

Summary of Proposal (Compile in English within 3 pages.)

Host institution: Nagoya University

Head of host institution: Seiichi Matsuo (President)

Research center: Institute of Transformative Bio-Molecules (ITbM)

Center director: Kenichiro Itami

Chief center-project officer (in December 2012): Kenichiro Itami (Director)

Administrative director: Tsuyoshi Matsumoto

1) Project summary

ITbM was launched at Nagoya University (NU) as a unique research center to develop “transformative bio-molecules” that make a marked change in the form and nature of biological science and technology. Many interdisciplinary research projects have emerged rapidly in the “Mix Lab”, where new unique ideas in research are being generated from daily communications among the researchers from different fields who work side-by-side. As a result, a number of new bio-functional molecules and molecular technologies has been developed. Many of the research outcomes have been filed for patents and published as joint publications between different research groups. According to the Center’s research progress, ITbM has defined its flagship projects as “Plant Chemical Biology”, “Chemical Chronobiology”, and “Chemistry-enabled Live Imaging”. ITbM will focus on these flagship research areas and will work to actively promote chemical biology research to “understand”, “see”, and “regulate” living organisms by establishing new interdisciplinary research fields between chemistry and biology. This is expected to lead to the creation of transformative bio-molecules.

2) Mission statement and/or center’s identity

The mission of ITbM is to develop diverse functional molecules that bring about innovative impact on the principle of biological systems. To accomplish this, we will harness our synthetic abilities based on molecule-activation chemistry. We seek to effect a paradigm shift in science by creating a new field of research that aims to implement programmed chemical transformations for precisely controlling the production of bio-functional molecules of requisite structures and their functional expressions. The identity of ITbM resides in the development of novel bio-molecules that will achieve this goal. To accomplish this, we will enlist the best synthetic chemists and plant and animal biologists worldwide.

3) Research fields

ITbM’s research to develop “transformative bio-molecules” is closely related to the fields of synthetic chemistry, molecular catalysis, functional molecular science, systems biology, plant science, plant genetics, plant developmental biology, animal physiology, protein science, and bio-imaging. These are areas in which NU has significant international competitive advantages. We plan to bring this to a new level by exploiting cutting-edge synthetic chemistry partnered with fundamental biological systems of plants and animals. This research endeavor will have significant impacts in 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.

4) Research objectives

Since ITbM’s establishment in 2013, novel synthetic small bio-molecules have been developed. Molecule-initiated biology (chemical biology) to create transformative bio-molecules is currently shifting to the next phase, i.e., understanding and controlling biological processes by utilizing the molecules

developed at ITbM.

At such a turning point, ITbM has defined the following flagship research areas based on ITbM's research achievements so far: **plant chemical biology**, **chemical chronobiology**, and **chemistry-enabled live imaging**. ITbM will focus on these flagship research areas and will work to actively promote chemical biology research to "understand", "see", and "regulate" living organisms by establishing new interdisciplinary research fields between chemistry and biology, which will lead to the creation of transformative bio-molecules.

5) Outline of management

ITbM will take number of measures to remove the barriers that hinder interdisciplinary research and internationalization thereby triggering a fundamental transformation of existing academic systems.

- The Center Director will have the authority to make the final decisions over the appointments of personnel, the Center budget, and research priorities etc.
- Steering Committee meeting and PI meeting are held to provide advice to the Center Director.
- A rigorous evaluation of researchers will be made, and the results will be reflected in the salaries of researchers.
- We will establish an effective and efficient Administrative Department with English-speaking staff for accelerating the internationalization of ITbM as well as promotion of the fusion of different research fields.
- The Administration Department is led by Administrative Director with a strong background of scientific research and is composed of Management Division, Research Promotion Division (RPD), and Strategic Planning Division (SPD).

6) Researchers and other center staffs, satellites, partner institutions

As of the end of FY2016, ITbM consists of 72 researchers including 13 PIs (8 NU PIs, 5 overseas PIs), 47 research support staffs, and 13 administrative staffs. In addition, students conducting research at each PI group are involved in the research projects at ITbM.

The overseas PIs are talented researchers in their field and will have double affiliations with their host institute and NU. We introduced a system of Co-Principal Investigators (Co-PIs) to: (1) ensure close contact with ITbM's researchers and continuity in research; and (2) mentor leading young researchers. Young faculties are appointed to overseas PI groups. The Co-PIs will be based at Nagoya, where they are selected and guided by the overseas PIs for actively managing their research groups in ITbM. This will facilitate research in Japan and also help train young researchers (Co-PIs) to become leaders of the next generation.

Cooperating Institutes: Queen's University (Canada), University of Washington (USA), ETH Zürich (Switzerland), University of Southern California (USA), University of Düsseldorf (Germany), National Science Foundation Center for Selective C-H Functionalization (NSF-CCHF, USA), Institute for Basic Science (IBS, KAIST, Korea), University of Freiburg (Germany), Academia Sinica (Taiwan), and RIKEN Center for Sustainable Resource Science (CSRS, Japan).

7) Outline of research environment

- (1) We established a Mix-Lab system, where international young researchers from different fields work together in order to accelerate multidisciplinary advances through informal discussions on a daily basis.
- (2) To make the overseas PIs' research at ITbM possible, ITbM decided to employ young researchers as Co-PIs who stay full time at ITbM and cooperate with the overseas PIs.
- (3) In order to enable NU PIs to focus on their research, NU provided permission to employ 7 Associate Professors and Lecturers as Co-PIs of ITbM to conduct educational tasks in the place of NU's PIs.
- (4) All postdoctoral researchers will be supervised by two PIs from different fields in order to accelerate collaboration and nurture the next generation of cutting-edge research, unrestricted by the bounds of traditional disciplines.
- (5) In order to ensure to welcome talented overseas researchers to ITbM, we will provide the following:

(a) a team for assisting overseas researchers in their applications for competitive domestic (Japanese) research grants; (b) opportunities for partners/spouses to hold positions in the University based on their skill sets; and (c) adequate information on education opportunities for the children of overseas researchers. Through these endeavors, we have set a platform for overseas PIs to allocate a significant portion of their activities at Nagoya, and we aim to attract a certain percentage of overseas researchers permanently to Nagoya.

