FY 2013 WPI Project Progress Report

World Premier International Research Center Initiative (WPI)

Host Institution	Nagoya University	Host Institution Head	Michinari Hamaguchi
Research Center	Institute of Transformative Bio-Molecules (ITbM)	Center Director	Kenichiro Itami

Summary of center project progress

The Institute of Transformative Bio-Molecules (ITbM) pre-launched in December 2012 and was officially established in April 2013. Under the slogan "changing the world with molecules", researchers and administrative officers work together to develop molecules to "understand", "see" and "regulate" biological systems and to establish a "world top-level research center".

1. Research System and Administrative Department

Nagoya University's seven PIs and three overseas PIs currently form the core of the research center. Following advances in the center's research, ITbM's organization was reviewed this year. Along with Center Director Kenichiro Itami and Vice-Director Tetsuya Higashiyama, Nagoya University PI, Shigehiro Yamaguchi is to be appointed as the second Vice-Director (April 2014). In order to strengthen ITbM's animal/plant science research, Steve Kay of the University of Southern California, a world leader in biological clock research is to be assigned as an overseas PI (April 2014). Tsuyoshi Matsumoto took the role of Administrative Director in place of Trustee Yoshihito Watanabe (January 2014).

Three Co-PIs have been assigned to support overseas PIs and seven faculty members have been appointed to carry out educational roles in place of Nagoya University's PIs. Postdoctoral researchers, technicians and secretaries have also been hired to promote ITbM's research.

In order to develop a platform where researchers can fully focus on their research, the Administrative Department was established consisting of the Research Promotion Division and the Management Division. The department consists of English competent staff, some with a scientific background, capable of organizing international symposia/seminars and supporting the framework of the center.

2. Mix-Labs and Interdisciplinary Research

Mix-Labs have been established where synthetic chemists, animal/plant biologists and theoretical scientists work side by side in the lab. The ITbM Research Award was implemented to promote interdisciplinary research of young researchers. These initiatives, which removed the barriers between research fields and groups, have led to initiation of new interdisciplinary research through integration of people, ideas, equipment and research. This Mix-Lab concept will continue to be the main core in ITbM's new building, which is expected to be finished in March 2015.

3. Exchange Programs with Partner Institutes

Fostering young researchers is also a key mission of this center. Programs to exchange young faculty and graduate students have officially started with partner institutes.

4. Environment and Safety Committee

The center is involved in creating new compounds that have action on animals/plants as well as generation of new species. The Environment and Safety Committee was established to address and guarantee the safety of ITbM's research activities. The committee consists of internal/external experts and the first meeting was held in January 2014.

5. Organization of International Symposia

To celebrate ITbM's official launch, ITbM's opening ceremony and the 1st International Opening Symposium was held in April 2013. In February 2014, the 10th Hirata Memorial Lecture was organized and hosted by ITbM.

6. Research Promotion Division

The division consists of faculty with PhD degrees in science and a science designer, who supports the center's research through international public relations, outreach activities and daily support for foreign researchers.

1. Summary of center project

<Plan at start of project>

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. Through this interaction, which is fundamental to the Center, transformative bio-molecules will be synthesized that can (1) **enhance biotic productivity and quality** and (2) **realize innovative bio-imaging**. To ensure the advancement of these projects, we will (3) **develop catalysts that enable incredibly efficient synthesis and molecule activation on demand**. The ultimate goal is to have a positive impact on global issues such as food production. Our team of PIs is an innovative mix of chemists and biologists from Japan and abroad. A Co-PI system, and an efficient administration with an English focus will ensure that international members will have significant involvement in the project.

The Center will start with 10 PIs, including 3 foreign researchers, and one Administrative Director. These founding members will then hire post-doctoral researchers, research assistants, administrative staff, and secretaries.

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

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

<Results/progress/alternations from plan at start of project >

Since the launch of the center one year ago, establishment of the center and the interdisciplinary research undergoing at ITbM are both making good progress. The two Mix-Labs, which were implemented to promote interdisciplinary research, have promoted the successful integration of synthetic chemists, plant/animal biologists, and theoretical scientists. The degree of mixing at ITbM has been more than what was initially expected and many research themes related to the creation of bio-functional molecules have arisen from young researchers. At this point, some seed molecules with the potential to become transformative bio-molecules have already been discovered (details on research results are stated in Section 3. Research objectives). Stated below is a summary of this year's main progress for the center.

Organization/Personnel Organization

Administrative Department

Led by the Administrative Director, the Administrative Department consists of the Management Division (General Affairs Unit and Accounting Unit) and the Research Promotion Division. More than 50% of the Management Division consists of personnel competent in English who are capable of conducting the appropriate administrative processes for foreign researchers. Most of the members in the Research Promotion Division are fluent in English and hold science PhD degrees. A science designer with a background in biology was hired to play an important role in carrying out effective outreach activities. The Administrative Department has been established to effectively manage international symposia/seminars and prepare official documents for the Center in both English and Japanese.

Employment of Faculty

Three faculty members (Co-PIs) were employed to conduct research at Nagoya University alongside the three overseas PIs. In addition, seven associate professors/lecturers were appointed by Nagoya University to give lectures and carry out educational activities in place of Nagoya University's seven PIs, enabling them to focus on their research. Secretaries competent in English along with postdoctoral researchers and technicians were also appointed to each PI.

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

An International Advisory & Review Board has already been assembled, which will support our research.

The Center will establish an effective and efficient administration staffed by talented individuals with a good command of English, as well as a global outlook and vision. In addition, resources will be allocated to hire a substantial number of technical staff in order to minimize the extra demands on the time of researchers, freeing them to concentrate on their core research activities.

Appointment of the Second Vice-Director
To support the work of the Center Director, a second Vice-Director, Shigehiro Yamaguchi is to be appointed in April 2014.

Appointment of the Fourth Overseas PI
Steve Kay of the University of Southern California (USA), who is one of the world leaders in biological clock research will be appointed as an overseas PI to join ITbM from April 2014. His group is currently screening molecules to control the circadian clock of mammals, which is expected to build upon ITbM's research in animal biology. A Co-PI with experience in animal science will also be appointed in May 2014 to work at ITbM and conduct interdisciplinary research.

Establishment of Committees
A Steering Committee was organized and gathered once a month to discuss and evaluate ITbM's research plans, management, personnel, budget and other important issues related to ITbM's overall operation. In addition, PI meetings are held twice a month including overseas PIs and the Administrative Department to share information regarding the management of the center.
ITbM is involved in creating new compounds that have action on animals and plants as well as generation of new species. The Environment and Safety Committee was established to evaluate and guarantee that ITbM's research activities comply with the laws and regulations governing these activities, and also to provide relevant advice.

Partner Institutes
In addition to the host institutes of the overseas PIs, Queen's University (Canada), the University of Washington (USA) and ETH Zürich (Switzerland), partnerships commenced with the Center for Selective C-H Functionalization (CCHF, NSF center, USA), Freiburg University (Germany), and RIKEN Center of Sustainable Resource Science (CSRS, Japan). Faculty and student exchange also started between ITbM and CCHF. NSF has already accepted fund applications from CCHF to send faculty/students to ITbM.

Implementation of ITbM Research Awards
The ITbM Research Award was established, calling for grant applications

twice a year in order to promote interdisciplinary research proposed by young researchers. PIs are not eligible to apply for this award. The first round of awards was selected in October 2013. Amongst the nine applications, awards of 200 million yen over 2 years were provided to four teams with outstanding project proposals.

Design and Construction of ITbM's New Building

The new building for ITbM is to be finished by the end of FY2014. The design of the building was proposed at the end of FY2012 and was finalized at the beginning of FY2013. Construction of the building commenced from the end of FY2013. The total area of the new six-floor building will be approximately 7,000 m^2 and is designed to incorporate the "Mix-Lab" concept to promote interdisciplinary research.

ITbM Opening Ceremony and International Symposia

To celebrate ITbM's official establishment, ITbM's opening ceremony was held in front of Nagoya University's Science and Agricultural building in April 2013. This was followed by the 1st International Opening Symposium of ITbM (ISTbM-1). In February 2014, the 10th Yoshimasa Hirata Memorial Lecture was organized and hosted by ITbM.

Presentation of Research Results

In 2013, 96 papers were published in peer-reviewed journals (46 papers published in journals with an Impact Factor (2012) > 7 and 31 papers published in journals with an Impact Factor (2012) > 10). From January to April 2014, 39 papers were published in peer-reviewed journals. There were 9 patent applications in 2013. Through press conferences and distribution of press releases, research outcomes have been covered over 100 times in a range of national and international newspapers, TV, magazines, journals and internet sites. PIs have presented their research in a total of 99 invited lectures at international symposia and a total of 16 international awards and honors have been granted to researchers at ITbM.

Research Grants

In FY2013, the total amount of research grants obtained by Nagoya University's PIs was 1,141 million yen. For FY2014, successful grant applications have been also been submitted by overseas PIs/Co-PIs.

2. Research fields

<Plan at start of project >	<Results/progress/alternations from plan at start of project >
Target research field: **Molecule-Activation Chemistry* for Advanced Systems Biology**** (This is an area in which Nagoya University has significant international competitive advantages: synthetic chemistry, molecular catalysis, systems biology, plant science, peptide science, live-cell imaging.) The interface of chemistry and molecular biology has already resulted in important new research fields of significant scientific impact, such as chemical biology and medicinal chemistry. We plan to bring this to a new level by exploiting newly developed molecule-activation chemistry partnered with fundamental biological systems of plants and animals. This research endeavor will have significant impacts in the closely related fields of chemical biology and medicinal chemistry, but most importantly, on areas that are of urgent global importance including world food production, medical care, and bioenergy. ***Molecule-Activation Chemistry**: The synthetic chemistry that enables the activation and direct transformation of stable molecules into target structures. This methodology can rapidly convert biologically active "lead" molecules into more selective and active derivatives. ****Systems Biology**: The biology to unveil the pivotal mechanism of how organisms function as a system. The discovery of key molecules operating biological systems at an individual organism level is crucial.	Target research field: **Molecule-Activation Chemistry for Advanced Systems Biology** (This is an area in which Nagoya University has significant international competitive advantages: synthetic chemistry, molecular catalysis, systems biology, plant science, peptide science, live-cell imaging.) The target research field of ITbM has not changed since the start of the project. In addition to scientists working in the fields of chemistry and biology, ITbM has employed new faculty members and researchers in order to enhance chemical biology research, which lies at the interface of these two disciplines. Co-PIs and associate professors specializing in plant/animal circadian clocks (Norihito Nakamichi, Taeko Ohkawa), plant stem cells (Naoyuki Uchida), plant development (Minako Ueda), and chemical biology (Shinya Hagihara, Masayasu Taki) have now joined ITbM. Their expertise boosts ITbM's strengths on molecular activation chemistry and systems biology to a higher level, and is also a strong driving force to promote interdisciplinary research. Within one year since the launch of ITbM, their input has resulted in the discovery of seed molecules with the potential to become transformative bio-molecules. The integration of molecular activation chemistry and systems biology has led to the establishment of animal/plant molecular chemistry as a new interdisciplinary field of research, which may lead to the creation of transformative bio-molecules. This is envisaged to be the key to solving significant social issues related to the environment, food production, medical technology and bio-energy.

3. Research objectives

< Plan at start of project >

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

I) Control of Biological Systems

(a) Molecules that dramatically enhance plant growth
(b) Molecules that improve animal reproduction innovatively
(c) Molecules that overcome the genome barrier to produce novel crops

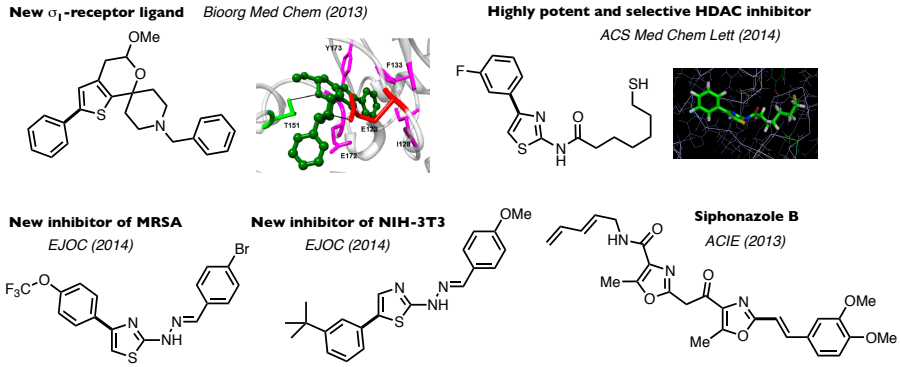
<Results/progress/alternations from plan at start of project >

Research objectives of ITbM have not changed since the start of the project. The main achievements are listed below.

