute to develop its own personnel policies and management. For a Japanese institution, this is remarkable latitude. In addition to establishing an efficient and effective administrate office to ensure both research and administrative business can be carried out in English, Nagoya University has also agreed to provide financial/personnel assistance and building space to the Institute.

Last but not least, Nagoya University has agreed to permit Yoshihito Watanabe, a Trustee and a Vice-President of Nagoya University and a Vice-President of the Chemical

Society of Japan, to take up the position of Administrative Director of this Institute. He has already demonstrated his talents in making the Global COE program in Chemistry a great success as the Project Leader, and also has been responsible for the Internationalization Initiatives of Nagoya University including the Global 30 program. Among his achievements in this mission, he launched international undergraduate and graduate courses, in which all classes are delivered in English. Thus by committing University Trustee Watanabe to this Institute, Nagoya University is clearly illustrating its strongest support for the Institute, and its willingness to accelerate reforms in the entire system of Nagoya University.

**Final remarks**

I am simply thrilled to head this ambitious, full-scale collaboration of synthetic chemists and systems biologists that is the crux of this application. What became obvious through extensive discussions between the chemists and biologists that are part of our team was the common recognition that "molecules" are the key not only for chemistry and biology, but also for exploring a new interdisciplinary research fields. With the recent exciting progress in molecule-activation chemistry and systems biology, the time has come to put in place the necessary means to develop a collaboration that will have impacts on science and society for decades to come.

In addition to these impacts, the present WPI project is also critical to further enhance the prestige and international visibility of Nagoya University, and also to lead a remarkable reformation of research culture. The importance of department-based conventional research and education is obvious. However, we believe that ITbM will be the lead example in drastically reforming the University in the long term. We will establish the "stage" on which researchers, sharing responsibility and problem awareness, can talk about their dreams freely and can put their innovative ideas into practice immediately. What our future success brings will not be limited to innovations in bio-molecular research. I strongly believe that the Institute, with researchers of various backgrounds, will accelerate the mixing/merging of people, ideas, and research, and also help nurture a new generation of scientists unrestricted by the bounds of traditional disciplines. This will surely have a positive influence on the way Japanese universities carry out research and education. In this regard, we must succeed by all means.

The Institute will connect molecules, create value, and change the world, one molecule at a time.

Kenichiro Itami

November 14, 2012

# Host Institution's Commitment

June 28, 2012

To MEXT

Nagoya University
Dr. Michinari Hamaguchi, President

I confirm that the measures listed below will be taken faithfully if "Institute of Transformative Bio-Molecules" is adopted under the World Premier International Research Center Initiative (WPI).

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

Nagoya University (hereinafter referred to as "NU") promotes its research activities based on our *Midterm Objectives*, which include establishing world-leading research centers. In addition, the manifesto of the incumbent President—also known as the "*Hamaguchi Plan*"—identifies the strong promotion of world-class research and the globalization of NU as top priorities.

This proposal for *the Institute of Transformative Bio-Molecules* (hereinafter referred to as *"the Center"*) coincides wholly with the current conception of NU. If this proposal is adopted, NU will amend its *Midterm Plans* and *Research Promotion and Strategy Plans* to specify the WPI and the Center, and fully commit to providing support for the Center based on clear objectives.

**＜Concrete Measures＞**

**(1) How it will support the center's need to secure resources that match or exceed the project grant through such means as competitive grants obtained by researchers participating in the project, in-kind contributions and other forms of assistance by the host institution (including partial payment of salaries, provision of research space), and/or external donations. In the case of project exploiting previously-initiated center-building efforts, how it will assist the center in securing sufficient independent resources to continue to secure the same scale of the measured amount through independent resources after that funding eventually ends.**

1) NU endorses the fully committed financial support for the Center that is larger than the support from WPI.
2) NU will continue to cover the equivalent amount of the salaries of those researchers at the Center who already hold posts at NU, and will provide 6,000 $m^2$ of the research space for the Center. Additional space will be given according to the progress of the research.
3) The total sum of competitive funding for those researchers at the Center who already hold posts at NU is $5.9 million (in FY2012), and receipt of competitive funding at an equal or greater level is promised from FY2013 onwards.
4) To help with the establishment and smooth operation of the Center, NU will assign 4 staff to the center and cover their salaries as well as employing new bilingual staff.
5) Although this proposal does not exploit previously-initiated center-building

efforts, NU has actively accepted some national projects such as the Global COE Program (“Advanced System-Biology: Designing The Biological Function”, “Elucidation and Design of Materials and Molecular Functions”) and the resulting research systems and facilities have made this proposal possible.

6) This proposal will affect not only related research fields but also all of the research activities in NU, coupled with the other national projects such as the Program for Leading Graduate Schools “Integrative Graduate Education and Research Program in Green Natural Sciences” and “MEXT Project of Integrated Research on Chemical Synthesis”.

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

1) NU will reorganize the Institute of Advanced Research, which is established as an institute independent from the other departments and research centers, and will place the Center as part of the Institute.
2) NU will support the Center Director in his leadership and give full mandate for his decisions on important matters such as personnel and the execution of the Center's budget.
3) In addition, the Vice Director and Administrative Director will make decisions depending on the matter, to avoid placing an excess burden on the Center Director and enable the progress of daily work at the Center.