- (6) Each PI group will be provided with sufficient research space and start-up funds.
- (7) We will be equipped with leading edge equipment and facilities at NU, staffed with expert technical managers, so that it is fully accessible for promoting research, international collaborations, and discoveries.
- (8) We will engage in high-profile recruitment campaigns to attract highly qualified postdoctoral researchers using web sites with high global status, outlining the current efforts of the Institute, University, and Nagoya as a city.

8) Outline of indicators for evaluating a center’s global standing

Three aspects are important for the global standing of ITbM:

- 1) research quality and impact, 2) breakthroughs resulting from interdisciplinary research activities, and 3) human resources development as an international institute.

The following quantitative metrics will be used for evaluation: number of peer-reviewed publications (impact factor, citations), application to patent files, technology transfer and commercialization, awards and honors, research grants, and career promotion of ITbM’s researchers.

9) Securing research funding

ITbM’s researchers have been constantly obtaining competitive funding from ITbM’s establishment. The total amount acquired nearly matches the project grant at the beginning, and became more than double in FY2013. The amount has further increased in the following years. We will continue our effort to secure competitive research funds. Major competitive funding obtained in FY2016 are as follows: JST-ERATO (2 projects), JST-CREST (2 projects), JST-PRESTO (2 projects), Grant-in-Aid for Scientific Research on Innovative Areas (2 project as Area Representative), JST-ALCA (1 project), Grant-in-Aid for Specially Promoted Research (1 project) etc. Overseas PIs have also been successful in obtaining KAKENHI (Grant-in-Aid for Scientific Research) from FY2014.

10) Appropriations plan

Appropriations plan	FY	2017	2018	2019	2020	2021	Total
(Exchange Rate: JPY/USD=100) Cost (\$ millions)		7.0	7.0	7.0	7.0	7.0	35.0

(Exchange Rate: JPY/USD=100)

11) Summary of host institution’s commitment

NU has placed ITbM as a significant research institute conducting world-leading frontier basic research at NU in the University’s mid-term plans and in “Nagoya University Matsuo Initiatives for Reform, Autonomy, and Innovation 2020 (NU MIRAI 2020)”. The presence of ITbM is essential for NU to become a research university that can compete with leading universities in the world. NU is committed to supporting ITbM through all means. Under the umbrella of the “Institute for Advanced Research”, ITbM will receive additional support needed to manage ITbM even after termination of funding from the WPI program. Representative concrete measures are 1) provision of space, 2) financial support towards construction of ITbM’s new building, 3) support towards the operation of the new building, 4) covering salaries of faculties, 5) ITbM’s priority to the use of hall of residence.

Research Center Project (in English)

Host institution: Nagoya University

Head of host institution: Seiichi Matsuo (President)

Research center: Institute of Transformative Bio-Molecules (ITbM)

Center director: Kenichiro Itami

Chief center-project officer (in December 2012): Kenichiro Itami (Director)

Project summary

- Briefly describe the general plan of the project.

ITbM was launched at Nagoya University (NU) as a unique research institute 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 our cutting-edge molecular synthesis expertise and intense interactions with leading plant/animal biology research, "transformative bio-molecules" will be developed. These are expected to enhance biotic productivity and quality, and to realize innovative bio-imaging. To ensure the advancement of these projects, we will develop catalysts that enable efficient synthesis and on demand molecule activation. The ultimate goal is to develop molecules that have a positive impact on major global issues such as food production. In late 2015, the following research areas were defined as ITbM's flagships: "**plant chemical biology**", "**chemical chronobiology**", and "**chemistry-enabled live imaging**". ITbM will focus on these flagship research areas and will work to actively promote chemical biology research to "understand", "see", and "regulate" living organisms by establishing new interdisciplinary research fields between chemistry and biology, to lead to the creation of transformative bio-molecules.

The synergy of the high research profile of ITbM researchers and the new research style at ITbM's facilitates interdisciplinary research.

"Mix" is our key concept to mix different disciplines. Mix Labs and Mix Offices established in ITbM have significantly contributed to promote bottom-up interdisciplinary projects among young researchers. These are places where new unique ideas in research are being generated from daily communications among the researchers from different fields who work side-by-side. New bio-functional molecules and molecular technologies have been emerged from these spaces. The ITbM Research Award, established to promote interdisciplinary research proposed by young researchers, further accelerates collaborations in a bottom-up manner. The ITbM Workshop, Mix Hour, and Tea Break Meetings were also started to share each other's research progress and to find seeds of collaboration and possible collaborators.

Upon development of molecules that modulate biological system in plants/animals, it is essential for ITbM to communicate to the general public widely that ITbM always addresses the environmental and safety issues carefully, and to gain the understanding from the international/domestic societies and local community. ITbM has set up an Environment and Safety Committee so that researchers at ITbM are constantly aware of these issues when conducting their research and can inform the general public accordingly.

<Major changes from initial project plan:>

In late 2015, we have defined the three research areas as ITbM's flagships, "plant chemical biology", "chemical chronobiology", and "chemistry-enabled live imaging". We focus on these three research areas and conduct respective interdisciplinary research projects categorized to these areas. To promote bottom-up interdisciplinary research of ITbM, the ITbM Research Award, ITbM Workshop, Mix Hour, and Tea Break Meetings are being held.

Strategic international/national collaboration network have been extended. In addition to the overseas PIs' host institutions, ITbM has started collaboration with the National Science Foundation Center for Selective C-H Functionalization (NSF-CCHF, USA) in 2013. Around 4 to 5 researchers per year are being exchanged between the institutes to conduct collaborating researches, which is envisaged to foster young scientists. Collaborations with the RIKEN Center for Sustainable Resource Science (CSRS, Japan),

University of Freiburg (Germany), and Academia Sinica (Taiwan) are also ongoing.

It is essential for ITbM to communicate to the general public widely that ITbM always addresses the environmental and safety issues carefully, and to gain the understanding from the international/domestic societies and local community. Accordingly, ITbM has set up an Environment and Safety Committee to seek the counsel of experts for ITbM's research to be conducted competently while complying with the laws and regulations.

