World Premier International Research Center Initiative (WPI)
Executive Summary (For Extension Application Screening)

Host Institution	Nagoya University	Host Institution Head	Seiichi Matsuo
Research Center	Institute of Transformative Bio-Molecules	Center Director	Kenichiro Itami

Instruction:
Based on the Center's Progress Report and Progress Plan, prepare this summary within 6 pages.

A. Progress Report of the WPI Center

I. Summary

ITbM was launched at Nagoya University (NU) as a unique research institute to develop innovative functional molecules "transformative bio-molecules" that make a marked change in the form and nature of biological science and technology. By taking full advantage of our cutting-edge molecular synthesis expertise and intense interactions with leading plant/animal biology research, ITbM has been conducting 'needs-inspired' basic research and explored new research areas of "plant chemical biology", "chemical chronobiology", and "chemistry-enabled live imaging".

The achievements of 2012.11-2019.3 (papers: 2012.11-2018.12)

- Journal publications: 770 peer-reviewed papers (191 papers = IF>10; 313 papers = IF>7; 51 Highly cited papers (Top 1%); 6 Hot papers (Top 0.1%),
  Nature x 5, *Science* x 7, *Cell* x 4, *Nature/Science sister journals* x 63)
- Awards and honors: 129
- Patent application: 120 (incl. 41 cases co-filed among several PI groups)
- Patent license agreement: 32
- Collaborative research with industries: 72
- Commercialization of molecules/catalysts: 15
- Spin-off ventures: 2 companies
- Total sum of external research funds: 7.45 billion yen

The synergy of ITbM researchers' high research profile and the new research style at ITbM has facilitated interdisciplinary research at a pace more rapidly than initially expected. ITbM's "Mix Labs" that mixes different disciplines has been highly effective, and has led to the development of a number of new bio-functional molecules and molecular technologies. The ITbM Research Award, established to promote interdisciplinary research proposed by young researchers, has accelerated collaborations in a bottom-up manner and most of the proposals have been making good progress to mature into ITbM's representative projects. Many of the research outcomes have been filed for patents and published as joint publications between different research groups. Their societal implementation is also in progress as represented by the development of molecules to combat parasitic plants *Striga*. ITbM launched a membership discussion forum "ITbM Consortium" in 2017 to provide matching opportunities with industries.

ITbM has been extending its global network to further advance its interdisciplinary research via extensive collaboration through researcher exchange. With the cutting-edge research outcomes, ITbM is now widely recognized as an international research hub of chem-bio research. ITbM is positioned as a flagship research institute of NU, and has induced system reforms of NU. In 2018, a new graduate program was launched with ITbM as a core, and ITbM will work proactively in nurturing PhD students who can pioneer new science at the interface of multiple disciplines.

ITbM has now become truly exciting and internationally visible institute where new interdisciplinary research fields emerge and new molecules are born every day. ITbM's unique "Mix" culture has led researchers from different fields to work together, take risks, think/act differently, thereby finding unique problems and solutions, discovering something new, and providing unique solutions to key global problems. Researchers world-wide have recognized the strength of ITbM. Our dream of changing the world with molecules is clearly bearing fruit, but the challenge continues.

II. Items

1. Overall Image of Your Center

ITbM has gathered top-researchers from the different disciplines including synthetic

chemistry, plant biology, animal biology, and theoretical sciences under one roof, who have been carrying out interdisciplinary research through extensive collaboration. In the 7 years, ITbM has grown to a size of 200 people including 13 PIs, 63 researchers, 62 support staff, and many PhD students. ITbM has also been proactive to appoint female researchers. Including three female PIs, 19 female researchers are on staff at ITbM, making up 25% of total researchers.

In order to mix the people to promote interdisciplinary research, ITbM installed Mix Labs and Mix Offices, where researchers and students from different fields discuss on a daily basis. This style has significantly promoted bottom-up interdisciplinary projects among young researchers. ITbM also installed "soft" measures to promote interdisciplinary research such as ITbM Research Award, which significantly accelerates collaborations in a bottom-up manner.

Collaboration with partner institutions is also a key to promote interdisciplinary research. ITbM's target ID platform is being developed through collaboration with RIKEN Center for Sustainable Resource Science (CSRS) and Institute of Chemistry (IoC) at Academia Sinica, Taiwan. International collaboration has also contributed to enhance the ITbM's internationalization and international visibility. ITbM has been proactive to organize outreach events and make international press releases, which also resulted in receiving world-wide recognition of ITbM.

2. Advancing Research of the Highest Global Level

Research Activities

ITbM has been promoting 'needs-inspired' basic research to develop transformative bio-molecules that make a marked change in the form and nature of biological science and technology. ITbM has also pioneered a new molecular nanocarbon science using its state-of-art synthetic chemistry, which will be a new pillar of ITbM in the future. Selected achievements are summarized below.

Development of molecules toward combating *Striga*: The parasitic plant *Striga* has been causing huge damage on crop production in Africa. ITbM has been tackling to provide molecular solutions to the food security in Africa. The fluorescent probe molecule "Yoshimulactone" Green (YLG) was developed, which enabled disclosure on the mechanism of germination and elongation of the *Striga* parasite. Researchers have also identified strigolactone receptors in *Striga* by the use of YLG, which further led to the development of *Striga* germinator sphynolactone-7 (SPL7). SPL7 has two functional modules, which cooperatively acted on the specific strigolactone receptor, and activated it with a high-affinity to provoke *Striga* germination with potency in the *femtomolar* (10^{-15} molar) range. The SPL7 is effective for reducing *Striga* parasitism on practical crop (maize) without impinging on host strigolactone-related processes. To test these molecules in environmentally challenged fields, ITbM starts collaboration with KALRO to bring them into societal implementation.

Discovery of key molecules that regulate plant reproduction: Following the discovery of the long sought pollen tube attractant molecules LURE, ITbM has identified anew two key biomolecules AMOR and CALL1 that control plant fertilization. The AMOR is a sugar chain molecule that increases the fertilization efficiency. Interestingly, the essential part of the AMOR was proved to be a disaccharide unit via structure-activity relationship study. This is a quite interesting finding because any specific sugar-chain unit of plant extracellular matrix has not been identified as a bioactive molecule.

Recently the target protein of the LURE has been identified and the structure was elucidated by the crystallographic analysis. The discovery of a series of biomolecules is expected to lead to advances in research to improve plant fertilization efficiency.

Molecular control of stomatal development and movements: ITbM has developed small molecules that enable stomatal control through an extensive mechanistic investigation and a screening of the chemical libraries. Accordingly, a series of molecules that have enhanced the number of stomata in *Arabidopsis thaliana* have been developed. The stomatal opening/closing mechanism was also investigated, which reveals that the stomatal aperture is a limiting factor of photosynthesis and plant growth. Several molecules that can control stomatal movements have also developed, which include those accelerate stomatal opening/closure and restrict stomatal dynamics reversibly. The stomatal closing molecules have prevented plant leaves from drying-up and suppress withering when sprayed onto the plants.

Molecular control of biological clock: A number of potent molecules controlling the animal/plant biological clocks have been discovered. Based on the identification of the target proteins, X-ray crystal structures, and evaluation of biological functions, some of the discovered molecules are under further investigation with pharmaceutical companies. Researchers have also demonstrated that modulation of the plant biological clock by molecules may lead to the development of an optimized variety of crops.

Using drug-repurposing approach, molecules that can either shorten or lengthen the circadian rhythm in human cells have been developed. DHEA (dehydroepiandrosterone), which is a hormone also known as a common anti-aging supplement, demonstrated notable period-shortening activities. When DHEA was fed to mice, jet lag symptoms were significantly reduced. Further screening of known bioactive compounds may lead to the discovery of other effective compounds that can treat circadian clock disorders arising from jet lag. In the study of seasonal clock, medaka fish was found to show different behavior upon seasonal changes, and the reason was revealed as that the genes encoding photopigments vary dynamically among seasons. It was also suggested that plasticity in color perception is crucial for the emergence of seasonally regulated behaviors.

Imaging molecules: ITbM has developed molecules that exhibit exceptionally high resistance to photobleaching that can accelerate cutting-edge and super-resolution bio-imaging such as STED microscopy. Researchers have also developed molecules that exhibit high responsive property to environment polarity and have discovered near infrared emissive phospha-fluoresceins. These super high performance molecules are commercially available and expected to serve a significant role in leading the bio-imaging field. Indeed, the molecule named as PREX 710 can be used to stain mitochondria in living cells, which allowed long-term and multi-color imaging in the vis-NIR range. The PREX 710 exhibits the high fluorescence longevity and applicable to a single-molecule microscopy under physiological conditions.

Catalysis and rapid molecule synthesis: ITbM has established epoch-making synthetic methodologies that allow rapid synthesis and modification of biologically active molecules. These include next-generation cross-coupling catalysts, C-H coupling catalysts, asymmetric reactions, and rapid peptide/protein synthesis. For example, Ooi has developed a new reaction to directly install amines into carbonyl compounds using their unique phase-transfer catalyst. This unprecedented method leads to the rapid formation of optically active (chiral) α-aminocarbonyls, which are structural moieties found in many biologically active compounds. These synthesis technologies have been applied to ITbM's interdisciplinary research, and towards developing candidate molecules for medicines and agrochemicals.

Molecular nanocarbons: Chemists have tried to synthesize carbon nanobelts for more than 60 years, but none have succeeded until now. Itami has reported the first organic synthesis of a carbon nanobelt. Carbon nanobelts are expected to serve as a useful template for building carbon nanotubes and open a new field of nanocarbon science. Itami has also developed a fast way to form nanographenes in a controlled fashion. This simple and powerful method for nanographene synthesis could help generate a range of novel optoelectronic materials and biological applications.

Societal implementation of the research outcomes

ITbM has strategically created a wide range of networks consisting of domestic/international industries toward societal implementation of the research outcomes. As summarized above, ITbM has filed 120 patent applications, and its 34% have been derived from the interdisciplinary researches between chemistry and biology. Base on the patents, 2 ITbM-based ventures have also launched and 15 molecules are commercially available as tool reagents for researches. For example, LipiDye, a novel fluorescent dye that stains the lipid droplets located in cells with high sensitivity, has widely spread to not only academia but industries including medical, pharmaceutical, agrochemical and cosmetic companies. ITbM concluded the license agreement of SPL7, which induces suicide germination of *Striga* and has decided to commercialize as a reagent for researchers. SPL7 is expected to be utilized as an agrichemical application in Africa and other countries.

ITbM has been conducting many collaborative research projects with companies and has concluded 25 MTAs to further promote the societal implementation. To create the opportunities for academia-industry partnership, ITbM launched a membership discussion forum "ITbM Consortium" in 2018, where 'Seeds' and 'Needs' meet each other.

3. Generating Fused Disciplines

Under the strong leadership of the Director, all members at ITbM have been working beyond their discipline and developing interdisciplinary research spanning chemistry, plant/animal biology, and theoretical sciences toward making transformative molecules. ITbM has defined three flagship research areas as 'plant chemical biology', 'chemical chronobiology', and 'chemistry-enabled live imaging', and has been exploring the research projects via extensive collaboration of chemistry and biology.

ITbM's interdisciplinary research has been making significant progress under the "Mix" concept, and the center's initiatives to promote interdisciplinary research have been effective so far. The ITbM Research Award, established to foster interdisciplinary collaboration among young researchers and students, was granted to 4 new projects in FY2017. The ITbM Workshop and Tea

break Meeting are also providing opportunities to find new partners and seeds for collaboration. These initiatives are organized by the Administrative Department of ITbM, in which the Research Promotion Division (RPD) and the Strategic Planning Division (SPD) are playing key roles. ITbM's 4 supporting centers (Molecular Structure Center, Live Imaging Center, Chemical Library Center, and Peptide Protein Center) are also making a major contribution to the promotion of ITbM's interdisciplinary research through their technical support.

The synergy of ITbM researchers' high research profile with the new research style at ITbM has facilitated interdisciplinary research, and has resulted in a number of innovative achievements that can never be obtained without extensive interactions of the different disciplines. The success of the interdisciplinary research is represented by the joint publications and patents. So far, 49 papers and 41 patents are co-authored by multiple PIs, and 260 papers are published by international collaboration. The numbers have been constantly increasing. The *Striga* project is a representative case, which launched as a bottom-up collaboration led by a PhD student and has become a flagship project of ITbM organized by the team *Striga.* Now the team has many researchers and administrative staff and is tackling to provide a molecular solution to the food security of Africa.

4. Realizing an International Research Environment

ITbM has 5 world-leading overseas PIs. They have been actively contributing to the activities of ITbM. They are staying in Nagoya for 1-2 months per year and attending the site visits and annual international symposia, ISTbM. Even when they are absent from Nagoya, they have close contact with their respective Co-PIs and postdoctoral researchers through regular TV conferences or e-mails. They also send a few researchers of his/her institutes to ITbM.

ITbM has hired 82 postdocs from over the world, and 53 (65%) are non-Japanese. Out of the 59 postdocs who left ITbM, 31 found faculty positions in academia in Japan and overseas. Thus ITbM has been involved in a global brain circulation.

The Administrative Department consists of staff with good correspondence in both English and Japanese to handle various tasks. The RPD has staff to provide support to foreign researchers and their families.

ITbM proactively offers PhD students the opportunities to conduct research abroad. So far 39 PhD students have visited overseas institutions to engage in collaborative research.

ITbM has been hosting annual international symposia (ISTbM) and three international awards (Hirata Award, Tsuneko & Reiji Okazaki Award, Nagoya Medal of Organic Chemistry), which have been contributing to increase ITbM's international visibility and extending international network.

5. Making Organizational Reforms

NU gave the executive authority to the Center Director to make top-down decisions over the appointments of ITbM's personnel, budget, research priorities, and incentive-based bonuses.

ITbM's efforts to support foreign researchers are spreading across the university. ITbM's Co-PI system, forming a team of top-level overseas PI in overseas institutes and a full-time Co-PI in NU, was incorporated to the WPI-next program established to support top-level science of NU.

ITbM's high research performance has largely contributed to establish various initiatives of NU, such as being selected as "Designated National University" by MEXT (2018), a basic agreement with RIKEN. NU launched the new graduate program "Graduate Program of Transformative Chem-Bio Research (GTR)" with ITbM as a core. ITbM's Mix Lab will provide a superb place to nurture young researchers who pioneer new science.

NU has been strongly supporting ITbM by such as (1) covering salaries, (2) provision of space, (3) financial support towards construction of ITbM's building, (4) support towards the operation of the building, and (5) ITbM's priority to the use of hall of residence. To secure the employment of ITbM's faculties and staffs, NU makes an organizational reform in 2019. NU will launch "Institutes for Advanced Research Excellence", and position ITbM under this umbrella.

6. Others

Upon development of molecules that modulate biological system in plants and animals, ITbM recognizes the importance of communication with the general public widely so that ITbM always addresses the environmental and safety issues carefully. Accordingly, ITbM has set up an Environment and Safety Committee so that researchers at ITbM are constantly aware of these issues when conducting their research. ITbM provides special safety training for the ITbM researchers suitable for interdisciplinary environments.

World Premier International Research Center Initiative (WPI)
Progress Report of the WPI Center
(For Extension Application Screening)

Host Institution	Nagoya University	Host Institution Head	Seiichi Matsuo
Research Center	Institute of Transformative Bio-Molecules	Center Director	Kenichiro Itami

Common Instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2019) situation of your WPI center.
* As a rule, keep the length of your report within the specified number of pages. (The attached forms are not included to this page count.)
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

1. Overall Image of Your Center (write within 2 pages including this page)

Describe the Center's current identity and overall image.
- List the Principal Investigators in Appendix 2, and enter the number of center personnel in Appendix 3-1, 3-2, diagram the center's management system in Appendix 3-3, draw a campus map in Appendix 3-4, and enter project funding in Appendix 3-5, 3-6.

ITbM was launched at Nagoya University (NU) as a unique research institute to develop innovative functional molecules "transformative bio-molecules" that make a marked change in the form and nature of biological science and technology. By taking full advantage of our cutting-edge molecular synthesis expertise and intense interactions with leading plant/animal biology research, ITbM has been conducting 'needs-inspired' basic research and explored new research areas of "plant chemical biology", "chemical chronobiology", and "chemistry-enabled live imaging".

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ITbM has gathered top-researchers from the different disciplines of synthetic chemistry, plant biology, animal biology, and theoretical sciences under one roof, who have been carrying out interdisciplinary research through extensive collaboration. ITbM started with 10 PIs, consisting of 7 PIs selected from NU (NU PIs) and 3 PIs from overseas institutions (overseas PIs). Later, ITbM appointed 3 more PIs (1 from NU, 2 from overseas) who were necessary to further advance the research at the time. ITbM now has 13 PIs. In order to enable world-class researchers to participate in ITbM as overseas PIs, ITbM introduced the Co-PI system. Through this system, ITbM employs brilliant young researchers as Co-PIs who are full time at ITbM and cooperate with the overseas PIs. This system enables the overseas PIs to carry out research at ITbM with continuity, and has contributed to improving the global visibility of ITbM. Co-PIs were also allocated to NU PIs to enable NU PIs to focus on their research. In the 7 years since its inception, ITbM has grown to a size of 200 people including 13 PIs, 63 researchers, 62 support staff, and many PhD students.

In order to "Mix" ITbM researchers to promote interdisciplinary research, ITbM installed Mix Labs and Mix Offices. In these spaces, researchers and students from different fields discuss and communicate about science, education and other administrative matters on a daily basis. This style has significantly promoted bottom-up interdisciplinary projects among young researchers. The ITbM Research Award, established to promote interdisciplinary research proposed by young researchers, further accelerates collaborations in a bottom-up manner. Regular ITbM Workshops, and Tea Break Meetings enable researchers to interact and start new collaborations from the ground up.

These endeavors have resulted in the development of a range of promising bio-functional molecules and the discovery of molecular mechanisms of important biological events. The most exciting example is the discovery/development of molecules to combat the parasitic plant *Striga*. These were developed from a bottom-up collaboration initiated at the Mix Lab. The molecules will soon enter an exciting phase of

testing in the fields of Africa. The societal implementation of ITbM's other achievements is also in progress. Many molecules have been commercialized, and patent licensing has been increasing. ITbM has also launched a membership forum "ITbM Consortium" with 17 companies, which is working extremely well.

ITbM's extraordinary achievements are also evident in the records of competitive funds, prestigious awards, and invited lectures. In the past 7 years, research funds amounting to 7.45 billion yen have been garnered by our PIs. Considering the relatively small number of PIs and the nature of ITbM's science focusing on basic research, this number is amazingly high as an institute in Japan. Overseas PIs has been constantly obtaining KAKENHI grants, patents and papers from their work at ITbM. In addition to many other awards, three PIs (Itami, Kay, Frommer) have been selected as "Highly Cited Researchers (Clarivate Analytics)" for two years in a row (2017 and 2018), which represents their high activity and visibility.

ITbM's research activities are supported by many capable and dedicated staff in ITbM. A key player is the Administrative Department of ITbM, especially members in the Research Promotion Division (RPD) and the Strategic Planning Division (SPD). The RPD finds inventions and scientific discoveries from each research group at an early stage, and the SPD promotes patent application and societal implementation. The RPD also has staff to provide local support to ITbM's foreign researchers and their families, enabling them to fully concentrate on their research. ITbM's four supporting centers (Molecular Structure Center, Live Imaging Center, Chemical Library Center, and Peptide Protein Center) also make major contributions to ITbM's interdisciplinary research.

ITbM has strategically extended its collaboration network. International collaboration has been considerably enhanced by ITbM internationalization and international visibility. These collaborations have been largely contributing to interdisciplinary research. ITbM's target ID platform is being developed through collaboration with RIKEN Center for Sustainable Resource Science (CSRS) and Institute of Chemistry (IoC) at Academia Sinica, Taiwan. ITbM has published 260 international joint papers.

Nurturing young researchers is a key mission of ITbM and critical for our future development. ITbM financially supports PhD students going abroad and have sent 39 PhD students on overseas exchanges. A notable number of postdoctoral researchers have carried out research at ITbM, and are currently in outstanding academic and industrial positions in Japan and overseas. The ITbM spirit is everywhere and ITbM has been recognized as a key hub in the global talent pool.

ITbM has also been proactive to appoint and foster female researchers. Including three female PIs, 19 female researchers are on staff at ITbM, making up 25% of total researchers as of March 31, 2019. Their remarkable activity is represented by a number of awards such as Arthur C. Cope Scholar Award (Crudden), Killam Research Fellowship (Crudden), ASPB Award (Torii), and Saruhashi Award (Torii).

ITbM's challenges have contributed to significant system reform at NU as a core research center. NU was recognized for its abilities to develop world-leading education and research activities and was named a "Designated National University", in part because of ITbM's high-profile activities. To achieve the goal, NU launched research supporting programs such as the "WPI-next" program to promote cutting-edge sciences at NU, which referred to ITbM's unique structures such as the Co-PI system. In 2019, NU made an organizational reform to establish "Institutes for Advanced Research Excellence", positioning ITbM under this umbrella to secure the employment of ITbM staff through providing the needed financial support.

ITbM has also influenced the education system. NU recognizes that ITbM's Mix Lab is one of the best places to nurture young researchers, and has launched a new graduate program entitled "Graduate Program of Transformative Chem-Bio Research (GTR)". In this program, ITbM is positioned as a hub, through which the pioneering spirit of ITbM will be more widely spread.

In order to disseminate ITbM's interdisciplinary research activities and accomplishments to a global audience, ITbM has organized outreach events and prepared international press releases. Through this endeavor, ITbM has been highlighted in various national/international media and is receiving recognition by the international community. ITbM has also participated in or hosted many international events to present its research activities, establish networks and foster the next generation of scientists. These endeavors are envisaged to increase the international recognition of ITbM and attract prominent researchers and industrial partners from abroad. For example, Itami receives more than 1,000 applications from abroad every year from researchers trying to land a position in ITbM (as a faculty member, postdoctoral researcher, or PhD student). ITbM is clearly an internationally visible institute.

ITbM has now become truly exciting and internationally visible institute where new interdisciplinary research fields emerge and new molecules are born every day. ITbM's unique "Mix" culture has led researchers from different fields to work together, take risks, think/act differently, thereby finding unique problems and solutions, discovering something new, and providing unique solutions to key global problems. Researchers world-wide have recognized the strength of ITbM. Our dream of changing the world with molecules is clearly bearing fruit, but the challenge continues.

2. Advancing Research of the Highest Global Level (within 12 pages)

2-1. Research results to date

Describe issues of a global level that the Center has challenged, and give the results. Select 15 representative results achieved during the period from 2012 through March 2019. Number them [1] to [15] and provide a description of each. Place an asterisk (*) in front of those results that could only have been achieved by a WPI center and explain the reason in the description.

- In Appendix 1-1, list the papers underscoring each research achievement (up to 30 papers) and provide a description of each of their significance. And in Appendix 1-4 list the center's research papers published in 2018.

ITbM has been promoting 'needs-inspired' basic research to develop transformative bio-molecules that make a marked change in the form and nature of biological science and technology, such as those enhance biotic productivity and quality, and realize innovative bio-imaging. To ensure that these targets are achieved, ITbM has developed catalysts that enable efficient synthesis and on demand molecular activation. ITbM has also pioneered a new molecular nanocarbon science using its state-of-the-art synthetic chemistry, which will be a new pillar of ITbM in the future.

In the 7 years, a number of outstanding research outcomes have been filed for patents and published in top journals as summarized in Section 1. Their societal implementation is also in progress as represented by the development of molecules to combat parasitic plants *Striga*.

[1] Unraveling strigolactone signaling and controlling parasitic plant behaviors in *Striga

The parasitic plant *Striga hermonthica* (*Striga*), so-called witchweed, has been causing huge damage on crop production in Africa. Infection of harvests by Striga leads to the loss of $10 billion U.S. dollars' worth of crops from the continent every year. However, genetic intractability of *Striga* stood as a significant barrier to understand Striga in detail and develop *Striga* science.