I) Control of Biological System

<u>Molecules that dramatically enhance plant growth</u>

Itami and his collaborators have synthesized a number of biologically active molecules in a rapid and unconventional fashion (mostly by C-H coupling) in addition to achieving streamlined syntheses of bioactive natural products and pharmaceutically relevant molecules, including an inhibitor of histone deacetylases, small-molecule ligands for σ-receptor proteins, and small molecules that have activities against Gram-positive bacterial strains, yeast strain Candida glabrata, and dermatophytic fungus Trichophyton mentragrophytes.



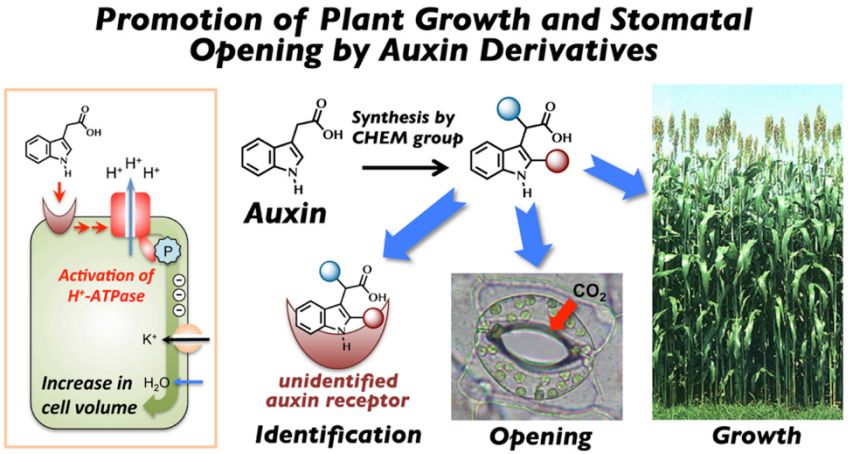
Examples of synthesized bioactive molecules

Through extensive collaboration with other groups at ITbM, Itami's group has successfully discovered a number of synthetic bio-molecules for plant and animal biology. Examples of small molecules include those that (1) control plant growth (with the Kinoshita-Takahashi group); (2) modulate the mammalian circadian clock (with the Yoshimura-Ohkawa group); (3) modulate the plant circadian clock (with the Kinoshita-Nakamichi group); (4) visualize strigolactone activity (with the Kinoshita-Tsuchiya group); (5)

control pollen tube guidance (with the Higashiyama group); and (6) visualize mitochondrial DNA (with the Higashiyama-Sasaki group).

Torii and Uchida have identified plant peptides regulating leaf shape as well as secondary growth of stems. Furthermore, their group has discovered novel receptor kinases influencing plant aging.

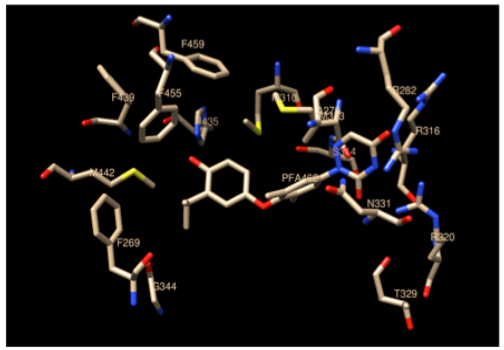
Kinoshita and his team have showed that stomatal aperture is a limiting factor in photosynthesis and plant growth, and that manipulation of stomatal opening by overexpressing H^+-ATPase in guard cells is useful for the promotion of plant growth. This work has resulted in a provisional patent and was published in the journal, PNAS. The research has received significant media coverage both nationally and internationally by distribution of a press release through global news services. Kinoshita also reported CHLH (Mg-chelatase H subunit)-transgenic plants that exhibited a closed stomata phenotype. The CHLH transgenic plants were more tolerant towards drought than WT plants, indicating that manipulation of stomatal aperture via overexpression of CHLH in guard cells improves drought tolerance in plants. These results indicate that H^+-ATPase and the Mg-chelatase H subunit may potentially be good target proteins for small molecules.



A gene circuit, 'a repressilator' in the Arabidopsis clock system, is believed to explain the generation of rhythmic pattern. However, it has been difficult to find the responsible genes using the classical genetic approach due to genetic redundancy. Nakamichi in the Kinoshita group has begun to identify novel factors involved in the clock system by using ITbM's chemical library and has identified 13 candidate molecules, which displayed lengthened or shortened circadian period activities.

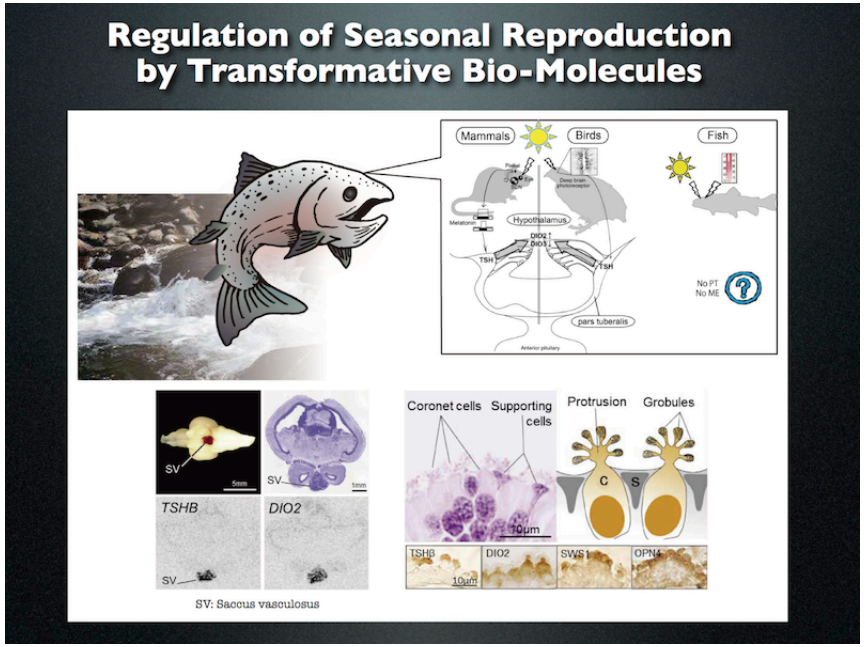
Molecules that improve animal reproduction

Yoshimura and his colleagues have discovered that thyroid hormones (TH) play a key role in the regulation of seasonal reproduction and that the thyroid hormone receptor (THRβ), is expected to be important in mediating the lowering of cholesterol and fat loss. Thus, he has started to identify THRβ-specific compounds to be applied towards treating obesity, type 2 diabetes, and atherosclerosis in collaboration with the Irle group (in silico docking studies) and the Crudden group (synthesis).



Irle's in silico docking study

Yoshimura described the regulatory mechanism of fish seasonal responses (reproduction) by observing the expression of key genes regulating seasonal reproduction and photoreception in the saccus vasculosus of masu salmon. The physiological role of the saccus vasculosus had been a mystery for more than 300 years.

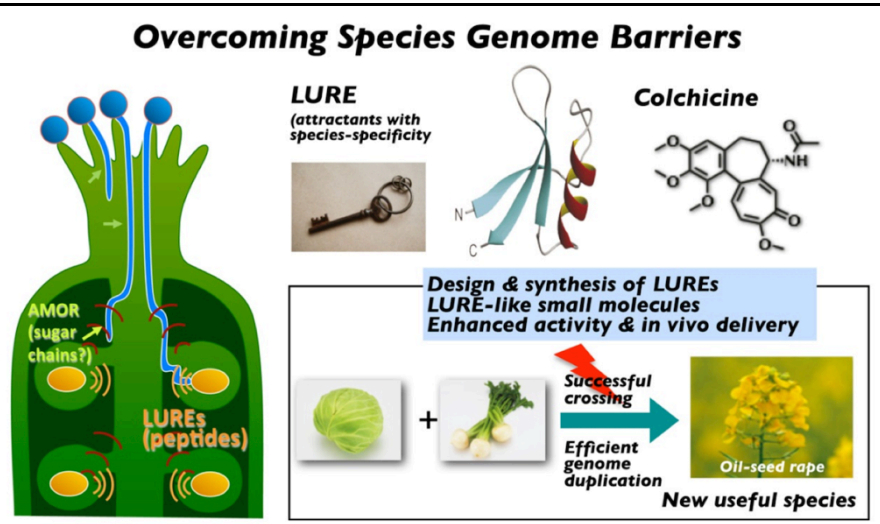


Molecules that overcome the genome barrier to produce novel crops

Higashiyama and his group have reported that fertilization of two female gametes of flowering plants, egg and central cells, were independently involved in the termination of pollen tube attraction. Along with this report, his research group demonstrated "hetero" fertilization, whereby the egg and central cells were fertilized by different pollen tubes. This phenomenon could be applied for overcoming genome barriers in endosperm development. Higashiyama's group has also showed that the molecules that induce "hetero" fertilization could be one of the targets for transformative bio-molecules.

Furthermore, Higashiyama has succeeded in the identification of two additional key signaling molecules along with LUREs.

In addition to investigating molecules related to pollen tube guidance, Higashiyama has developed a new technology, a microfluidic device, which can deliberately control plant fertilization.



II) Visualization of Biological Systems

(a) Targeting plant fertilization, embryogenesis, and animal season sensing
(b) Highly efficient, full-color fluorescent molecules
(c) Specific conjugation technologies for peptide labeling

II) Visualization of Biological Systems

<u>Highly efficient, full-color fluorescent molecule</u>

Yamaguchi and his collaborators have found triphenylborane derivatives that exhibit interesting multi-fluorescence properties, including dual emissions that change their ratio depending on temperature. Detailed studies based on time-resolved spectroscopy as well as quantum chemical calculations in the excited state were conducted in close collaboration with the Irle group to reveal that an unusual plane-to-bowl structural change in the excited state is the origin of these properties.

Yamaguchi has succeeded in synthesizing an anthraceneimide dimer that can demonstrate RGB three primary color emissions, namely, a blue emission in a polymer matrix, a green emission in a solution, and a red emission in the crystalline state. Systematic studies including the structure-property relationship study revealed the origin of this unusual behavior and provided a design principle for the molecule's multiluminescent properties. These classes of molecules are expected to have great potentials in various imaging applications.

The Yamaguchi group has continuously developed a series of phosphole oxide-based π-conjugated systems. Yamaguchi's group found that one derivative with an *o*-phenol moiety at the 2-position of the benzophosphole skeleton showed intense fluorescence <u>even in polar solvents</u>. Detailed studies on their application of these molecules to

bio-imaging is now in progress via a strong collaboration with the Higashiyama group.

Yamaguchi's multiluminescent flapping π system

Molecular Nanocarbons

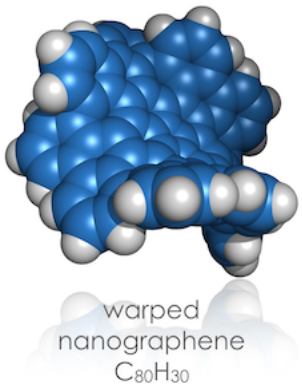
Synthesis of nanocarbons such as carbon nanotubes and graphenes still remain a science resulting in mixtures of molecules with a range of structures and properties. Itami and his collaborators are trying to address this Holy Grail in nanocarbon science through the development of the selective and controlled synthesis of structurally uniform nanocarbons. In 2013, Itami made significant progress toward this end. For example, Itami succeeded in the diameter-selective synthesis of carbon nanotubes using cycloparaphenylenes (CPPs; shortest segments of carbon nanotubes) as templates.

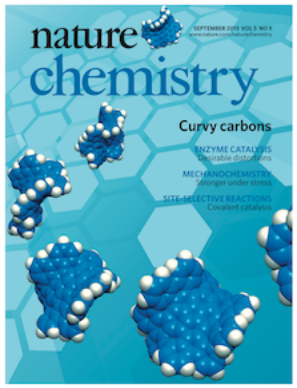
In addition to the controlled synthesis of carbon nanotubes (one-dimensional nanocarbons) and graphene nanoribbons (two-dimensional nanocarbons), Itami and his co-workers created a completely novel, three-dimensional curved nanocarbon (warped nanographene) that contains both positive and negative curvatures on its π-surface. These warped nanographenes have an uneven structure that is unique and clearly distinct from any other nanocarbon synthesized so far, and are expected to possess unprecedented functionality (such as solubility, fluorescent property, etc.).