<Mission statement and/or center's identity>

- Briefly and clearly describe the mission statement and/or the project's identity as WPI center.

The mission of ITbM 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 catalytic chemistry. We seek to cause a paradigm shift in science by creating a new field of research that aims at implementing programmed chemical transformations for precisely controlling the production of biofunctional molecules of requisite structures and their functional expressions. The identity of ITbM resides in the development of novel bio-molecules, "transformative bio-molecules", in order to achieve this goal. To accomplish this, we will enlist the best synthetic chemists and plant and animal biologists worldwide.

1. Research fields

- Specifying the inter-disciplinary field(s) to which the project may be closely related.

ITbM's research to develop "transformative bio-molecules" is closely related to the fields of synthetic chemistry, molecular catalysis, functional molecular science, systems biology, plant science, plant genetics, plant developmental biology, animal physiology, protein science, and bio-imaging. These are areas in which NU has significant international competitive advantages.

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

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 cutting-edge synthetic chemistry partnered with fundamental biological systems of plants and animals. This research endeavor will have significant impacts in 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.

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

Center for Sustainable Resource Science (CSRS) at RIKEN, Japan

CSRS, focusing on plant biology and synthetic chemistry was established at almost the same time as ITbM. Both institutes concluded the "Agreement on the Association and Cooperation" and held the 1st CSRS-ITbM Joint Workshop in January 2014. The workshop takes place annually in either Nagoya or Wako. In January 2016, both directors made a joint statement on the joint use of the research support platform, and confirmed further promotion of collaboration between CSRS and ITbM. Several collaborating research projects are ongoing.

Other institutions

Apart from CSRS at RIKEN, no national/international center exists for leading-edge chemistry targeting fundamental biological systems of plants and animals. Thus many Japanese and overseas researchers who want to produce and/or use new bio-molecules are expected to benefit from our campaign.

2. Research objectives

- Describe in a clear and easy-to-understand manner the research objectives that the project seeks to achieve by the end of the grant period. In describing the objectives, the following should be articulated in an easily understandable manner: What kind of research do you plan to

implement by fusing various fields within the environmental domain? In the process, what world-level scientific issues are sought to be resolved? What is the expected impact of the scientific advances to be achieved on society in the future?

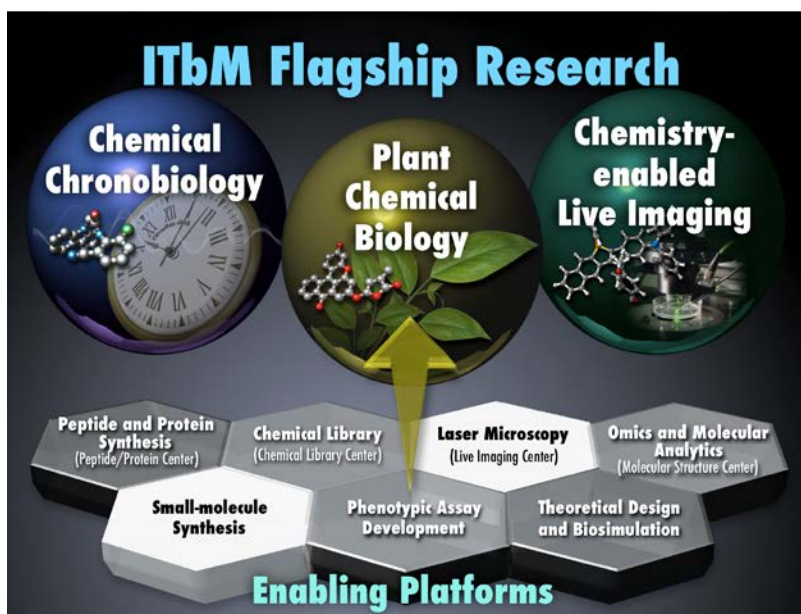
- Describe concretely the research plan to achieve these objectives.

Since ITbM's establishment in 2013, the novel synthetic small molecules designed and synthesized by the synthetic chemistry groups, the Chemical Library Center, and the Peptide/Protein Center of ITbM have been screened and distributed to the biologists of ITbM. Thus, within three years, all the biologists at ITbM now have their desired molecules for further studies. Molecule-initiated biology (chemical biology) to create transformative bio-molecules is currently shifting to the next phase, i.e., understanding and controlling biological processes by utilizing the molecules developed at ITbM.

At such a turning point, ITbM has defined the following flagship research areas based on ITbM's research achievements so far.

1. **Plant chemical biology**
2. **Chemical chronobiology**
3. **Chemistry-enabled live imaging**

We will focus on these flagship research areas and will work to actively promote chemical biology research to "understand", "see", and "regulate" living organisms by establishing new interdisciplinary research fields between chemistry and biology. This is expected to lead to the creation of transformative bio-molecules.



Research objectives;

- (1) Plant chemical biology
 - Development of molecules that combat *Striga* and related parasitic plants.
 - Development of molecules that control plant stomata.
 - Development of molecules that overcome genome barriers to produce new hybrid plant species.
 - Discovery of unidentified protein receptors of plant hormones.
- (2) Chemical chronobiology
 - Development of molecules that control mammalian circadian rhythm.
 - Development of molecules that control plant circadian rhythm.
- (3) Chemistry-enabled live imaging
 - Development of high photo-resistant fluorescent dyes towards 3D/4D super-resolution and single-molecule fluorescence imaging.
 - Development of fluorescent probes enabling unprecedented visualization of cellular microstructures and biological events.

To accomplish these objectives, we also improve and develop our platforms of small-molecule synthesis, peptide and protein synthesis, chemical library, laser microscopy, omics and molecular analysis, phenotypic assay, theoretical design, and bio-simulation.

ITbM's next challenge is how to utilize ITbM's outcomes and to contribute to the society. Upon the development of novel products based on ITbM's molecules and molecular technologies, this will largely improve ITbM's international/national visibility and recognition by the general public.

ITbM currently has several industrial partners in the chemical, pharmaceutical, and agrochemical industries. In order to achieve the best matches with industries, ITbM will launch a consortium by enrolling firms of related fields and will aim to expand its network. The consortium will also function to understand the needs of industries and societies in related fields.

