

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?

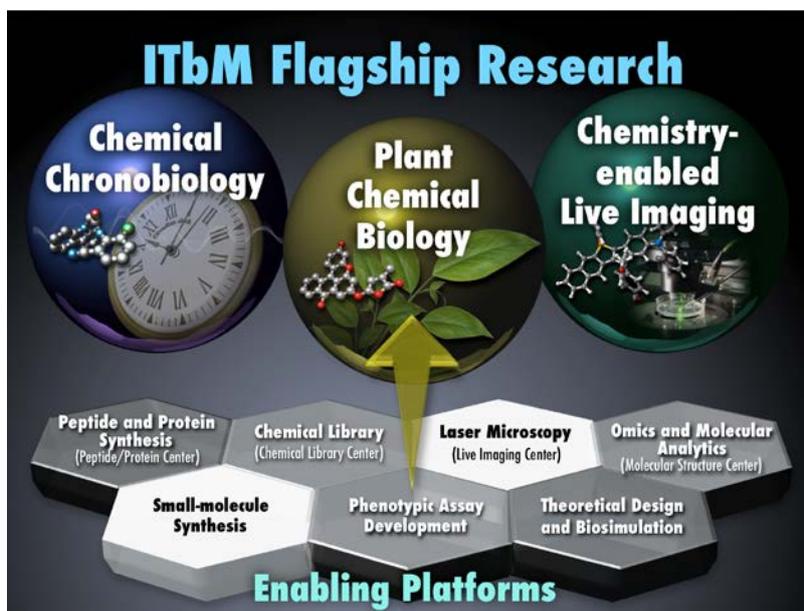
- Describe concretely the research plan to achieve these objectives.

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.