III)Synthesis of New Bio-Functional Molecules

(a) Catalysts activating C-H bonds for direct transformations of bio-molecules
(b) Catalysts acting without heavy metals
(c) Catalysts for protein ligation

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



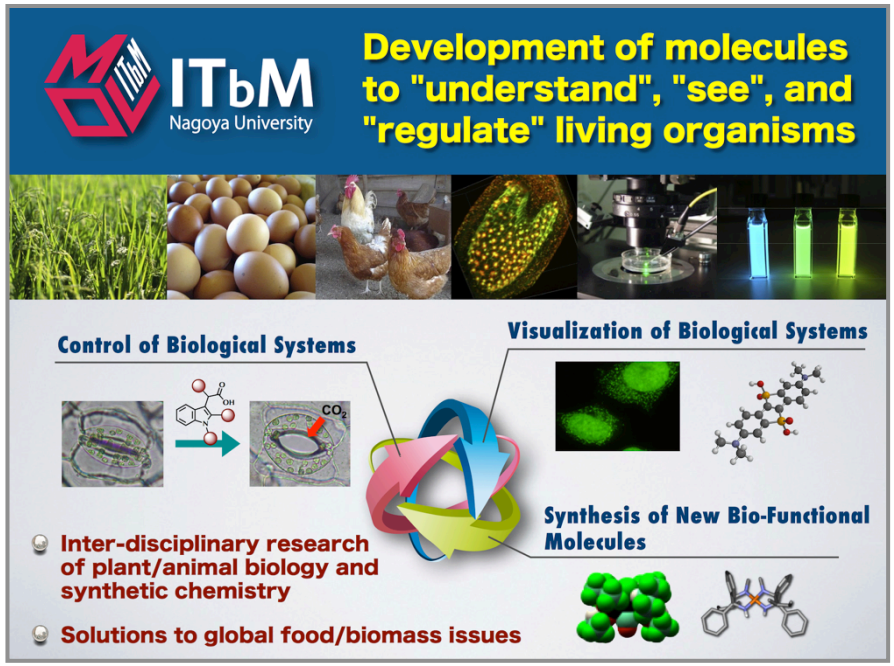


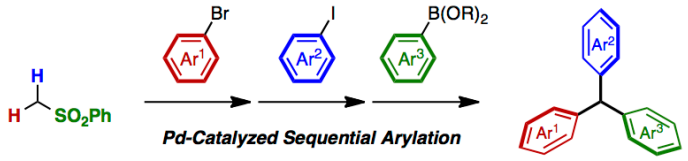
III) Synthesis of New Bio-Functional Molecules

Catalysts activating C-H bonds for direct transformations of bio-molecules

Representative achievements in the Itami group include (1) the development and mechanistic study of nickel-diphosphine catalysts for activating both C-H and C-O bonds, (2) the development of palladium-based catalysts for C-H coupling of hindered substrates, and (3) the development of site-selective C-H coupling of thiazoles realizing a programmed synthesis of all possible arylthiazoles. These catalysts were used in exploring plant/animal biology and creating nanocarbons.
One of the nickel catalysts (Ni-dcype) developed by Itami became commercially available from Kanto Chemicals from September 2013.

The Crudden-Nambo group developed a new method for the modular synthesis of triarylmethanes, which are valuable structures in materials and pharmaceuticals, through a palladium-catalyzed stepwise arylation of a methane derivative. With high functional group compatibility, readily available substrates and catalysts, they synthesized a variety of triarylmethane derivatives and prepared a small focused chemical library. This is being utilized to discover new biological functions at ITbM.

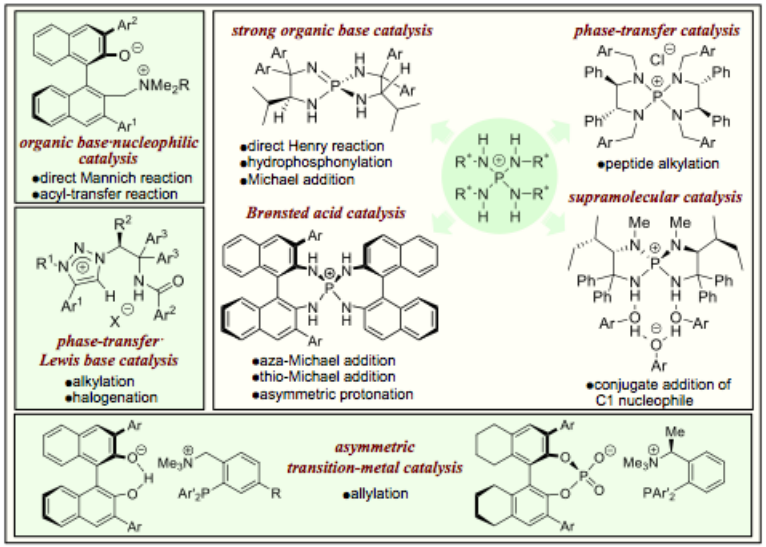




Modular synthesis of unsymmetrical triarylmethanes from readily available, bench-stable reagents

Catalysts acting without heavy metals

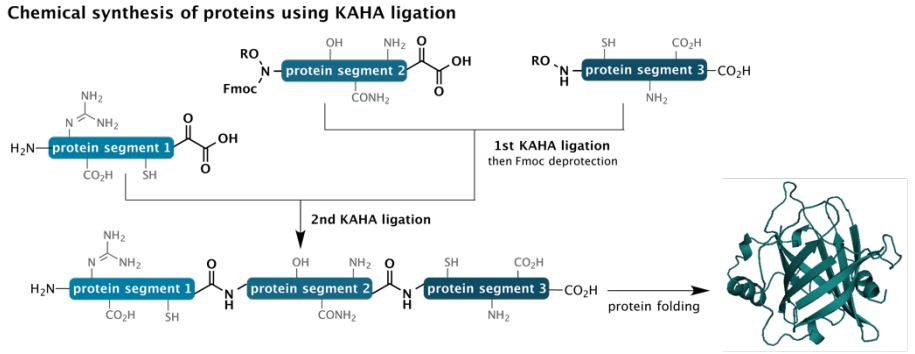
Ooi and his group reported the highly enantioselective oxidation of *N*-sulfonyl imines with their iminophosphorane catalyst. This is an excellent method for preparing chiral oxaziridine derivatives. Ooi and Ohmatsu have succeeded in the development of 1,2,3-triazolium salt catalysts. The synthetic utility of this catalytic protocol was clearly demonstrated in the concise asymmetric synthesis of a pyrrolidinoindole derivative, which is the ubiquitous core structure in a wide array of biologically relevant natural products. They also reported a novel approach for the asymmetric construction of contiguous all-carbon quaternary stereocenters via palladium-catalyzed [3+2] cycloaddition of oxazolidinones with trisubstituted alkenes.



Catalysts for protein ligation

The Bode group has developed a new amide-forming reaction of α-ketoacid and hydroxylamines (KAHA ligation) that enables the synthesis of proteins by combining peptide segments under aqueous conditions without the use of coupling reagents or side chain protecting groups. By using this method, Bode and his Co-PI Oishi were able to synthesize the LURE protein as well as its fluorescently labeled analogue. These synthetic proteins will be utilized to explore the yet to be known 3D structure of LURE, to understand structure-activity relationships in LURE, and spatiotemporal analyses for how pollen tubes are attracted. Bode's group has also succeeded in the synthesis of Nitrophorin 4 consisting of 184 amino acids.

Bode and Oishi have accomplished the synthesis of structural and activity defined fluorescence labeled LURE proteins with their original peptide formation reactions (KAHA ligation), to investigate complex signaling pathways of pollen tube guidance.



4. Management

<Plan at start of project >	<Results/progress/alternations from plan at start of project >
	At the start of the center on April 1, 2013, Nagoya University Trustee Yoshihito Watanabe, who was initially appointed as the Director of the Establishment Preparation Office in FY2012, assumed the post as the Administrative Director of the center. Also, the staff of the Establishment Preparation Office in FY2012 were reassigned as Administrative Department staff of the center.
1) Composition of administrative staff	1) Composition of administrative staff
i) The Administrative Director manages six units of administration: 1) general affairs unit, 2) accounting unit, 3) international promotion unit, 4) research administration unit, 5) public relations unit, and 6) environmental affairs unit, with the support of Associate Administrative Directors.	In FY2013, two Associate Administrative Directors (the Head of Management and the Head of Research Promotion) were assigned to support the Administrative Director. The Head of Research Promotion Tsuyoshi Matsumoto (Associate Professor) was also assigned as the Deputy Administrative Director to assist the work of the Administrative Director Watanabe who concurrently holds a position as the Trustee of Nagoya University.
ii) Two Associate Administrative Directors will be appointed. One is for internal affairs (to manage the general affairs unit and the accounting unit) and the other is for external relations (to manage the international promotion unit, the research administration unit, the public relations unit, and the environmental affairs unit).	**Management Division** Under the Head of Management, four full-time staff from Nagoya University (two competent English speakers included), four contract employees (three competent English speakers included) and one part-time employee were assigned to construct the framework of the Management Division (four staff in the General Affairs Unit and five staff in the Accounting Unit, including five English-speakers overall).
iii) Beneath the Administrative Director and the Associate Administrative Directors, a total of 18 experts will be involved in 6 units: 4 in the general affairs unit, 3 in the accounting unit, 3 in the public relations unit, 3 in the research administration unit (including 2 PhDs to support foreign PIs in their applications for Japanese domestic research grants), 3 in the international promotion unit (including 2 PhDs), and 2 in the environmental affairs unit. Each unit will have 1 unit chief.	**Research Promotion Division** Under the Head of Research Promotion Matsumoto (PhD in bioinorganic chemistry), Chief of Research Promotion Ayato Sato (Lecturer, PhD in synthetic chemistry and chemical biology), an Assistant Professor (PhD in organometallic chemistry), a science designer and a URA (University Research Administrator, PhD in inorganic chemistry; concurrent post) were assigned to the Research Promotion Division to conduct international promotion of research, research administration, public relations and outreach activities. Also, a contract employee who is a competent English speaker was
iv) A total of 15 bilingual laboratory secretaries will be assigned to assist the PIs. These secretaries will assist with paper work and matters regarding foreign researchers and students.	

	employed to support the daily living of non-Japanese researchers in the center. In addition to the five secretaries for Nagoya University PIs, one secretary to assist the three overseas PIs was assigned (total of four competent English speakers). On January 1, 2014, a year after being selected as a WPI center and nine months since the center's establishment, ITbM had a change in personnel for the Administrative Director. The Head of Research Promotion Matsumoto assumed the post of the full-time Administrative Director in the place of Nagoya University's Trustee Watanabe. The university supported this shift by ensuring the center's autonomy through establishment of the center's system. This has enabled the role of the Administrative Department to change its phase from establishment to organization of the research environment. Nagoya University has given approval for Nagoya University's Trustee Watanabe to continue to be involved in ITbM's administrative reform. Arising from this change in personnel, Sato, Lecturer at the Research Promotion Division has been appointed as the Head of Research Promotion. As of January 2014, the Research Promotion Division consists of the Head of Research Promotion, an Assistant Professor, a science designer, a URA (concurrent post) and a contract employee.
2) Decision-making system The Center Director will have the authority to make final decisions over the appointment of personnel, the Center budget and research priorities in addition to other matters as they arise. The Center Director needs to maintain good communications with the Administrative Directors and the PIs in the Center. To this end, we envisage establishing the following councils and committees. In order to ensure sufficient time for the scientific goals of the Center, **the number of meetings will be kept to a minimum.** i) **Joint Management Council** *Mission*: To discuss and to propose issues of fundamental importance to the Center	2) Decision-making system **Steering Committee** In FY2013, the Steering Committee, which integrates the Councils and Committees listed in ii) - iv) on the left, was held once a month to discuss and deliberate on important matters in the center including research plans, operation and management, personnel affairs and the budget. The Steering Committee is a place for discussion and provides advice to the Center Director to make final decisions. The Center Director conducts operation and management of the Center in consultation with the Steering Committee. Committee Members: Center Director, Vice-Center Director, Administrative Director, Head of

Members: The Center Director, the Vice Center Director, the Administrative Director, the Associate Administrative Directors, the President of Nagoya University, the Director-General of Nagoya University, any member of the International Advisory and Review Board, and/or the representatives of Cooperating Institutes may also be invited to join the Council Meeting.