Since the launch of the center, ITbM's general principle has been to conduct curiosity-driven cutting-edge basic research. As a consequence, the center does not necessarily customize or prioritize its research projects according to industrial needs. Following the center's general principle, ITbM does not plan to extensively use its resources for technological applications. Instead, the center will focus on establishing relationships with industries, where the industries take initiative in implementing ITbM's research outcomes.

ITbM will act to make sure that this principle is followed by providing additional roles to the Environment and Safety Committee. As described in the Project Summary, ITbM had set up this committee and has been holding annual meetings to ensure that the center's research projects comply with the laws and regulations. The committee member includes the Senior Councilor of the NPO "Life & Bio plaza 21", and ethical aspects of the center's research are under discussion. ITbM will expand the committee's role to discuss and provide advice regarding the prioritization of the center's research projects according to the needs of societies.

3. Management

i) Center director

- Provide the name of the center director, his/her age (as of 1 April 2017), specialties, and brief career profile (within 5 lines).
- If there is a plan to change the center director, how does the new center director intend to construct the center and what is his/her vision of objectives to be achieved? Provide a synopsis written by the new center director (free format).

Kenichiro Itami (age: 45)

Specialties: Organic Synthesis, Catalysis, Pharmaceutical Science, Nanocarbon Chemistry
Ph.D. from Kyoto University (1998, Synthetic Chemistry and Biological Chemistry), Assistant Professor of Kyoto University (1998-2005), Associate Professor of Nagoya University (2005-2007), Professor of Nagoya University (2008-present), Director & PI of ITbM (2013-present), Director of JST-ERATO Itami Molecular Nanocarbon Project (2013-present).

ii) Administrative director

- Provide the name of the administrative director, his/her age (as of 1 April 2017), and his/her brief career profile (within 5 lines).

Tsuyoshi Matsumoto (age: 50)

Ph.D. from the University of Tokyo (1995, Main Group Chemistry), Researcher of TORAY Industries Inc., (1995-1998), Assistant Professor of Nagoya University (1998-2012), Visiting researcher of University of Rochester (2012), Designated Associate Professor of Nagoya University (2013-2016), Deputy Administrative Director of ITbM (2013-2014), Administrative Director of ITbM (2015-present), Designated Professor of Nagoya University (2016-present).

iii) Composition of administrative staff

- Concretely describe how the administrative staff is organized.

Led by the Administrative Director, the Administrative Department consists of Management Division, Research Promotion Division, and Strategic Planning Division.

Management Division

With the Head of Management, the Management Division consists of the General Affairs Unit (5 staff) and the Accounting Unit (5 staff). The 10 staff in the Management Division consists of 4 full-time administrative staff from the university (including 2 competent English speakers), 6 contract employees (including 3 competent English speakers).

Research Promotion Division (RPD)

With the Head of Research Promotion (Associate Professor, PhD in synthetic chemistry and chemical biology), the Research Promotion Division consists of an Assistant Professor (PhD in organometallic chemistry) and a science designer (Masters degree in molecular biology) to conduct international promotion of research, research administration, public relations, outreach activities, along with event management, and a University Research Administrator (PhD in bioinorganic chemistry holding a concurrent post), and a contract employee (Bachelors degree in plant biology) to support the daily living of foreign researchers at ITbM. Many of the members at the RPD are proficient in English.

Strategic Planning Division (SPD)

In strong cooperation with the Research Promotion Division, the Strategic Planning Division plays a key role in realization of the practical use of the research outcomes at ITbM by working out strategies for the acquisition of intellectual property rights and business matching with companies. This enables ITbM to enhance the value of research outcomes and share the benefit to the society. At the Strategic Planning Division, an Associate Professor (Masters degree in organic chemistry, pharmaceutical science) with prior experience as the head of the chemistry department at a pharmaceutical venture company and a good fluency in English was employed as of April 2016. A Lecturer (Patent attorney/ degree in catalytic chemistry) in charge of intellectual property management was transferred from RPD to the SPD.

iv) Decision-making system

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

The Center Director has the authority to make final decisions over all matters concerning the operation and management of ITbM. To support the work of the Center Director, two Vice-Directors are assigned from chemistry and biology for further promotion of interdisciplinary research and risk management at ITbM. The Center Director has good communications with the Vice-Directors, Administrative Director, and PIs. Steering Committee meetings and PI meetings are held to provide advice to the Center Director.

Steering Committee meetings

The Steering Committee was organized to discuss and consider important matters of ITbM, including research plans, operation and management, personnel affairs and the budget.

The Committee meeting is held once a month to serve as a place for discussion and provides advice for the Center Director to make the final decisions. The Center Director operates and manages ITbM in consultation with the Steering Committee.

Having Trustee (in charge of WPI affairs) as a member and the Directors of the Research Cooperation Department and the Manager of the Research Support Division as observers, ITbM is operated under the strong support of the NU headquarters and seek advice when needed.

The Committee Members:

Center Director, Vice-Center Directors, Administrative Director, Head of Research Promotion Division, Head of Strategic Planning Division, Nagoya University PIs, Trustee (in charge of WPI affairs)

Observers:

Overseas PIs, Co-PIs of overseas PIs, Sub-Center Chief Coordinators, Director of the Research Cooperation Department, Director of the Manager of the Research Support Division

PI Meetings

Regular PI meetings to discuss research and major matters among all PIs are held on a regular basis. Overseas PIs also participate in all PI meetings through the TV conference system. The PI meeting involves discussions on matters related to the management of ITbM, along with the progress of interdisciplinary research with the Co-PIs. PI meetings play an indispensable role to discuss and determine the direction of the interdisciplinary research for ITbM.

v) **Allocation of authority between the center director and the host institution's side**

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

The NU Rules restrict the role of the President of NU only to the appointment of the Center Director. All matters concerning the operation and management of ITbM fall under the purview of the Center Director. According to the "Implementation Guidelines for the Special Bonus System for Persons in the Service of Nagoya University Institute of Transformative Bio-Molecules", which provides special bonuses to the Center Director, the Vice-Center Directors, PIs, and the Administrative Director based on their performance and evaluations, the selection of eligible persons and the bonus amount is left to the discretion of the Center Director. On the other hand, the Executive Board of NU determines the bonus amount of the Center Director.