To overcome the genetic intractability of the *Striga* that has previously interfered with identification of the strigolactone receptors (ShHTLs), ITbM chemists (Itami, Hagihara), biologists (Tsuchiya, Kinoshita), the Molecular Structure Center, the Live Imaging Center and their co-workers designed and developed a fluorescent turn-on probe, Yoshimulactone Green (YLG), which activates strigolactone (SL) signaling and illuminates signal perception by the ShHTLs. Using YLG, they demonstrated that ShHTLs function as SL receptors in *Striga* for the first time. Moreover, Live-imaging revealed that a dynamic wavelike propagation of SLs' perception wakes up *Striga* seeds (Appendix 1-2 (1): *Science* 2015). Their chemical approach have made *Striga* experimentally accessible to researchers world-wide for analyzing the functions of SL receptors, leading discovery of number of the receptor agonists / antagonists, from ITbM chemical library (Appendix 1-2 (3): *ACS Cent. Sci.* 2018).

Using the assay system enabled by YLG, ITbM chemists (Uraguchi, Ooi), biologists (Tsuchiya, Kinoshita), theoretical sciences group (Hijikata, Irle), and the Molecular Structure Center identified hit molecule (SAM690) from a high throughput chemical screening and succeeded in developing of sphynolactone-7 (SPL7), a hybrid molecule of SAM690 and natural strigolactone, as a *Striga*-selective agonist. They revealed that two functional modules of SPL7 cooperatively acted on strigolactone receptor ShHTL7, and activated it with a high-affinity to provoke *Striga* germination with potency in the *femtomolar* (10^{-15} molar) range, SPL7 is effective for reducing *Striga* parasitism on a common crop (maize) in Africa without impinging on host strigolactone-related processes, unlike synthetic SL agonist GR24 showing multiple actions in plants and fungi (Appendix 1-2 (2): *Science* 2018). The discovery of SPL7 has motivated all ITbM scientists to tackle the issue of *Striga* through the practical use of SPL7 in Kenyan fields.

***[2] Identification of a series of molecules that control plant reproduction**

Identification of key molecules of plant reproduction is critically important to achieve molecular control of crop production and breeding. The Higashiyama group discovered the long sought (nearly 140 years) pollen tube (PT) attractant molecules "LURE" as defensin-like polypeptide secreted from synergid cells (Higashiyama *et al.* Nature 2009). However, the mechanism by which the PT receives LURE peptides and the following signal transduction remains largely unknown.

The Higashiyama group succeeded in showing that tip-localized pollen-specific receptor-like kinase 6 (PRK6) is an essential receptor for sensing of the LURE1 attractant peptide in *Arabidopsis thaliana* under semi-*in-vivo* conditions, and is important for ovule targeting in the pistil. They also revealed that PRK6 interacted with pollen-expressed ROPGEFs (Rho of plant guanine nucleotide-exchange factors), which are important for PT growth through activation of the signaling switch Rho GTPase ROP1. As a result, they concluded that PRK6 acts as a key membrane receptor for external AtLURE1 attractants, and recruits the core tip-growth machinery, including ROP signaling proteins. This work provides a major breakthrough not only to investigate ligand-receptor interaction but also to discover molecules that break species-specific reproductive barriers (Appendix 1-1 (1): *Nature* 2016).

Followed by the discovery of LURE receptor, the Higashiyama group identified that an ovular glycochain, methyl-glucuronosyl arabinogalactan (AMOR), induces competency of the PT to respond to ovular attractant LURE peptides in Torenia. With the Itami group, they determined that the terminal disaccharide residue of AMOR was necessary and only the β-isomer of methyl-glucuronosyl galactose (4-Me-GlcA-β-(1/6)-Gal) showed AMOR activity through an extensive structure-activity relationship study (Jiao *et al.* Plant Physiol. 2018). No specific sugar-chain structure of plant extracellular matrix has been identified as a bioactive molecule involved in intercellular communication. This study suggested that the AMOR sugar chain in the ovary renders the PT competent to the chemotropic response prior to final guidance by LURE peptides (Appendix 1-1 (2): *Curr. Biol.* 2016)

The discovery of PT attractant polypeptides (LUREs) and their receptor PRK6 led the Higashiyama group to investigate ligand-receptor interactions. They found that the extracellular domain of the leucine-rich repeat receptor kinase (LRR-RK) PRK6 from *Arabidopsis thaliana* directly interacts with AtLURE1 peptides. A C-terminal loop of the LRR domain (AtPRK6LRR) is responsible for the recognition of AtLURE1.2, mediated by a set of residues largely conserved among PRK6 homologs from *Arabidopsis lyrata* and *Capsella rubella*, as supported by in vitro mutagenesis and semi-*in-vivo* PT growth assays.

This study provided strong evidence that PRK6 actually functions as a receptor of the LURE peptides in *Arabidopsis thaliana*, and revealed a unique ligand recognition mechanism of LRR-RKs (Appendix 1-1 (3): *Nature Commun*. 2017). In addition, this study leads to the collaboration between plant reproduction group (Higashiyama) and computational sciences group (Tama group), and will give a great potential for designing small molecule PT attractant to overcome genetic barrier.

***[3] Elucidation of mechanisms involved in early embryogenesis of plants**

In flowering plants, the detailed mechanism of early embryogenesis remains largely unknown despite an immense amount of effort of the scientific community. The Higashiyama group has been tackling this challenge using live-imaging.

Higashiyama and Maruyama discovered that the fusion of the persistent synergid cell and the endosperm selectively inactivate the persistent synergid cell in *Arabidopsis thaliana*. They unveiled, through live-imaging, that the synergid-endosperm fusion causes rapid dilution of a PT attractant in the persistent synergid cell and selective disorganization of the remaining synergid nucleus during the endosperm proliferation, preventing further attraction of multiple PTs after fertilization. They also revealed that synergid-endosperm fusion is induced by fertilization of the central cell, while the egg cell fertilization predominantly activates ethylene signaling, an inducer of the synergid nuclear disorganization. Finally, two female gametes (the egg and the central cell) control independent pathways yet coordinately accomplish the elimination of the persistent synergid cell by double fertilization (Appendix 1-1 (4): *Cell* 2015). Only two other examples of plant cell fusion have been observed so far, and over 110 years have passed since the identification of the two cell fusions, which occurred between two sets of gametes during fertilization.

Higashiyama and Ueda successively revealed the dynamics of organelles in early plant embryogenesis. They utilized live-cell imaging with Arabidopsis zygotes to visualize the dynamics of the major elements of the cytoskeleton, microtubules (MTs) and actin filaments (F-actins), during the entire process of zygote polarization.

By combining image analysis and biological experiments, they found the preexisting alignment of MTs and F-actin in the egg cell is lost in fertilization, and then, MTs organize into a transverse ring defining the zygote subapical region and driving cell outgrowth in the apical direction. On the other hand, F-actin forms an apical cap and longitudinal arrays and is required to position the nucleus to the apical region of the zygote, setting the plane of the first asymmetrical division (Appendix 1-1 (5): *PNAS* 2016). In addition, they revealed by live-imaging that the vacuoles form tubular strands around the apically migrating nucleus, which gradually accumulates at the basal region and filled the space, resulting in an asymmetric distribution in the mature zygote. They also identified that shoot *gravitropism2* (*sgr2*), in which the vacuolar structural change was impaired, failed to form tubular vacuoles and to polarly distribute the vacuole, and revealed in *sgr2* that large vacuoles occupied the apical tip and thus nuclear migration was blocked, resulting in failure to undergo asymmetrical division. Furthermore, they observed that both tubular vacuole formation and asymmetric vacuolar distribution depended on the longitudinal array of F-actins. These results showed that vacuolar dynamics is crucial not only for the polar distribution along F-actins but also for adequate nuclear positioning, and consequently asymmetrical zygote-division (Appendix 1-1 (6): *PNAS* 2019).

***[4] Elucidation of stomatal development mechanism and its molecular control**

Plant stomata, the cellular interface between a plant and the atmosphere, develop according to positional cues, which include a family of secreted peptides called epidermal patterning factors (EPFs).

Although stomatal development is considered to play a key role in crop plant productivity and water-use efficiency, the mechanism of stomatal development at a molecular level remains unclear.

The Torii group has made a number of remarkable discoveries on biomolecules, such as genes, receptors, transcription factors and peptides, involved in controlling the number and density of plant stomata, and leads the field of developmental biology of plant stomata at the molecular level. They identified stomagen peptide (also called EPF-LIKE9) in Arabidopsis, which promotes stomatal development, requires ERECTA (ER)-family receptor kinases and interferes in the inhibition of stomatal development through interaction with Epidermal Patterning Factor 2 (EPF2)–ER complex. They revealed that the stomagen peptide competitively replaces EPF2 binding to ER and induces rapid phosphorylation of downstream signaling components in vivo. Their findings demonstrate how plant receptor agonists/antagonists define inductive/inhibitory cues to fine-tune tissue patterning on the plant epidermis (Appendix 1-1 (7): *Nature* 2015).

In ITbM, the Torii-Uchida group has been exploring small molecules that affect the density and/or patterning of stomata through chemical screening. They succeeded in identifying the first-in-class synthetic molecules enhancing the number of stomata in *Arabidopsis thaliana* with the Itami group and the Chemical Library Center. Several promising lead compounds have further been optimized through structure-activity relationship study of hit compounds by using C–H functionalization reactions at late stage of the synthesis. In addition, some compounds could promote root growth in various plant species such as *Arabidopsis thaliana* as well as edible plants (cucumber, lettuce, etc.) (Appendix 1-2 (4): *Chem. Commun.* 2017). These results have inspired the development academia-industry collaborations towards the practical use of molecules in the field.

***[5] Control of stomatal opening/closing**

Control of stomatal movements (opening/closing) have long been considered to be critical not only an environmental responses of plant as basic science but also an application to future agriculture, such as increase of biomass (plant growth) and drought tolerance. The Kinoshita group has successively identified a major component of blue light-dependent stomatal opening such as blue light-receptor phototropins, protein phosphatase 1, and the plasma membrane H^+-ATPase. However, the signaling mechanisms between blue light perception and the H^+-ATPase activation have remained largely unknown.

The Kinoshita group demonstrated that the transgenic Arabidopsis plants overexpressing H^+-ATPase show enhanced light-induced stomatal opening and photosynthesis, leading to plant growth. They also revealed stomata in the transgenic plants closed normally in response to darkness and abscisic acid. In contrast, the overexpression of the other key components, phototropin or inward-rectifying K^+ channels, in guard cells had no effect on these phenotypes. These results demonstrate 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 (Appendix 1-1 (8): *PNAS* 2014). This research outcome has gained a significant amount of attention, leading to the initiation of several academia-industry joint research projects and licensing of the research to agrochemical companies by using commercial cultivar (rice, mays, and rape seed). This result has inspired a study of regulation of stomatal aperture by synthetic small molecules towards an increase of photosynthesis and plant growth.

The Kinoshita group identified a Raf-like protein kinase, **b**lue light-dependent **H**$^+$-ATPase **p**hosphorylation (BHP) as a novel positive regulator for the H^+-ATPase activation in the stomatal opening by an elegant combination of chemical screening and reverse genetics. They revealed that BHP is abundantly expressed in the cytosol of guard cells and interacts with BLUS1, a serine/threonine protein kinase that is identified as a positive regulator between the phototropin and the H^+-ATPase, both *in vitro* and *in vivo*. Based on these results, BHP has now being recognized as a novel signaling mediator in blue light-dependent stomatal opening, likely downstream of BLUS1 (Appendix 1-1 (9): *Sci. Rep.* 2017). This work fills in the missing piece of the blue light signaling in guard cells, and provides important insights into understanding of the stomatal opening and plant photobiology, and suggests a potential strategy for the artificial control of stomata.

The Kinoshita group and the Chemical Library Center have screened more than 30,000 molecules from various chemical libraries, identified compounds that affect stomatal movements (opening or closing) in *Commelina benghalensis* and characterized the underlying molecular mechanisms. They also revealed that SCL1 and SCL2 (**s**tomata **cl**osing compounds) suppressed blue light-induced phosphorylation of plasma membrane H^+-ATPase for stomatal opening and had no effect on ABA-dependent responses. In addition, they demonstrated that spraying the leaves of both of dicot and monocot plants with SCL1 suppressed strongly withering of leaves and confers tolerance to drought stress in plants (Appendix 1-2 (5): *Plant Cell*

Physiol. 2018).

***[6] New approach to ligand-receptor pair: delineation of specific auxin response**

Evolution often diversifies a peptide hormone family into multiple subfamilies, which exert distinct activities through exclusive peptides (ligands)-receptor interaction. The Torii-Uchida group focused on the two plant peptide hormones, CLV3 and CLE25, which belong to the CLE (**Cl**avata3/**E**mbryo Surrounding Region-related) family and have root-shortening activity. On the other hand, amino acid sequence homolog CLE41 peptide, also known as tracheary element differentiation inhibitory factor (TDIF), promotes the stem cell activity in the vascular meristem without affecting root/shoot stem cells. Through systematic swapping the amino acid sequences of CLV3 and CLE25, they succeeded in creating a novel synthetic bifunctional peptide, KIN, that exhibits vascular-thickening function in addition to the original root-shortening function. Computational studies suggest that the KIN peptide binds to both CLV1 and TDR, receptors for CLV3/CLE25 and TDIF/CLE25, respectively. Thus, it could be possible to create novel synthetic plant peptide hormones which can effectively control plant growth even if the structural basis of the specificity between ligands and receptor has not been fully understood (Appendix 1-2 (6): *Nature Commun.* 2017).

The phytohormone auxin regulates nearly all aspects of plant growth and development. Despite substantial progress in understanding of auxin biology, delineating specific auxin response remains as a major challenge. Auxin regulates transcriptional response via its receptors, TIR1/AFB F-box proteins. Through extensive collaborations with Hagihara (Itami group), the Torii-Uchida group developed that an engineered, orthogonal auxin-TIR1 receptor pair, which triggers auxin signaling without affecting endogenous auxin or TIR1/AFBs. A synthetic convex IAA (cvxIAA), designed by docking study of IAA-TIR1complex, hijacks the downstream auxin signaling *in vivo* both at the transcriptomic level and in specific developmental contexts, only in the presence of a complementary, concave TIR1 (ccvTIR1) receptor. Harnessing the cvxIAA-ccvTIR1 system, they provided conclusive evidence for the role of the TIR1-mediated pathway in auxin-induced seedling acid growth. The cvxIAA-ccvTIR1 system serves as a powerful tool for uncovering long-sought-after questions in auxin biology and for precise manipulation of auxin-mediated processes as a controllable switch (Appendix 1-1 (10): *Nature Chem. Biol.* 2018).

[7] Mechanistic elucidation of seasonal clock in animals

Organisms are exposed to seasonal changes in environment, such as photoperiod, temperature, and precipitation. Among them, organisms are using changes in photoperiod for seasonal adaptation to maximize their survival. Although this phenomenon attracts tremendous general interest, its underlying molecular mechanism remains unknown. The Yoshimura group has tackled the elucidation of a long-standing mystery of how living organisms sense the season and respond to the changes in the four seasons. The pars tuberalis of the pituitary gland is the regulatory hub for seasonal reproduction in birds and mammals. Fish also exhibit robust seasonal responses. However, they do not possess an anatomically distinct pars tuberalis and how fish respond to seasonal change still remains largely unknown. They identified the photoperiodic center in fish (masu salmon), the saccus vasculosus, which is the sensor of seasonal changes in day length. They revealed that expression of key genes, rhodopsin family genes, regulates seasonal reproduction in coronet cells of the saccus vasculosus of masu salmon. In addition, they demonstrated that an isolated saccus vasculosus has the capacity to respond to photoperiodic signals and its removal abolishes photoperiodic response of the development of gonad (Appendix 1-1 (11): *Nature Commun.* 2013).

Then, the Yoshimura group revealed that in quail, novel photopigment (OPN5)-positive neurons existing deep inside the brains, respond directly to light and regulate seasonal reproduction. They identified the neurons capable of phototransduction by whole-cell patch-clamp recordings. Separately, they carried out a siRNA knockdown experiment of OPN5 in vivo inhibits the secretion of the thyroid-stimulating hormone (TSH), so-called the ‘spring hormone’ which triggers spring breeding in birds (Appendix 1-1 (12): *Curr. Biol.* 2014). As OPN5 also exists in humans, it will contribute to understanding how mammals regulate their biological clocks. This result may also lead to improvements in animal breeding and provide a deeper understanding of the evolution of eyes and photoreceptors.

Subsequently to the discoveries of the photoperiodic center in both fish (masu salmon) and birds (quail), the Yoshimura group revealed dynamic plasticity in phototransduction regulates seasonal changes in color perception in medaka fish. They demonstrated the medaka kept in summer conditions are more attracted to computer-generated orange-red-colored medaka (nuptial coloration) than medaka kept in winter conditions. Then, they revealed that the genes encoding photopigments such as opsin and their downstream pathway varies dynamically among seasons. In addition, they demonstrated photopigment-null fish showed significant differences from wild type in behavioral analysis and suggested plasticity in

color perception is crucial for the emergence of seasonally regulated behaviors (Appendix 1-1 (13): *Nature Commun.* 2017). As the effects of environmental changes on opsin gene expression have been reported in several teleosts, seasonal plasticity in color perception may be a common mechanism shared by many species including human beings. These findings have been led to further results including the discovery of a novel, long non-coding RNA (lncRNA) responding to day length (*Nature Ecol. Evol.* 2019) and identification of molecules that affect sociability (manuscript in preparation).

***[8] Development of molecules that control biological clock**

Chronic circadian disruption due to shift work or frequent travel across time zones leads to jet-lag and an increased risk of diabetes, cardiovascular disease, and cancer. The development of new drugs to treat circadian disorders, however, is costly and hugely time-consuming. The Yoshimura group and the Chemical Library Center performed a high-throughput chemical screen of existing drugs for circadian clock modulators in human U2OS cells (so called drug repositioning). They identified that approximately 5% of the drugs screened altered circadian period, including the period-shortening compound dehydroepiandrosterone (DHEA; also known as prasterone). They demonstrated that dietary administration of DHEA to mice accelerated re-entrainment to advanced light–dark (LD) cycles, thereby reducing jet-lag. They also revealed tyrosine kinases, ABL1 and ABL2, and the BCR serine/threonine kinase are involved in regulating circadian period. Thus, drug repositioning is a useful approach to identify new circadian clock modulators and potential therapies for circadian rhythms related disorders (Appendix 1-2 (9): *EMBO Mol. Med.* 2018).

Inspired by the discovery of KL001 (*Science* 2012), the groups of Yoshimura and Kay-Hirota identified clock-modulating molecules by cell-based phenotypic chemical (Appendix 1-2 (8): *Angew. Chem. Int. Ed.* 2015) and established the practical design of small-molecule cryptochrome modulators by a computational approach (*ChemMedChem* 2015) through extensive collaboration with synthetic chemistry groups (Itami, Ooi) and theoretical scientists (Irle and Tama). Through affinity-based target deconvolution, the groups of Kay-Hirota and Itami succeeded in identifying GO289 as a lead compound, which strongly lengthened circadian period, and is a potent and selective inhibitor of casein kinase 2 (CK2) with outstanding physicochemical properties. They also identified multiple phosphorylation sites inhibited by GO289 on clock proteins, including PER2 with the help of the Molecular Structure Center and Tama group. In addition, they demonstrated GO289 exhibited selective inhibition of cancer cell growth that correlated with cellular clock function. Furthermore, they revealed that the interactions between GO289 and CK2-specific residues by X-ray crystal structure of the CK2α-GO289 complex and no direct interaction of GO289 with the hinge region that is highly conserved among kinases. The discovery of well-defined GO289 provides a direct link between the circadian clock and cancer regulation, and reveals some unique design principles underlying kinase selectivity (Appendix 1-1 (14): *Science Adv.* 2019).

***[9] Novel characteristic probes applicable to the advanced live imaging**

The development of super-resolution stimulated emission depletion (STED) microscopy represents a major breakthrough in cellular and molecular biology. Nonetheless, the intense laser beams are required for STED microscopy, which give rise to photobleaching of fluorescent probes. The Yamaguchi group has developed the outstanding photostable fluorescent dye C-Naphox (diarylmethylene bridged **na**phtho-**ph**osphole P-**ox**ide) and reported several distinct advantages relative to conventional dyes, such as intense fluorescence emission by the combination of an electron-donating group (diphenylamino moiety) with an electron-accepting group (the core structure of C-Naphox), high quantum yields even in polar and protic solvents, large Stokes shift arising from an intramolecular charge transfer, solvent polarity sensitivity from bluish green to reddish orange. They demonstrated that almost all (99.5%) C-Naphox remained intact even after irradiation with a Xe lamp for 12 hours although representative STED imaging probes (Alexa Flour 488 and Atto 488) significantly diminished their fluorescence intensities under the same conditions. In addition, they applied C-Naphox in repeated STED imaging of HeLa cells and recorded 83% of the initial fluorescence intensity persisted even after 50 STED images (Appendix 1-1 (15): *Angew. Chem. Int. Ed.* 2015).

However, C-Naphox still has drawbacks for practical use in bio-imaging, *i.e.* water insolubility, target selectivity, and polarity-sensitivity fluorescence. The groups of Yamaguchi and Higashiyama, and the Live Imaging Center succeeded in developing a new super-photostable dye, PhoxBright 430 (PB430), comprising a fully ring-fused π-conjugated skeleton with an electron-accepting phosphole P-oxide unit. PB430 also has high solubility in water, is capable of labeling proteins with maintaining high fluorescence quantum yields, also exhibits outstanding resistance to photoirradiation even under STED conditions, and allows continuous acquisition of STED images. Indeed, using a PB430-conjugated antibody, they succeed in creating a 3-D

reconstruction of super-resolution STED images as well as photostability-based multicolor STED imaging of fluorescently labeled cytoskeletal structures (Appendix 1-1 (16): *JACS* 2017). They succeeded in further development of super-photostable fluorescent probe and the results will be published soon (Yamaguchi *et al. PNAS*, to be accepted).

The groups of Yamaguchi and Higashiyama, and the Live Imaging Center also developed a highly photostable and water-soluble near-infrared phosphorus-substituted rhodamine, PREX 710 (Appendix 1-1 (17): *Angew. Chem. Int. Ed.* 2018). By the nature of membrane permeability and localization in the mitochondria, they demonstrated that PREX 710 can be used to stain mitochondria in living cells, which allowed long-term and multi-color imaging in the vis-NIR range. Moreover, they showed the high fluorescence longevity of PREX 710 by tracking a dye-labeled biomolecule (IgG, NeutrAvidin) by single-molecule microscopy under physiological conditions. Furthermore, they achieved deep imaging of blood vessels in mice brain using the bright NIR emitting PREX 710-dextran conjugate.

***[10] New avenues of catalysis for efficient molecular synthesis**

The development of a general catalytic method for the direct and stereoselective construction of contiguous all-carbon quaternary stereocenters in a single synthetic operation remains a formidable challenge and largely unexplored in design of catalysts and development of chemical synthesis. The Ooi group has developed a catalytic system to establish stereocenters of contiguous quaternary carbons. Specifically, they achieved a highly enantio- and diastereoselective [3+2] annulation reaction catalyzed by a palladium complex bearing a newly devised phosphine ligand with a chiral ammonium salt component, which enables the single-step construction of three contiguous stereocenters, including vicinal all-carbon quaternary stereocenters, in a five-membered heterocyclic framework. This stereoselective cycloaddition protocol relies on the remarkable ability of the chiral ligand to rigorously control the absolute stereochemistry of each chiral center associated with the multiple bond-forming events, and provides a reliable catalytic process for the asymmetric synthesis of densely functionalized pyrrolidines (Appendix 1-1 (18): *Nature Chem.* 2013).

The Suzuki–Miyaura cross-coupling (Nobel Prize in Chemistry, 2010) is one of the most often utilized reactions in the synthesis of pharmaceutical compounds and functional materials to afford a planer biaryl or polyene compounds, in which these substructures are widely found in natural products and small molecules. However, the creation of carbon-carbon bonds with stereochemistry using the Suzuki-Miyaura reaction has only been demonstrated in the last few years. The Crudden group made significant advance in this approach, in which multiply functionalized chiral cross-coupling partners can be employed in iterative coupling without the use of protecting groups. Through extensive investigation on the reaction system, they identified that the orthogonal reactivity of boron-carbon bonds in different positions in a single molecule permits the chemo- and stereoselective sequential coupling of aromatic and aliphatic molecules. This method permits the rapid generation of multiply arylated, chiral organic molecules with control of stereochemistry, without the need for protection/deprotection sequences. (Appendix 1-1 (19): *Nature Commun.* 2016). The approach now allows the preparation of a range of chiral enantioenriched compounds, which are likely to provide interesting lead compounds for pharmaceutical and medicinal applications, by escaping from ‘flatland’.