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

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

iv) **Budget Committee**
Mission: To design a budgetary plan
Members: The Center Director, the Vice Center Director, the Administrative Director, the Associate Administrative Directors, and 2 members appointed by the Center Director selected from the PIs

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

Research Promotion, Five Nagoya University PIs, a Lecturer in the Research Promotion Division
Observers:
Three Co-PIs, Three Sub-Center Chief Coordinators

PI Meeting
The Center has launched a regular PI meeting in FY2013 to discuss research and major matters among all PIs. Overseas PIs also participate in all PI meetings through the TV conference system. The PI meeting is not only a place to discuss matters related to management of the center, but is also a place to discuss the progress of interdisciplinary research with young researchers. PI meetings play an indispensable role to discuss and determine the direction of the interdisciplinary research for the center.

Environmental and Safety Committee
As the center aims to create chemical compounds that affect plants and animals, as well as generate new plant and animal species, the Environmental and Safety Committee has been established to seek the counsel of experts for ITbM's research to be conducted competently while complying with the laws and regulations.

Mission:
To evaluate 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 Center Director.

Members:
One Nagoya University PI
- Toshinori Kinoshita, Director of Center for Gene Research, Nagoya University

Two Internal Experts within Nagoya University
- Director of Collaboration Office, Academic Research & Industry-Academia-Government Collaboration Office
- Professor of Jurisprudence, Graduate School of Law

Three External Experts outside Nagoya University
- Trustee/Vice-President of Okayama University
- Head of Natural Environment Division, Department of the

	Environment, Aichi Prefecture - Senior Councilor, Life & Bio Plaza 21 (NPO) **Other Committees** Concerning the Joint Management Council listed as i) in the left column, the Executive Board of Nagoya University will take the role of the Council for the time being, depending on the subject to be discussed. The Internal Evaluation Committee listed as v) in the left column is to be established in the second half of FY2014, including external experts outside Nagoya University in order to conduct an objective assessment of the center's research and the activities of each PI.
3) Allocation of authority between center director and host institution **The Center Director** The Center Director will have the authority to make the final decisions over the appointments of personnel, the Center budget, and research priorities in addition to other matters as they arise. To enable this, Nagoya University has taken the significant step of revising its rules in order to give executive authority to the director to make top-down decisions. Nagoya University will also reform its regulations to allow the Center the prerogative to establish its own system for pay structures, employment periods, and other preferential treatment such as the conferment of appropriate titles for its members including project managers and guest researchers. **Host Institution (Nagoya University)** The host institution has the authority and responsibility to allocate some part of the University budget for appropriate financial support of the Center. The host institution has the authority to inspect the management of the Center, and to audit the Center accounts.	3) Allocation of authority between center director and host institution As determined at the time of establishment, the Institute Rules limits the role of the President of Nagoya University only to the appointment of the Center Director. All matters concerning operations and management of the center 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 is the system to provide special bonuses to the Center Director, the Vice-Center Director, PIs, and the Administrative Director based on their performance and evaluations, the determination of eligible persons and amount of bonus is left to the discretion of the Center Director. The Executive Board of Nagoya University determines the bonus of the Center Director. The Administration Bureau of Nagoya University allocates the budget of the center, and the center has authority independent from other Schools of the university in the execution of its budget. However, the budget of the center is subject to internal and external audits as is the case with other budgets in Nagoya University.

5. Researchers and center staffs

i) "Core" to be established within host institution

Principal investigators

	At beginning	Final goal (Date: month, year)	Results at end of FY 2013	Results at end of April 2014
Researchers from within host institution	7	7	7	7
Foreign researchers invited from abroad	3	5	3	4
Researchers invited from other Japanese institutions	0	3	0	0
Total principal investigators	10	15	10	11

All members

- 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.
- In the "Administrative staffs" column, put the number and percentage of bilingual staffs in the ( ) brackets.

	At beginning	Final goal (Date: month, year)	Results at end of FY 2013	Results at end of April 2014
Researchers	20 < 5, 25% > [4, 20%]	70 < 35, 50% > [14, 20%]	53 < 21, 40% > [10, 19%]	50 < 20, 40 % > [10, 20%]
Principal investigators	10 < 3, 30% > [2, 20%]	15 < 5, 33% > [3, 20%]	10 < 3, 30% > [2, 20%]	11 < 4, 36% > [2, 18%]
Other researchers	10 < 2, 20% > [2, 20%]	55 < 30, 55% > [11, 20%]	43 < 18, 42% > [8, 19%]	39 < 16, 41 % > [8, 21%]
Research support staffs	10	40	19	23
Administrative staffs	10	20	11 (6, 56%)	11 (6, 56%)
Total	40	130	83	84

ii) Satellites <Plan at start of project > Satellite institutes are NOT applicable.	<Results/progress/alternations from plan at start of project> As initially planned, satellite institutes are NOT established.
iii) Partner institutions < Plan at start of project >	<Results/progress/alternations from plan at start of project> In addition to the three institutes stated on the left, ITbM has started partnerships with the following institutes: The Center for Selective C-H Functionalization (CCHF, National Science Foundation (NSF) Center, USA), Freiburg University (Germany), RIKEN Center for Sustainable Resource Science (CSRS, Japan).
Institution (1): Queen's University, Canada	Institution (1): Queen's University, Canada - Role Queen's University collaborates with ITbM as a host institution affiliated with Cathleen Crudden, an overseas PI, who is carrying out research to develop transformative bio-molecules through her research on novel molecular transformation catalysis. - Personnel composition and structure Prof. Cathleen Crudden (Double affiliation with ITbM and Queen's University) - Collaborative framework ITbM has employed one Co-PI (Assistant Prof. Masakazu Nambo) from March 2013 and three postdoctoral researchers to conduct research in close collaboration with Crudden at Nagoya University.
Institution (2): University of Washington, USA	Institution (2): University of Washington, USA - Role The University of Washington collaborates with ITbM as a host institution affiliated with Keiko Torii, an overseas PI, who is carrying out research to define key molecules for plant growth and to promote plant growth research using synthetic molecules. - Personnel composition and structure Prof. Keiko Torii (Double affiliation with ITbM and the University of

	Washington) - Collaborative framework ITbM has employed one Co-PI (Associate Prof. Naoyuki Uchida), three postdoctoral researchers and one technician during FY2013 to conduct research in close collaboration with Torii at Nagoya University.
Institution (3): ETH Zürich, Switzerland	Institution (3): ETH Zürich, Switzerland - Role ETH Zürich collaborates with ITbM as a host institution affiliated with Jeffrey Bode, an overseas PI, who is carrying out research to develop transformative bio-molecules using his novel method for polypeptide synthesis. - Personnel composition and structure Prof. Jeffrey Bode (Double affiliation with ITbM and ETH Zürich) - Collaborative framework ITbM has employed one Co-PI (Assistant Prof. Shunsuke Oishi), three postdoctoral researchers and one technician during FY2013 to conduct research in close collaboration with Bode at Nagoya University. During FY2013, Oishi and one postdoctoral researcher underwent training at the Bode laboratory in ETH Zürich. With their knowledge and experience from ETH Zürich, the exact same synthetic equipment and analytical devices were installed in the Mix-Lab to create a "clone lab" at Nagoya University. Institution (4): The Center for Selective C-H Functionalization (CCHF, National Science Foundation (NSF) Center, USA) - Role The CCHF was recently established as an NSF center, comprised of leading researchers in the USA working in the field of C-H activation chemistry. Since C-H activation chemistry constitutes an important area of ITbM's research, collaboration with CCHF is to promote research as well as internationalization. - Personnel composition and structure The following top leading 23 PIs and their research groups working in the field of C-H activation chemistry in 14 universities/institutes across

	the USA are members of CCHF partnered with ITbM: Emory University (Huw Davies, Simon Blakey, Cora MacBeth, Djamaladdin Musaev), University of Washington (Christine Luscombe), University of California, Berkeley (Richmond Sarpong), Stanford University (Justin DuBois, Richard Zare), University of California, Irvine (Brian Stoltz, Andy Borovik), University of California, Los Angeles (Ken Houk), The Scripps Research Institute (Donna Blackmond, Jin-Quan Yu), University of Utah (Matthew Sigman), University of Wisconsin at Madison (John Berry), University of Chicago (Jared Lewis), University of Michigan, Ann-Arbor (John Montgomery, David Sherman), Massachusetts Institute of Technology (Mohammad Movassaghi), Princeton University (Erik Sorensen), Georgia Institute of Technology (Stefan France, Christopher Jones, Seth Marder) - Collaborative framework Collaborative research is conducted between CCHF and ITbM through mutual exchange of researchers with each other's center. In order to send researchers to ITbM, CCHF makes a joint application with ITbM to the NSF to secure funds. On the other hand, ITbM sends researchers abroad through WPI funds. During FY2013, ITbM has received two researchers from CCHF. At this point, ITbM is planning to send two researchers and to accept three researchers and one faculty from CCHF during FY2014. ITbM is connected with CCHF through TV conferences, which are held on a regular basis. <u>Institution (5)</u>: Freiburg University, Germany - Role ITbM has collaborated with Freiburg University, which is Europe's main center for biochemical research. Through interaction and collaborative research with Freiburg University, ITbM aims to promote its research and internationalization. - Personnel composition and structure Prof. Gunther Neuhaus (Vice-President and Vice Rector for Research, Freiburg University), Freiburg University's researchers working in natural sciences including Prof. Hermann Grabert, Prof. Ralf Reski and Prof. Thomas Laux.

	- Collaborative framework Nagoya University's European Center is established in Freiburg and strong collaborative relationships already exist with Freiburg University. In addition, ITbM's Vice-Director Tetsuya Higashiyama and Minako Ueda (Lecturer) have started collaborative research in plant biology with Freiburg University. ITbM's PI Takashi Ooi has already published papers with Freiburg University in the area of synthetic chemistry. Based on these achievements, ITbM will conduct further collaborative research in biochemistry and chemistry with Freiburg University. In March 2013, the president and vice-president of Freiburg University arrived at ITbM to discuss research and potential areas for collaboration. ITbM's researchers and the Administrative Director will visit Freiburg University in June 2014 to hold a joint symposium and initiate collaborative research. <u>Institution (6)</u>: RIKEN Center for Sustainable Resource Science (CSRS), Japan - Role Based on the following three keywords, "plant science", "chemical biology" and "chemistry" that are common to both centers, ITbM and CSRS will interact effectively to generate new interdisciplinary research. - Personnel composition and structure Prof. Kazuo Shinozaki (CSRS Center Director) and researchers of CSRS - Collaborative framework CSRS Center Director Kazuo Shinozaki was invited as a speaker at ITbM's international symposium in April 2013. ITbM's Center Director Kenichiro Itami presented a special lecture at RIKEN CSRS opening symposium in October 2013. In addition, Itami serves as an evaluation committee member of the CSRS. As part of the partnership, ITbM participated in the UK-Japan Workshop "Rhizosphere Interactions – towards Global Food Security" sponsored by the British Embassy and RIKEN.

6. Summary of center's research environment

< Plan at start of project >

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

Mix-Lab System

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

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

Co-supervising system

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

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

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

<Results/progress/alternations from plan at start of project>

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

Mix-Lab System

Through the establishment of "Mix-Labs", ITbM continues its challenge to achieve extensive mixing of different disciplines. This approach is different from conventional collaborative research and joint seminars in the sense that chemists, biologists and theoreticians share the same space and work side by side in the lab. Through daily discussions ranging from simple practical questions to sophisticated research hypotheses, innovative ideas that arise from young researchers enable the propagation of new research fields. In these "Mix-Labs", many interdisciplinary research themes to create new molecules have arisen from among various combinations of PI group members, e.g. Itami-Kinoshita, Kinoshita-Ooi, Crudden-Yoshimura, Higashiyama-Bode, Yamaguchi-Higashiyama-Irle, Torii-Yamaguchi, and Yoshimura-Itami. These new research projects are aimed at elucidating biological phenomena and to discovering new functional bio-molecules.

In order to realize new areas of research and to promote further mixing, personnel of the Research Promotion Division attends all ITbM seminars to cover ITbM's research. In addition, ITbM's researchers attend seminars of other PIs groups to share and exchange ideas from different perspectives. Some of the informal meetings held by young researchers have evolved into regular seminars, involving many researchers including students. For example, the "Mix-Plant" seminar, which mainly consisted of plant biologists, now involves chief coordinators of the three sub-centers (see below) to cooperate efficiently and accelerate ITbM's research. This enables the chief coordinators to understand the latest research in the plant field and suggest necessary methods accordingly.