4. **Researchers and other center staffs, 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 2016	Final goal (Date: month, year)
Researchers from within the host institution	7	8	8
Foreign researchers invited from abroad	3	5	5
Researchers invited from other Japanese institutions	0	0	0
Total principal investigators	10	13	13

- Describe the concrete plan to achieve final staffing goal, including steps and timetables.
- Attach a list of principal investigators using the Appendix. Place an asterisk (*) by names of the investigators considered to be ranked among the world's top researchers. Describe the policy and strategy for inviting the PIs who are to be included after 1 April 2017.

b) **Total members**

	Numbers		
	At beginning	At end of FY 2016	Final goal (Date: □ month, year)
Researchers	20 < 5, 25%> [4, 20%]	72 < 24, 33%> [19, 26%]	80 < 27, 34%> [21, 26%]
Principal investigators	10 < 3, 30%> [2, 20%]	13 < 6, 46%> [3, 23%]	13 < 6, 46%> [3, 23%]
Other researchers	10 < 2, 20%> [2, 20%]	59 < 18, 31%> [16, 27%]	67 < 21, 31%> [18, 27%]
Research support staffs	10	47	50
Administrative staffs	10	13	13
Total number of people who form the "core" of the research center	40	132	143

- Enter the total number of people in the columns above. In the "Researchers" column, put the number and percentage of overseas researchers in the < > brackets and the number and percentage of female researchers in the [] brackets.

- Enter matters warranting special mention, such as concrete plans for achieving the Center's goals, established schedules for employing the main researchers, particularly principal investigators.

ii) Collaboration with other institutions

- If the "core" forms linkages with other institutions, domestic and/or foreign, by establishing satellite functions, Provide the name of the partner institution(s), and describe the role of the satellite functions, personnel composition and structure, and collaborative framework between the host institution and the said partner institutions (e.g., contracts to be concluded, scheme for resource transfer).
- If some of the principal investigators will be stationed at satellites, attach a list of these principal investigators and the name of their satellite organizations using the Appendix.
- If the "core" forms organic linkages with other institutions, domestic and/or foreign, without establishing satellite functions, provide the names of the partner institutions and describe their roles and linkages within the center project.

Whereas satellite institutes are not established to ITbM, we have cooperating institutions. In addition to the overseas PIs' host institutions designated at start, we are strategically expanding collaborating network with national/international institutions to augment the research activity of ITbM.

Queen's University (Canada), University of Washington (USA), ETH Zürich (Switzerland), University of Southern California (USA), and University of Düsseldorf (Germany) are partners as host institutions of the overseas PIs, and have been collaborating in various aspects.

National Science Foundation Center for Selective C-H Functionalization (NSF-CCHF, USA) is an international partner collaborating in the field of C-H activation chemistry constituting an important area of ITbM's research. CCHF is a virtual institute with top leading 23 PIs and their research groups working in the field of C-H activation chemistry in 14 universities/institutes across the USA. Around 4 to 5 researchers per year (duration: 3-6 months) are being exchanged between the institutes. The network expanded to include other related institutes such as the **Institute for Basic Science (IBS, KAIST, Korea)**.

RIKEN Center for Sustainable Resource Science (CSRS, Japan) is an important national partner. CSRS, focusing on plant biology and synthetic chemistry, was established at almost the same time as ITbM. Directors of ITbM and CSRS made a joint statement on the joint use of the research support platform, and confirmed further promotion of collaboration between CSRS and ITbM. The CSRS-ITbM Joint Workshop is annually held.

University of Freiburg (Germany) and **Academia Sinica (Taiwan)** are also international partners of ITbM. We conduct collaborating research projects with these institutions through exchange of the researchers.

5. Research Environment

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

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

Mix-Labs: Key to interdisciplinary research

At ITbM's Mix Labs, researchers and students from different fields share the same space and are able to discuss and communicate about science, education and other administrative matters on a daily basis. The Mix Lab concept has also been reflected in ITbM's new building that was constructed in April 2015, where over 60 new interdisciplinary research projects are being generated across 11 research groups and 4 centers, some of which have already led to patent applications, journal publications and technology transfers. The continuous merging and reassembling of research projects that have arisen from the Mix Lab effect, have led to the establishment of new interdisciplinary research fields at ITbM, such as plant chemical biology, chemical chronobiology, and chemistry-enabled live imaging.

Co-PI system

ITbM introduced the Co-PI system to enable world-class researchers in related research fields participate in ITbM's research activities. To make the overseas PIs' research at ITbM possible, ITbM decided to employ young researchers as Co-PIs who stay full time at ITbM and cooperate with the overseas PIs. This system has led to increased attention of ITbM's research results and activities from the international science community, and has contributed to improving the global visibility of

ITbM.

Co-PIs are also allocated to NU PIs. In order to enable NU PIs to focus on their research, NU provided permission to employ 7 Associate Professors and Lecturers as Co-PIs of ITbM to conduct educational tasks in the place of the NU PIs.

Administrative Department and Secretaries

As described in section 3-iii), the Administrative Department is staffed by talented individuals with a good command of English, as well as a global outlook and vision. The Department has been established to effectively manage international symposia/seminars and prepare official documents in both English and Japanese for ITbM. Secretaries allocated to PIs and sub-centers work along with the Administrative Department staff to support the administrative tasks.

Research Promotion Division (RPD) works closely with researchers and supports research through international public relations, outreach activities, education and organization of events. ITbM's researchers and research have been covered over 1,800 times in international and domestic media. To allow the researchers from abroad to settle down in Japan and focus on their research, ITbM has assigned a staff in RPD to support the daily lives of foreign researchers and their families. The staff provides a wide range of support such as assistance in registrations at city council and banks, linguistic support (interpretation and translation) and giving advice on daily lives, education and health care.

Realization of the research outcomes of ITbM improves international/national visibility and recognition by the general public. To achieve this, the Strategic Planning Division (SPD) was established and works with RPD and researchers to make strategies and prepare a roadmap to contribute to the scientific community and society.

Secretaries are also playing important roles to support researchers. A total of 15 bilingual secretaries were 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 over the need to apply immediately for competitive grants.