Carbon-carbon bond formations between prochiral nucleophiles and electrophiles represent a powerful synthetic tool of general utility, affording four possible stereoisomeric products. The development of a catalytic process capable of producing each and all of those stereoisomers from the same starting materials (diastereodivergent catalysis) poses a formidable challenge, especially when simultaneous control of other selectivity factors, such as chemo- and regioselectivity, is needed. The Ooi group established a catalyst-directed pinpoint inversion of diastereochemical preference in the 1,6-addition of azlactones to δ-aryl dienyl carbonyl compounds with full control over other selectivities preserved. This rigorous diastereodivergence was enabled by the slight structural adjustment of a chiral iminophosphorane catalyst developed by themselves, providing access to all the stereoisomers with high regio-, distereo- and enantioselectivity. They demonstrated the utility of this method in the facile stereodivergent preparation of densely functionalized proline derivatives. In addition, they elucidated the origin of the diastereodivergence experimentally and computationally. This study significantly expands the potential of catalyst-controlled stereodivergent chemical synthesis (Appendix 1-1 (20): *Nature Commun.* 2017).

[11] Unprecedented approach to peptide/protein synthesis

The chemical syntheses of peptides and conjugated proteins are in great demand for understanding biological processes and developing new protein-based therapies. Ordinary solid-phase peptide synthesis can routinely provide peptide fragments up to 40 amino acid residues but is not suited for the preparation

of proteins. The Bode group has discovered and developed a bio-mimetic peptide ligation reaction, which is known as the KAHA ligation (*JACS* 2006). Recently they have developed a new method 'synthetic fermentation'. Microbial fermentation is known to rapidly provide potent molecules as a mixture that can be easily screened based on biological activity, and then the active components can be isolated. Its success in drug discovery has inspired extensive efforts to modulate and control the products. This reaction proceeds without additional organisms, enzymes, and reagents, and can be used to synthesize a number of peptides/proteins in water. They applied their KAHA ligation method into a microbial fermentation process and succeeded in demonstrating that bioactive, unnatural peptides can be grown from a mixture of amino acid building blocks in water. As a proof-of-concept, they identified a hepatitis C virus NS3/4A protease inhibitor among c.a. 6,000 unnatural peptides produced from just 23 amino acid building blocks (Appendix 1-1 (21): *Nature Chem.* 2014).

The Bode group has been developing the KAHA ligation and has synthesized various proteins not accessible by expression or bioengineering approaches. Actually, this ligation has proven to be remarkably robust, but has limitations including the introduction of a non-canonical homoserine residue at the ligation site, the formation of esters as the primary ligation products, and a preference for relatively high concentrations (10–20 mM) and temperatures (50–60 °C). They reported the synthesis of an N-terminus-protected oxazetidine as a canonical serine precursor for use in the KAHA ligation and demonstrated, when incorporated at the N-terminus of a peptide segment, that the four-membered oxazitidine can be used for rapid serine-forming ligations with C-terminus of peptide. They also revealed this ligation operates at lower concentration (100 μM–5 mM) and milder temperatures (20–25 °C). The utility of the reaction was demonstrated by the synthesis of S100A4, a 12 kDa calcium-binding protein that is not easily accessible by the conventional methods, such as native chemical ligation (NCL) or other amide forming reactions due to its primary sequence and properties (Appendix 1-1 (22): *Nature Chem.* 2015).

***[12] Development of biology-friendly functional materials**

The formation of organic films on gold employing N-heterocyclic carbenes (NHCs) has been previously shown to be a useful strategy for generating stable organic films. However, NHCs or NHC precursors typically require inert atmosphere and harsh conditions for their generation and use. The Crudden group has developed a simple direct method to form self-assembled NHC monolayers on gold. Using the bench-stable benzimidazolium hydrogen carbonate as a replacement for conventional air-sensitive NHCs or NHC precursors, NHC films were able to be prepared much more easily in solution or by vapor-phase deposition from the solid state. They applied these materials into surface plasmon resonance (SPR)-type biosensing and revealed that NHC-based films provide specific physicochemical durability, such as thermal stability and stability in extreme pH, versus conventional thiol-based ones (Appendix 1-1 (23): *Nature Commun.* 2016). The advantages over conventional thiol-based gold complex led the Crudden-Nambo group to develop the size-controlled synthesis of water-soluble NHC-gold nanoparticles (Salorinne *et al. Angew. Chem. Int. Ed.* 2017), ultra-stable gold nanoparticles modified with novel multivalent NHC ligands (Man *et al. JACS* 2018), and NHC-stabilized gold nano-clusters (Narouz *et al. Nature Chem.* 2019), and to apply the gold nanoparticles to genome modification by a particle bombardment method in collaboration with the groups of Higashiyama and Yamaguchi.

[13] Synthesis of carbon nanorings, nanobelts and pure nanotubes

Currently, carbon nanotubes (CNTs) can only be produced as mixtures with regard to diameter and sidewall structure. Given that the electronic properties of CNTs are primarily determined by the sidewall structures, structural uniformity is critically important for CNT-based electronics. Thus, the selective and predictable synthesis of structurally uniform CNTs and ultra-short carbon nanotubes (carbon nanorings and nanobelts) is recognized as one of the greatest challenges in science and technology. The Itami group has made significant progress toward this Holy Grail.

The Itami group achieved the first selective synthesis of carbon nanorings, representing the shortest sidewall segments of armchair CNTs (*Angew. Chem. Int. Ed.* 2009). In 2013, they succeeded in the first diameter-selective synthesis of CNTs using nanorings as templates (Appendix 1-1 (24): *Nature Chem.* 2013). The diameter of the nanoring template, which can be controlled using Itami's method, determines the diameter of the final CNT. A range of carbon nanorings of varying sizes is also commercially available, thus encouraging others to explore the bottom-up synthesis of CNTs and their use in materials and biology.

In 2017, the Itami group successively achieved the first synthesis of a carbon nanobelt - a long-sought-after ultra-short CNT (Appendix 1-1 (25): *Science* 2017). The synthesis of these highly strained, belt-shaped aromatic compounds had been one of the most difficult problems in chemistry for the last 60 years (even before the discovery of CNTs). This achievement is both an experimental tour de force and a triumph of

synthetic chemistry. Itami's carbon nanobelt, which can be synthesized from *p*-xylene (petroleum feedstock), was commercialized in 2018, thereby accelerating the discovery of extraordinary properties, functions, and applications.

[14] Synthesis of nanographenes and graphene nanoribbons

The Itami group has developed a number of unique catalysts for single-step aromatic π-extension and aromatic C-H activation that allows for the rapid synthesis of nanocarbon molecules in a programmable fashion. Recently, they have introduced the concept of "annulative π-extension (APEX) chemistry", which permits the facile synthesis of fused aromatic systems and molecular nanocarbons from simple aromatic compounds. For example, they have developed one-shot APEX reactions that occur at the K-region (convex armchair edge) of polycyclic aromatic hydrocarbons by the original $Pd(OAc)_2$/*o*-chloranil catalytic system with silicon-bridged aromatics as π-extending agents (Appendix 1-1 (26): *Nature Commun.* 2015). In addition, they revealed that the complete K-region selectivity stems from the electronic (olefinic) character of the K-region with density functional theory calculations.

The Itami group has also developed a single-step synthesis of fused aromatics with a triphenylene core by the palladium-catalyzed APEX dimerization of structurally and functionally diverse chlorophenylenes through double C-H activation (Appendix 1-1 (27): *Science* 2018). The partially fused polyaromatics can be transformed into fully fused, small graphene nanoribbons, which are otherwise difficult to synthesize. This simple, yet powerful method allows access to functional nanographenes of interest in optoelectronics and biological research. As the properties of nanographenes depend heavily on the degree of π-extension, shape, width and edge topology, the APEX reactions are expected to significantly contribute for those who need fine-tuned nanographenes.

Very recently, they have developed a new living APEX polymerization that enables rapid and modular synthesis of **g**raphene **n**ano**r**ibbons (GNRs) with control over width, edge structure, and length (*Nature* 2019). In the presence of palladium/silver salts, *o*-chloranil and an initiator (phenanthrene or diphenylacetylene), the benzonaphthosilole monomer polymerizes in an annulative manner to furnish a range of GNRs. The length of GNRs can be controlled by simply changing the initiator to monomer ratio, and the synthesis of GNR block copolymers has been accomplished for the first time. Itami's living APEX polymerization allows a range of previously inaccessible molecular nanocarbon materials to be synthesized with ease. Moreover, all of the structurally uniform GNRs will be commercially available in the near future.

[15] Synthesis of topologically unique, three-dimensional nanocarbons

The Itami group has also created completely novel, topologically unique nanocarbons. Aside from theoretical studies that predict interesting properties for these types of species, three-dimensionally curved nanocarbons are a virtually unexplored group of materials. In 2013, they accomplished the synthesis of a novel **w**arped **n**ano**g**raphene (WNG) containing both positive and negative curvatures on its π-surface (Appendix 1-1 (28): *Nature Chem.* 2013). WNG is unique and clearly distinct from any other existing nanocarbon. The negatively curved geometry of WNG engenders a flexible configuration in solution, thereby displaying significant solubility. As WNG is also commercially available, many industries are now using WNG as a key molecule in optoelectronic devices.

The groups of Itami and Higashiyama, and the Live Imaging Center have also synthesized a water-soluble WNG that exhibits green-yellow fluorescence with a long lifetime, good photostability and notably low cytotoxicity to cells (Appendix 1-2 (10): *Angew. Chem. Int. Ed.* 2018). Furthermore, the water-soluble WNG was readily introduced into HeLa cells and induced cell death upon light irradiation, demonstrating the applicability for photodynamic therapy.

2-2. Research environment including facilities and equipment

Describe the degree to which the Center has prepared a research environment appropriate for a world premier international research center, including facilities, equipment and support systems, and describe the functionality of that environment.

Mix Lab & Mix Office: The new 6-storey ITbM building was completed at the end of FY2014, in a design that reflects the "Mix" concept. The Mix Labs on the second and fourth floors consist of a large Bio Mix Lab and a Chem Mix Lab, which are located next to each other and are accessible through a single door. There are no barriers within the Bio Mix Labs and the Chem Mix Labs, along with the Mix Office spaces located directly above. This design removes the conventional barriers between research groups, thus creating huge Mix Labs and Mix Offices to promote interdisciplinary research. The building is also equipped with a childcare room for researchers and visiting researchers accompanied by small children. In addition, NU has provided 5,400 m^2 of research space for ITbM around the ITbM building, enabling easy access to the provided spaces. The arrangement has provided significant opportunities for ITbM

researchers to collaborate with each other and with others on campus.

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

Facilities and equipments: NU is very well equipped with top-level major instruments necessary for ITbM's research, such as multiconfocal laser microscopes, and mass spectrometers. Many of these are set up at one of ITbM's four supporting centers. The quality and number of these instruments rivals the best institutions in the world.

Administrative Department and Secretaries: The Administrative Department is staffed by talented individuals with a good command of English, as well as a global outlook and vision. The Research Promotion Division (RPD) and Strategic Planning Division (SPD) in the Department work closely with researchers and supports research through international public relations, outreach activities, education, and organization of events. Another important and unique role is to make a seamless support of the research by following-up the research progress and making strategies and roadmaps to societal implementation. The RPD also has staff tasks with supporting the daily lives of foreign researchers and their families. The staff provides a wide range of support such as assistance in registration at city council and banks, linguistic support (interpretation and translation) and giving advice on daily life, education and health care. Secretaries allocated to PIs are also playing important roles in support of researchers and students, especially those coming from/going to abroad (see Sections 3-2 and 4-3).

2-3. Competitive and other funding

Describe the results of the Center's researchers to date in securing competitive and other research funding.
- In Appendix 3-6, describe the transition in acquiring research project funding.

At the start of ITbM, the amount of competitive funding in FY2012 was 528 million yen. In FY2013, it was 1,141 million yen, more than double the amount in FY2012. The amount further increased or was comparable in the following years, and the sum for the 7 years (FY2012-FY2018) amounts to 7.45 billion yen. Major competitive funding successes include JST-ERATO (2 projects), JST-CREST (3 projects), JST-PRESTO (11 projects), Grant-in-Aid for Scientific Research on Innovative Areas (2 project as Area Representative), JST-ALCA (1 project), AMED (2 Projects), and Grant-in-Aid for Specially Promoted Research (1 project) among others. In FY2019, one more project of Grant-in-Aid for Specially Promoted Research was awarded.

Overseas PIs have also been successful in obtaining KAKENHI (Grant-in-Aid for Scientific Research), such as Bode (KIBAN A, Scientific Research on Innovative Areas), Crudden (KIBAN B, Scientific Research on Innovative Areas), Torii (KIBAN A, B, Scientific Research on Innovative Areas), Frommer (KIBAN A from FY2019). In addition, ITbM collected the JSPS Bilateral Program (Joint Research Projects) for FY2015-2016 to strengthen the research collaboration with NSF-CCHF.

All together, considering the relatively small number of research groups and the nature of ITbM's science focusing on basic research, this number is amazingly high as an institute in Japan.

2-4. State of joint research

Describe the results of joint research conducted with other research organizations both in and outside Japan.

ITbM has strategically extended its collaborating networks with academia and industries to expand the range of joint research activities. ITbM and the overseas PIs' host institutions are extensively collaborating, and have published co-authored papers with ETH-Zürich (Switzerland), Queen's University (Canada), University of Washington (USA), the University of Southern California (USA), and the Heinrich Heine University Düsseldorf (HHUD, Germany). ITbM has been conducting the collaborative research with the other organizations as described below.

NSF Center for Selective C-H Functionalization (CCHF) (USA): ITbM became a partner of NSF-CCHF that consists of 23 research groups spread over 15 top institutions in the USA, along with the involvement of some major pharmaceutical and agrochemical companies. ITbM and CCHF exchange graduate students each year, and many collaborative research projects have been conducted, some of which have been published as joint papers in top journals. In 2016, ITbM hosted a joint workshop "2016 International C–H Functionalization Workshop", inviting members of CCHF (7 faculties, 3 postdoctoral researchers, 12 students, and 1 staff), and IBS (2 faculties, 4 postdoctoral researchers, and 11 students). This joint workshop will be held in Seoul in this July.

Academia Sinica (Taiwan): ITbM and Institute of Chemistry (IoC) in Academia Sinica have organized joint workshops in 2016 & 2017 and deepened the collaborative relationship. As a result, Hirota (ITbM) and Prof. Yu-Ju Chen (Director of IoC) initiated a project aimed at target protein identification related to circadian rhythms. Itami will soon assume the first Joint Appointment Research Fellow in Academia Sinica and start organizing a research group in IoC, which will accelerate the collaboration of ITbM and IoC.

Freiburg University (Germany): Nagoya University and Freiburg University concluded an MOU for promotion and collaboration, and they established the co-funding system for their collaborative research. The proposal entitled “Multicomponent Supramolecular Catalysts for Sustainable Chemical Synthesis” organized by Ooi and Itami of ITbM and Prof. Breit of Freiburg University was selected to the fund in 2015, and collaborative research towards the development of new catalysts has been launched. The groups have exchanged researchers, and a joint symposium "1st International Symposium on Catalysis for Sustainable Chemical Synthesis" was held at Freiburg University in 2017, inviting 8 world-leading synthetic chemists.

RIKEN Center for Sustainable Resource Science (CSRS) (Japan): In 2015, both institutes decided to enter a partnership to collaborate in chemistry and plant biology. In 2016, both directors made a joint statement on the combined use of the research support platform and confirmed further promotion of collaboration between ITbM and CSRS. A number of collaborations involving the ITbM Chemical Library Center have started, and hit molecules have been identified in several projects. The joint workshop takes place annually in either Nagoya or Wako/Yokohama. In 2017, RIKEN NP-Depo (Headed by Dr. Hiroyuki Osada) and ITbM Chemical Library Center established an ITbM-CSRS Authentic Library. The Library can be applicable to validate newly established assay systems. The Library is accessible to researchers inside and outside of Japan to conduct chemical screening.

Collaboration with industries: ITbM has been involved with a total of 72 collaborative research projects with 34 companies, including 40 for chemistry, 28 for biology, and 4 for theoretical sciences. In the early days of ITbM, the scale of industrial collaboration was small, mainly focusing on fundamental studies. However, as the research achievements of ITbM have become more visible, large collaborative research toward practical applications are increasing.

2-5. Appraisal by society and scientific organizations

Describe how society and/or scientific organizations in and outside Japan have recognized the Center’s research achievements.

- To substantiate the above evaluation, list the main awards received and invitational/Keynote lectures given by the Center’s researchers in Appendix 1-3.

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

Three PIs (Itami, Kay, Frommer) have been designated as “Highly Cited Researchers (Clarivate Analytics)” for two years in a row (2017 and 2018), which is a global standard for high activity and visibility. In 2017, Frommer received the Alexander von Humboldt Professorship and transferred to his present position. Frommer was also awarded the 11th Tsungming Tu Award from Taiwan, the most prestigious academic honor conferred to foreign scholars. Yoshimura became the first Japan-based animal biologist to receive the Van Meter Award, which was established in 1930 by the American Thyroid Association. Itami became the youngest Japanese chemist to receive the Arthur C. Cope Scholar Award by the American Chemical Society in 2015. Crudden awarded a highly competitive Killam Research Fellowship from the Canada Council in recognition of her exceptional career achievements in 2015. Crudden is also a 2019 Arthur C. Cope Scholar. Torii was awarded the Saruhashi Award in 2015, which is granted each year to a female scientist in recognition for their distinguished research in natural sciences. Torii’s accomplishments have been widely covered in the media, including 12 national newspapers, and over 60 websites and magazines.

ITbM PIs have been invited to give lectures at nearly 400 international conferences held worldwide and at over 500 academic meetings, as well as at public workshops, where they have successfully promoted their research along with the activities of ITbM. It is noteworthy that ITbM researchers have recently been invited to the conferences of different disciplines. For instance, Itami was invited as a keynote speaker to “Cold Spring Harbor Asia Conference on Latest Advances in Plant Development & Environmental Responses” (2016), “The Annual Conference of Japan Society for Chronobiology” (2016), and “The Annual Meeting of the Japanese Society of Nephrology” (2019).

All ITbM PIs serve on editorial boards of major scientific journals and many of them are on the organizing committee of various international conferences, thus reflecting their presence in the science community.

In addition to the huge number of awards and honors, ITbM’s molecules developed via

interdisciplinary collaboration are influential. In particular, the molecule developed to combat the parasitic plant *Striga* has been widely covered in the public media (see Section 2-1[1]), and is highlighted in the Recommendation to the 7th Tokyo International Conference on African Development (TICAD7), which will be held in August 2019. ITbM will be recognized more widely when the molecule is developed as a tool in Kenya and becomes available widely to all the farmers in Africa.

2-6. Feeding Research Outcomes Back into Society

2-6-1. Applications of research results

Describe the applications created from research results, their effect in spawning innovation, intellectual properties (IPs) obtained, and joint research activities conducted with corporations, etc.

ITbM has created a wide range of networks consisting of domestic/international industries geared towards the societal implementation of the research outcomes. As a result, ITbM has contributed globally to technological and social development.

ITbM has developed innovative technologies which meet the needs of society. Based on the ITbM research, 120 patent applications have been filed; 85 for national patent applications and 35 for PCT applications. It should be noted that 41 out of 120 applications have been based on inventions derived from the interdisciplinary researches between chemistry and biology. With these patents, 32 patent license agreements have been concluded. The licensees including global leading companies have actively promoted R&D results with significant societal implications. In 2018, the license agreements on nanocarbon-based materials was concluded, which are expected to be a novel core for future functional materials.

ITbM-based patents were also concluded with Nagoya University-initiated ventures, and 2 ITbM-based ventures were established. Gra&Green Inc., supported by JST-START program, was established in 2017, which aims to innovate seeds & seedlings industry to impact next-generation food & agriculture by using cutting-edge biotechnology, such as its own and novel “inter-family” grafting technology including genome editing. Craftide Co., Ltd., supported by NEDO Entrepreneurs Program (NEP) and Venture Fund of Nagoya University and Tokai Area’s Universities, was established in 2018 to develop research tools for peptide-based drug discovery using cutting-edge peptide synthesis technology.

ITbM has created opportunities for licensing and collaborative research with overseas companies by working closely with Technology Partnership of Nagoya University, Inc. (NU Tech) in USA. At the NU Tech Round Table, which is a technology-matching event held in North Carolina, ITbM researchers describe their unique technologies every year. In 2018, when Torii released the technology of commercialized synthetic auxin (cvxIAA), a large number of foreign companies approached her about this technology. To date, NU Tech’s support has led to conclude 7 agreements in the agrochemical and research reagent field with foreign companies including major global foreign companies.

Based on these patents, 15 molecules developed at ITbM are now commercially available. For example, LipiDye, a novel fluorescent dye that stains the lipid droplets located in cells with high sensitivity, has widely spread to not only academia but several industries including medical, pharmaceutical, agrochemical and cosmetic companies. Also, ITbM concluded the license agreement of SPL7, which induces suicide germination of *Striga* and has decided to commercialize this as a reagent for researchers. Furthermore, due to its extremely high activity, SPL7 is expected to be utilized as not only a reagent for basic research, but also an agrichemical application in Africa.

ITbM has conducted many collaborative research projects with companies as denoted above. To promote this, ITbM has concluded 25 MTAs with a variety of companies in the field of medical, agrochemical, and electronic material. The results have been fed back to the researchers through SPD and some go on to the next stage, such as further collaborative research agreement or are utilized by the researchers to develop their research further.

To create more opportunities for academia-industry partnership, ITbM launched a membership discussion forum “ITbM Consortium” in 2018, where ‘Seeds’ and ‘Needs’ meet each other. The organization of the consortium offers industrial partners the opportunity to access the latest science, technologies and researchers in ITbM. In return, industrial partners provide ITbM researchers with information on societal needs that can be solved with ITbM cutting-edge technologies. The consortium has 17 companies covering a variety of businesses such as agrichemical, chemical, pharmaceutical, food, functional materials, and automotive. ITbM has co-organized an “ITbM consortium workshop” twice a year. As a result of the latest research presentation at the workshops, new license and collaborative research agreements have been concluded. ITbM expects to enter into further licensing and collaboration agreements continuously, through these consortium activities.

2-6-2. Achievements of Center's outreach activities

* Describe what was accomplished in the center's outreach activities during the period from 2012 through March 2019 and how the activities have contributed to enhancing the center's "globally visibility." In Appendix 5, describe the concrete contents of these outreach activities and media reports or coverage of the activities.

ITbM has strategically created a wide range of networks with top scientists, journalists, artists, high school teachers/students, and the general public. Based on this network, ITbM has actively organized various outreach activities including scientific symposia/seminars, exhibitions, international press releases, public lectures, science education and so on.

International press releases

In 2013, ITbM established an international press release platform in RPD and has been regularly releasing international press releases on ITbM's interdisciplinary research outcomes, international awards/events and other outreach activities, through international press release services such as EurekAlert!, ResearchSEA and AlphaGalileo in North America, Asia, and Europe, respectively. These are released in a way that complex scientific results are conceivable to people in different fields, and that the excitement from the research can be understood quickly and shared with the readers, *in combination with writing skills and science design*. To date, ITbM has distributed over 60 press/event releases, held over 30 press conferences about their research activities and has been covered over 10,000 times in the media. A number of ITbM's research news items have been translated in various languages, such as Chinese, Dutch, French, Germany, Indonesian, Korean, Portuguese, Russian, and Spanish. The distribution of press releases and subsequent media coverage are considered to have been a highly effective method for dissemination of ITbM's activities, thus leading to increased attention from the academic, industrial, public and media sectors. For example, a press release on SCL1, molecule that close stomata for drought tolerance, developed by the collaboration between Kinoshita group and Chemical Library Center in 2018, received a number of inquiries from both the academia and industry within a few days and led to international collaborations with agrochemical companies. ITbM is also working together with its partner institutes, Emory University and RIKEN CSRS to release joint press releases and strengthen the collaboration.