In order to promote interdisciplinary research, the ITbM Research Award was established. This provides an opportunity for young faculty members, postdoctoral researchers and students to write research proposals and obtain funding for their research. In October 2013, the first round of selection for the ITbM Research Award was held, which has led to the discovery of promising areas for interdisciplinary research.

smooth operation of analytical instruments etc.
In order to reduce the educational and administrative burden of PIs, the University will furnish the original faculty of PIs with additional staff (a total of 7 associate professors).
A total of 15 bilingual secretaries will be assigned to the PIs in 2013 to help the Investigators cope with their paper work and any matters regarding foreign researchers and students in the groups.

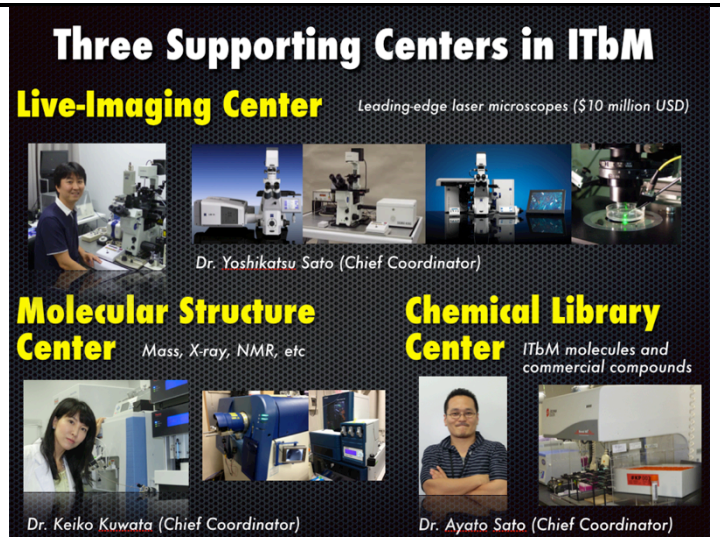
ITbM Mix-Lab Concept

Researchers and students from different fields work together in one big lab

Establishment of 3 Sub-Centers

In order to support the cutting-edge research of ITbM, the following three sub-centers were set up: Chemical Library Center, Molecular Structure Center and Live-Imaging Center. Chief coordinators were appointed for each center in March, April and May 2013.

1. Chemical Library Center
   This center was launched at the end of FY2013 and has started distributing compounds to ITbM researchers and cooperating researchers.
2. Molecular Structure Center
   The latest mass spectrometers, NMR machines and a high performance X-ray diffractometer were installed, which supports the omics research of ITbM.
3. Live-Imaging Center
   This center was established by expanding upon Nagoya University's imaging center through installation of large-scale microscopes. It has started to function as a national hub for imaging, utilized by researchers from within Japan and abroad (47 national, 1 international).



Strengthening the activity of the Research Promotion Division

The Research Promotion Division supports ITbM's research through organizing symposia/seminars, carrying out international public relations, outreach activities and providing daily support to foreign researchers and their families. In FY2012, the Research Promotion Division consisted of an administrative director, chief and a university research administrator (URA; concurrent post). Three additional personnel were recruited and employed at the Research Promotion Division to support ITbM's activities. All personnel have experience abroad in countries including Canada, Singapore, UK and USA, with the ability to communicate effectively in both English and Japanese.

(1) Science Designer

A science designer was considered relevant to carry out public relation activities and was recruited through the internet using SNS tools including Twitter and Facebook. Twitter was successful in finding Haruko Hirukawa who was then studying science design in the USA and also had previous experience in studying biology. Employment of personnel with science designing skills has enabled effective outreach activities and communication of ITbM's research using visual tools, which greatly improves the visibility of the center.

Journal of Computational Chemistry
Volume 34, Issues 29-30, 2013

Angewandte Chemie
Volume 53, Issue 3 Pages 601–887
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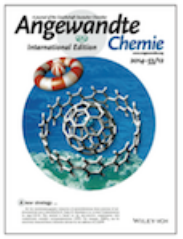
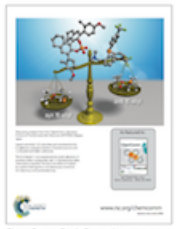
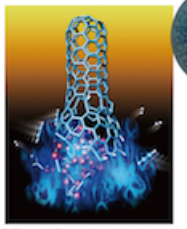
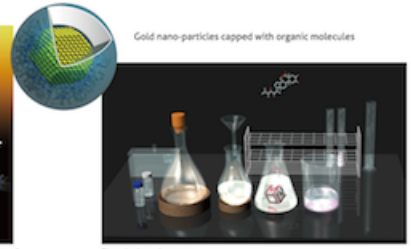
Chemical Science
Volume 5, Number 4, April 2014



Angewandte Chemie (Inside Back Cover)
Volume 53, Issue 12, page 3281,
March 17, 2014


ChemComm Back Cover, Issue35, 2014


CNT growth (Press release, May 31, 2014)



Chemical equipments

(2) International Public Relations Officer

In order to effectively communicate ITbM's research outcomes and activities to journalists around the world, it was necessary to establish a route to distribute news internationally. Conventional approaches for distributing press releases have relied on Nagoya University's public relation's office, which is mainly directed towards the national media. Ayako Miyazaki who obtained her PhD in the UK, specializing in synthetic/organometallic chemistry and chemical biology, was recruited as an Assistant Professor to devise strategies to build ITbM's international network and promote science communication. Three international press release services (EurekAlert!, Science Media Center and ResearchSEA) were implemented to distribute ITbM's research activities to the international audience. This has enabled the international distribution of ITbM's press releases accompanied by science design artwork, which has contributed to improving the international visibility of ITbM.

(3) Administrative Assistant to provide daily support to foreign researchers

The Research Promotion Division employed Hanae Tsuchiya with a science background, as an administrative assistant to support the daily

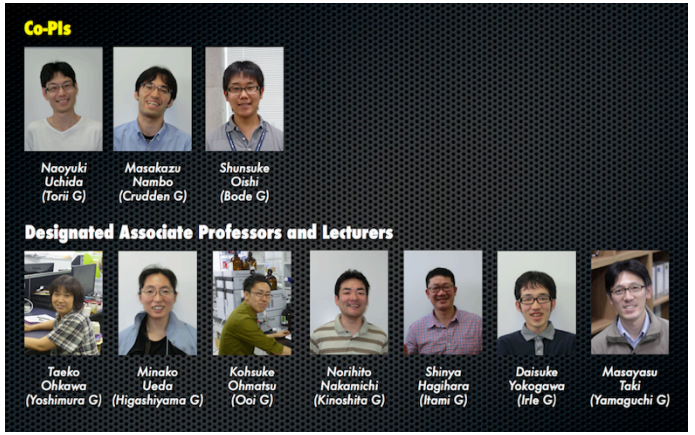
lives of foreign researchers and their families. This includes support for immigration, finding accommodation, registrations at city council and banks, accompaniment to hospitals along with providing advice for daily life in Japan. Educational support is also provided for foreign children to help them enter local public schools in Nagoya. Although internationalization in Nagoya is ongoing, much of the support has been in Chinese, Korean, Portuguese, and Filipino with limited correspondence in English. Therefore, ITbM established a network with Nagoya University and Nanzan University to provide linguistic support in English and Japanese for young children of foreign researchers. Liaisons with Nagoya city and Aichi prefecture's Board of Education are also in place to help the children of foreign researchers to attend local schools.

Employment of Associate Professors and Lecturers

In order to enable Nagoya University's seven PIs to focus on their research, Nagoya University gave their approval to employ seven Associate Professors and Lecturers to give lectures and handle educational affairs in the place of the PIs. Recruitment was started from FY2012. Three faculty members were employed in April 2013 and the remaining four faculty members were also employed during FY2013.

2) Startup research funding

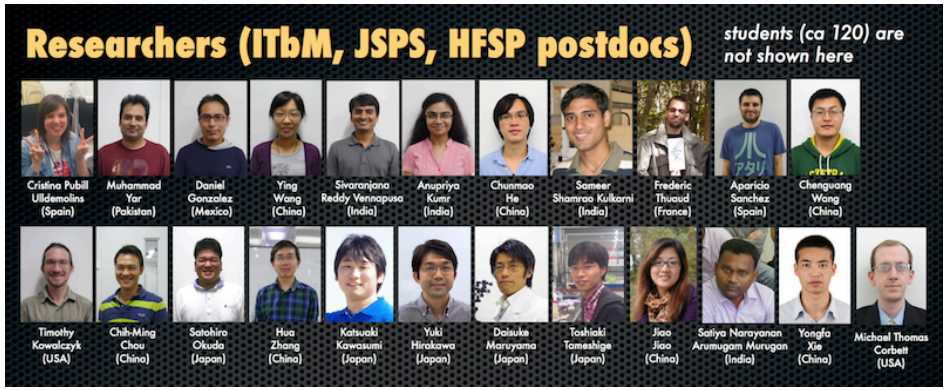
We will provide each of the new researchers with research space and start-up funds with an average value of $125,000 USD. If necessary, the start-up money will be increased for top-caliber researchers by using a discretionary budget allocated to the Center Director.
We will furnish the new researchers with full access to instruments in the Center. Except for the start-up funds, all of the following costs are covered by our Center: lab spaces fee, utility costs including electricity and water fees, employment costs of two postdoctoral researches, one secretary, and one technical staff.



Employment of Technicians and Secretaries
In order to support ITbM's research, six technicians were employed in FY2013.
In addition, five secretaries with good fluency in English were employed in April 2013 and one secretary with good English competence was employed in July 2013 to assist the three overseas PIs.

2) Startup research funding

Communal equipment to conduct Mix-Lab's interdisciplinary research were purchased and installed. A high performance computer was also purchased in the server room to conduct theoretical calculations. In addition, large equipment was purchased for the three sub-centers (refer to Section 12). To support the start-up of the research at ITbM for overseas PIs Crudden, Bode and Torii, ITbM provided 3 million yen to each overseas PI, which includes their costs to travel and stay at ITbM. To promote research activities for groups of young researchers, the ITbM Research Award was established, which provides an opportunity to apply for research grants twice a year. The first selection of awards was carried out in October 2013 and 2 million yen/2 years was granted to the successful projects.

3) Postdoctoral positions through open international solicitations We will engage in high-profile recruitment campaigns to attract highly qualified postdoctoral researchers using web sites with global appeal describing the current efforts of the Center, University, and Nagoya City for internationalization. We will keep channels open to world premier chemists and biologists, and solicit their recommendations for suitable candidates as postdoctoral researchers.	3) Postdoctoral positions through open international solicitations Open recruitment for postdoctoral researchers (one year contract, renewal up to three years) was announced on the ITbM website. Positions were also announced on international websites including Nagoya University, PI's websites, as well as the careers websites of Science, Nature and JREC-IN. In addition, recruitment flyers were distributed at the WPI presentation held at the AAAS Annual Meeting 2013 in Boston (USA). There were 103 applicants, including 25 female applicants from 23 countries around the world. Amongst the applications, eight foreign researchers were successfully recruited. Seven additional postdoctoral researchers were recruited through the website and through recommendation of candidates from the network of prestigious chemists and biochemists from around the world, to make a total of 15 postdoctoral researchers at the center. ITbM will continue its recruitment to secure talented researchers. 
4) Administrative personnel who can facilitate the use of English in the work process The research groups of the PIs are international in outlook, and have excellent track records in inviting foreign researchers as visiting professors, postdoctoral researchers, and exchange students. English is routinely used in their research groups. Not only our WPI Center but also all of Nagoya University is internationalized as Nagoya University has started the Global 30 International program to accept foreign undergraduate and graduate	4) Administrative personnel who can facilitate the use of English in the work process Personnel fluent in English and with thorough experience in handling administrative affairs were employed in the General Affairs and the Accounting Unit of the Management Division. In addition to their regular jobs related to administration, the administrative staff were actively involved in ITbM's international symposia, which were held twice in FY2013. Daily notifications from the university are sent out to ITbM researchers in both English and Japanese. This initially included grants and