Provide each of PI groups with research space and start-up funds with an average value of 30,000,000 JPY. In addition to the start-up funds, all of the following costs for each PI group are covered by ITbM: utility costs including electricity and water fees, employment costs of two postdoctoral researches, one secretary, and one technical staff. All the researchers are furnished with full access to instruments of ITbM and those available in NU.

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

We engage in high-profile recruitment campaigns to attract highly qualified postdoctoral researchers using web sites of ITbM and international top journals. We also 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.

Personnel who are fluent in English and with thorough experience in handling administrative affairs were employed in the General Affairs and Accounting Unit of the Management Division. In addition to their usual work related to administration, the Management Division is actively involved in preparing ITbM's international symposia, such as reception, performing the MC, and handling the registration. ITbM regularly sends notices from the university to ITbM researchers in both English and Japanese.

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

researchers from outside the host institution. As a basic rule, the salaries of researchers who were already employed at the host institution prior to the centers' establishment are to be paid by the host institution.)

Based on the performance and evaluations, special bonuses are provided to the Center Director, the Vice-Director, NU PIs and the Administrative Director. They receive full bonuses during the starting period of the project and the amount will vary according to their evaluation.

All ITbM researchers are required to submit an activity report regarding their research activity in March. For the PIs, the Center Director will reflect the results of the Site Visit report to the special bonuses. As for other faculty and postdoctoral researchers, each PI will conduct the first evaluation, followed by a secondary evaluation by the Center Director, and the results will be reflected in their salary upon renewal of their contract.

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

At start of ITbM, NU has provided 5,400 m² of research space for ITbM, which contains 2,400 m² of new space on top of the existing 3,000 m² of space designated to NU PIs.

The new building for ITbM was completed at the end of FY2014. The total area of the new six-floor building is 7,934 m² and has a unique structure where a pre-existing building (floor area 463 m²) is incorporated within the new building. In addition, the university provided the area from the pre-existing building. The new building is designed to reflect the "Mix-Lab" concept. The second and fourth floors consist of large biology and chemistry labs and the third and fifth floors consist of the office space for the researchers. The first floor contains the administrative office and the lecture room. On the top (sixth) floor are the Live Imaging Center, Chemical Library Center, and greenhouses. Both labs on the second and fourth floors consist of a large Bio Mix Lab and a Chem Mix Lab, which are located next to each other and are accessible through a single door. There are no barriers within the Bio Mix Labs and the Chem Mix Labs, along with the Mix Office spaces located directly above. This removes the conventional barriers between research groups, thus creating huge Mix Labs and Mix Offices to promote interdisciplinary research. The new building is also equipped with a childcare room for researchers and visiting researchers accompanied by small children.

Upon increase of two PI groups in FY2016, additional 200 m² space was provided in the building next to ITbM, in which biology groups of Graduate School of Science have their spaces. A bridge connecting the building and ITbM was constructed, enabling easy access to the provided spaces and providing the opportunities of ITbM's collaboration on campus.

NU is very well equipped with top-level major instruments necessary for ITbM's research. The quality and number of these instruments rivals the best institutions in the world. The researchers can access all these facilities.

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

ITbM organizes 4 symposia and awards annually; International Symposium on Transformative Bio-Molecules (ISTbM), Hirata Award, Tsuneko and Reiji Okazaki Award, and Nagoya Medal of Organic Chemistry.

International Symposium on Transformative Bio-Molecules (ISTbM)

ITbM organizes its annual international symposium (ISTbM), by inviting 5-8 prestigious researchers from around the world, who are closely related to ITbM's research fields of systems biology, biochemistry, synthetic chemistry, and theoretical science. ITbM organized its first symposium (ISTbM-1) in April 2013 to commemorate the launch of the institute, and are held annually.

Hirata Memorial Lecture and Hirata Award

In memory of NU's late honorary professor Yoshimasa Hirata, the Hirata Memorial Lecture had been held each year. ITbM became the organizer of the Hirata Memorial Lecture on its 10th anniversary year and held the symposium in February 2014. From 2015 onwards, the Hirata Memorial Lecture

was renamed as the Hirata Award and the 11th award lecture was carried out at the same time as ISTbM-3. ITbM holds the award annually.

Tsuneko and Reiji Okazaki Award

The Tsuneko and Reiji Okazaki Award was established to recognize rising stars in the field of molecular biology. ITbM organized the 1st award along with ISTbM-3, and are held annually.

Nagoya Medal of Organic Chemistry

From 2014, Itami was selected to become the chair of the Nagoya Medal of Organic Chemistry, which is an international award in organic chemistry that has been granted to many prestigious researchers across the world. The Nagoya Medal was established in 1995 by Professors Hisashi Yamamoto (University of Chicago/Chubu University) and Nobel Laureate Ryoji Noyori and is held each year with the financial support by the Banyu Life Science Foundation International. In October 2014, ITbM organized the 20th Nagoya Medal of Organic Chemistry at NU, and has been held annually.

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

In order to provide a better environment for foreign researchers to focus on their research, arrangements have been made with the university's accommodation facilities, and university rules have been revised so that ITbM postdoctoral researchers can stay in the accommodation facilities for up to 2 years (initially 1 year before changing the regulations). Also, ITbM helps foreign researchers who are looking for an apartment outside the campus by providing linguistic support when signing an apartment lease contract and other procedures required for living, and helps them settle in the neighborhood.

ITbM has also been cooperating with the Nagoya City Board of Education and other universities in the region by providing assistance to enter local public schools in Nagoya, supporting communications between school and families and introducing private Japanese teachers and educational materials to learn Japanese. ITbM has also negotiated with the international schools near NU to accept preschool children of the researchers arriving from overseas.

ITbM's staff has collected information of hospitals with English services in Nagoya to cover major 9 medical departments. ITbM supports the health care of foreign researchers and their families by accompanying them to hospitals, supporting pregnant mothers for childbirth, along with providing advice in selecting hospitals, and providing information on vaccination for children.

6. Indicators for evaluating a center's global standing

• Describe concretely the following points.

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

The global standing of ITbM 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 ITbM.