Outreach and network

The RPD has also been involved in various outreach activities, including the largest event: Science Agora. Lab tours and seminars to introduce ITbM have been also held for students, teachers, and the general public from local and overseas high schools as well as for other visitors. ITbM's activities are also introduced to the academic community by means of booth exhibitions at international events, including the AAAS Annual Meetings (USA) to the public, Super Science High School Presentation, and various kinds of the exhibitions to industries. PIs, staff and RPD members are also involved in holding public lectures in high schools and science cafés. ITbM's research activities were presented to over 5,000 high school students in these two years (in FY2017 and 2018), and the RPD held many outreach events to the general public (over 50 outreach events every year). In 2018, ITbM organized the 7th WPI Science Symposium entitled "Transformative Science", which collected more than 800 participants including 400 high school students, and shared the excitement of science with all. These events not only are effective for fostering future scientists (high school students) but they are effective for the younger generation elementary school students, including their parents, to develop a curiosity towards molecules. This led to the establishment of ITbM's "MoleQrious!" project. The final goal of this campaign is to create a society in which molecules are recognized at the same level as common scientific words, such as the "genome".

The 7-year-educational campaign has had a substantial payoff in the form of collaboration with one of the oldest department stores in Japan, Matsuzakaya. This is the first attempt to receive private financial support for management of the event and is considered a good strategy towards sustainable management of the center. In April 2019, ITbM will start a series of ITbM lectures at Chunichi Culture Center in Sakae, the downtown of Nagoya, to introduce the general public to ITbM's cutting-edge science and potential contribution to society.

The 7-year networking with high schools resulted in joint events including the annual WPI science symposium and Kagaku-zanmai, the largest science event in the Tokai area, an extensive network for University-High School Collaboration, and the involvement of ITbM as a committee member at designated high schools of the Super Science High School Program, MEXT.

3. Generating Fused Disciplines (within 3 pages)

3-1. State of strategic (or "top-down") undertakings toward creating new interdisciplinary domains

Under the strong leadership of the Director, all members at ITbM have been working beyond their discipline and developing interdisciplinary research spanning chemistry, plant/animal biology, and theoretical sciences toward making transformative molecules.

Following the success of the distinctive 'Mix' strategy in ITbM, ITbM succeeded in creating more than 100 interdisciplinary research projects. In 2015, ITbM has defined three flagship research areas as 'plant chemical biology', 'chemical chronobiology', and 'chemistry-enabled live imaging'. These flagship projects are also enabled by ITbM's unique set of platforms: (i) small-molecule synthesis, (ii) phenotypic assay development, (iii) theoretical design and bio-simulation, (iv) chemical library generation/curation (Chemical Library Center), (v) laser microscopy (Live Imaging Center), (vi) omics and molecular analysis (Molecular Structure Center, see also 3-2), and (vii) peptide and protein synthesis (Peptide/Protein Center). Through sharing these platforms among all of ITbM's researchers, interdisciplinary research was strongly promoted.

During the 1st phase of ITbM (2012-2016), ITbM selected the *Striga* project as a flagship project. The project emerged via a bottom-up collaboration and has been highly successful as denoted in Section 2-1[1].

3-2. State of "bottom-up" undertakings from the center's researchers toward creating new interdisciplinary domains

Describe the content of measures taken by the Center to advance research by fusing disciplines. For example, measures that facilitate doing joint research by researchers in differing fields.

ITbM's Mix concept as described in Section 2-2 has facilitated bottom-up interdisciplinary projects among young researchers. Particularly, Mix Labs and Mix Offices function as places where new unique ideas in research are being generated based on daily communications among the researchers from different fields working side-by-side. Other strategic measures listed below are also contributing effectively to facilitate interdisciplinary research.

ITbM Research Award was established to foster interdisciplinary collaboration among young researchers and students. All ITbM members (except PIs) including postdoctoral researchers and students are eligible to apply. Selected proposals are each awarded 2 million yen to be spent over 2 years. The proposals prepared in English are pre-evaluated, and finally selected through oral presentation in English followed by paper screening, adjudicated by all NU PIs, several overseas PIs, and in some cases, visiting professors with high research profiles. So far, 15 proposals among 28 were selected after careful evaluation, and most proposals have made good progress to mature into ITbM's representative research projects including the *Striga* project. The award also contributes to motivate young researchers and students to apply for external grants, and provides them practice with writing grants and defending their ideas.

ITbM Workshop is held annually to share research progress and to provide an opportunity for new collaboration in ITbM. Members who participate in the workshop are those engaged in ITbM research including faculty members, postdoctoral researchers, technical staff, students, and administrative staff. At these workshops, extensive discussions about the details and plans of research are held in one – two days. The workshop functions to highlight and expand the bottom-up collaborations generated during daily discussions around the bench to all ITbM members and encourage further participants.

ITbM Tea Break Meeting started from 2015 to promote "Mix" based on casual discussions such as on research progress and Mix Lab/Mix Office management. The meeting has been providing an important opportunity to mix researchers, students, technical staff, and administrative staff, to enable network-building among ITbM's researchers who come from various disciplines and backgrounds.

Research Promotion Division (RPD) has been playing a critical role as a catalyst to initiate collaboration. RPD staff attend all PI's group meetings to enable collaborations between groups of different research fields. Thus, the RPD can assist in strategic planning at an early stage of the research, including early feedback on research that should be covered under intellectual property and developing industrial collaborations with the help of the SPD (see below). By having a detailed understanding of the science, the RPD is able to carry out effective public relations, science visualization, public outreach, and so on.

Strategic Planning Division (SPD) was separated from RPD in 2016 to focus on promotion of societal implementation of the research outcomes, which is also critical for ITbM's sustainability. The SPD is spearheading initiatives to promote collaborative research with industry. The SPD has been building strong ties with the Academic Research & Industry–Academia–Government Collaboration Department of NU, which is enabling them to further promote, expand and strengthen collaborations with industry.

The four supporting centers (Molecular Structure Center, Live Imaging Center, Chemical Library

Center, and Peptide Protein Center) have also been making remarkable contributions to the promotion of ITbM's interdisciplinary research. To date, ITbM has collaborated with over 1000 users inside and outside of ITbM and has been a part of nearly 100 publications on interdisciplinary research. For example, the Live Imaging Center cooperated on two Grant-in-Aid for Scientific Research on the Innovative Areas, and has been elected the most used center in Japan in 2017. The Chemical Library Center has distributed ca one million compounds for 88 collaborators inside/outside Japan, filing 11 patens, and expanding its activities such as on drug discovery and development, metabolomics, and predictive toxicology. The Molecular Structure Center plays a key role in identifying target proteins by installing immunoprecipitation, stable isotope labeling of amino acids in cell culture (SILAC), phosphoproteomics, and mass spectrometry (MS) imaging through collaborations with Academia Sinica and RIKEN CSRS. The Peptide/Protein Center is a critical part of ITbM, delivering tailor-made peptides for plant and animal biologists. The center has established a spin-off company "Craftide" and was successfully funded for early stage support of startups.

New research groups have advanced the interdisciplinarity of ITbM. A computational group led by Tama (since 2016) has been collaborating extensively with the Kay-Hirota, Torii-Uchida, and Higashiyama groups and the results have been published in interdisciplinary research journals such as chemical chronobiology (Proteins, 2018), plant chemical biology (Nature Plants, accepted), and plant reproduction, respectively. The Frommer-Nakamura group is also actively initiating interdisciplinary collaborations with chemistry groups (Itami, Yamaguchi, Bode), the computational sciences group (Tama), and the supporting centers such as the Live Imaging Center, Chemical Library Center, and Molecular Structure Center. Their proposals were selected to receive ITbM Awards in FY2017 and 2018, and are expected to open up new avenues in ITbM. The Yanai group, which joined ITbM in 2018, and has just started collaborations with Itami and Yamaguchi groups to explore the electronic properties of carbon nanobelts and design new fluorescent molecules initiated by theory, respectively. They also started to collaborate toward in silico drug discovery and development.

3-3. Results of research in fused research fields

Describe the Center's record and results by interdisciplinary research activities yielded by the measures described in 4-1 and 4-2.

- In Appendix 1-2, list up to 10 of the Center's main papers on interdisciplinary research that substantiate the above record of results, and describe their content.

The synergy of ITbM researchers' high research profile and the new research style at ITbM has facilitated interdisciplinary research in the three flagship research areas that ITbM had defined. A number of collaborative research projects have been promoted, and joint publications and patent filings by multiple PI groups are constantly increasing in number. So far, 49 papers and 41 patents are co-authored by multiple PIs, and 260 papers are published by international collaboration. Representative outcomes are denoted below.

Striga project

The progress of the *Striga* project denoted in Section 2-1[1] has never been achieved without the full Mix of the ITbM. Yoshimulactone Green (YLG) was developed by naturally-occurred collaboration among the ITbM chemists (**Itami** group), biologists (**Kinoshita** group), **Molecular Structure Center**, and **Live Imaging Center** (Appendix 1-2 (1): *Science* 2015). The discovery has accelerated the development of sphynolactone-7 (SPL7) by further collaboration among the ITbM chemists (**Ooi** group), biologists (**Kinoshita** group), **theoretical science** group, and **Molecular Structure Center** (Appendix 1-2 (2): *Science* 2018). These achievements further led to the identification of strigolactone receptors agonists/antagonists in collaboration with the **Chemical Library Center** (Appendix 1-2 (3): *ACS Cent. Sci.* 2018). The collaborative network is further expanding toward practical use of SPL7 in the field of Kenya.

Plant Chemical Biology

The **Torii-Uchida** group has recently been exploring small molecules that can control the density and/or patterning of stomata through chemical screening of ITbM chemical library. They collaborated with the **Itami** group and the **Chemical Library Center**, and identified the first-in-class synthetic molecules that increase the number of stomata in *Arabidopsis thaliana*. In addition, some of the molecules were found to promote the root growth in various plant species such as *Arabidopsis thaliana* and edible plants (cucumber, lettuce, etc.) (Appendix 1-2 (4): *Chem. Commun.* 2017).

The **Kinoshita** group and the **Chemical Library Center** have conducted chemical screening over 30,000 compounds, and succeeded in identifying nine stomatal closing molecules (SCL1–SCL9) that suppress light-induced stomatal opening. They have also revealed that SCL1 and SCL2 do not show any negative effect on ABA-dependent responses, such as inhibition of seed germination (Appendix 1-2 (5): *Plant Cell Physiol.* 2018). Now, they are collaborating with agrochemical companies and trading companies toward practical use of the both molecules.

The **Torii-Uchida** group's study on ligand-receptor interaction in plant was led to the development of the novel bifunctional synthetic peptide, KIN, that exhibits double effects of vascular-thickening and root-shortening. They collaborated with **computer scientists** and indicated that the KIN could bind to two receptors CLV1 and TDR that regulate the two phenotypes, respectively (Appendix 1-2 (6): *Nature Commun.* 2018). Inspired by this success, the groups of **Torii-Uchida**, **Kinoshita**, and **Itami** have engineered an orthogonal auxin-TIR1 receptor pair through a bump-and-hole strategy, which triggers the auxin signaling without interfering with endogenous auxin or TIR1/AFBs. Through this study, they provided conclusive evidence for the role of the TIR1-mediated pathway in auxin-induced seedling acid growth (Appendix 1-1 (12): *Nature Chem. Biol.* 2018).

Nambo (Crudden group) established a chemical library consisting of diverse compounds containing the triarylmethanes which are thought to be promising compounds for anti-proliferative activities. By utilizing this library, **Ueda** and **Kurihara** (Higashiyama group), **Ohkawa** (Yoshimura group), and **Kuwata** (Molecular Structure Center) have cooperatively demonstrated one of the compounds, (3-furyl)-diphenylmethane, showed specific antiproliferative activity for plant cells (Nicotiana tabacum) but not for animal cells (HeLa) and yeast (Saccharomyces cerevisiae) (Appendix 1-2 (7): *Plant Cell Physiol*. 2016).

Chemical chronobiology

Through extensive collaborations in ITbM, the groups of **Yoshimura**, **Itami**, **Kay-Hirota**, and **computational sciences**, have demonstrated that transformation of a period-lengthening molecule KL001 resulted in the development of period-shortening derivatives synthesized via catalytic C-H coupling reactions by the **Itami** group (Appendix 1-2 (8): *Angew. Chem. Int. Ed.* 2015). Further collaborations of the groups of **Kay-Hirota**, **Itami**, **Tama** and **Molecular Structure Center** resulted in development of the small molecule GO289 as a potent and selective inhibitor of CK2 with outstanding physicochemical properties *in cells*. They have recently started joint R&D research with a pharmaceutical company to optimize GO289 targeting circadian clock related-diseases and to develop candidate molecules for clinical trial (Appendix 1-1 (15): *Science Adv.* 2019).

The **Yoshimura** group and the **Chemical Library Center** succeeded in identifying the period-shortening compound dehydroepiandrosterone (DHEA; also known as prasterone) accelerated re-entrainment to advanced light–dark (LD) cycles *in vivo*, thereby reducing jet-lag of mice. They also revealed that the mechanism regulating circadian period involves tyrosine kinases, ABL1 and ABL2, and the BCR serine/threonine kinase (Appendix 1-2 (9): *EMBO Mol. Med*. 2018).

Chemistry-enabled live imaging

Collaboration of the groups of **Yamaguchi**, **Higashiyama**, and **Live Imaging Center** resulted in a new design of super-photostable dye, PhoxBright 430 (PB430) as a biology-friendly fluorescent molecule. The PB430 gives rise to intense fluorescence insensitive to environment in terms of fluorescence colors and intensity, and bright fluorescence even in aqueous media. Indeed, using a PB430-conjugated antibody, they succeed in attaining a 3D reconstruction of super-resolution STED images as well as photostability-based multicolor STED imaging of fluorescently labeled cytoskeletal structures (Appendix 1-1 (16): *JACS* 2017).

The groups of **Itami**, **Higashiyama** and **Live Imaging Center** have cooperatively developed a water-soluble warped nanographene (WNG) and revealed that the WNG has unique properties suited to biological applications. They demonstrated that the water-soluble WNG was readily encaptured into HeLa cells and induced cell death upon light irradiation. The result indicates the future application of WNG toward photodynamic therapy (Appendix 1-2 (10): *Angew. Chem. Int. Ed.* 2018).

Target ID platform

According to the research progress, their target protein identification (target ID) became indispensable to elucidate the molecular mechanisms of biological functions and to develop transformative bio-molecules. Thus, ITbM has been developing the target ID platform. The **Molecular Structure Center** plays a central role to proteomics research applicable to identify target proteins and to explore signal transduction by installation of many methods, such as pull-down assay (**Hirota** and **Itami** *et al. Science Adv.* 2019: **Nakamichi** and **Itami** *et al. PNAS* 2019), co-immunoprecipitation (**Kinoshita** *et al. Sci. Rep.* 2017), phosphoproteomics (**Higashiyama-Ueda** *et al. PNAS* 2016 & 2019), shotgun proteomics for identification of target proteins of GO289 against AML cells, stable isotope labeling of amino acids in cell culture (SILAC) for target ID of natural product picrotoxinin that shortens circadian clock (collaboration of **Ooi** and **Yoshimura**), and mass spectrometry imaging (collaboration of **Crudden-Nambo** and **Yoshimura**). ITbM is also planning to establish a global target identification platform with the other institutions, such as the **Institute of Chemistry of Academia Sinica** and **RIKEN CSRS**. ITbM has also started collaboration with a **bio-informatician** (Dr. Shimamura) from the Division of System Biology in the Medical School of NU to accelerate omics research.

4. Realizing an International Research Environment (within 4 pages)

4-1. International Circulation of Best Brains

4-1-1. Center's record of attracting and retaining top-world researchers from abroad

Describe the participation of top-world researchers as PIs and their stays as joint researchers at the Center.

・ In Appendix 3-2, give the number of overseas researchers among all the Center's researchers, and the yearly transition in their numbers. In Appendix 4-2 give the achievements of overseas researchers staying at the center to substantiate this fact.

All of the five world-leading ITbM overseas PIs have been actively contributing to the various activities of ITbM. They live in Nagoya for 1-2 months per year and attend site visits and annual international symposia, ISTbM. Even when they are absent from Nagoya, they have close contact with their respective Co-PIs and postdoctoral researchers through regular video conferences or e-mails. They also regularly send young researchers from their own institutes to ITbM.

Frommer, who joined ITbM as the fifth overseas PI in FY2016, is a good example of a world-class researcher who was intrigued by ITbM. While Frommer was first planning to start collaborative research with ITbM researchers, he became aware of ITbM's unique research environment and approached us to become a PI.

4-1-2. Employment of young researchers at the Center and their job placement after leaving the Center

Describe the Center's employment of young researchers, including postdoctoral researchers, and the positions they acquire after leaving the Center.

・ Enter the following to substantiate the facts provided above:
- In Appendix 4-3, describe the Center's state of international recruitment of postdoctoral researchers, the applications received, and selections made.
- In Appendix 3-2, give the percentage of postdoctoral researchers employed from abroad
- In Appendix 4-4, describe the positions that postdoctoral researchers acquire upon leaving the Center.

Mentoring young researchers is a key to the future development and global standing of ITbM. Since ITbM's launch, a notable number of postdoctoral researchers have carried out research at ITbM, and are now in key positions in academia or industry in Japan and overseas. Thus, ITbM has been a key part of the global talent stream.

ITbM postdoctoral researchers hired by WPI fund are predominantly non-Japanese, although Japanese researchers have also been affiliated as JSPS Research Fellows. By the end of FY 2018, ITbM hired 82 postdocs, of which 53 (65%) are non-Japanese. On average, 25-30 postdoctoral researchers are resident at ITbM every year.

The employment of postdoctoral researchers is on a one-year contract, which can be renewed up to three years. ITbM has been able to recruit these highly trained personnel from various research institutions in the world such as UC Berkeley, University of North Carolina, University of Washington, Queen's University, University of British Columbia, University of Toronto, Max Planck Institutes, Free University of Berlin, University of Münster, University College London, University of Edinburgh, National University of Singapore, and Academia Sinica.

Out of the 59 postdocs who left ITbM, 31 found faculty positions in academia. Of note is Dr. Wang who got the Professor position of Peking University, China. Thus, affiliation to ITbM is obviously a successful career path.

Academic promotion of young faculty members is also notable. Dr. Hagihara was recruited as Team Leader of RIKEN CSRS, Dr. Yamaguchi as Professor of Waseda University, Dr. Yokogawa as Associate Professor (PI) at the University of Tokyo, Dr. Hijikata as Associate Professor of Hokkaido University, and Dr. Fukazawa as Professor of Kyoto University.

4-1-3. Overseas satellites and other cooperative organizations

・ In Appendix 4-1, describe the state of cooperation with overseas satellites and other cooperative organizations. In Appendix 4-5, describe the state of the Center's agreements concluded with these organizations.

Although satellite institutes are not established, ITbM has several international cooperating institutions. In addition to the overseas PIs' host institutions designated from the inception of ITbM, we have strategically expanded our collaboration network with national/international institutions to augment the research activities of ITbM. ITbM has published 260 international joint papers.

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

Frommer is a member of CEPLAS, which is a joint initiative of HHUD, University of Cologne (UoC), Max Planck Institute for Plant Breeding Research Cologne (MPIPZ) and Forschungszentrum Jülich (FZJ). The CEPLUS is the only plant research center selected as the Cluster of Excellence supported by the German Research Excellence Initiative, and a world-leading institute of plant science. HHUD has communicated a significant interest in collaborating with ITbM, and has concluded research collaboration agreements and tuition-free student exchange in 2018.

National Science Foundation Center for Selective C-H Functionalization (NSF-CCHF, USA) is an international partner that has been extensively collaborating in the field of C-H activation chemistry constituting an important area of ITbM's research. CCHF is a virtual institute with 23 world leading PIs and their research groups working in the field of C-H activation chemistry in 14 universities/institutes across the USA. Around 4 to 5 researchers per year carry out research exchanges of 3-6 months between the institutes. The network also expanded to include other related institutes such as the Institute for Basic Science (IBS, KAIST, Korea). In 2019, ITbM, CCHF, and IBS are holding joint workshop. ITbM organized the 1st workshop at ITbM in 2016, and IBS will host the 2nd workshop in July 2019 in Korea.

RIKEN Center for Sustainable Resource Science (CSRS, Japan) is an important partner in Japan. CSRS, focusing on plant biology and synthetic chemistry, was established at almost the same time as ITbM. Directors of ITbM and CSRS made a joint statement on the joint use of the research support platform, and confirmed further promotion of collaboration between CSRS and ITbM. The CSRS-ITbM Joint Workshop is an annual event. In 2018, Hagihara (ex Itami group) had transferred to the CSRS as Team Leader of the CSRS, and collaboration has been largely promoted. Several collaborative research are ongoing.

University of Freiburg (Germany) and **Academia Sinica (Taiwan)** are also international partners of ITbM. Based on research agreements, collaborative research projects are ongoing with these institutions through the exchange of researchers. Recently ITbM and **A*STAR (Singapore)** have started discussions to enter extensive collaboration especially in the field of chemical biology, which will advance ITbM's chemical plant biology and societal implementation of bio-functional molecules developed at ITbM.

NU and **Kenya Agricultural & Livestock Research Organization (KALRO)** will soon conclude a MOU to start "African food security project" (see Section 7 and the Progress Plan). In this framework, the molecules to combat *Striga* will be tested in the research fields of KALRO in Kenya.

4-2. Center's record of holding international symposia, workshops, research meetings, training meetings and others

- In Appendix 4-6, describe the main international research meetings held by the Center.

ITbM has hosted international symposia (ISTbM) and three international awards (Hirata Award, Tsuneko & Reiji Okazaki Award, Nagoya Medal of Organic Chemistry) annually, which have contributed to increasing ITbM's international visibility.

ITbM International Symposium on Transformative Bio-Molecules (ISTbM)

ITbM organizes an international symposium every year in Nagoya by inviting world leading researchers who carry out research in ITbM-related fields, such as organic chemistry, animal/plant biology and theoretical science. To date, 71 speakers have been invited, in which 19 from organic chemistry, 20 from plant/animal biology, 6 from theoretical sciences, and 26 from ITbM.

Hirata Award

The Hirata Award (former name: the Hirata Memorial Lecture) started in 2005 at NU in memory of the great achievements of the late Dr. Yoshimasa Hirata, an Honorary Professor of Nagoya University, and is an international award given to a rising star in the field of organic chemistry. Previous winners of the award are: Drs. Justin Dubois (2004), David R. Liu (2005), Phil S. Baran (2006), Peter H. Seeberger (2007), Scott J. Miller (2008), Jeffrey W. Bode (2009), Jin-Quan Yu (2010), Mohammad Movassaghi (2011), Tobias Ritter (2012), Martin D. Burke (2013), Ashraf Brik (2015), Emily Balskus (2016), David A. Nicewicz (2017), and Ruben Martin (2018).

Tsuneko & Reiji Okazaki Award

The Tsuneko & Reiji Okazaki Award was established in 2015 by ITbM in memory of the great achievements of Dr. Tsuneko Okazaki, University Professor and the late Dr. Reiji Okazaki, Honorary Professor of NU. Previous winners of the award are: Drs. Feng Zhang (2015), Yukiko Yamashita (2016), Maria Barna (2017), and Cyril Zipfel (2018).

Nagoya Medal of Organic Chemistry

The Nagoya Medal Prize was initially proposed by Drs. Hisashi Yamamoto and Ryoji Noyori, and founded in 1995 through the financial support of MSD Life Science Foundation (previously: Banyu Life Science Foundation International). The Nagoya Gold Medal Prize has been awarded every year to an organic chemist who has made significant original contributions to the field in its broadest sense. The Silver Medal, established in 1999, has been presented every year to a front-runner based in Japan whose research has had a major impact on the field of synthetic organic chemistry. Currently ITbM is hosting the Nagoya Medal from 2013 along with Itami as the chair of the Nagoya Medal selection committee.