students (all of classes and experimental courses are taught in English). The G30 students are also in the laboratory of the PIs. The Administrative Director is fluent in English, and the projected administrative staff will also have high English skills.	funding information. Nagoya University gradually realized the importance of this endeavor, and the university administration office took over this process and started to send grants and funding information in both languages from the end of FY2013.
5) Rigorous system for evaluating research and system of merit-based compensation	5) Rigorous system for evaluating research and system of merit-based compensation
A rigorous evaluation of researchers will be made by an external evaluation committee, with the assistance of the International Advisory and Review Board. The annual salary of researchers hired from outside the host institute will be adjusted based on the evaluation. There will also be a merit-based fringe benefit system for internal hires.	Special bonuses are provided to the Center Director, the Vice-Director, Nagoya University PIs and the Administrative Director based on their performance and evaluations. They will receive full bonuses during the starting period of the project (January 2013 to March 2014), and the amount will vary according to their evaluation in FY2013, from FY2014 onwards. ITbM plans to set up an evaluation committee including external experts during FY2014 to evaluate the research activities of the center as well as the PIs. All ITbM researchers submit an activity report regarding their research activity for the previous fiscal year in April. After evaluation by the evaluation committee, the Center Director will reflect the results to the special bonuses for that year. As for postdoctoral researchers, evaluation will be carried out by each PI followed by a secondary evaluation by the Center Director, which will be reflected in the renewal of their contract.
6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center	6) Equipment and facilities, including laboratory space, appropriate to a top world-level research center
Nagoya University will provide 6,000 m^2 of research space for the Center. The Science and Agricultural Building and Science South Building are regarded as the premier global facilities, and 3,000 m^2 of the building space will be allocated to the WPI Research Center. These two buildings, which are directly connected, were built in 2011 to accelerate the collaboration of science and agriculture research within Nagoya University. A brand-new live-cell imaging center space of 300 m^2, which was originally part of our G-COE program and will be further developed by our WPI program, is also in the Science South building. A teatime room of 70 m^2 will also be placed in the Science and Agricultural Building to facilitate communication among members of our WPI	Nagoya University has provided 5,165 m^2 of research space for the center, which contains 2,165 m^2 of new space on top of the existing 3,000 m^2 of space designated to Nagoya University PIs. In order to install new equipment, an additional 58 m^2 was allocated to the center in FY2013. Hence, Nagoya University provided a total of 5,223 m^2 of research space to ITbM during FY2013. Upon appointment of Steve Kay of the University of Southern California (USA) as an overseas PI from FY2014, 134 m^2 of new space will be allocated to accommodate his research group. The new building for ITbM is to be finished by the end of FY2014. The design for the building was proposed at the end of FY2012 and was finalized at the beginning of FY2013. Construction of the building started from the end of FY2013. The total area of the new six-floor building will be

Center. Nagoya University will provide additional laboratory space of 1,500 m^2 by the end of FY2012, and the other 1,500 m^2 as soon as possible As also noted in the host institution's commitment, Nagoya University will draw up a plan of further allocation of space and a new building for gathering not only activities of the WPI Center but also other organizations relating to the field of our WPI Center. Nagoya University will provide financial support for maintaining the research environment at a world-class level including the enforcement of appropriate safety measures. Nagoya University is very well equipped with top-level major instruments necessary for our WPI research. The quality and number of these instruments rivals the best institutions in the world. The following lists representative instruments that can be used by our WPI research team.	approximately 7,000 m^2 and is designed to incorporate the "Mix-Lab" concept. Lab space and office space will each consist of two floors and are designed to become a huge open-spaced "Mix-Lab", which removes the conventional barriers between research groups. This is expected to accelerate the interdisciplinary research of ITbM. There will also be childcare space for researchers and visiting researchers accompanied by small children, enabling them to keep a good balance between their research and families.
7) International research conferences or symposiums held regularly to bring world's leading researchers together A large-scale international research conference will be organized each year, primarily at Nagoya University. A limited number of international workshops of a small-to-medium size will be organized each year. For the first year of the Center, the 1st international research conference is scheduled at the end of FY2012 in March 2013. In Japanese universities, such international meetings are usually managed mainly by researchers, including administrative matters. However in our WPI Center, the Administrative Office directed by the Administrative Director and Associate Administrative Directors will manage meetings according to the decision of the subject, candidates of invited speakers, and schedule of each meeting by PIs, in order to avoid further encroachment on researcher's time.	7) International research conferences or symposia held regularly to bring world's leading researchers together To celebrate the launch of ITbM, the first international symposium of ITbM (ISTbM-1) was held in April 2013. Lectures were presented by ITbM's ten PIs and by eight invited speakers, who are all world-class international researchers working in life science systems, biochemistry, synthetic chemistry and theoretical science, which are fields strongly related to ITbM's research. As a result of building close relationships between ITbM's PIs and the invited speakers, ITbM was able to start collaborations with the Center for Selective C-H Functionalization, an NSF center led by Director Prof. Huw Davies of Emory University (USA) and RIKEN's Center for Sustainable Resource Science (CSRS) led by Center Director Prof. Kazuo Shinozaki of RIKEN (Japan). This symposium was fully organized by the Administrative Department, and the administrative staff also chaired the symposium. The symposium was a great success with over 400 participants including attendees from MEXT, JSPS, President of Nagoya University Michinari Hamaguchi and Professor of Nagoya University, President of RIKEN and Nobel Laureate Ryoji Noyori.

In memory of Nagoya University's late Emeritus Professor, Yoshimasa Hirata, the 10th Yoshimasa Hirata Memorial Lecture was held in February 2014. Prof. Martin Burke of the University of Illinois (USA) who was selected as the 10th Hirata award winner spoke along with special speakers, Prof. Yoshito Kishi of Harvard University (USA), Prof. Justin DuBois of Stanford University (USA), and Prof. Daisuke Uemura of Kanagawa University (Japan). This symposium was also organized by the Administrative Department and also ended with great success.

8) Other measures, if any As our foreign PIs are truly world-leading scientists, we are confident that they can maintain their excellent funding profiles in the future. However, there are special challenges to carrying out research in Japan for foreign PIs, in particular access to information only in Japanese, when they seek competitive funding in Japan. We wish to strongly encourage PIs and Co-PIs to become actively involved in the procurement of external funding from Japanese sources, therefore, the Center will provide **a support team**, which will collect Japanese information and translate application documents (Japanese to English and English to Japanese). The team in the research administration unit includes two PhD administrators from chemistry and biology fields. To facilitate both domestic and international research collaboration by our foreign PIs, the Center and Nagoya University will establish a more efficient and flexible administrative structure to process travel expenses and acceptance of outside researchers. The Center and Nagoya University will provide opportunities for partners/spouses to hold positions in the University on the basis of proper evaluation (Dual Career Support). Nagoya University will give priority to the principal and collaborative researchers in assigning university accommodations. In addition, the WPI Center will collect and provide information on international education opportunities, which are increasingly developed in Nagoya City, for the children of overseas researchers. Nagoya University established a nursery in its campus (as a part of the program to support female employees and researchers), and it will accept the children of foreign researchers at the Center. Nagoya University is very well equipped with top-level major instruments necessary for our WPI research. The quality and number of these instruments rivals the best institutions in the world. We will hire some expert operators and computer programmers for these facilities, which includes 5 postdoctoral researchers. They will strongly support the leading-edge research by the foreign PIs and other researchers.	8) Other measures, if any (1) Conclude Memorandum of Understanding (MOU) with partner institutions In FY2012, ITbM's Research Promotion Division visited ETH Zürich, Howard Hughes Medical Institute / University of Washington, and Queen's University to discuss the MOU with the board of directors, administrative director and intellectual property officer of each institute. As a result, MOUs were concluded to allow the employment of the three overseas PIs as part-time lecturers and visiting professors at Nagoya University. The MOU for intellectual property with partner institutes is also under negotiation. In FY2013, the MOU for intellectual property was concluded with ETH Zürich, and the Howard Hughes Medical Institute / University of Washington. The final version of the MOU with Queen's University is under construction and is planned to finalize by the end of FY2014. ITbM has exchanged MOUs with Center for Selective C-H Functionalization (CCHF) in March 2013 and further negotiations are currently undergoing. (2) Arrangements for overseas PIs to apply for external grants from FY2014: MOUs were concluded with Nagoya University appointing the three overseas PIs as visiting professors to become eligible to apply for grant applications in Japan. With the support from Co-PIs and the Administrative Department, the overseas PIs submitted application forms for the KAKENHI Grants-in-Aid for Scientific Research in autumn 2013. Two projects were selected as Scientific Research B and one project was selected as Scientific Research on Innovative Areas in April 2014. In addition to the KAKENHI, ITbM is collaborating with Nagoya University's URA to collect information and support the application for other research grants and supporting funds. (3) Setting up the environment to accommodate overseas PIs, foreign researchers, and researchers with children at Nagoya University. Appointment of the three overseas PIs as visiting professors of Nagoya University gives them priority to stay at Nagoya University's accommodation facilities during their time at ITbM. ITbM has also negotiated with international schools near Nagoya

Nagoya University has grasped the opportunity offered by being selected to host numerous Global-Centers of Excellence and the Global-30 program both to accelerate globalization of its campus and to promote high-level international research. In addition, we have implemented the mid- and long-term mutual exchange of doctoral students and young faculty members, as exemplified by the very successful "International Research Training Group (IRTG)" Program with the University of Münster (FY2005-2011). This program was followed by another Strategic Young Researcher Overseas Visits Program for Accelerating Brain Circulation, "Innovative Molecular Catalysis and Novel Functional Materials" (FY2011-2014). The Center will take full advantage of these international programs to ensure active international research activities.	University to allow the short time entry of an overseas PI's child. Liaisons have also been carried out with local public schools to accept the entry of international children from abroad. Arrangements have been made with Nagoya University so that foreign researchers can use the university's accommodation facilities, and university rules have been revised so that they can stay in the accommodation facilities for up to two years (initially one year before changing the regulations). Since the number of university facilities able to accommodate foreign researchers is still limited, ITbM's Associate Administrative Director has been attending working groups within the university to increase these facilities. (4) Promotion of ITbM's international research activities utilizing Nagoya University's international programs: Nagoya University is currently conducting international programs including the Japanese-German Graduate Externship program, and ITbM is continuously working along with this program to promote international collaborative research and to improve the international visibility of ITbM through building of networks. (5) Scientific outreach activities by PIs and the Research Promotion Division ITbM's PIs and the Research Promotion Division are carrying out lectures and supervision of experiments at high schools as part of ITbM's outreach activities. As a result of these activities, many of the newly enrolled students who attended Nagoya University's fresher's orientation were already aware of the word "transformative" and the presence of Center Director Itami, which gives a good indication for the growing visibility of the center. The Research Promotion Division was involved in the invitation and organization of the "24th UK Science Experiment Seminar / 2013 Christmas Lecture" at Nagoya University. In addition, Ayato Sato of the Research Promotion Division played a main role in the operation of the Tokai region's Chemistry Grand Prix, which is the Japan preliminary contest of the Chemistry Olympics. He will also serve as the chair of the FY2014 Chemistry Grand Prix. The Research Promotion Division provided supervision to students of

	Sendai First High School, who were to give a presentation on their research at the WPI Joint Symposium (December 2013). Along with Center Director Itami's inspiring lecture at the symposium, ITbM was selected as the center with the top impression amongst the students. ITbM's collaboration with Sendai First High School is to continue in FY2014.

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

< Plan at start of project >	<Current assessment>
The global standing of the Center depends firstly on the performance of the individual researchers, and we will use a set of quantitative metrics combined with more qualitative methods to assess the performance of individual researchers and their contributions to the Center. We consider there are three aspects important to the global standing of the WPI: 1) **research quality and impact**, 2) **breakthrough from the interdisciplinary research activities**, and 3) **human resources development**.	
1) Publishing our work in top journals is absolutely required. The number of papers published in top journals will be counted for evaluation. A selection of such data for our PIs clearly indicates we have a group of outstanding individuals that together will give our Center a very high global profile. Highly cited work is clearly an indication of high quality research and a significant impact. Citations can be quantified by bibliometrics such as total citations, citations per paper, and h-index. ***Total number of papers cited more than 80 times (10 PIs): 86*** These types of bibliometrics will be gathered for the researchers and used in evaluation throughout the life of the Center. Two more important indicators of research quality and impact are success in obtaining external funding and the number of invited lectures at international conferences and these will also be monitored.	1) Research quality and impact The Research Promotion Division uses Thomson Reuter's Researcher ID and EndNote to monitor and manage research publications of the Center. During the calendar year of 2013, 96 papers were published in peer-reviewed journals. As of April 2014, 39 papers are already published in peer-reviews journals. From January 1st to December 31st, 2013: **Number of papers**: 96, with 46 papers published in journals with an Impact Factor (2012) > 7 and 31 papers published in journals with an Impact Factor (2012) > 10. This includes papers whose authors are not noted in the institutional affiliations as WPI-ITbM. **Plenary and invited lectures in international symposium:** 99

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

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

Awards and Honors: 16

- Kenichiro Itami (Center Director, PI): The Aldrich Lectureship Award, The JSPS Prize, Novartis Chemistry Lectureship Award, Mukaiyama Award, Asian Rising Star Award
- Tetsuya Higashiyama (PI): Hirase Award 2013
- Takashi Ooi (PI): Inoue Prize for Science
- Takashi Yoshimura (PI): Animal Science Journal Excellent Paper Award
- Jeffrey Bode (PI): Fellow of the Royal Society of Chemistry
- Cathleen Crudden (PI): The Aldrich Lectureship Award, The Keith Fagnou Memorial Lectureship, Distinguished Speaker, Annual Beckman Scholars and Young Investigator Symposium
- Kohsuke Ohmatsu (Associate Prof.): Chemical Society of Japan Lecture Award for Young Chemists
- Norihito Nakamichi (Associate Prof.): Japanese Society of Plant Physiologists Young Investigator Award
- Masakazu Nambo (Assistant Prof., Co-PI): Inoue Research Award for Young Scientists
- Shunsuke Oishi (Assistant Prof., Co-PI): 2013 Reaxys PhD Prize Finalist

Patent applications: 9 (6 domestic, 3 overseas)

2) Breakthroughs from the interdisciplinary research activities will be monitored and evaluated by number of joint papers by PIs from chemistry and biology fields. Grants and patents resulting from collaboration of PIs from chemistry and biology fields will be also monitored.
We have already begun some interdisciplinary collaborations, which are expected to be published in the initial phase of our WPI program.