We consider there are three aspects important to the global standing of ITbM as a WPI center:

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) Research quality and impact

Since ITbM's launch, we have been publishing our work in top journals. The number of papers

published in top journals indicates our high performance. Highly cited work is clearly an indication of high quality research and a significant impact.

ITbM's researchers are being widely recognized by the international science community as well as by the society. This is evident by the significant number of prestigious international awards and honors, competitive research funds, as well as invitations to major international symposia that have been granted to ITbM's PIs.

2) Breakthroughs from the interdisciplinary research activities

ITbM's interdisciplinary research has been promoted by the "Mix" concept. As a result, the activities related to IP and technological transfers have made significant progress. This is evident in a good number of joint papers, patent files, joint R&Ds, technology transfers, and commercialization.

3) The development of human resources

Mentoring of young researchers is a key to the future development and global standing of ITbM. To evaluate our progress, we will use indicators such as the career paths and academic success of former researchers of ITbM. Since ITbM's launch, a notable number of ITbM researchers and students have got positions in academia in Japan and overseas. Many awards of young scientists and students garnered clearly indicate nurturing of the next-generation.

iii) **Goals to be achieved through the project (at time of final evaluation)**

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 PIs and intense interactions with our leading plant/animal biology PIs. Our dream is to have a positive impact on global issues such as food production.

7. Securing research funding

Future prospects

- Describe the concrete prospects for securing resources that match or exceed the project grant.

ITbM researchers have been constantly obtaining competitive funding from the time of the center's establishment. The total amount was approximately matched the project grant at the beginning, and became more than double in FY2013. The amount has been further increased in the following years. We will continue our effort to secure competitive research funds.

- Calculate the total amount of research funding (e.g., competitive funding) based on the percentage of time the researchers devote to research activities at the center vis-à-vis the total time they spend conducting research activities. Be sure the prospects are realistically based on the past record.

The total amount of competitive funding obtained in FY2012 was 528 million yen. In FY2013, it is 1,141 million yen, which is more than double the amount obtained in FY2012. The amount of funding further increased or comparable in the following years (FY2014: 1,290 million yen, FY2015: 1,185 million yen, FY2016, 1,036 million yen). Major competitive funding obtained in FY2016 are JST-ERATO (2 projects), JST-CREST (2 projects), JST-PRESTO (2 projects), Grant-in-Aid for Scientific Research on Innovative Areas (2 project as Area Representative), JST-ALCA (1 project), Grant-in-Aid for Specially Promoted Research (1 project) etc. Overseas PIs have also been successful in obtaining KAKENHI (Grant-in-Aid for Scientific Research) from FY2014. In addition, ITbM applied for the JSPS Bilateral Program (Joint Research Projects) to strengthen the research collaboration with NSF-CCHF (cf. 2-3) and the project was selected for FY2015-2016. The total competitive fund we have secured for 2012-2016 amounts to 5 billion yen.

Others

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

NU has committed to sustain ITbM's pioneering research activities after the WPI-grant period ends. In order to accomplish this, NU will include ITbM 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.

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, NU will accelerate system reform of the university to ensure that ITbM is maintained.

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

The 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.

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

- ITbM's wealth and safety training for interdisciplinary research

While the interdisciplinary research is rapidly in progress at the Mix Labs, ITbM has to provide special safety training suitable for interdisciplinary environments. The training also provides an opportunity to explain to the foreign researchers about the difference among the safety rules of Japan and their countries. ITbM started the original safety training in FY2014. The course consists of 3 sections; general safety lecture, specific lab safety lecture, and practical training. All the researchers of ITbM learn about safety of both chemistry and biology labs/experiments, such as safe use/disposal of chemicals in the Chem Mix-Lab and contamination of exogenous germs and seeds in the Bio Mix-Lab. Differences in domestic and foreign regulations of chemicals and biological materials, such as a color and contents of a gas cylinder are covered. The ITbM safety course has been authorized as the official training of NU from FY2015.

- Concern for the environment and safety

Upon development of molecules that modulate biological system in plants/animals, it is essential for ITbM to communicate to the general public widely that ITbM always addresses the environmental and safety issues carefully, and to gain the understanding from the international/domestic societies and local community. Accordingly, ITbM has set up an Environment and Safety Committee to seek the counsel of experts for ITbM's research to be conducted competently whilst complying with the laws and regulations. The Committee evaluates whether new compounds and species generated through ITbM's research along with their methods address environmental and safety issues appropriately, comply with laws and regulations, and thus provide relevant advice to the Director. Thus, the researchers at ITbM are constantly aware of these issues when conducting their research. The committee also contributes to prepare and improve the ITbM's safety training course stated above.

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 $78\text{ }^\circ\text{C}$, 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 proteins, 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, Irlé, 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 Pacificchem 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 devices. 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 administrative 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 (in English)

February 21, 2017

To MEXT

Nagoya University
Dr. Seiichi Matsuo, President



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

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

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

Nagoya University (hereinafter referred to as "NU") has positioned the Institute of Transformative Bio-Molecules (hereinafter referred to as "the Center") as an important research center conducting world-leading frontier basic research at NU in the University's mid-term plans and "Nagoya University Matsuo Initiatives for Reform, Autonomy, and Innovation 2020 (NU MIRAI 2020)". The Center's presence is essential for NU to become a research university that can compete with leading universities around the world. NU is committed to supporting ITbM through all means. Under the umbrella of the "Institute for Advanced Research", the Center will receive additional support needed to manage the center even after termination of funding from the WPI program.

<Concrete Measures>

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

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

- 1) NU is fully committed to provide financial support for the Center that is comparable to the support from WPI.
- 2) NU has provided 5,400 m² of the research space for the Center, and this allocation will be continued. Additional space will be given according to the progress of the research when needed.
- 3) NU has provided financial support towards construction of ITbM's new building. NU will continue to provide full support for the operation of the building.
- 4) NU will continue to cover the equivalent amount of the salaries of those researchers at the Center who already hold posts at NU.
- 5) NU will assign 4 capable administrative staff to the Center and cover their salaries as well as employing new bilingual staff.
- 6) The total sum of competitive funding for those researchers at the Center who already hold posts at NU was 1,036 million JPY (in FY2016), and the acquisition of competitive funding at an equal or greater level is promised onwards.
- 7) NU has actively accepted several programs to promote internationalization of NU, and the resulting research systems and facilities are available at the Center.