CSRS-ITbM Joint Workshop

ITbM and CSRS concluded the “Agreement on the Association and Cooperation” and held the 1st CSRS-ITbM Joint Workshop in January 2014. The workshop takes place annually in either Nagoya or Wako/Yokohama. In 2015, both institutes decided to enter a partnership to collaborate in chemistry and plant biology. In 2016, both directors made a statement on the joint use of the research support platform and confirmed further promotion of collaboration between ITbM and CSRS.

Others

As part of the collaboration with international partner institutions, the following activities were organized:

- 1st international joint workshop with NSF-CCHF and IBS-KAIST (Nagoya, 2016)
- 1st joint workshop of ITbM and IoC, Academia Sinica (Nagoya, 2016)
- 1st international symposium by ITbM and the University of Freiburg "Multicomponent Supramolecular Catalysts for Sustainable Chemical Synthesis" (Freiburg in Germany, 2017): Ooi served as one of the chairs of the symposium.
- 2nd joint workshop of ITbM and IoC, Academia Sinica (Taipei in Taiwan, 2017)
- 2nd international joint workshop with NSF-CCHF and IBS-KAIST (Daejeon in Korea, 2019)

ITbM researchers have been appointed to organize the following international symposia/workshops:

- International Symposium on Biological Rhythms “Towards understanding the molecular clockwork” (Nagoya, 2016): Yoshimura served as one of the organizers of the symposium.
- The 25th International Congress on Sexual Plant Reproduction (Gifu, 2018): Higashiyama and Ueda served as members of the organizing committee.
- Japan-Taiwan Plant Biology 2019 (Nagoya, 2019): Kinoshita, Nakamura, and Kanaoka served as organizing committee.

The EMBO Practical Course “Functional live imaging of plants” will be held in ITbM, Nagoya, from May 21-30, 2019 (Organizer: Higashiyama). The 9th Chemical Protein Synthesis Meeting is scheduled for 2021 in Nagoya (Organizer: Bode).

4-3. System for supporting the research activities of overseas researchers

Describe the Center’s preparations to provide an environment conducive for overseas researchers to concentrate on their work, including for example living support in various languages or living support for their families.

To allow the researchers from abroad to settle down in Japan and focus on their research, ITbM has been establishing various support systems. Especially, dedicated staff in ITbM’s Administrative Department are responsible for providing local support to **ITbM’s foreign researchers and their families** staying in Japan. The main purpose of this role is to offer a comfortable environment to ITbM’s researchers, so that they are able to fully concentrate on their research activities. Many foreign researchers who come to work in Japan have difficulties with the language barrier, as almost all the procedures at local government offices and medical centers are carried out in Japanese only. ITbM has assigned the **Local Support Officer** to the RPD, who is responsible to provide on-scene support to foreign researchers at ward offices, including help with national health insurance and the pension system, as well as assistance in immigration affairs and other matters that may arise in their daily lives.

The Administrative Department has been sending all notices from the university to researchers in both English and Japanese. All meetings at ITbM with participation of non-Japanese-speaking researchers are held in English and all documents and meeting minutes are prepared in both English and Japanese. Many documents for university administrative procedures have been translated into English by ITbM’s Administrative Department. The Administrative Department especially focuses on providing attentive support in the employment and resignation of non-Japanese researchers and provides detailed explanations of Japanese tax and the social insurance system in English.

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

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

The Local Support Officer has collected information of hospitals with English services in Nagoya to cover major medical departments. To provide advanced support, ITbM signed a contract with International SOS Japan Ltd. in 2016 to provide advanced medical service information 24 hours a day.

In order to provide more useful information, some beneficial services from the International Education & Exchange Center (IEEC) in NU are being shared with ITbM's foreign researchers. The IEEC mainly provides assistance for international students, but in recent years, the ITbM has started expanding their services to support foreign faculty members and postdoctoral fellows as well. Services include: seminars on tax adjustment, orientation for renting an apartment in Japan, health consultations, and information on cultural events such as Japanese flower arranging (Kado) and Origami lessons.

By contribution of ITbM, NU has recently established the **Dual Career Program**, which provides opportunities for partners/spouses to hold positions in NU on the basis of proper evaluation. This program will largely promote the recruiting of top researchers around the world.

4-4. Others

Describe the Center's policy for sending Japanese researchers overseas to gain international experience, and give examples of how the Center is working to create career paths for its researchers within a global environment of researcher mobility.

Fostering young researchers is a key mission of ITbM. For this purpose, ITbM launched the program "Overseas Training of PhD Students", which financially supports the PhD students to conduct research at overseas institutions. Annually, 2-4 PhD students have travelled for 3-6 months to various institutions in such as the US and Germany. On the other hand, ITbM has provided various opportunities for faculty members and postdocs to make international networks. Many of them are involved in collaborative research with overseas PI groups. Several researchers have started collaborations with overseas researchers who had visited ITbM. ITbM's annual international symposia described in Section 4-2 have also helped in this regard. ITbM is also utilizing the international programs run by NU, such as "Top Global University Project (MEXT)", "Dispatching Young Researchers Abroad Program at the Graduate School of Science (NU)", and the Core-to-Core Program "Elements Function for Transformative Catalysis and Materials". The total number of the PhD students travelled overseas institutions amounts to 39 as of the end of FY2018.

5. Making Organizational Reforms (within 3 pages)

5-1. Decision–making system in the center

Describe the strong leadership that the director is giving on the Center's operation and its effect, and the division of roles and authority between the Center and its host institution.
In Appendix 3-3, draw a concrete diagram of the Center's management system.

The Director has the authority to make final decisions over all matters concerning the operation and management of ITbM, such as the appointment of personnel, the Center budget and research priorities, and incentive-based bonuses. The role of the President of NU is limited to the appointment of the Director according to suggestion by the WPI program committee.

The ITbM Steering Committee is held monthly, which is a place for discussion and provides advice to the Director to make the final decisions. The Committee members include the Trustee of NU (in charge of WPI affairs). The Director operates and manages ITbM in consultation with the Steering Committee.
In addition, the Director and core members of ITbM hold a meeting with the President of NU once a month to discuss over any issues related to the management of ITbM.

5-2. Arrangement of administrative support staff and effectiveness of support system

Describe the assignment of the Center's administrative support staff who have English language and other specialized skills, effort made in establishing the support system, and the system's effectiveness.

The Administrative Department was organized to provide the environment for ITbM researchers to fully focus on their research projects. Led by the Administrative Director, the Department consists of 3 divisions; Management Division, Research Promotion Division (RPD), and Strategic Planning Division (SPD). The Management Division has 10 staff consisting of Division Head, 4 staff in the General Affairs Unit and 5 staff in the Accounting Unit. Half of the staff are competent English speakers, and the Department is able to manage all issues requiring English.

The RPD & SPD units have 8 staff including the Division Heads, who are experienced individuals with specialized skills, such as a science designer and a patent attorney. Most of them hold a PhD or a Masters Degree in related fields and are proficient in English. Their high performance strongly supports ITbM's interdisciplinary research in various aspects.

ITbM has 10 secretaries employed to assist NU/overseas PIs and the 4 supporting centers to make a smooth communication with the groups via cooperation with the Administrative Department.

5-3. System reforms advanced by WPI program and their ripple effects

Concisely itemize the system reforms made to the Center's research operation and administrative organization, and describe their background and results. Describe the ripple effects that these reforms have on the host institution. (If any describe the ripple effects on other institutions.)

Under President Matsuo's vision for Reform, Autonomy and Innovation 2020 (NU MIRAI 2020), NU has been carrying out extensive system reform to become a world-class research university. In the initiative, ITbM is positioned as a core research center of Nagoya University, and thus the basic policy and the measures of system reform have been established to match ITbM's needs.

Named to "Designated National University" by MEXT: NU was recognized for its abilities to develop world-leading education and research activities and was selected as a "Designated National University" as of March 20, 2018. ITbM's high-profile activities significantly contributed to this designation. NU will make all efforts to become an international leading university and play a leading role in the reform of national universities by actively disseminating the concrete results of their influence and efforts that have contributed to the development of the society and economy.

Conclusion of a Basic Agreement of NU with RIKEN: NU concluded a basic agreement on June 13, 2017 with RIKEN regarding the promotion of their partnership and cooperation to begin an inter-institutional partnership with the aim to produce world-class, top-level research achievements and innovation. In the past, ITbM and the Graduate School of Bioagricultural Sciences have both collaborated separately with the RIKEN Center for Sustainable Resource Science (CSRS). As other collaborative research is projected between the two institutions, the agreement between the two institutions was considered to be very comprehensive, aiming for cooperation in all fields in which collaboration is possible.

"Graduate Program of Transformative Chem-Bio Research (GTR)": NU recognizes the significance of the "Mix" concept to nurture young researchers. NU and ITbM drew up a concept for the "*Excellet Graduate School Program"*, which was selected in 2018. In the program, ITbM is positioned as a hub for promoting interdisciplinary research in the field of natural sciences. Through this program, ITbM's Mix concept will be more widely spread.

"WPI-next" and related programs at NU: In 2014, NU launched the "WPI-next" program to support world-leading science at NU, which referred to ITbM's unique concepts such as the Co-PI system. This program was reorganized as the "Cutting-edge International Research Units" program, and two more programs, "Research Units Geared toward Young International Researchers" and "Young Researcher Units for the Advancement of New and Undeveloped Fields" were launched in the framework of the Program for Promoting the Enhancement of Research Universities.

International Public Relations: ITbM has shared its expertise and experience on international public relations to the Academic Research and Industry-Academia-Government Collaboration Department and public relations office of NU. As a result, NU has started to prepare international press releases on research accomplishments for the entire university.

Information distributed in English: With respect to the English e-mail distribution by ITbM, NU started to circulate information of grants, funding and other information in both English and Japanese from the end of FY2013.

Department for "Academic Research & Industry-Academia-Government Collaboration": In order to promote technology transfer and research outcomes from ITbM and other NU's institutes,

NU conducted organizational reform of research supporting units to establish this department in 2015. At the same time, the URA system that started in 2013 was also reviewed extensively with respect to the role of the RPD at ITbM. Through this mutual feedback, ITbM's activities have largely advanced.

5-4. Support by Host Institution

The following two items concern the support that the host institution provides the Center. Describe the functional measures that the host institution has taken to sustain and advance the Center's project. That include those items of support that it committed to at the time of the initial project proposal submittal or in its revised commitment following the project's interim evaluation.

5-4-1. Record of host institution support and its effects

- In Appendix 6-1, describe the concrete measures being taken by the host institution.

NU has strongly supported ITbM in many aspects. Representative concrete measures are 1) covering salaries, 2) provision of space, 3) financial support towards construction of ITbM's building, 4) support towards the operation of the building, and 5) ITbM's priority to the use of the residence hall. More details are available in Appendix 6-1.

To secure the employment of ITbM's faculty members and staff, NU will institute organizational reform in 2019. NU will launch the "Institutes for Advanced Research Excellence", and position ITbM under this umbrella.

According to this plan, NU requested faculty positions from MEXT to strengthen ITbM's activities in 2018. This request was partially approved and 2 positions have been allocated to ITbM. NU will continue this request in the following several years.

5-4-2. Position of the Center within the host institution's mid-term plan

- To Appendix 6-2, excerpt the places in the host institution's "Mid-term objectives" and/or "Mid-term plan" that clearly show the positioning of the WPI center within its organization.

Following the launch of ITbM in 2012, NU immediately amended its 2nd phase 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)" including the promotion of ITbM's research in the plan.

In 2015, President Matsuo formulated the vision "NU MIRAI 2020", which states "Through excellence in its education and research, Nagoya University aspires to become one of the world's leading universities", "Research: Inspired by our Nobel laureates, we are committed to the creation and discovery of knowledge through research, ... supporting frontier research led by ... ITbM for WPI program".

In 2016, the 3rd phase mid-term plan was issued (revised partially in March 2019), in which ITbM has been included both in education and research; "(K2) ... NU will improve its international compatibilities by developing joint degree programs with world class partner universities. NU will provide the education program in the doctoral course integrated with the advanced researches conducted in various NU institutes such as the Institute of Transformative Bio-Molecules (ITbM) to attract capable doctoral candidates." "(K11) NU will promote the world-leading fundamental research and establish an international and original research center engaged in cross-section study, international collaborative study, and comprehensive study by promoting "World Premier International Research Center Initiative"".

In 2018, NU was named a "Designated National University". In the plan, NU has identified four key research areas, in which the first area is "interdisciplinary research in chemistry and biology led by ITbM". The plan clearly states that NU will invest human and financial resources intensively into the key areas, and following the president's initiative, ITbM is positioned to be a core research center of NU for the foreseeable future.

5-5. Others

Describe efforts advanced to foster young researchers (e.g., start-up funding, autonomous research environment) and to enlist female researchers.

- In Appendix 3-1, 3-2, give the transition in the number and ratio of female researchers.

Efforts to Foster Young Researchers (e.g., start-up funding)

The ITbM Research Award is a key way in which ITbM nurtures young researchers. For example, the novel fluorescent probe "Yoshimulactone" arose from the proposal of Masahiko Yoshimura (a PhD student in Itami group at the time) in 2014. This project paved a way to the development the *Striga*'s suicide germinator SPL7.

Personnel exchange between overseas institutes, such as NFS-CCHF has been active every year. ITbM has sent 39 students to universities in US and Europe, and accepted 36 students from those countries. ITbM holds the Joint Workshop with NSF-CCHF (USA) and IBS (Korea) on a regular basis as denoted above.

In the workshop, postdoctoral researchers and PhD students who met for the first time are requested to form several groups, and each group prepares a research proposal in English within a day. This is a big challenge especially for the Japanese PhD students, but it is an excellent training environment.

On the educational front, to establish a system for students to learn “chemical biology”, ITbM has started a lecture series on chemical biology. Three of the PhD students have been awarded the prestigious JSPS “IKUSHI Prize”, which is awarded to outstanding PhD students expected to contribute to Japan’s future scientific advancement in the presence of the Emperor. In 2018, NU launched the “Graduate Program of Transformative Chem-Bio Research (GTR)”, which has ITbM as a hub for promoting interdisciplinary research in the field of natural sciences.

Appointment and activities of Female Researchers

At the inception of ITbM, two female PIs (Torii, Crudden) were founding members, and they are leading the world by conducting cutting-edge science. Their remarkable achievements are evident in their collected number of awards as represented by the Saruhashi award to Torii in 2015 (see Section 2-5, Appendix 1-3). One more female PI (Tama) joined ITbM in 2016, and has been promoting various research projects via strengthening of the theoretical platform. ITbM has 16 female researchers, with 19 in total, this is 25% of all researchers.

ITbM has taken a proactive approach to supporting female researchers. Recently JST launched the “Jun Ashida Award” to foster female researchers, and Torii assumed the chair. Dr. Yoko Mizuta from the Higashiyama group has recently received JST-PRESTO and A-STEP, and is appointed as a YLC Assistant Professor of NU in 2019. ITbM has 2 JSPS Restart Postdoctoral Fellows to support parental leaves of female researchers. ITbM has installed a childcare room in the ITbM building to support the researchers with children.

The activity of female PhD students is also remarkable. For example, Dr. Akiko Yagi of the Itami group and Dr. Maki Hayashi in the Kinoshita group were awarded the “L’Oreal-UNESCO Award for Women in Science, Japan Encouragement Prize” in 2014 and 2015.

As a part of the GTR activity, two special lectures to foster female top leaders have been organized in early 2019 to raise awareness of gender equity issues. NU has been actively engaged in developing female leaders and young female researchers who can play a leading role in the world, by preparing nursery schools and after-school childcare center on campus ahead of other universities in Japan. Due to their efforts, the President of NU was selected as one of the 10 world universities that have made advanced efforts to promote gender equality under the IMPACT 10x10x10 program of United Nation Women’s HeForShe movement. ITbM is fully utilizing these platforms to support female researchers.

6. Others

In addition to the above 1.-5. evaluation items, note any of the Center's leading activities, distinctive features or other important points that denote its status as an "internationally visible research center."

ITbM’s safety training for interdisciplinary research

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

Concern for the environment and safety

Upon development of molecules that modulate biological system in plants/animals, it is essential for ITbM to communicate to the general public widely that ITbM always addresses environmental and safety issues carefully. Accordingly, ITbM has set up an Environment and Safety Committee (see below) so that researchers at ITbM are constantly aware of these issues when conducting their research. The committee also contributes to prepare and improve the ITbM’s safety training course stated above. In addition, ITbM has been actively involved in public outreach events as denoted above and explaining ITbM’s concern for safety and environmental issues. In the media, ITbM also weighs in on safety issues when needed.

Environmental and Safety Committee

As ITbM aims to create chemical compounds that affect plants and animals, as well as generate new plant and animal species, the Environmental and Safety Committee was established to seek the counsel of experts for ITbM's research to be conducted competently whilst 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 Director.

Members:

1 Nagoya University PI
- Toshinori Kinoshita, Director of Center for Gene Research, Nagoya University

1 Internal Expert within Nagoya University
- Associate Professor of Jurisprudence, Graduate School of Law, NU

4 External Experts outside Nagoya University
- Trustee/Vice-President of Okayama University
- Senior Research Administrator, Strategic Program Support Unit, Okayama University
- Head of Natural Environment Division, Department of the Environment, Aichi Prefecture
- Senior Councilor, Life & Bio Plaza 21 (NPO)

7. Center's Response to Results of FY 2018 Follow-up (including Site Visit Results)

* Describe the Center's response to results of FY 2018 follow-up. Note: If you have already provided this information, please indicate where in the report.

(1) ITbM should prepare a more strategic and concrete plan for maintaining its momentum for the long-term (10 years), including a plan after the support from the WPI program ends. ITbM needs thorough discussion about its future research direction including selection of transformative biomolecules next to SPL7, facilitation of target ID project and others.

<response>

In posting this report on the website, the response herein was omitted since it was on the premise that the extension application was approved.

(2) NU and ITbM should cooperate to solve organization issues and make every effort for sustaining ITbM as a role model (institute) within the NU structure. The Excellent Graduate School program, a new MEXT program for which NU has now been selected, may be coupled with the system reform including ITbM.

<response>

To secure the employment of ITbM's faculty members and staff, NU has made significant organizational reform in 2019. NU will launch the "Institutes for Advanced Research Excellence", and will position ITbM under this umbrella. Through this reorganization, the Director of ITbM will retain the authority to make key decisions at ITbM. NU has promised to make all efforts to secure personnel for ITbM. In 2019, NU requested funding to MEXT to further develop its activities, and was given 2 positions in 2019. NU considers this request to provide positions to ITbM as its highest priority, and continues in the following years. In addition to this request, 7 more faculty positions for ITbM will be secured within FY2019. NU will also make a full support to collect

Appendix 1-1 List of Papers Underscoring Each Research Achievement

* List papers underscoring each research achievement [1] ~ [15] listed in the item 2-1 “Research results to date” of 2. “Advancing Research of the Highest Global Level” (up to 30 papers) and provide a description of the significance of each (within 10 lines).
* For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is the same. If a paper has many authors, underline those affiliated with the Center.
* If a paper has many authors (say, more than 10), all of their names do not need to be listed.
* Place an asterisk (*) in front of those results that could only have been achieved by a WPI center.

*[1] Unraveling strigolactone signaling and controlling parasitic plant behaviors in *Striga*

The discoveries of Yoshimulactone (*Science* 2015) and SPL7 (*Science* 2018) had a huge and global impact not only on researchers of both academia and industries but also for those who have been involved in food security. It should be strongly emphasized that these astonishing achievements have emerged via a bottom-up collaboration initiated at the Mix Lab between chemists, biologists, and theoretical scientists. We will provide a description of the significance of them in Appendix 1-2.

* "Probing strigolactone receptors in *Striga hermonthica* with fluorescence", Tsuchiya, Y., Yoshimura, M., Sato, Y., Kuwata, K., Toh, S., Holbrook-Smith, D., Zhang, H., McCourt, P., Itami, K., Kinoshita, T., and Hagihara, S. *Science* **349**, 864 (2015)
DOI: 0.1126/science.aab3831

* "A femto-molar range suicide germination stimulant for the parasitic plant *Striga hermonthica*", Uraguchi, D., Kuwata, K., Hijikata, Y., Yamaguchi, R., Imaizumi, H., Sathiyanarayanan, A. M., Rakers, C., Mori, M., Akiyama, K., Irle, S., McCourt, P., Kinoshita, T., Ooi, T., and Tsuchiya, Y. *Science* **362**, 1301 (2018)
DOI: 10.1126/science.aau5445

*[2] Identification of a series of molecules that control plant reproduction

(1) "Tip-localized receptors control pollen tube growth and LURE sensing in Arabidopsis", Takeuchi, H., and Higashiyama, T. *Nature* **531**, 245 (2016)
DOI:10.1038/nature17413

The Higashiyama group succeeded in identifying that pollen-specific receptor-like kinase 6 (PRK6) is an essential receptor for sensing of the LURE1 attractant peptide in *Arabidopsis thaliana* under semi-*in-vivo* conditions, and is essential for ovule targeting in the pistil. They revealed PRK6 interacted with pollen-expressed ROPGEFs (**R**ho **o**f **p**lant **g**uanine nucleotide-**e**xchange **f**actors), which are important for pollen tube growth through activation of the signaling switch Rho GTPase ROP1. As a result, they concluded that PRK6 acts as a key membrane receptor for external AtLURE1 attractants, and recruits the core tip-growth machinery, including ROP signaling proteins. This work provides a major breakthrough not only to investigate ligand-receptor interaction but also to discover molecules that break species-specific reproductive barriers.

*(2) "The AMOR arabinogalactan sugar chain induces pollen-tube competency to respond to ovular guidance", Mizukami, A. G., Inatsugi, R., Jiao, J., Kotake, T., Kuwata, K., Ootani, K., Okuda, S., Sankaranarayanan, S., Sato, Y., Maruyama, D., Iwai, H., Garénaux, E., Sato, C., Kitajima, K., Tsumuraya, Y., Mori, H., Yamaguchi, J., Itami, K., Sasaki, N., and Higashiyama, T. *Curr. Biol.* **26**, 1091 (2016)
DOI: org/10.1016/j.cub.2016.02.040

Based on a finding that pollen tubes growing through a cut style acquired a response capability in the medium by receiving a sufficient amount of a factor derived from mature ovules of *Torenia fournieri*, the Higashiyama group identified that ovular glycochain, methyl-glucuronosyl arabinogalactan (AMOR), induces competency of the pollen tube to respond to ovular attractant LURE peptides in Torenia. With the Itami group, they further revealed the essential part of the AMOR was proved to be a terminal disaccharide unit and only the β-isomer of methyl-glucuronosyl galactose (4-Me-GlcA-β-(1/6)-Gal) showed AMOR activity via structure-activity relationship study (see also, Jiao *et al. Plant Physiol.* 2018). This is a quite interesting finding because any specific sugar-chain unit of plant extracellular matrix has not been identified as a bioactive molecule.

(3) "Structural basis for receptor recognition of pollen tube attraction peptides", Zhang, X., Liu, W., Nagae, T. T., Takeuchi, H., Zhang, H., Han, Z., Higashiyama, T., and Chai, J. *Nat. Commun.* **6**, 1331 (2017)

DOI: 10.1038/s41467-017-01323-8

The Higashiyama group revealed that the extracellular domain of the leucine-rich repeat receptor kinase (LRR-RK) PRK6 from *Arabidopsis thaliana* directly interacts with AtLURE1 peptides. Structural study revealed that a C-terminal loop of the LRR domain (AtPRK6LRR) is responsible for recognition of AtLURE1.2, mediated by a set of residues largely conserved among PRK6 homologs from *Arabidopsis lyrata* and *Capsella rubella*, supported by in vitro mutagenesis and semi-in-vivo pollen tube growth assays. This study provided a strong evidence that PRK6 actually functions as a receptor of the LURE peptides in *A. thaliana* and revealed a unique ligand recognition mechanism of LRR-Rs as well as giving a great potential for a design of small molecule pollen tube attractants to overcome genetic barrier.