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

1) NU will assign 7 associate professors, who will mainly take charge of education in each department to take PIs duty, and to maintain high-level education.
2) NU will give priority to female researchers at the Center to enable their children to enter the nursery school operated by NU.
3) NU will support foreign researchers at the Center in their daily life and the education of their children, making full use of facilities and knowledge base which has been obtained through the operation of international projects such as the “Global 30 Internationalization Program (G30)” and “CAMPUS Asia Support for the Formation of a Core Center”, and so on.
4) NU will provide opportunities for partners/spouses of foreign PIs to hold positions in NU on the basis of proper evaluation (Dual Career Support).

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

1) NU will give full mandate to the Center Director for a flexible management system by implementing the Center as a “Special Research Zone”, and by introducing ground breaking working rules and salary system which give the

researchers and staff extra allowance to encourage their activities.
2) NU will gradually implement the Center's trial across the entire university in order to give other researchers and staff incentives to apply.

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

1) NU commits to accommodate the Center with research space equivalent to 6,000 $m^2$.
2) 7 PI candidates who work for NU already occupy approximately 3,000 $m^2$. NU will provide additional 1,500 $m^2$ by the end of FY2012, and the other 1,500 $m^2$ as soon as possible.
3) NU will rearrange and relocate the facilities of the existing departments and centers, and will establish the Center's core facility, making it possible to collaborate intensively with the researchers of other departments and research centers.
4) NU will reauthorize the University's Facility Management Plan and will make the Center's core facility a top priority.

**(6) How it will support to sustain the center as a world premier international research center after the WPI-grant period ends.**

1) NU commits to sustain the Center's pioneering research activities after the WPI-grant period ends. In order to do so, NU will allocate the Center as part of the Institute of Advanced Research, which has been established as an institute independent from the other departments and research centers at NU, and will ensure permanent positions for the newly employed researchers.
2) Depending on the achievement and influence of the Center, NU will advance the scheme to reorganize the departments and institutes.

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

1) Learned from the existing WPI centers, sustainability is the vital issue they face, but still they are struggling against their host institution's leadership.
2) To overcome these issues, NU has decided to assign a member of Board of Trustee/Vice-President as the Administrative Director to bridge the gap between the Center and the University's headquarters.
3) The Administrative Director will organize a team with his two associates and keep the administrative office active enough to enable the Center's research activities at a maximum performance.
Two associates are; Associate Administrative Director for Management who is a high-level expert of administration affairs, and Associate Administrative Director for External Relations who has strong expertize in chemistry related science, with a good command of English.
4) We recognize one of the important aspects of WPI is to accelerate system reform of Japanese universities such as deregulation, internationalization, and so on.
5) Intensive commitment of NU's leadership to the Center is critically important to accelerate the system reform in not only the Center but also the entire university.

(Appendix 1)

# List of Principal Investigators

| | Name | Age | Current affiliation (organization, department) | Academic degree and current specialties | Notes |
|---|---|---|---|---|---|
| 1 | Kenichiro ITAMI* | 41 | Department of Chemistry, Graduate School of Science, Nagoya University | Dr.Eng<br>*Specialties*: Organic Synthesis, Catalysis, Pharmaceutical Science, Nanocarbon Chemistry | |
| 2 | Tetsuya HIGASHIYAMA* | 41 | Division of Biological Science, Graduate School of Science, Nagoya University | Dr.Sci<br>*Specialties*: Live Cell Biology, Plant Reproduction, Bio-active molecules, Peptides | |
| 3 | Jeffrey W. BODE* | 38 | Department of Chemistry and Applied Biosciences, ETH Zürich, Switzerland | Doctoral of Natural Science<br>*Specialties*: Organic Synthesis, Peptide and Protein Chemistry, Catalysis, Ligation and bioconjugation reactions | Double Affiliation |
| 4 | Cathleen M. CRUDDEN* | 46 | Department of Chemistry, Queen's University, Canada | Ph.D<br>*Specialities*: Catalysis, Organic Synthesis, Materials Chemistry, Chirality | Double Affiliation |
| 5 | Stephan IRLE* | 45 | Department of Chemistry, Graduate School of Science, Nagoya University | Ph.D.<br>*Specialties*: Electronic Structure Theory, Computational Materials Science, Quantum Chemistry of Complex Systems | |
| 6 | Toshinori KINOSHITA* | 44 | Division of Biological Science, Graduate School of Science, Nagoya University | Dr.Sci<br>*Specialities*: Plant Molecular Physiology | |
| 7 | Takashi OOI* | 47 | Department of Applied Chemistry, Graduate School of Engineering, Nagoya University | Dr. Engineering<br>*Specialties*: Organic Synthesis, Catalysis, Molecular Recognition | |
| 8 | Keiko TORII* | 46 | Department of Biology, University of Washington, USA | Ph.D.<br>*Specialties*: Plant Development, Signal Transduction, Stem Cell Maintenance/Differentiation in Plants | Double Affiliation |
| 9 | Shigehiro YAMAGUCHI* | 43 | Research Center for Materials Science, Nagoya University | Dr. Engineering<br>*Specialties*: Main Group Chemistry, Physical Organic Chemistry | |
| 10 | Takashi YOSHIMURA* | 42 | Department of Applied Molecular Biosciences, Graduate School of Bioagricultural Sciences, Nagoya University | Dr. Agriculture<br>*Specialties*: Animal Physiology, Systems Biology, Neuroendocrinology | |