- 8) The Center will not only activate related research fields but also have an effect to all of the research activities at NU, through collaboration with the other national projects such as the Program for Leading Graduate Schools "Integrative Graduate Education and Research Program in Green Natural Sciences".

(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 reorganized the Institute of Advanced Research, which is established as an institute independent from the other departments and research centers, and placed the Center as part of the Institute as a significant research institute conducting frontier basic research of NU.
- 2) In order for the Center Director to operate the Center under his leadership, NU will give full authority to the Center Director for final decisions on relevant matters such as personnel and the execution of the Center's budget.
- 3) In addition, the Vice Directors and Administrative Director will make decisions depending on the issue, to avoid placing an excess burden on the Center Director and to enable speedy execution 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 has assigned 7 associate professors/lecturers, who will mainly take charge of education in each department to take PIs duty, and to maintain high-level education. Their salaries are covered by NU.
- 2) NU gives priority to female researchers at the Center to enable their children to enter the nursery school operated by NU.
- 3) NU will continue its support towards foreign researchers at the Center in their daily life and education of their children, making full use of the 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".
- 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 authority 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 a salary system which will 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 incentives to other researchers and staff as well.

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

- 1) NU has provided 5,400 m² of research space to accommodate the Center. This commitment will be continued. Additional space will be allocated when needed.
- 2) NU will rearrange and relocate the facilities of 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.
- 3) 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 places the Center as a significant research institute in the University's mid-term plans, and commits to sustain the Center's pioneering research activities after the termination of the WPI grant support. In order to do so, NU allocated 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 financial support and permanent positions for the researchers employed at the Center.
- 2) Depending on the achievement and influence of the Center, NU will advance the scheme to reorganize other departments and institutes within the university.

(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) Looking at the existing WPI centers, there seemed to be situations where they faced struggles with their host institution's headquarters. To overcome these issues, NU had assigned a member of Board of Trustee/Vice-President as the Administrative Director to bridge the gap between the Center and the University's headquarters. Through these endeavors, the Center's management system and guidelines were built. As of January 2014, the Trustee stepped down as the Administrative Director and a new Administrative Director was appointed. The Center Director has been holding a regular meeting with the President of NU once a month to discuss any issues related to the management of the Center.
- 2) The newly assigned Administrative Director has a research background and leads the administrative department. NU will continue the Center so that it's research activities at a maximum performance.
- 3) NU recognizes one of the important aspects of the WPI is to accelerate system reform of Japanese universities such as flexible operation and, internationalization.
- 4) Intensive commitment of NU's leadership to the Center is critically important to accelerate the system reform in not only the Center but also for the entire university.

List of Principal Investigators

- If the number of principal investigators exceeds 10, add columns as appropriate.
- Place an asterisk(*) by the name of the investigators who are considered to be ranked among the world's top researchers.
- Give age as of 1 April 2017.
- For investigators who cannot participate in the center project from 1 April 2017, indicate the time that their participation will start in the "Notes" column.

Name	Age	Current affiliation (organization, department and specialties)	Academic degree	Notes
1 Kenichiro ITAMI*	45	Department of Chemistry, Graduate School of Science, Nagoya University	Dr.Eng <i>Specialties</i> : Organic Synthesis, Catalysis, Pharmaceutical Science, Nanocarbon Chemistry	
2 Tetsuya HIGASHIYAMA*	45	Division of Biological Science, Graduate School of Science, Nagoya University	Dr.Sci <i>Specialties</i> : Live Cell Biology, Plant Reproduction, Bio-active molecules, Peptides	
3 Jeffrey W. BODE*	43	Department of Chemistry and Applied Biosciences, ETH Zürich, Switzerland	Doctoral of Natural Science <i>Specialties</i> : Organic Synthesis, Peptide and Protein Chemistry, Catalysis, Ligation and bioconjugation reactions	Double Affiliation
4 Cathleen M. CRUDDEN*	50	Department of Chemistry, Queen's University, Canada	Ph.D <i>Specialties</i> : Catalysis, Organic Synthesis, Materials Chemistry, Chirality	Double Affiliation
5 Stephan IRLE*	49	Department of Chemistry, Graduate School of Science, Nagoya University	Ph.D. <i>Specialties</i> : Electronic Structure Theory, Computational Materials Science, Quantum Chemistry of Complex Systems	
6 Toshinori KINOSHITA*	48	Division of Biological Science, Graduate School of Science, Nagoya University	Dr.Sci <i>Specialties</i> : Plant Molecular Physiology	
7 Takashi OOI*	51	Department of Applied Chemistry, Graduate School of Engineering, Nagoya University	Dr. Engineering <i>Specialties</i> : Organic Synthesis, Catalysis, Molecular Recognition	
8 Keiko TORII*	51	Department of Biology, University of Washington, USA	Ph.D. <i>Specialties</i> : Plant Development, Signal Transduction, Stem Cell Maintenance/Differentiation in Plants	Double Affiliation
9 Shigehiro YAMAGUCHI*	48	Research Center for Materials Science, Nagoya University	Dr. Engineering <i>Specialties</i> : Main Group Chemistry, Physical Organic Chemistry	
10 Takashi YOSHIMURA*	47	Department of Applied Molecular Biosciences, Graduate School of Bioagricultural Sciences, Nagoya University	Dr. Agriculture <i>Specialties</i> : Animal Physiology, Systems Biology, Neuroendocrinology	
11 Steve KAY*	57	Dornsife College of Letters, Arts and Sciences, University of Southern California, USA	Ph.D. <i>Specialties</i> : Chronobiology, Genetics, Biochemistry, Systems Biology	Double Affiliation
12 Florence M. TAMA*	42	Research Center for Materials Science, Nagoya University	Ph.D. <i>Specialties</i> : Computational Biophysics, In Silico Drug Design	
13 Wolf B. FROMMER*	59	Institute for Molecular Physiology, Heinrich Heine Universität Düsseldorf, Germany	Dr. rer. nat. <i>Specialties</i> : Plant Biology	Double Affiliation