*[3] Elucidation of mechanisms involved in early embryogenesis of plants

*(4) "Rapid elimination of the persistent synergid through a cell fusion mechanism", Maruyama, D., Völz, R., Takeuchi, H., Mori, T., Igawa, T., Kurihara, D., Kawashima, T., Ueda, M., Itoh, M., Umeda, M., Nishikawa, S., Groß-Hardt, R., and Higashiyama, T. *Cell* **161**, 907 (2015)
DOI: org/10.1016/j.cell. 2015.03.018

The Higashiyama group disclosed by live imaging that two female gametes (the egg and the central cell) coordinately prevent attractions of excess number of pollen tubes known as “polytubey block”. They observed in *Arabidopsis thaliana* that the synergid-endosperm fusion causes rapid dilution of pollen tube attractant in the persistent synergid cell and selective disorganization of the synergid nucleus, preventing further attractions of pollen tubes. Simultaneously, the synergid-endosperm cell fusion is induced by fertilization of the central cell, while the egg cell fertilization activates ethylene signaling, an inducer of the synergid nuclear disorganization. In case of unsuccessful fertilization, the persistent synergid cell attracts a second pollen tube to recover the failure of earlier fertilization. Over 110 years have passed since the identification of the two cell fusions in plant, the findings have possibilities to replace the principles that rewrite existing textbooks.

*(5) “Cytoskeleton dynamics control the first asymmetric cell division in Arabidopsis zygote”, Kimata, Y., Higaki, T., Kawashima, T., Kurihara, D., Sato, Y., Yamada, T., Hasezawa, S., Berger, F., Higashiyama, T., and Ueda, M. *Proc. Natl. Acad. Sci. USA* **113**, 14157 (2016)
DOI: www.pnas.org/cgi/doi/10.1073/ pnas.1613979113

The zygote divides unequally and the daughter cells inherit different developmental fates. However, the cytological events leading to zygote polarization have remained unknown in flowering plants. Higashiyama and Ueda unveiled the dynamics of the major elements of the cytoskeleton, microtubules (MTs) and actin filaments (F-actins), during the entire process of zygote polarization by using live imaging with Arabidopsis. By combining image analysis and biological experiments using specific inhibitors of the cytoskeleton, they revealed the preexisting alignment of MTs and F-actin in the egg cell is lost in fertilization. Then, they revealed that MTs organize into a transverse ring defining the zygote subapical region and driving cell outgrowth in the apical direction. In addition, they revealed F-actin forms an apical cap and longitudinal arrays, and is required to position the nucleus to the apical region of the zygote, setting the plane of the first asymmetrical division.

*(6) “Polar vacuolar distribution is essential for accurate asymmetric division of Arabidopsis zygotes”, Kimata, Y., Kato, T., Higaki, T., Kurihara, D., Yamada, T., Segami, S., Morita, M. T., Maeshima, M., Hasezawa, S., Higashiyama, T., Tasaka, M., and Ueda, M. *Proc. Natl. Acad. Sci. USA* **116**, 2338 (2019)
DOI: 10.1073/pnas.1814160116

Higashiyama and Ueda revealed by live imaging that the vacuoles formed tubular strands around the apically migrating nucleus, which gradually accumulated at the basal region and filled the space, resulting in asymmetric distribution in the mature zygote. They also revealed that mutant *shoot gravitropism2* (*sgr2*), in which the vacuolar structural change was impaired, failed to form tubular vacuoles and to polarly distribute the vacuole. In *sgr2*, they further revealed that large vacuoles occupied the apical tip and thus nuclear migration was blocked, resulting in fail of asymmetrical division. Furthermore, they observed that both tubular vacuole formation and asymmetric vacuolar distribution depended on the longitudinal array of actin filaments. These results provided new insight of vacuole in asymmetric zygote division, in which its dynamics is crucial not only for the polar distribution along actin filaments but also for adequate nuclear positioning.

***[4] Elucidation of stomatal development mechanism and its molecular control**

*(7) "Competitive binding of antagonistic peptides fine-tunes stomatal patterning", Lee, J. S., Hnilova, M., Maes, M., Lin, Y. C. L., Putarjunan, A., Han, S. K., Avila, J., and Torii, K. U. *Nature* **522**, 439 (2015)
DOI: 10.1038/nature14561

The Torii group revealed in Arabidopsis that stomagen (also called EPF-LIKE9) peptide, which promotes stomatal development, requires ERECTA (ER)-family receptor kinases and interferes in the inhibition of stomatal development through interaction with epidermal patterning factor 2 (EPF2)–ER complex. They further revealed that the stomagen competitively replaced EPF2 binding to ER and induces rapid phosphorylation of downstream signaling components in vivo. Their findings demonstrated how a plant receptor agonists/antagonists define inductive/inhibitory cues to fine-tune tissue patterning on the plant epidermis. As stomatal development is considered to play a key role in crop plant productivity and water-use efficiency, this study is expected to be important for understanding the productivity of plants in both natural and agricultural systems, and give a potential strategy for the control of stomatal development by small molecules.

***[5] Control of stomatal opening/closing**

*(8) "Overexpression of plasma membrane H^+-ATPase in guard cells promotes light-induced stomatal opening and enhances plant growth", Wang, T., Noguchi, K., Ono, N., Inoue, S., Terashima, I., and Kinoshita, T. *Proc. Natl. Acad. Sci. USA* **111**, 533 (2014)
DOI: 10.1073/pnas.1305438111

The Kinoshita group revealed that the transgenic Arabidopsis plants overexpressing H^+-ATPase using the guard cell promoter GC1 showed enhanced light-induced stomatal opening, photosynthesis, and plant growth. The transgenic plants produced larger and increased numbers of rosette leaves, with greater fresh and dry weights than the wild type. The dry weights of total flowering stems, including seeds, siliques, and flowers, also were greater than those of the wild type. In addition, stomata in the transgenic plants closed normally in response to darkness and abscisic acid. Overexpression of the other key components, phototropin or inward-rectifying K^+ channels, in guard cells had no effect on these phenotypes. This research outcome has gained a significant amount of attention, leading to the initiation of several academia-industry joint research and licensing of the research to agrochemical companies by using commercial cultivar (rice, maize, and rape seed).

*(9) "A Raf-like protein kinase BHP mediates blue light-dependent stomatal opening", Hayashi, M., Inoue, S., Ueno, Y., and Kinoshita, T. *Sci. Rep.* **7**, 45586 (2017)
DOI: 10.1038/srep45586

The Kinoshita group has successively identified a major component of blue light-dependent stomatal opening, such as blue light-receptor phototropins, protein phosphatase 1, and the plasma membrane H^+-ATPase. In addition, they identified a Raf-like protein kinase, **b**lue light-dependent **H**$^+$-ATPase **p**hosphorylation (BHP), as a novel positive regulator for the H^+-ATPase activation in the stomatal opening by a combination of chemical screening and reverse genetics. They demonstrated that BHP is abundantly expressed in the cytosol of guard cells and interacts with BLUS1 in vitro and in vivo. This work fills in the missing piece of the blue light-dependent stomatal opening, provides important insights into understanding of the stomatal opening and plant photobiology, proposes a potential strategy for the artificial control of stomatal aperture.

***[6] New approach to ligand-receptor pair: delineation of specific auxin response**

*(10) "Chemical hijacking of auxin signaling with an engineered auxin-TIR1 pair", Uchida, N., Takahashi, K., Iwasaki, R., Yamada, R., Yoshimura, M., Endo, T. A., Kimura, S., Zhang, H., Nomoto, M., Tada, Y., Kinoshita, T., Itami, K., Hagihara S., and Torii, K. U. *Nat. Chem. Biol.* **14**, 299 (2018)
DOI: 10.1038/nchembio.2555

The groups of Torii-Uchida, Itami and Kinoshita developed that an engineered, orthogonal auxin-TIR1 receptor pair, which triggers auxin signaling without affecting endogenous auxin or TIR1/AFBs. A synthetic convex IAA (cvxIAA), designed by docking study of IAA-TIR1complex, hijacks the downstream auxin signaling in vivo both at the transcriptomic level and in specific developmental

contexts, only in the presence of a complementary, concave TIR1 (ccvTIR1) receptor. Harnessing the cvxIAA-ccvTIR1 system, they provided conclusive evidence for the role of the TIR1-mediated pathway in auxin-induced seedling acid growth. The cvxIAA-ccvTIR1 system serves as a powerful tool for solving outstanding questions in auxin biology and for precise manipulation of auxin-mediated processes as a controllable switch.

[7] Mechanistic elucidation of seasonal clock in animals

*(11) "The saccus vasculosus of fish is a sensor of seasonal changes in day length", Nakane, Y., Ikegami, K., Iigo, M., Ono, H., Takeda, K., Takahashi, D., Uesaka, M., Kimijima, M., Hashimoto, R., Arai, N., Suga, T., Kosuge, K., Abe, T., Maeda, R., Senga, T., Amiya, N., Azuma, T., Amano, M., Abe, H., Yamamoto, N., and Yoshimura, T. *Nat. Commun.* **4**, 2018 (2013)
DOI: 10.1038/ncomms3108

The pars tuberalis of the pituitary gland is the regulatory hub for seasonal reproduction in birds and mammals. Although fish also exhibit robust seasonal responses, they do not possess an anatomically distinct pars tuberalis. The Yoshimura group identified the photoperiodic center in fish (masu salmon), the saccus vasculosus, which is the sensor of seasonal changes in day length. They revealed that expression of key genes, rhodopsin family genes, regulates seasonal reproduction in coronet cells of the saccus vasculosus of masu salmon. In addition, they demonstrated that an isolated saccus vasculosus has the capacity to respond to photoperiodic signals and its removal abolishes photoperiodic response of the development of gonad.

*(12) “Intrinsic photosensitivity of a deep brain photoreceptor”, Nakane, Y., Shimmura, T., Abe, H., and Yoshimura, T. *Curr. Biol.* **24**, R596 (2014)
DOI: 10.1016/j.cub.2014.05.038

In most mammals including humans, eyes are the exclusive photoreceptor organs. On the other hand, it has been said that vertebrates apart from mammals sense seasonal changes by receiving light directly inside their brains. The Yoshimura group revealed that in quail, novel photopigment (OPN5)-positive neurons, existing deep inside the brains, respond directly to light and regulate seasonal reproduction. They identified the neurons capable of phototransduction by whole-cell patch-clamp recordings. Separately, they carried out a siRNA knockdown experiment of OPN5 in vivo inhibits the secretion of the thyroid-stimulating hormone (TSH), so-called the ‘spring hormone’, which triggers breeding in birds. This is the first demonstration of the intrinsic photosensitivity of deep brain neurons in birds, may also lead to improvements in animal breeding, and provides a deeper understanding of the evolution of eyes and photoreceptors.

*(13) “Dynamic plasticity in phototransduction regulates seasonal changes in color perception”, Shimmura, T., Nakayama, T., Shinomiya, A., Fukamachi, S., Yasugi, M., Watanabe, E., Shimo, T., Senga, T., Nishimura, T., Tanaka, M., Kamei, Y., Naruse, K., and Yoshimura, T. *Nat. Commun.* **8**, 412 (2017)
DOI: 10.1038/s41467-017-00432-8

Subsequently to the discovery of the photoperiodic center in fish and birds, the Yoshimura group revealed dynamic plasticity in phototransduction regulates seasonal changes in color perception in medaka fish. They demonstrated that medaka are active and exhibit clear phototaxis in summer conditions, but remain at the bottom of the tank and fail to exhibit phototaxis in winter ones. In addition, they demonstrated the medaka kept in summer conditions are more attracted to computer-generated orange-red-colored medaka (nuptial coloration) than medaka kept in winter conditions. Then, they revealed that the genes encoding photopigments such as opsin and their downstream pathway varies dynamically among seasons. In addition, they demonstrated photopigment-null fish showed significant differences from wild type in behavioral analysis and suggested plasticity in color perception is crucial for the emergence of seasonally regulated behaviors.

*[8] Development of molecules that control biological clock

*(14) “Cell-based screen identifies a new potent and highly selective CK2 inhibitor for modulation of circadian rhythms and cancer cell growth”, Oshima, T., Niwa, Y., Kuwata, K., Srivastava, A., Hyoda, T., Tsuchiya, Y., Kumagai, M., Tsuyuguchi, M., Tamaru, T., Sugiyama, A., Ono, N., Zolboot, N., Aikawa, Y., Oishi, S., Nonami, A., Arai, F., Hagihara, S., Yamaguchi, J., Tama, F., Kunisaki, Y., Yagita, K., Ikeda, M., Kinoshita, T., Kay, S. A., Itami, K., and Hirota, T. *Sci. Adv.* **5**, eaau9060 (2019)

DOI: 10.1126/sciadv.aau9060

The groups of Kay-Hirota and Itami succeeded in identifying GO289 as a lead compound, which strongly lengthened circadian period, and is a potent and selective inhibitor of CK2 with outstanding physicochemical properties. They also identified multiple phosphorylation sites inhibited by GO289 on clock proteins, including PER2 with the help of the Molecular Structure Center and Tama group. In addition, they demonstrated that GO289 exhibited selective inhibition of cancer cell growth. They further revealed the interactions between GO289 and CK2-specific residues by X-ray crystal structure of the CK2α-GO289 complex, and revealed that GO289 does not interact with the hinge region of CK2 that is highly conserved among kinases. The discovery of well-defined GO289 provides a direct link between the circadian clock and cancer regulation, and reveals some unique design principles underlying kinase selectivity.

***[9] Novel characteristic probes applicable to the advanced live imaging**

*(15) "A Phosphole Oxide Based Fluorescent Dye with Exceptional Resistance to Photobleaching: A Practical Tool for Continuous Imaging in STED Microscopy", Wang, C., Fukazawa, A., Taki, M., Sato, Y., Higashiyama, T., and Yamaguchi, S. *Angew. Chem. Int. Ed.* **54**, 15213 (2015)
DOI: 10.1002/anie.201507939

The Yamaguchi group has developed the outstanding photostable fluorescent dye C-Naphox (diaryl-methylene bridged **na**phtho**ph**osphole P-**ox**ide) and reported several distinct advantages relative to conventional probes, such as intense fluorescence emission by the combination of an electron-donating group (diphenylamino moiety) with an electron-accepting group (the core structure of C-Naphox), high quantum yields, large Stokes shift, and solvent polarity sensitivity (environment-responsiveness). They demonstrated that almost all (99.5%) of C-Naphox remained intact even after irradiation with a Xe lamp for 12 hours although representative STED imaging probes significantly diminished their fluorescence intensities under the same conditions. In addition, they applied C-Naphox into repeated STED imaging of HeLa cells and recorded 83% of the initial fluorescence intensity of C-Naphox persisted even after recording 50 STED images.

*(16) "Super-Photostable Phosphole-Based Dye for Multiple-Acquisition Stimulated Emission Depletion Imaging", Wang, C., Taki, M., Sato, Y., Fukazawa, A., Higashiyama, T., and Yamaguchi, S. *J. Am. Chem. Soc.* **139**, 10374 (2017)
DOI: 10.1021/jacs.7b04418

C-Naphox still has drawbacks for practical use in bio-imaging, i.e. water insolubility, target selectivity, and polarity-sensitivity fluorescence. The groups of Yamaguchi and Higashiyama, and the Live Imaging Center succeeded in developing a new super-photostable dye, PhoxBright 430 (PB430). They revealed that PB430 also has high solubility in water, and is capable of labeling proteins with maintaining high fluorescence quantum yields. This dye also exhibits outstanding resistance to photoirradiation even under the STED conditions and allows continuous acquisition of STED images. Indeed, using a PB430-conjugated antibody, they succeed in creating a 3-D reconstruction of super-resolution STED images as well as photostability-based multicolor STED imaging of fluorescently labeled cytoskeletal structures.

*(17) "A Highly Photostable Near-Infrared Labeling Agent Based on a Phospha-rhodamine for Long-Term and Deep Imaging", Grzybowski, M., Taki, M., Senda, K., Sato, Y., Ariyoshi, T., Okada, Y., Kawakami, K., Imamura, T., and Yamaguchi, S. *Angew. Chem. Int. Ed.* **57**, 10137 (2018)
DOI: 10.1002/anie.201804731

The Yamaguchi group and the Live Imaging Center also developed a highly photostable and water-soluble near-infrared phosphorus-substituted rhodamine, PREX 710. By the nature of membrane permeability and localization in the mitochondoria, they demonstrated that PREX 710 can be used to stain mitochondria in living cells, which allowed long-term and multi-color imaging in the vis-NIR range. Moreover, they showed the high fluorescence longevity of PREX 710 by tracking a dye-labeled biomolecule (IgG, NeutrAvidin) by single-molecule microscopy under physiological conditions. Furthermore, they achieved deep imaging of blood vessels in mice brain using the bright NIR emitting PREX 710-dextran conjugate.

*[10] New avenues of catalysis for efficient molecular synthesis

(18) “Ligand-enabled multiple absolute stereocontrol in metal-catalysed cycloaddition for construction of contiguous all-carbon quaternary stereocentres”, Ohmatsu, K., Imagawa, N., and Ooi, T. *Nat. Chem.* **6**, 47 (2013)
DOI: 10.1038/NCHEM.1796

The development of a general catalytic method for the stereoselective construction of contiguous all-carbon quaternary stereocenters in a single synthetic operation remains a formidable challenge. The Ooi group has developed a catalytic system to establish stereocenters of contiguous quaternary carbons with a high enantio- and diastereoselective [3+2] annulation reaction. This reaction is catalyzed by a palladium complex bearing a novel phosphine ligand and a chiral ammonium salt, which enables the single-step construction of three contiguous stereocenters, including vicinal all-carbon quaternary stereocenters. This stereoselective cycloaddition protocol relies on the remarkable ability of the chiral ligand to rigorously control the absolute stereochemistry of each chiral center associated with the multiple bond-forming events, and provides a reliable catalytic process for the asymmetric synthesis of densely functionalized pyrrolidines.

(19) “Iterative protecting group-free cross-coupling leading to chiral multiply arylated structures”, Crudden, C. M., Ziebenhaus, C., Rygus, J. P. G., Ghozati, K., Unsworth, P. J., Nambo, M., Voth, S., Hutchinson, M., Laberge, V. S., Maekawa Y., and Imao, D. *Nat. Commun.* **7**, 11065 (2016)
DOI: 10.1038/ncomms11065

The Crudden group made significant advance in cross-coupling chemistry, in which multiply functionalized chiral cross-coupling partners can be employed in iterative coupling without the use of protecting groups. Through extensive investigation on the reaction conditions, they identified that the orthogonal reactivity of boron-carbon bonds in different positions in a single molecule permits the chemoselective, sequential coupling of aromatic, aliphatic and stereochemistry-bearing B–C bonds. This method permits the rapid generation of multiply arylated, chiral organic molecules with control of stereochemistry, without the need for protection/deprotection sequences. The approach is expected to be the preparation of chiral enantioenriched compounds, which are likely to provide interesting lead compounds for pharmaceutical and medicinal applications, by escaping from ‘flatland’.

*(20) "Complete diastereodivergence in asymmetric 1,6-addition reactions enabled by minimal modification of a chiral catalyst", Uraguchi, D., Yoshioka, K., and Ooi, T. *Nat. Commun.* **8**, 14793 (2017)
DOI: 10.1038/ncomms14793

The development of a catalytic process capable of producing each and all of those stereoisomers from the same starting materials (diastereodivergent catalysis) poses a formidable challenge. The Ooi group established a catalyst-directed pinpoint inversion of diastereochemical preference in the 1,6-addition of azlactones to δ-aryl dienyl carbonyl compounds with full control over other selectivities preserved. This rigorous diastereodivergence was enabled by the slight structural adjustment of a chiral iminophosphorane catalyst developed by themselves, providing access to all the stereoisomers with high regio-, distereo- and enantioselectivity. They demonstrated the utility of this method in the facile stereodivergent preparation of densely functionalized proline derivatives. In addition, they elucidated experimentally and computationally the origin of the diastereodivergence.

[11] Unprecedented approach to peptide/protein synthesis

(21) "Synthetic fermentation of bioactive non-ribosomal peptides without organisms, enzymes or reagents", Huang, Y. L., and Bode, J. W. *Nat. Chem.* **6**, 877 (2014)
DOI: 10.1038/NCHEM.2048

Microbial fermentation can rapidly provide potent molecules as a mixture that can be easily screened based on biological activity, and then the active components can be isolated. Its success in drug discovery has inspired extensive efforts to modulate and control the products. The Bode group has discovered and developed a bio-mimetic peptide ligation reaction, known as the KAHA ligation (JACS. 2006). This reaction proceeds without additional organisms, enzymes, and reagents, and can be used to synthesize a number of peptides/proteins in water. They applied this KAHA ligation into a microbial fermentation process, named “synthetic fermentation”, and succeeded in demonstrating that bioactive,

unnatural peptides can be grown from a mixture of amino acid building blocks in water. As a proof-of-concept, they identified a hepatitis C virus NS3/4A protease inhibitor (IC50 = 1.0 μM) among c.a. 6,000 unnatural peptides produced from just 23 amino acid building blocks.

(22) “An oxazetidine amino acid for chemical protein synthesis by rapid, serine-forming ligations”, Pusterla, I., and Bode, J. W. *Nat. Chem.* **7**, 668 (2015)
DOI: 10.1038/NCHEM.2282

The KAHA ligation, developed by the Bode group, has proven to be remarkably robust, but has limitations including the introduction of a non-canonical homoserine residue at the ligation site, and a preference for relatively high concentrations (10**-**20 mM) and temperatures (50**-**60 °C). They reported the synthesis of an N-terminus protected oxazetidine as a canonical serine precursor for use in the KAHA ligation and demonstrated, when incorporated at the N-terminus of a peptide segment, that the four-membered oxazitidine can be used for rapid serine-forming ligations with C-terminus of peptide. In addition, they demonstrated this ligation operates at lower concentration (100 μM**-**5 mM) and milder temperatures (20**-**25 °C). The utility of the reaction was demonstrated by the synthesis of S100A4, a 12 kDa calcium-binding protein that is not easily accessible by the conventional methods, such as native chemical ligation (NCL) or other amide forming reactions.

*[12] Development of biology-friendly functional materials

*(23) “Simple direct formation of self-assembled N-heterocyclic carbene monolayers on gold and their application in biosensing”, Crudden, C. M., Horton, J. H., Narouz, M. R., Li, Z., Smith, C. A., Munro, K., Baddeley, C. J., Larrea, C. R., Drevniok, B., Thanabalasingam, B., McLean, A. B., Zenkina, O. V., Ebralidze, I. I., She, Z., Kraatz, H. B., Mosey, N. J., Saunders, L. N., and Yagi, A. *Nat. Commun.* **7**. 12654 (2016)
DOI: 10.1038/ncomms12654

The formation of organic films on gold employing ***N*-h**eterocyclic **c**arbenes (NHCs) has been previously shown to be a useful strategy for generating stable organic films. However, NHCs or NHC precursors typically require inert atmosphere and harsh conditions for their generation and use. The Crudden group has developed a simple direct method to form self-assembled NHC monolayers on gold. Using the bench-stable benzimidzolium hydrogen carbonate as a replacement for conventional air-sensitive NHCs or NHC precursors, NHC films were able to be prepared much more easily in solution or by vapor-phase deposition from the solid state. They applied these materials into surface plasmon resonance (SPR)-type biosensing and revealed that NHC-based films provide specific physicochemical durability, such as thermal stability and stability in extreme pH, versus conventional thiol-based ones.

[13] Synthesis of carbon nanorings, nanobelts and pure nanotubes

(24) "Initiation of carbon nanotube growth by well-defined carbon nanorings", Omachi, H., Nakayama, T., Takahashi, E., Segawa, Y., and Itami, K. *Nat. Chem.* **5**, 572 (2013)
DOI: 10.1038/NCHEM.1655

Currently, carbon nanotubes (CNTs) can only be produced as mixtures with regard to diameter and sidewall structure. Given that the electronic properties of CNTs are primarily determined by the sidewall structures, structural uniformity is critically important for CNT-based electronics and biology. The Itami group succeeded in the first diameter-selective synthesis of CNTs using carbon nanorings as templates. This method is extremely simple; it only involves reacting ethanol (as a carbon source) at 500 °C with carbon nanorings coated onto a sapphire substrate. The diameter of the nanoring template, which can be controlled using Itami’s method, determines the diameter of the final CNT. A range of carbon nanorings of varying sizes is also commercially available, thus encouraging others to explore the bottom-up synthesis of CNTs.