2) Breakthroughs from the interdisciplinary research activities

Two special laboratories called "Mix-Labs" were established in the existing buildings to achieve mixing/merging of chemists, biologists and theoreticians. The ITbM Research Award was established to promote ITbM's interdisciplinary research and to enable young researchers to independently conduct their own research. For each research project, 200 million yen/2 years was awarded. Four projects are currently in progress at ITbM.

Other projects are also underway at ITbM's PI groups and Sub-Centers.

Since the selection of the center as a WPI program, ITbM's ten research groups have been publishing their high impact research in many prestigious journals (over 100 papers since the launch of the center, including 6 papers in Nature Chemistry, 6 in Nature Communications, and 1 in the Proceedings of the National Academy of Sciences, USA). In addition, these research outcomes have been covered over 100 times in a range of national and international media including newspapers, TV, magazines, journals and internet sites.

The collaborative projects have officially started from April 2013. Some of the research has already been filed for patents.

3) The development of human resources is key to the future development and global standing of the Center. To evaluate our progress, we will use indicators such as the career paths and academic success of former researchers of the Center and the flow of visitors to and from other international institutions. Six Japanese PIs from Nagoya University have been involved in many international exchange programs and already have good track records of exchanging researchers. In the

3) Development of human resources

As of May 2014, ITbM has sent five researchers abroad and have accepted three researchers from its international partner institutes. ITbM will continue to carry out international exchange of approximately 10 researchers/year with its partner institutes.
The career path for researchers is also assumed as a measure for human

last three years alone, they have welcomed ***75*** foreign visitors and arranged for ***85*** students and researchers to be sent abroad. The number of student awards garnered will be also monitored as an important evidence of nurturing the next-generation. For example, the prospective Center Director Itami has produced a number of talented young chemists who have been recognized in the community. Our focus on quantitative measurements of achievements reflects a worldwide trend in the evaluation of research. However, we are also aware that some aspects of research cannot be easily quantified. The importance of truly original contributions may not be recognized immediately and citation numbers may not directly reflect the quality of research. In using research metrics to assess the performance of individual researchers, it is important to take into account their age and career stage. In addition, because our Center will consist of researchers from diverse fields, we will also be conscious of the ways in which these metrics may be influenced by different research styles and conventions in different fields. We will, therefore, establish an Internal Evaluation Committee consisting of directors, PIs and administrative directors to evaluate research activity within the Center. These results will be used together with the recommendations of the International Advisory and Review Board to carry out a rigorous evaluation of the Center and PIs by an external evaluation committee.	resource development of the center. In FY2013, four researchers were promoted as follows: researcher in overseas research institution (2) (one researcher will be promoted in May 2014), JSPS postdoctoral fellow (1), JSPS postdoctoral fellow for foreign researchers (1), Assistant Professor in the YLC Program at the Institute of Advanced Research, Nagoya University (1). PIs of the ITbM have been invited as speakers in many international institutes and ITbM has invited 17 overseas lecturers to the center in FY2013.

8. Securing competitive research funding

<Plan at start of project > Prospects for securing resources for each fiscal year (full-year basis) - Salaries of PIs who hold posts at Nagoya University, Administrative staff and new hired additional researchers 1.4 million USD / year - Partial support to the costs of utility, maintenance and renovation of laboratory and office space, provided by Nagoya University 0.8 million USD / year	<Results/progress/alternations from plan at start of project> Nagoya University pays the salaries for Nagoya University's seven PIs, four administrative staff and seven faculty members associated to Nagoya University's PIs. The university provides financial aid to cover partial costs for utilities, maintenance and renovation of the building, which follows the initial plan and brings about good progress in building the research center. - Competitive funding acquired by Nagoya University's PIs in FY2013 **Sum: 1,141 million yen** (increase of 216% compared to FY2012)

- Competitive funding based on the past record by PIs 7.7 million USD / year (the average of FY 2007-2011) **Sum: 9.9 million USD / year** * At least the following amount of Japanese grants has been already acquired by PIs: the total amount of **5.5 million** USD / year for the first (FY 2012) and the second (FY 2013) years, and the total amount of **4.0 million** USD / year for the third (FY 2014) and the fourth (FY 2015) years.	Breakdown of competitive funding obtained in FY2013 ・ NEXT (3; Itami, Ooi, Yoshimura): 107 million yen ・ ERATO (2; Itami, Higashiyama): 797 million yen ・ CREST (2; Yamaguchi, Ooi): 88 million yen ・ ALCA (1; Kinoshita): 23 million yen The center will continue to acquire new competitive funding in FY2014 onwards.

9. Other important measures taken to create a world premier international research center

<Plan at start of project >	<Results/progress/alternations from plan at start of project>
Nagoya University has recently launched the Graduate School of Pharmaceutical Science in cooperation with Graduate Schools of Science, Bioagricultural Sciences, Engineering, and Medicine. The central area of Japan, represented by Nagoya City, is very famous as the industrial center of Japan. The establishment of the Graduate School of Pharmaceutical Science in Nagoya University was based on strong demand from industrial community. The achievements of our WPI Center will be directly applied through the activities of Nagoya University and Nagoya City. Thus profound ripple effects are expected not only in Nagoya University but also in other research institutions in central Japan. To establish a truly top world-level research center, the commitment of the host institution is essential. In particular, setting up an efficient and effective administration is crucial. The benefits to the research goals of the Center through assisting the researchers to concentrate on their core research activities cannot be overestimated. In addition, appointing talented individuals, who are capable of handling administration with a global view, is also an essential ingredient to establishing a truly world premier research center. The word "transformative" implies that our molecules will also make a marked change in human society. Thus another important measure is how novel products based on our molecules and resultant new plant species developed by overcoming reproductive barriers are spread and recognized	As stated in the previous sections, the Administrative Department consists of experienced staff with good correspondence in both English and Japanese. Two more English competent speakers were employed in April 2013, who prepare meeting documents and grant information in both English and Japanese and also served as MCs at international symposia. Their ability to communicate effectively with foreign researchers has enabled ITbM to function smoothly as an international center. Led by the Administrative Director, the Administrative Department is composed by the Management Division and Research Promotion Division, which work collaboratively and provide full support for the research activities at ITbM. The transformative molecules generated by ITbM's research will be communicated and announced through research publications, press releases and at meetings/conferences. ITbM also plans to distribute these molecules to research institutes and industries in order to extend their application and become molecules that can potentially change the society in a positive manner. Improving the international visibility of ITbM's research is of high significance to be established as an international research center. As ITbM's research consists of developing molecules that change the biological systems of plants and animals, it is extremely important for the contents of the research to be communicated precisely. It is equally

by the general public.	important for the public to correctly understand the environmental and safety issues associated with ITbM's research. 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. This year, ITbM carried out two large public outreach events. Academic lectures were held during Nagoya University's homecoming day inviting Nobel Laureate and Nagoya University's Emeritus Professor, Osamu Shimomura who spoke about his work on Green Fluorescent Protein (GFP), which is a molecule closely linked to the research goals of ITbM. Center Director Kenichiro Itami and PI Takashi Yoshimura also gave talks about their research at ITbM in front of more than 200 public attendants. Booths exhibitions and posters were also presented to introduce ITbM's research to the public. On March 21, 2014, Vice-Director Tetsuya Higashiyama spoke about the nature of flowers at Nagoya University's open lecture to the public. He described in detail about new breeding methods of plants along with his research at ITbM to generate new plant species through overcoming genome barriers.

10. Host institution's commitment

<Plan at start of project > -Provision in host institution's mid-to-long-term plan Nagoya University promotes its research activities based on our *Midterm Objectives*, which include establishing world-leading research centers. In addition, the manifesto of the incumbent President—also known as the "*Hamaguchi Plan*"—identifies the strong promotion of world-class research and the globalization of NU as top priorities. This proposal for *the ITbM* (hereinafter referred to as *"the Center"*) coincides wholly with the current conception of NU. If this proposal is adopted, NU will amend its *Midterm Plans* and *Research Promotion and Strategy Plans* to specify the WPI and the Center, and fully commit to providing support for the Center based on clear objectives. - Concrete Measures (1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc. i) NU endorses the fully committed financial support for the Center that	<Results/progress/alternations from plan at start of project> -Provision in host institution's mid-to-long-term plan Nagoya University has amended its mid-term plans by adding the following statement "Establishment of core research centers by promoting the projects including the "World Premier International Research Initiative" and the "International Science Innovation Center Development Project (COI)" and continuing the promotion of ITbM's research in FY2013. In addition, the Hamaguchi Plan of Nagoya University specifies that "Establishment of the World Premier International Research Initiative (WPI) – Institute of Transformative Bio-Molecules" for the promotion of world class research. -Concrete Measures (1) Competitive grants obtained by researchers participating in the project and in-kind contributions, etc. Nagoya University covers the salaries of Nagoya University's seven PIs,

is larger than the support from WPI. ii) NU will continue to cover the equivalent amount of the salaries of those researchers at the Center who already hold posts at NU, and will provide 6,000 m^2 of the research space for the Center. Additional space will be given according to the progress of the research. iii) The total sum of competitive funding for those researchers at the Center who already hold posts at NU is $5.9 million (in FY2012), and receipt of competitive funding at an equal or greater level is promised from FY2013 onwards. iv) To help with the establishment and smooth operation of the Center, NU will assign 4 staff to the center and cover their salaries as well as employing new bilingual staff. (2) System under which the center's director is able to make substantive personnel and budget allocation decisions i) NU will reorganize the Institute of Advanced Research, which is established as an institute independent from the other departments and research centers, and will place the Center as part of the Institute. ii) NU will support the Center Director in his leadership and give full mandate for his decisions on important matters such as personnel and the execution of the Center's budget. iii) In addition, the Vice Director and Administrative Director will make decisions depending on the matter, to avoid placing an excess burden on the Center Director and enable the progress of daily work at the Center. (3) Support for the center director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments	seven associate professors/lecturers and four administrative officers. The university continues to provide 5,165 m^2 plus an additional 58 m^2 adding to a total of 5,223 m^2 research space for the center. The total amount of competitive funding for Nagoya University was approximately 528 million yen for FY2012. Arising from the success of Center Director Kenichiro Itami starting the ERATO project and young Co-PIs acquiring grants, the competitive funds for FY2013 doubled to 1,141 million yen. Moreover, overseas PIs have gained KAKENHI grants in FY2014, hence securing sufficient funds for research. At the beginning of FY2013, the Administrative Department has appointed ten administrative staff (four are staff from Nagoya University) to the Management Division (General Affairs and Accounting units), which includes staff competent in English. The Research Promotion Division consists of five members who can correspond in English, including one Nagoya University URA jointly affiliated to ITbM. (2) System under which the center's director is able to make substantive personnel and budget allocation decisions Nagoya University has established the center based on the basic philosophy of the Institute for Advanced Research of Nagoya University, which is "promotion of the world's most advanced project research". Nagoya University has authorized the Center Director to manage and make decisions on important matters of the center. In addition, Nagoya University has established rules for the center such as Steering Committee Rules, which enables the Center Director to exercise strong leadership in the center concerning important matters such as personnel and execution of the budget (details in Section 4. Management), while authorizing the Administrative Director to make decisions accordingly, for the Center Director to be exempt from excessive work. (3) Support for the Center Director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments

i) NU will assign 7 associate professors, who will mainly take charge of education in each department to relieve the PIs of this responsibility, and to maintain high-level education. ii) NU will give priority to female researchers at the Center to enable their children to enter the nursery school operated by NU. iii) NU will support foreign researchers at the Center in their daily life and the education of their children, making full use of facilities and knowledge base which has been obtained through the operation of international projects such as the "Global 30 Internationalization Program (G30)" and "CAMPUS Asia Support for the Formation of a Core Center", and so on. iv) NU will provide opportunities for partners/spouses of foreign PIs to hold positions in NU on the basis of proper evaluation (Dual Career Support).	・ Nagoya University has employed seven associate professors/lectures to carry out educational activities in place of Nagoya University's seven PIs. ・ To support the progress of the center, a second Vice-Director Shigehiro Yamaguchi will be appointed in April 2014 to lead the chemistry field of research, alongside the current Vice-Director Higashiyama who will lead the biology field. ・ Children of female researchers are granted the opportunity to apply for entry to international schools outside the university. ・ The Research Promotion Division has assigned staff to provide support to foreign researchers and their families during their stay at ITbM.
(4) Revamping host institution's internal systems to allow introducing of new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation i) NU will give full mandate to the Center Director for a flexible management system by implementing the Center as a "Special Research Zone", and by introducing ground breaking working rules and salary system which give the researchers and staff extra allowance to encourage their activities. ii) NU will gradually implement the Center's trial across the entire university in order to give other researchers and staff incentives to apply.	(4) Revamping host institution's internal systems to allow introducing of new management methods (e.g., English-language environment, merit-based pay, top-down decision making) unfettered by conventional modes of operation ・ Nagoya University has established "Implementation Guidelines for the Special Bonus for Persons in the Service of Nagoya University Institute of Transformative Bio-Molecules" in FY2012, which is the system to provide special bonuses to the Center Director, Vice-Director, Nagoya University PIs and the Administrative Director based on their performance and evaluations. ・ All members of the Research Promotion Division and more than half of the Management Division are competent in English. The Management Division translates notifications on administrative affairs in English. This is considered a highly technical skill, which is reflected in the relatively high salaries of contract employees.
(5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.) i) NU commits to accommodate the Center with research space equivalent to 6,000 m^2.	・ As grants and funding information from the university were initially provided in Japanese, these were translated into English by the ITbM administrative office. The host institution realized the importance of these endeavors and subsequently, the university administration decided to take over this activity and started to distribute grants and

ii) 7 PI candidates who work for NU already occupy approximately 3,000 m^2. NU will provide additional 1,500 m^2 by the end of FY2012, and the other 1,500 m^2 as soon as possible. iii) NU will rearrange and relocate the facilities of the existing departments and centers, and will establish the Center's core facility, making it possible to collaborate intensively with the researchers of other departments and research centers. iv) NU will reauthorize the University's Facility Management Plan and will make the Center's core facility a top priority. (6) Support for other types of assistance i) <u>NU has decided to assign a member of the Board of Trustees/Vice-President as the Administrative Director to bridge the gap between the Center and the University's headquarters</u>. ii) The Administrative Director will organize a team with his two associates and keep the administrative office active enough to enable the Center's research activities at a maximum performance. Two associates are: Associate Administrative Director for Management who is a high-level expert of administration affairs, and Associate Administrative Director for External Relations who has strong expertize in chemistry related science, with a good command of English. iii) We recognize one of the important aspects of WPI is to accelerate system reform of Japanese universities such as deregulation, internationalization, and so on. Intensive commitment of NU's leadership to the Center is critically important to accelerate the system reform in not only the Center but also the entire university.	funding information in both English and Japanese from the end of FY2013. ・ Nagoya University's Institute for Advanced Research and COI programs are following the footsteps of ITbM and have started to incorporate ITbM's system and activities in their programs, such as employment of foreign researchers, Co-PI system, and incentive-based salary systems. (5) Accommodation of center's requirements for infrastructural support (facilities, e.g., laboratory space; equipment; land, etc.) ・ Nagoya University continues to provide 5,165 m^2 of space at the beginning of FY2013. An additional 58 m^2 was allocated at the end of FY2013 adding to a total of 5,223 m^2 research space for the center. At the beginning of FY2014, 134 m^2 of research space will be provided to accommodate the new overseas PI Steve Kay's research group. ・ Towards the end of FY2014, Nagoya University is planning to provide 1,000 m^2 of space, which will be connected to ITbM's new building. This space will be shared with schools related to ITbM, including the School of Science to promote further collaboration. (6) Support for other types of assistance ・ The Administrative Department is comprised of the Management Division dealing with administrative/accounting affairs and the Research Promotion Division consisting of scientists to promote ITbM's research. This enables interactive communication between the management staff and faculty to enhance the job performance on both sides. ・ During the launch of the center, Nagoya University's Trustee Yoshihito Watanabe served as the Administrative Director who liaised and coordinated with the university's executive board. Through these endeavors, the center's management system and guidelines were built. As of January 2014, Watanabe stepped down as the Administrative Director and Research Promotion Director Tsuyoshi Matsumoto took the place of the Administrative Director. Watanabe continues to be involved with ITbM as a Trustee and coordinates with the executive board.

11. Efforts to improve points indicated as requiring improvement in application review and results of such efforts

- Major points to be improved	- Efforts to improve them and results
The following points were recommended in the Follow Up Report in FY2013.	ITbM's response to the recommendations is stated as follows.
1. Although the Program Committee has suggested increasing the number of animal/pharmaceutical researchers, the Working Group advises that achieving a balance between plant and animal researchers is not a high priority but that ITbM focuses on plant biology as an institutional strategy.	1. One of ITbM's strengths is in plant science and there are many well-known researchers at Nagoya University working in this field (some of the researchers are already cooperating with ITbM). On the other hand, ITbM considers integration of plant and animal science to be a highly unique area of research. Currently, research on the circadian clock is one of the core projects at ITbM. In order to accelerate this research, Steve Kay of the University of Southern California (USA) who is one of the world leaders in biological clock research was invited to talk at ITbM in March, 2013 and has been appointed as an overseas PI to join ITbM from April 2014. His group is currently screening molecules to control the circadian clock of mammals, which is expected to build upon ITbM's research in animal biology. Associate Prof. Tsuyoshi Hirota who has been working with Kay is to be assigned as a Co-PI, and his expertise in animal science is expected to enhance interdisciplinary research with plant science and synthetic chemistry.
2. The mission of ITbM states that is should become a novel institute for the discovery, development and production of transformative bio-molecules. Although ITbM presented a roadmap towards reaching this mission, it needs clarity and refinement. ITbM should continue to focus on groundbreaking fundamental research and the identification of opportunities to benefit society, including collaboration with pharmaceutical and agricultural researchers.	2. As indicated in the roadmap presented at the WPI program committee 2013, ITbM is currently targeting the following molecules and is conducting research to discover and create lead compounds. ・ Molecules that control the growth of plants ・ Molecules that control the reproduction of animals ・ Peptide molecules that overcome the genome barrier of species ・ Molecules that control the biological clocks of plants ・ Molecules that control the reproduction of plants ・ Molecules that control sudden mutation of plants ・ Molecules that mimic animal hormones ・ Molecules that control the cell cycle ・ Small fluorescent proteins ・ Fluorescent peptides that control plant growth ・ Small fluorescent molecules for super-high resolution microscopy In parallel to synthesizing lead molecules, ITbM is conducting

	collaborative research with its cooperating researchers. In the research on plant growth, PI Toshinori Kinoshita determined the factor controlling plant growth and has started collaborative research with cooperating researchers in Nagoya University's Department of Agriculture. This research is expected to lead to development of molecules to solve social problems such as food production and carbon dioxide emissions.
3. The Working Group recommends hiring computer and/or theoretical scientists to complement and advance research on transformative bio-molecules.	3. As indicated at the 2013 WPI program committee, ITbM currently involves many theoretical chemists. In addition, ITbM is collaborating with Nagoya University's Structural Biology Research Center to elucidate the structure of proteins and is conducting structure optimization based on structure activity relationships.
4. ITbM is recommended to make good use of a unique opportunity to train a new generation of national and international researchers in synthetic chemistry, biology and computational science.	4. As indicated at the WPI program committee 2013, the Center for Selective C-H Functionalization (CCHF, NSF center, USA) has become a partner institution of ITbM. CCHF consists of 23 research groups across 14 universities in USA carrying out extensive research in the fields of synthetic chemistry, medicinal chemistry, and theoretical chemistry. Based on intense support from NSF, ITbM has started exchange of researchers (students and faculty) between NSF. ITbM is expecting an annual exchange of over 10 researchers with NSF along with invitation of faculty to carry out courses at ITbM. In addition to ITbM's PI groups, Nagoya University's eight research groups (from the School of Pharmaceutical Sciences, Science, and Engineering and Bioagricultural Sciences) are also participating in this exchange program. IBS (Korea) and Catalysis@Cambridge (UK) are also expected to become involved in this program. Following conclusion of agreement with Freiburg University (Germany), Nagoya University is also starting exchange programs and collaborative research, in which ITbM will also be involved.

12. FY2013 Funding

(the exchange rate used:)

i) Overall project funding

1 million yen

Cost Items	Details	Costs (1 million yen)
Personnel	Center Director and Administrative Director	23
	Principal Investigators (no. of persons): 9	75
	Other researchers (no. of persons): 33	137
	Research support staff (no. of persons): 8	9
	Administrative staff (no. of persons): 33	57
	Total	301
Project activities	Gratuities and honoraria paid to invited Principal Investigators (no. of persons): 0	0
	Cost of dispatching scientists (no. of persons): 4	2
	Research startup cost (no. of persons): 20	207
	Cost of satellite organizations (no. of satellite organizations): 0	0
	Cost of international symposia (no. of symposia): 2	3
	Rental fees for facilities	10
	Cost of consumables	4
	Cost of utilities	0
	Other costs	10
	Total	236
Travel	Domestic travel costs	3
	Overseas travel costs	10
	Travel and accommodations cost for invited scientists (no. of domestic scientists): 6 (no. of overseas scientists): 13	7

WPI grant for FY2013	609
Costs of establishing and maintaining facilities in FY2013	0
Establishing new facilities: Institute of Transformative Bio-Molecules (Number of facilities: 6,400m²) Costs paid:	0
Repairing facilities (Number of facilities: , m²) Costs paid:	0
Others	0
Cost of equipment procured in FY2013	678
Name of equipment: Analysis Equipment (Server) Number of units: 1Set Costs paid	10
Name of equipment: Mouse Facility Number of units: 1Set Costs paid	12
Name of equipment: Growth Chamber Number of units: 1Set Costs paid	3
Name of equipment: High Performance Liquid Chromatography Number of units: 1Set Costs paid	16
Name of equipment: Isolera Dalton System Number of units: 1Set Costs paid	10
Name of equipment: Multi Preparative High Performance Liquid Chromatography Number of units: 1Set Costs paid	5
Name of equipment: Femtosecond Laser System Number of units: 1Set Costs paid:	25
Name of equipment: High Resolution Quadrupole Time-of-flight Hybrid Mass Spectrometry System Number of units: 1Set Costs paid	7
Name of equipment: Representative Diversity Set Number of units: 1Set Costs paid	90
Name of equipment: Molecular Analysis System Number of units: 1Set Costs paid	288
Name of equipment: Molecular Imaging System Number of units: 1Set Costs paid	184
Name of equipment: Fully Automated Peptide Synthesizer Number of units: 1Set Costs paid:	28

	Travel cost for scientists on secondment (no. of domestic scientists): 3 (no. of overseas scientists): 7	5
	Total	25
Equipment	Depreciation of buildings	0
	Depreciation of equipment	180
	Total	180
Other research projects	Projects supported by other government subsidies, etc.	244
	Commissioned research projects, etc.	515
	Grants-in-Aid for Scientific Research, etc.	187
	Total	946
Total		1688

ii) Costs of Satellites and Partner Institutions

Cost Items	Details	Costs (1million yen)
Personnel	Principal Investigators (no. of persons):	
	Other researchers (no. of persons):	
	Research support staff (no. of persons):	
	Administrative staff (no. of persons):	
	Total	0
Project activities		
Travel		
Equipment		
Other research projects		
Total		0