(25) "Synthesis of a Carbon Nanobelt", Povie, G., Segawa, Y., Nishihara, T., Miyauchi, Y., and Itami, K. *Science* **356**, 172 (2017)
DOI: 10.1126/science.aam8158

The Itami group achieved the first synthesis of a carbon nanobelt - a long-sought-after ultra-short CNT. The synthesis of these highly strained, belt-shaped aromatic compounds had been one of the most difficult problems in chemistry for the last 60 years (even before the discovery of CNTs). Itami

synthesized the carbon nanobelt through iterative Wittig reactions followed by a nickel-mediated aryl-aryl coupling reaction. The cylindrical shape of its belt structure was confirmed by X-ray crystallography, and its fundamental optoelectronic properties were elucidated by ultraviolet-visible absorption, fluorescence, and Raman spectroscopic studies. This achievement is both an experimental tour de force and a triumph of synthetic chemistry. Itami's carbon nanobelt, which can be synthesized from *p*-xylene (petroleum feedstock), was commercialized in 2018, thereby accelerating the discovery of extraordinary properties, functions, and applications.

[14] Synthesis of nanographenes and graphene nanoribbons

(26) "One-shot K-region-selective annulative π-extension for nanographene synthesis and functionalization", Ozaki, K., Kawasumi, K., Shibata, M., Ito, H., and Itami, K. *Nat. Commun.* **6**, 6251 (2015)
DOI: 10.1038/ncomms7251

The Itami group has developed a number of unique catalysts for single-step aromatic π-extension and aromatic C-H activation that allows for the rapid synthesis of nanocarbon molecules in a programmable fashion. Recently, they have introduced the concept of "annulative π-extension (APEX) chemistry", which permits the facile synthesis of fused aromatic systems and molecular nanocarbons from simple aromatic compounds. For example, they have developed one-shot APEX reactions that occur at the K-region (convex armchair edge) of polycyclic aromatic hydrocarbons by the original $Pd(OAc)_2$/*o*-chloranil catalytic system with silicon-bridged aromatics as π-extending agents. In addition, they revealed that the complete K-region selectivity stems from the electronic (olefinic) character of the K-region with density functional theory calculations.

(27) "Synthesis of partially and fully fused polyaromatics by annulative chlorophenylene dimerization", Koga, Y., Kaneda, T., Saito, Y., Murakami, K., and Itami, K. *Science* **359**, 435 (2018)
DOI: 10.1126/science.aap9801

The Itami group has also developed a single-step synthesis of fused aromatics with a triphenylene core by the palladium-catalyzed APEX dimerization of structurally and functionally diverse chlorophenylenes through double C-H activation. One of the triphenylene derivatives performs exceptionally well as a high-molecular-orientation electron-transport material in OLEDs, which is now seriously investigated in a company. The resulting partially fused polyaromatics can be transformed into fully fused, small graphene nanoribbons, which are otherwise difficult to synthesize. This simple, yet powerful method allows access to functional nanographenes of interest in optoelectronics and biological research. As the properties of nanographenes depend heavily on the degree of pi-extension, shape, width and edge topology, the APEX reactions are expected to significantly contribute for those who need fine-tuned nanographenes.

[15] Synthesis of topologically unique, three-dimensional nanocarbons

(28) "A grossly warped nanographene and the consequences of multiple odd-membered-ring defects", Kawasumi, K., Zhang, Q., Segawa, Y., Scott, L. T., and Itami, K. *Nat. Chem.* **5**, 739 (2013)
DOI: 10.1038/NCHEM.1704

The Itami group has also created completely novel, topologically unique nanocarbons. Aside from theoretical studies that predict interesting properties for these types of species, three-dimensionally curved nanocarbons are a virtually unexplored group of materials. They accomplished the synthesis of a novel warped nanographene (WNG) containing both positive and negative curvatures on its π-surface. A WNG ($C_{80}H_{30}$) that incorporates five 7-membered rings and one 5-membered ring embedded in a hexagonal lattice has been synthesized by stepwise chemical methods using Itami's original C-H activation catalyst. Its grossly warped structure is revealed by single crystal X-ray crystallography. WNG is unique and clearly distinct from any other existing nanocarbon. As WNG is also commercially available, many academic research groups and industries are now using WNG as a key molecule in optoelectronic devices and biology.

Appendix1-2 List of Papers of Representative of Interdisciplinary Research Activities

* List **up to 10 papers** underscoring each interdisciplinary research activity and give brief accounts (within 10 lines).
* For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is the same. If a paper has many authors, underline those affiliated with the Center.
* If a paper has many authors (say, more than 10), all of their names do not need to be listed.

(1) "Probing strigolactone receptors in *Striga hermonthica* with fluorescence", Tsuchiya, Y., Yoshimura, M., Sato Y., Kuwata, K., Toh, S., Holbrook-Smith, D., Zhang, H., McCourt, P., Itami, K., Kinoshita, T., and Hagihara, S. *Science* **349**, 864 (2015)
DOI: 10.1126/science.aab3831.Yoshimulactone

A molecular approach has been used to identify the protein responsible for germination of *Striga* seeds by green fluorescence. *Striga*, a parasitic plant known as witchweed, has seriously affected millions of hectares of the fields in Africa that poses a major threat to food security. Nevertheless, the exact mechanism on how *Striga* seeds detect host crops has not been fully understood up to now. In a new study reported in *Science*, ITbM chemists (**Itami group**) and biologist (**Kinoshita group**) and their team have come together to develop a fluorescent molecule “Yoshimulactone” Green (YLG) to examine the process of *Striga* germination. The outcome of this study is expected to accelerate research to control *Striga* growth and to save crop losses worth of billions of U.S. dollars every year.

(2) "A femto-molar range suicide germination stimulant for the parasitic plant *Striga hermonthica*", Uraguchi, D., Kuwata, K., Hijikata, Y., Yamaguchi, R., Imaizumi, H., Sathiyanarayanan, A. M., Rakers, C., Mori, M., Akiyama, K., Irle, S., McCourt, P., Kinoshita, T., Ooi, T., and Tsuchiya, Y. *Science* **362**, 1301 (2018)
DOI: 10.1126/science.aau5445

ITbM chemists (**Ooi group**), biologist (**Kinoshita group**), theoretical sciences group (**Irle group**), and the **Molecular Structure Center** have also developed *Striga* germinator sphynolactone-7 (SPL7). SPL7 has two functional modules, which cooperatively acted on the specific strigolactone receptor, and activated it with a high-affinity to provoke *Striga* germination with potency in the *femtomolar* (10^{-15} molar) range. The SPL7 is effective for reducing *Striga* parasitism on practical crop (maize) without impinging on host strigolactone-related processes even though synthetic SL agonist GR24 showed multiple actions to plant because of pan-agonist of ShHTLs. The discovery of SPL7 gets all ITbM scientists motivated to tackle the issue of *Striga* by practical use of SPL7 in near future in the field of Kenya, Africa.

(3) “Discovery of shoot branching regulator targeting strigolactone receptor DWARF14”, Yoshimura, M., Sato, A., Kuwata, K., Inukai, Y., Kinoshita, T., Itami, K., Tsuchiya, Y., and Hagihara, S. *ACS Cent. Sci.* **4**, 230 (2018)
DOI: 10.1021/acscentsci.7b00554

DWARF14 (D14) is a strigolactone receptor that plays a central role in suppression of shoot branching, and hence is a potential target to increase crop productions and biomass. The groups of **Itami** and **Kinoshita**, and the **Chemical Library Center** succeeded in identifying SL receptor agonists/antagonists from ITbM chemical library by using the Yoshimulactone, and among them, they revealed that a novel small molecule DL1 acts as a potent antagonist of D14-type strigolactone receptors They revealed that DL1 competes with endogenous strigolactones, thereby increasing the number of shoot branching in a model plant Arabidopsis as well as in rice. Thus, DL1 is expected to be useful not only as a tool to understand the biological roles of D14 receptors in plant growth and development, but also as a potent agrochemical to improve the crop yield.

(4) “Discovery of synthetic small molecules that enhance the number of stomata: C-H functionalization chemistry for plant biology”, Ziadi, A., Uchida, N., Kato, H., Hisamatsu, R., Sato, A., Hagihara, S., Itami, K., and Torii, K. U. *Chem. Commun.* **53**, 9632 (2017)
DOI: 10.1039/c7cc04526c

The **Torii-Uchida group** has explored small molecules that enhanced the density and/or patterning of stomata through chemical screening. They succeeded in identifying the first-in-class

synthetic molecules enhancing the number of stomata in *Arabidopsis thaliana* with the **Itami group** and the **Chemical library Center**. Several promising lead compounds have further been optimized through structure-activity relationship study of hit compounds by using C–H functionalization reactions at late stage of the synthesis. In addition, some compounds could promote root growth in various plant species such as *Arabidopsis thaliana* as well as edible plants (cucumber, lettuce, etc.). These results motivated them to initiate not only stomatal (chemical) biology as basic research but also develop academia-industry collaboration towards practical use of molecules in the field.

(5) "Identification and characterization of compounds that affect stomatal movements", Toh, S., Inoue, S., Toda, Y., Yuki, T., Suzuki, K., Hamamoto, S., Fukatsu, K., Aoki, S., Uchida, M., Asai, E., Uozumi, N., Sato, A., and Kinoshita, T. *Plant Cell Physiol.* **59**, 1568 (2018)
DOI:10.1093/pcp/pcy061

The **Kinoshita group** and **Chemical Library Center** have been screened more than 30,000 molecules from various chemical libraries to identify compounds that affect stomatal movements (opening/closing) in *Commelina benghalensis* and characterized the underlying their molecular mechanisms. They further revealed that the **s**tomatal **cl**osing compounds (SCLs) suppressed blue light-induced phosphorylation of PM H^+-ATPase for stomatal opening and had no negative effect on ABA-dependent responses including seed germination and expression of ABA-induced genes. In addition, they demonstrated that SCLs prevented plant leaves from drying-up and suppress withering when sprayed onto the plants (both of dicot (Chinese cabbage and rose) and monocot (oat) plants).

(6) "Cryptic bioactivity capacitated by synthetic hybrid plant peptides", Hirakawa, Y., Shinohara, H., Welke, K., Irle, S., Matsubayashi, Y., Torii, K. U., and Uchida, N. *Nat. Commun.* **8**, 14318 (2016)
DOI: 10.1038/ncomms14318

The groups of **Torii-Uchida** and **computational sciences group (Irle)** focused on the two plant peptide hormones, CLV3 and CLE25, which have root shortening activity. On the other hand, amino acid sequence homolog CLE41 peptide promotes the stem cell activity in the vascular meristem without affecting root / shoot stem cells. Through systematic swapping the amino acid sequences of CLV3 and CLE25, they succeeded in creating a novel synthetic bifunctional peptide, KIN, that exhibits vascular-thickening function as well as the original root-shortening function. They also exhibited computationally that KIN peptide binds to both CLV1 and TDR, receptors for CLV3/CLE25 and TDIF/CLE25, respectively. This result indicated that it could be possible to create novel synthetic plant peptide hormones even if the structural basis of the specificity between ligands and receptor has not been fully understood.

(7) "Combination of synthetic chemistry and live-cell imaging identified a rapid cell division inhibitor in Tobacco and Arabidopsis thaliana", Nambo, M., Kurihara, D., Yamada, T., Nishiwaki-Ohkawa, T., Kadofusa, N., Kimata, Y., Kuwata, K., Umeda, M., and Ueda, M. *Plant Cell Physiol.* **57**, 2255 (2016)
DOI:10.1093/pcp/pcw140

Nambo (**Crudden group**), Ueda (**Higashiyama group**), Ohkawa (**Yoshimura group**), and Kuwata (**Molecular Structure Center**) succeeded in identifying (3-furyl)diphenylmethane as a strong and reversible modulator for cell division. They revealed that the molecule has antiproliferative activity in developing organs of *Arabidopsis thaliana* without any defects in cell morphology, and induced rapid cell division arrest independent of the cell cycle stage. They further revealed that the molecule did not affect the growth of a human cell line (HeLa) and a budding yeast (Saccharomyces cerevisiae), and concluded that the molecule acts as a specific antiproliferative agent for plants. As molecular tools for controlling cell proliferation of plants remain still poor, this molecule is expected to give significant opportunities for plant biologists as a molecular tool.

(8) "C-H activation generates period-shortening molecules that target cryptochrome in the mammalian circadian clock", Oshima, T., Yamanaka, I., Kumar, A., Yamaguchi, J., Ohkawa, T. N., Muto, K., Kawamura, R., Hirota, T., Yagita, K., Irle, S., Kay, S. A., Yoshimura, T., and Itami, K. *Angew. Chem. Int. Ed.* **54**, 7193 (2015)
DOI: 10.1002/anie.201502942

Inspired by the discovery of KL001 (Hirota, Kay *et al.*, *Science* 2012), the **groups of Itami**, **Yoshimura**, and **theoretical sciences** identified clock-modulating molecules by cell-based phenotypic chemical screening. By using cutting-edge C-H activation chemistry, Itami G constructed a focused library of KL001 derivatives, and succeeded in uncovering the critical sites on KL001 derivatives that induce a rhythm-changing activity and rhythm-lengthening/shortening selectivity towards the cryptochrome (CRY)-mediated circadian clock regulation. Through structure-activity relationship study, they further succeeded in identifying the first period-shortening molecules that target CRY among library compounds. These compounds are expected to provide a tool to investigate the regulatory mechanism of CRY in the circadian timekeeping mechanism.

(9) "Identification of circadian clock modulators from existing drugs", Tamai, T. K., Nakane, Y., Ota, W., Kobayashi, A., Ishiguro, M., Kadofusa, N., Ikegami, K., Yagita, K., Shigeyoshi, Y., Sudo, M., Nishiwaki-Ohkawa, T., Sato, A., and Yoshimura, T. *EMBO Mol. Med.* **10**, e8724 (2018)
DOI 10.15252/emmm.201708724

Using drug-repurposing approach, the **Yoshimura group** and the **Chemical Library Center** performed a high-throughput chemical screening of existing drugs and have identified circadian clock modulators in human U2OS cells (drug repositioning). They identified that approximately 5% of the drugs screened altered circadian period, including the period-shortening compound dehydroepiandrosterone (DHEA; also known as prasterone). They demonstrated that dietary administration of DHEA to mice accelerates re-entrainment to advanced light–dark (LD) cycles, thereby reducing jet-lag. Their drug screening also revealed the involvement of tyrosine kinases, ABL1 and ABL2, and the BCR serine/threonine kinase in regulating circadian period. They concluded that drug repositioning is a useful approach to identify new circadian clock modulators and potential therapies for circadian disorders.

(10) "A water-soluble warped nanographene: synthesis and applications for photoinduced cell death", Lin, H. A., Sato, Y., Segawa, Y., Nishihara, T., Sugimoto, N., Scott, L. T., Higashiyama, T., and Itami, K. *Angew. Chem. Int. Ed.* **57**, 2874 (2018)
DOI: 10.1002/anie.201713387

The biological applications of nanographenes, such as bioimaging, cancer therapies and drug delivery, provide significant opportunities for breakthroughs in the field. However, the intrinsic aggregation behavior and low solubility of nanographenes, which stem from their flat structures, hamper their development for biological applications. The **Itami group** has synthesized a water-soluble warped nanographene (WNG) by sequential regioselective C-H borylation and cross-coupling. A water-soluble WNG exhibits green-yellow fluorescence with a long lifetime, good photostability and notably low cytotoxicity to cells. With the **Live Imaging Center**, they revealed that the water-soluble WNG was readily introduced into HeLa cells and induced cell death upon light irradiation, demonstrating the applicability for photodynamic therapy.

Appendix 1-3
Major Awards, Invited Lectures, Plenary Addresses (etc.) (within 2 pages)

*Prepare the information below during the period from the start of the center through March 2019.

1. Major Awards

*List main internationally-acclaimed awards received/unofficially announced in order from the most recent.
*For each, write the recipient's name, the name of award, and the date issued.
In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
Apr. 2, 2019	Cathleen Crudden	2019 Arthur C. Cope Scholar Award (Announcement September 2018)
Mar. 29, 2019	Shigehiro Yamaguchi	Humboldt Research Award
Mar. 25, 2019	Tetsuya Higashiyama	BBB Awards for Excellence to Authors
Dec. 7, 2018	Kenichiro Itami	The Netherlands Scholar Award for Supramolecular Chemistry
Nov. 27, 2018 (Announcement)	Kenichiro Itami, Wolf Frommer, Steve Kay	2018 Highly Cited Researchers
Sep. 15, 2018	Tetsuya Higashiyama	15th Academic Award of The Botanical Society of Japan
Aug. 27, 2018, Sep. 15, 2015, Sep. 17, 2013	Jeffery Bode (2018), Shigehiro Yamaguchi (2015), Kenichiro Itami (2013)	Mukaiyama Award
May 31, 2018, May 31, 2017	Tetsuya Higashiyama (2018), Kenichiro Itami (2017)	Chunichi Cultural Award
May 23, 2018	Cathleen Crudden	2018 IPMI Carol Tyler Award
May 8, 2018	Wolf Frommer	Tsungming Tu Award, Taiwan
May 1, 2018	Keiko Torii	2018 Clayton Person Lecture (Department of Botany, University of British Columbia, Canada)
Apr. 25, 2018	Kenichiro Itami	Guthikonda Lectureship in Organic Chemistry 2018
Feb. 7, 2018, Feb. 10, 2013, Feb. 4, 2012	Takeshi Yanai (2018), Kenichiro Itami (2013), Shigehiro Yamaguchi (2012)	The JSPS Award
Feb. 2, 2018, Feb. 4, 2015, Feb. 4, 2014	Tetsuya Higashiyama (2018), Keiko Torii (2015), Takashi Ooi (2013)	Inoue Prize for Science
Jan. 15, 2018	Takashi Ooi	The Society of Synthetic Organic Chemistry Award
May 19, 2017	Tetsuya Higashiyama	Kihara Foundation Award
Apr. 20, 2017, Apr. 17, 2014	Kenichiro Itami (2017), Tetsuya Higashiyama (2014)	Yomiuri Techno Forum Gold Medal Prize, Yomiuri Shimbun, Japan
Oct. 31, 2016	Kenichiro Itami	The Holger Erdtman Lecture, KTH, Sweden
Sep. 23, 2016	Kenichiro Itami	The Nagase Prize, Japan,
Sep. 1, 2016	Steve Kay	Funding Award: National Institutes of Health; National Institute of Diabetes and Digestive and Kidney Diseases
Jul. 15, 2016	Keiko Torii	Distinguished Lecture, Institute of Plant Molecular Biology, Academia Sinica, Taipei
Apr. 22, 2016	Shigehiro Yamaguchi	Nagase Foundation Award
Mar. 26, 2016	Shigehiro Yamaguchi	33rd Academic Award, Chemical Society of Japan

Oct. 19, 2015	Takashi Yoshimura	2015 Van Meter Award, American Thyroid Association
Jun. 26, 2015	Keiko Torii	2015 ASPB Fellow Award, American Society of Plant Biologists
May 23, 2015	Keiko Torii	35th Saruhashi Award
Dec. 25, 2014	Kenichiro Itami	Swiss Chemical Society Lectureship Award
Dec. 19, 2014	Tetsuya Higashiyama	NISTEP Award
Aug. 12, 2014	Kenichiro Itami	Arthur C. Cope Scholar Award, American Chemical Society
Aug. 20-23, 2013	Kenichiro Itami	Asian Rising Star Award

2. Invited Lectures, Plenary Addresses (etc.) at International Conferences and International Research Meetings

*List up to 10 main presentations in order from most recent.
*For each, write the lecturer/presenter's name, presentation title, conference name and date(s)

Date(s)	Lecturer/ Presenter's name	Presentation title	Conference name
Nov. 18, 2018	Wolf Frommer	In vivo biochemistry with sensors for signaling molecules and transporters.	Plenary Lecture: International Meeting on Optical Biosensors In memory of Roger Y. Tsien on the 10th year anniversary of his Nobel prize: VIB, Ghent, Belgium
Sep. 24, 2018	Keiko Torii	Making a pore: signaling and transcription factor control of stomatal differentiation.	Plenary Lecture: Annals of Botany Lecture, COMBIO 2018, Sydney, Australia
Jun. 29, 2018	Tetsuya Higashiyama	Cruising inside flowers: from cellular dynamics to key signaling molecules.	Keynote speaker: International Conference on Arabidopsis Research ICAR 2018, Turku, Finland
Jan. 24, 2018	Kenichiro Itami	Exploring Molecular Nanocarbon Science.	Prof. Bäckvall 70th Anniversary Symposium, The Royal Swedish Academy of Sciences
Jun. 26-29, 2017	Shigehiro Yamaguchi	Main Group Strategy for Functional pi-Electron Materials.	Gordon Research Conference 2017, Physical Organic Chemistry Symposium, Holderness, NH, USA
Jun. 26, 2017	Kenichiro Itami	Creation of molecular nanocarbons by metal catalysis.	19th IUPAC International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis (OMCOS19), Jeju Island, Korea
Jun. 9, 2017	Takashi Yoshimura	Understanding the molecular basis of vertebrate seasonal adaptation.	18th International Congress of Comparative Endocrinology, Lake Louise, Canada
Sep. 2-3, 2016	Steve Kay	Circadian Rhythm Networks in Health and Disease.	Nobel Prize Laureate Summit, Chengdu, China
Aug. 25, 2016	Takashi Yoshimura	Universality and diversity in the photoperiodic signal transduction in vertebrates.	Plenary Lecture: 28th Conference of European Comparative Endocrinologists Leuven, Belgium

Jul. 20-25, 2014	Keiko Torii	Receptor Kinase Specificity and Integration in Stomatal Patterning.	Gordon Research Conference, Plant Development, Holderness, NH, USA

Appendix 1-4 2018 List of Center's Research Results

Refereed Papers

- List only the Center's papers published in 2018. (Note: The list should be for the calendar year, not the fiscal year.)

(1) Divide the papers into two categories, A and B.
   A. WPI papers
      List papers whose author(s) can be identified as affiliated with the WPI program (e.g., that state "WPI" and the name of the WPI center (WPI-center name)). (Not including papers in which the names of persons affiliated with the WPI program are contained only in acknowledgements.)
   B. WPI-related papers
      List papers related to the WPI program but whose authors are not noted in the institutional affiliations as WPI affiliated. (Including papers whose acknowledgements contain the names of researchers affiliated with the WPI program.)

      Note: On 14 December 2011, the Basic Research Promotion Division in MEXT's Research Promotion Bureau circulated an instruction requiring paper authors to include the name or abbreviation of their WPI center among their institutional affiliations. As some WPI-affiliated authors of papers published up to 2011 may not be aware of this requirement, their papers are treated as "WPI-related papers." From 2012, the authors' affiliations must be clearly noted.

(2) Method of listing paper
   - List only refereed papers. Divide them into categories (e.g., original articles, reviews, proceedings).
   - For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is consistent. (The names of the center researchers do not need to be underlined.)
   - If a paper has many authors (say, more than 20), all of their names do not need to be listed.
   - Assign a serial number to each paper to be used to identify it throughout the report.
   - If the papers are written in languages other than English, underline their serial numbers.
   - Order of Listing
      A. WPI papers
         1. Original articles
         2. Review articles
         3. Proceedings
         4. Other English articles

      B. WPI-related papers
         1. Original articles
         2. Review articles
         3. Proceedings
         4. Other English articles

(3) Use in assessments
   - The lists of papers will be used in assessing the state of WPI project's progress.
   - They will be used as reference in analyzing the trends and whole states of research in the said WPI center, not to evaluate individual researcher performance.
   - The special characteristics of each research domain will be considered when conducting assessments.

(4) Additional documents
   - After all documents, including these paper listings, showing the state of research progress have been submitted, additional documents may be requested.

A. WPI papers (Jan 1, 2018 – Dec 31, 2018)

1. Original Articles

(1) Piyali Bhanja, Sabuj K. Das, Kousik Bhunia, Debabrata Pradhan, Taku Hayashi, Yuh Hijikata, Stephan Irle, and Asim Bhaumik, ACS Sustainable Chem. Eng. 2018, 6, 202−209. "A New Porous Polymer for Highly Efficient Capacitive Energy Storage" (DOI: 10.1021/acssuschemeng.7b02234)

(2) "Hsing-An Lin, Nobuhiko Mitoma, Lingkui Meng, Yasutomo Segawa, Atsushi Wakamiya and Kenichiro Itami, Mater. Chem. Front. 2018, 2, 275−280. "Hole-transporting materials based on thiophene-fused arenes from sulfur-mediated thienannulations" (DOI: 10.1039/c7qm00473g)

(3) Sujan Mondal, Ramana Singuru, Subhash Chandra Shit, Taku Hayashi, Stephan Irle, Yuh Hijikata, John Mondal, and Asim Bhaumik, ACS Sustainable Chem. Eng. 2018, 6, 1610−1619. "Ruthenium Nanoparticle-Decorated Porous Organic Network for Direct Hydrodeoxygenation of Long-Chain Fatty Acids to Alkanes" (DOI: 10.1021/acssuschemeng.7b02772)

(4) Renee W. Y. Man, Chien-Hung Li, Michael W. A. MacLean, Olena V. Zenkina, Matthew T. Zamora, Lisa N. Saunders, Alexander Rousina-Webb, Masakazu Nambo, and Cathleen M. Crudden, J. Am. Chem. Soc. 2018, 140, 1576−1579. "Ultrastable Gold Nanoparticles Modified by Bidentate N-Heterocyclic Carbene Ligands" (DOI: 10.1021/jacs.7b08516) *Highly Cited Paper*.

(5) Hiroaki Ogasawara, Marek Grzybowski, Riho Hosokawa, Yoshikatsu Sato, Masayasu Taki and Shigehiro

Yamaguchi, Chem. Commun. 2018, 54, 299–302. "A far-red fluorescent probe based on a phospha-fluorescein scaffold for cytosolic calcium imaging" (DOI: 10.1039/C7CC07344E)

(6) Zachary T. Ariki, Yuuki Maekawa, Masakazu Nambo, and Cathleen M. Crudden, J. Am. Chem. Soc. 2018, 140, 78−81. "Preparation of Quaternary Centers via Nickel-Catalyzed Suzuki-Miyaura Cross-Coupling of Tertiary Sulfones" (DOI: 10.1021/jacs.7b10855) *Highly Cited Paper*.

(7) Arifin, Daisuke Yokogawa, Udo Schnupf, and Stephan Irle, J. Phys. Chem. B 2018, 122, 290−296. "Statistical Mechanics-Based Theoretical Investigation of Solvation Effects on Glucose Anomer Preferences" (DOI: 10.1021/acs.jpcb.7b10270)

(8) Ashutosh Srivastava, Tsuyoshi Hirota, Stephan Irle, Florence Tama, Proteins 2018, 86, 344–353. "Conformational dynamics of human protein kinase CK2a and its effect on function and inhibition" (DOI: 10.1002/prot.25444)

(9) J. J. Clarke, P. Eisenberger, S. S. Piotrkowski and C. M. Crudden, Dalton Trans. 2018, 47, 1791−1795. "Azaborenium Ions: Synthesis and Use in the Generation of Stabilized Carbenium Ions" (DOI: 10.1039/C7DT01329A)

(10) Shu Jan Yip, Tetsushi Yoshidomi, Kei Murakami, and Kenichiro Itami, Chem. Lett. 2018, 47, 329–331. "Synthesis of α-Fluoroimines by Copper-catalyzed Reaction of Diarylacetylenes and N-Fluorobenzenesulfonimide" (DOI: 10.1246/cl.171097)

(11) Yosuke Ota, Shin Miyamura, Misaho Araki, Yukihiro Itoh, Shusuke Yasuda, Mitsuharu Masuda, Tomoyuki Taniguchi, Yoshihiro Sowa, Toshiyuki Sakai, Kenichiro Itami, Junichiro Yamaguchi, Takayoshi Suzuki, Bioorg. Med. Chem. Lett. 2018, 26, 775−785. "Design, synthesis and evaluation of c-turn mimetics as LSD1-selective inhibitors" (DOI: 10.1016/j.bmc.2017.12.045)

(12) Barbara Glöckle, Wojciech J. Urban, Shiori Nagahara, Ellen D. Andersen, Tetsuya Higashiyama, Paul E. Grini, Arp Schnittger, Development 2018, 145, dev152645. "Pollen differentiation as well as pollen tube guidance and discharge are independent of the presence of gametes" (DOI: 10.1242/dev.152645)

(13) Yuka Kimura, Masao Tasaka, Keiko U. Torii, Naoyuki Uchida, Development 2018, 145, dev156380. "ERECTA-family genes coordinate stem cell functions between the epidermal and internal layers of the shoot apical meristem" (DOI: 10.1242/dev.156380)

(14) Kenta Kato, Yasutomo Segawa, Lawrence T. Scott and Kenichiro Itami, Angew. Chem. Int. Ed. 2018, 57, 1337–1341. "A Quintuple [6]Helicene with a Corannulene Core as a C5-Symmetric Propeller-Shaped π-System" (DOI: 10.1002/anie.201711985) *Highly Cited Paper.*

(15) Mari Shibata, Hideto Ito, and Kenichiro Itami, J. Am. Chem. Soc. 2018, 140, 2196−2205. "C–H Arylation of Phenanthrene with Trimethylphenylsilane by Pd/o-Chloranil Catalysis: Computational Studies on the Mechanism, Regioselectivity, and Role of o-Chloranil" (DOI: 10.1021/jacs.7b11260)

(16) Soichiro Ogi, Kentarou Matsumoto and Shigehiro Yamaguchi, Angew. Chem. Int. Ed. 2018, 57, 2339–2343. "Seeded Polymerization through the Interplay of Folding and Aggregation of an Amino-Acid-based Diamide" (DOI: 10.1002/anie.201712119)

(17) Naoyuki Uchida, Koji Takahashi, Rie Iwasaki, Ryotaro Yamada, Masahiko Yoshimura, Takaho A Endo, Seisuke Kimura, Hua Zhang, Mika Nomoto, Yasuomi Tada, Toshinori Kinoshita, Kenichiro Itami, Shinya Hagihara & Keiko U Torii, Nature Chem. Biol. 2018, 14, 299–305. "Chemical hijacking of auxin signaling with an engineered auxin–TIR1 pair" (DOI: 10.1038/nchembio.2555) *Highly Cited Paper*.

(18) Yoshito Koga, Takeshi Kaneda, Yutaro Saito, Kei Murakami, Kenichiro Itami, Science 2018, 359, 435–439. "Synthesis of partially and fully fused polyaromatics by annulative chlorophenylene dimerization" (DOI: 10.1126/science.aap9801) *Highly Cited Paper.*

(19) Kazuki Motomura, Tomokazu Kawashima, Frédéric Berger, Tetsu Kinoshita, Tetsuya Higashiyama, Daisuke Maruyama, J. Cell Sci. 2018, 131, jcs204123. "A pharmacological study of Arabidopsis cell fusion between the persistent synergid and endosperm" (DOI: 10.1242/jcs.204123)

(20) Hsing-An Lin, Yoshikatsu Sato, Yasutomo Segawa, Taishi Nishihara, Nagisa Sugimoto, Lawrence T. Scott, Tetsuya Higashiyama and Kenichiro Itami, Angew. Chem. Int. Ed. 2018, 57, 2874 –2878. "A Water-soluble Warped Nanographene: Synthesis and Applications for Photo-induced Cell Death" (DOI: 10.1002/anie.201713387)

(21) Yoko Mizuta, Tetsuya Higashiyama, J. Cell Sci. 2018, 131, jcs208447. "Chemical signaling for pollen tube guidance at a glance" (DOI: 10.1242/jcs.208447)

(22) Naoya Suzuki, Kayo Suda, Daisuke Yokogawa, Hirotaka Kitoh-Nishioka, Stephan Irle, Akihiro Ando, Luis M. G. Abegao, Kenji Kamada, Aiko Fukazawa and Shigehiro Yamaguchi, Chem. Sci. 2018, 9, 2666–2673. "Near infrared two-photon-excited and -emissive dyes based on a strapped excited-state intramolecular proton-transfer (ESIPT) scaffold" (DOI: 10.1039/c8sc00066b)

(23) Daisuke Uraguchi, Hitoshi Sasaki, Yuto Kimura, Takaki Ito, and Takashi Ooi, J. Am. Chem. Soc. 2018, 140, 2765−2768. "Molecular Design, Synthesis, and Asymmetric Catalysis of a Hexacoordinated Chiral Phosphate Ion" (DOI: 10.1021/jacs.7b13433)

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(9) Daisuke Yokogawa, Bull. Chem. Soc. Jpn. 2018. 91, 1540-1545. "New Generation of the Reference Interaction Site Model Self-Consistent Field Method: Introduction of Constrained Spatial Electron Density Distribution (cSED)" (DOI: 10.1246/bcsj.20180179)

(10) Iain A Stepek, .and Jeffrey W. Bode, Curr. Opin. Chem. Biol. 2018, 46, 18-24. "Synthetic fermentation of bioactive molecules" (DOI: 10.1016/j.cbpa.2018.03.014)

(11) Michihisa Toya, Hideto Ito, Kenichiro Itami, Tetrahedron Lett. 2018, 59, 1531–1547. "Recent advances in acetylene-based helical oligomers and polymers: Synthesis, structures, and properties" (DOI: 10.1016/j.tetlet.2018.03.018)

(12) Subramanian Sankaranarayanan and Tetsuya Higashiyama, Trends Plant Sci. 2018, 23, 129–139. "Capacitation in Plant and Animal Fertilization" (DOI: 10.1016/j.tplants.2017.10.006)

3. Proceedings

N/A

4. Other English Articles

(1) Meng-Xiang Sun, Wei-Cai Yang, Tetsuya Higashiyama, Plant Reprod. 2018, 31, 1–2. "Special issue on plant reproduction research in Asia" (DOI: 10.1007/s00497-018-0330-9)

(2) Tetsuya Higashiyama, Curr. Biol. 2018, 28, R266–R269. "Plant Reproduction: Autocrine Machinery for the Long Journey of the Pollen Tube" (DOI: 10.1016/j.cub.2018.01.067)

(3) Daisuke Yokogawa, J. Chem. Theory Comput. 2018, 14, 3272-3278. "Toward Accurate Solvation Free Energy Calculation with the Reference Interaction Site Model Self-Consistent Field: Introduction of a New Bridge Function" (DOI: 10.1021/acs.jctc.8b00314)

(4) Toshinori Kinoshita, Peter McCourt, Tadao Asami, Keiko U Torii, Plant Cell Physiol. 2018, 59, 1483–1486. "Plant Chemical Biology" (DOI: 10.1093/pcp/pcy142)

(5) Yoko Mizuta and Katsutoshi Tsuda, Plant Transcription Factors, 257-268. "Three-Dimensional Multiphoton Imaging of Transcription Factor by ClearSee" (DOI: 10.1007/978-1-4939-8657-6_15)

(6) Ai Shinomiya and Takashi Yoshimura, Reproductive and Developmental Strategies: The Continuity of Life, 2018, 103-122. "Seasonal Regulation of Reproduction in Vertebrates: Special Focus on Avian Strategy" (DOI: 10.1007/978-4-431-56609-0_6)

B. WPI-related papers (Jan 1, 2018 – Dec 31, 2018)

1. Original Articles

(1) Christopher J. White and Jeffrey W. Bode, ACS Cent. Sci. 2018, 4, 197−206. "PEGylation and Dimerization of Expressed Proteins under Near Equimolar Conditions with Potassium 2-Pyridyl Acyltrifluoroborates" (DOI: 10.1021/acscentsci.7b00432)

(2) Jonathan G. Hubert, Iain A. Stepek, Hidetoshi Noda and Jeffrey W. Bode, Chem. Sci. 2018, 9, 2159−2167. "Synthetic fermentation of β-peptide macrocycles by thiadiazole-forming ring-closing reactions" (DOI: 10.1039/C7SC05057G)

(3) Masayoshi Nakamura, Jelmer J. Lindeboom, Marco Saltini, Bela M. Mulder, and David W. Ehrhardt, J. Cell Biol. 2018, 217, 915-927. "SPR2 protects minus ends to promote severing and reorientation of plant cortical microtubule arrays" (DOI: 10.1083/jcb.201708130)

(4) Margaret Bezrutczyk, Thomas Hartwig, Marc Horschman, Si Nian Char, Jinliang Yang, Bing Yang, Wolf B. Frommer, Davide Sosso, New Phytol. 2018, 218, 594–603. "Impaired phloem loading in zmsweet13a,b,c sucrose transporter triple knock-out mutants in Zea mays" (DOI: 10.1111/nph.15021)

(5) Motomu Endo, Masayasu Yoshida, Youhei Sasaki, Katsuya Negishi, Kobo Horikawa, Yasufumi Daimon, Ken-Ichi Kurotani, Michitaka Notaguchi, Mitsutomo Abe and Takashi Araki, Plant Cell Physiol. 2018, 59, 1621-1629. "Re-Evaluation of Florigen Transport Kinetics with Separation of Functions by Mutations That Uncouple Flowering Initiation and Long-Distance Transport" (DOI: 10.1093/pcp/pcy063)

(6) Chalupat Jindakun, Sheng-Ying Hsieh and Jeffrey W. Bode, Org. Lett. 2018, 20, 2071–2075. "Iridium-catalyzed Synthesis of Saturated N-Heterocycles from Aldehydes and SnAP Reagents with Continuous Flow Photochemistry" (DOI: 10.1021/acs.orglett.8b00611)

(7) Sizhou M. Liu, Dino Wu, and Jeffrey W. Bode, Org. Lett. 2018, 20, 2378−2381. "One-Step Synthesis of Aliphatic Potassium Acyltrifluoroborates (KATs) from Organocuprates" (DOI: 10.1021/acs.orglett.8b00720)

(8) Giorgio Perrella, Mhairi L. H. Davidson, Liz O'Donnell, Ana-Marie Nastase, Pawel Herzyk, Ghislain Breton, Jose L. Pruneda-Paz, Steve A. Kay, Joanne Chory, and Eirini Kaiserli, PNAS 2018, 115, E4503–E4511. "ZINC-FINGER interactions mediate transcriptional regulation of hypocotyl growth in Arabidopsis" (DOI: 10.1073/pnas.1718099115)

(9) Tomoya Shiro, Anne Schuhmacher, Moritz K. Jackl and Jeffrey W. Bode, Chem. Sci. 2018, 9, 5191−5196. "Facile synthesis of a-aminoboronic acids from amines and potassium acyltrifluoroborates (KATs) via trifluoroborate-iminiums (TIMs)" (DOI: 10.1039/c8sc01486h)

(10) Chin-Mei Lee, Ann Feke, Man-Wah Li, Christopher Adamchek, Kristofor Webb, José Pruneda-Paz, Eric J. Bennett, Steve A. Kay, and Joshua M. Gendron, Plant Phys. 2018, 177, 1170–1186. "Decoys Untangle Complicated Redundancy and Reveal Targets of Circadian Clock F-Box Proteins" (DOI: 10.1104/pp.18.00331)

(11) Jin Wen, Takayuki Uto, Jakub Chalupský, Deborah L. Casher, Gerhard Raabe, Joerg Fleischhauer, Takeshi Yanai, Hayato Tsuji, Koichi Komatsu, Josef Michl, J. Phys. Org. Chem. 2018, 31, e3854. "Magnetic circular dichroism of an unaromatic planar [8]annulene" (DOI: 10.1002/poc.3854)

(12) Rui Wu, Lina Duan, Jose L. Pruneda-Paz, Dong-ha Oh, Michael Pound, Steve Kay, and Jose R. Dinneny, Plant Physiol. 2018, 177, 1650-1665. "The 6xABRE Synthetic Promoter Enables the Spatiotemporal Analysis of ABA-Mediated Transcriptional Regulation" (DOI: 10.1104/pp.18.00401)

(13) Moritz K. Jackl, Anne Schuhmacher, Tomoya Shiro, and Jeffrey W. Bode, Org. Lett. 2018, 20, 4044−4047. "Synthesis of N,N-Alkylated α-Tertiary Amines by Coupling of α-Aminoalkyltrifluoroborates and Grignard Reagents" (DOI: 10.1021/acs.orglett.8b01613)

(14) Dominik Schauenburg, Alberto Osuna Galvez and Jeffrey W. Bode, J. Mater. Chem. B 2018, 6, 4775–4782. "Covalently functionalized amide cross-linked hydrogels from primary amines and polyethylene glycol acyltrifluoroborates (PEG-KATs)" (DOI: 10.1039/c8tb01028e)

(15) Thibault J. Harmand, Claudia E. Murar, Hikaru Takano and Jeffrey W. Bode, Org. Synth. 2018, 95, 142-156. "Enantioselective Synthesis of (S)-Ethyl 2-((tertbutoxycarbonyl)((tert-butyldimethylsilyl)oxy)amino)-4-oxobutanoate" (DOI: 10.15227/orgsyn.95.0142)

(16) Claudia E. Murar, Thibault J. Harmand, Hikaru Takano and Jeffrey W. Bode, Org. Synth. 2018, 95, 157-176. "Preparation of (S)-N-Boc-5-oxaproline" (DOI: 10.15227/orgsyn.95.015)

(17) Artemis Perraki, Thomas A. DeFalco, Paul Derbyshire, Julian Avila, David Séré, Jan Sklenar, Xingyun Qi, Lena Stransfeld, Benjamin Schwessinger, Yasuhiro Kadota, Alberto P. Macho, Shushu Jiang, Daniel Couto, Keiko U. Torii, Frank L. H. Menke & Cyril Zipfel, Nature 2018, 561, 248–252. "Phosphocode-dependent functional dichotomy of a common co-receptor in plant signalling" (DOI: 10.1038/s41586-018-0471-x)

(18) Qiyu Jin, Osamu Miyashita, Florence Tama, Jie Yang, and Slavica Jonic, IET Image Process. 2018, 12, 2264-2274. " Poisson image denoising by piecewise principal component analysis and its application in single-particle X-ray diffraction imaging" (DOI: 10.1049/iet-ipr.2018.5145)

(19) "Gabor N. Boross, Satomi Shimura, Melissa Besenius, Norbert Tennagels,Kai Rossen, Michael Wagner and Jeffrey W. Bode, Chem. Sci. 2018, 9, 8388–8395. "Facile folding of insulin variants bearing a prosthetic C-peptide prepared by a-ketoacidhydroxylamine (KAHA) ligation" (DOI: 10.1039/c8sc03738h)

(20) Yuwei Gu, Dominik Schauenburg, Jeffrey W. Bode, and Jeremiah A. Johnson, J. Am. Chem. Soc. 2018, 140, 14033-14037. "Leaving Groups as Traceless Topological Modifiers for the Synthesis of Topologically Isomeric Polymer Networks" (DOI: 10.1021/jacs.8b07967)

(21) Michael U. Luescher, Chalupat Jindakun and Jeffrey W. Bode, Org. Synth. 2018, 95, 345-356. "Preparation of Tributyl(iodomethyl)stannane" (DOI: 10.15227/orgsyn.095.0345)

(22) Michael U. Luescher, Chalupat Jindakun and Jeffrey W. Bode, Org. Synth. 2018, 95, 357-373. "Stannylamine Protocol (SnAP) Reagents for the Synthesis of C–Substituted Morpholines from Aldehydes" (DOI: 10.15227/orgsyn.095.0357)

2. Review Articles

(1) Xingyun Qi and Keiko U. Torii, BMC Biol. 2018, 16, 21. "Hormonal and environmental signals guiding stomatal development" (DOI: 10.1186/s12915-018-0488-5)

(2) Miya Mizutani and Masahiro M. Kanaoka, Semin. Cell Dev. Biol. 2018, 83, 69-77. "Environmental sensing and morphological plasticity in plants" (DOI: 10.1016/j.semcdb.2017.10.029)

(3) Masahiro M. Kanaoka, J. Plant Res. 2018, 131, 37-47. "Cell–cell communications and molecular mechanisms in plant sexual reproduction" (DOI: 10.1007/s10265-017-0997-2)

3. Proceedings

N/A

4. Other English Articles

(1) Takashi Yoshimura, Gen. Comp. Endocrinol. 2018, 260, 162–163. "Editorial – The Japan Society for Comparative Endocrinology" (DOI: 10.1016/j.ygcen.2018.03.002)

(2) Huw M. L. Davies, Kenichiro Itami and Brian M. Stoltz, Chem. Soc. Rev. 2018, 47, 7828-7829. "New directions in natural product synthesis" (DOI: 10.1039/c8cs90115e)

Appendix 2　FY 2018 List of Principal Investigators

NOTE:

*Underline names of principal investigators who belong to an overseas research institution.

*In the case of researcher(s) not listed in the latest report, attach a “Biographical Sketch of a New Principal Investigator”(Appendix 2a).

<Results at the end of FY2018> **Principal Investigators Total: 13**

Name	Age	Affiliation (Position title, department, organization)	Academic degree, Specialty	Effort (%)*	Starting date of project participation	Status of project participation (Describe in concrete terms)	Contributions by PIs from overseas research institutions
Kenichiro ITAMI*	47	Director, Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr.Eng Specialties: Organic Synthesis, Catalysis, Pharmaceuti-cal Science, Nanocarbon Chemistry	80	from the beginning	usually stays at the center	
Tetsuya HIGASHIYAMA*	47	Vice-Director, Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr.Sci Specialties: Live Cell Biology, Plant Reproduction, Bio-active molecules, Peptides	90	from the beginning	usually stays at the center	
Jeffrey W. BODE*	45	Professor of Organic Chemistry Department of Chemistry and Applied Biosciences, ETH Zürich, Switzerland	Doctoral of Natural Science Specialties: Organic Synthesis, Peptide and Protein Chemistry, Catalysis, Ligation and Bioconjugati-on reactions	21	from the beginning	Stayed at the center for two weeks in FY2018. Connected 24 hours through iPad to the center. Holds on-line group meeting once a week. Joins PI meeting online.	
Cathleen M. CRUDDEN*	52	Professor Department of Chemistry, Queen's University, Canada	Ph.D Specialities: Catalysis, Organic Synthesis, Materials Chemistry, Chirality	21	from the beginning	Stayed at the center for six weeks in FY2018. Holds Skype group meeting once a week. Joins PI meeting online.	
Toshinori KINOSHITA*	50	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr.Sci Specialities: Plant Molecular Physiology	90	from the beginning	usually stays at the center	
Takashi OOI*	53	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Engineering Specialties: Organic Synthesis, Catalysis, Molecular Recognition	90	from the beginning	usually stays at the center	

Keiko TORII*	53	Distinguished Professor Department of Biology, University of Washington Investigator Howard Hughes Medical Institute and Gordon and Betty Moore Foundation (HHMI-GBMF)	Ph.D. Specialties: Plant Development, Signal Transduction, Stem Cell Maintenance/Differentiati-on in Plants	21	from the beginning	Stayed at the center for one month in FY2018. Holds on-line plant biology meeting “Mixplant meeting” once a week. Joins PI meeting online.	
Shigehiro YAMAGUCHI*	50	Vice-Director, Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Engineering Specialties: Main Group Chemistry, Physical Organic Chemistry	90	from the beginning	usually stays at the center	
Takashi YOSHIMURA*	49	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Agriculture Specialties: Animal Physiology, Systems Biology, Neuroendoc-rinology	70	from the beginning	usually stays at the center	
Steve A. Kay*	59	Dean and Anna H. Bing Dean's Chair, Professor of Biological Sciences, Professor of Neurology, Physiology and Biophysics, Dornsife College of Letters, Arts and Sciences, University of Southern California	Ph.D. Specialties: Chronobiolo-gy, Genetics, Biochemistry, Systems Biology	21	from April 1st 2014	Holds on-line meeting on an as-needed basis. Joins PI meeting online.	
Florence Tama*	44	Professor Institute of Transformative Bio-Molecules / Department of Physics, Graduate School of Science, Nagoya University	Ph.D Specialties: computational biophysics	50	from April 1st 2016	usually stays at the center	
Wolf B. Frommer*	61	Professor Heinrich Heine University Dü sseldorf and Max Planck Institute for Breeding Research, Germany	Dr. rer. nat. Specialties: Biology	21	from October 16th 2016	Stayed at the center for three weeks in FY2018. Holds on-line group meeting once a week. Joins PI meeting online.	
Takeshi Yanai*	44	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr.Eng Specialties: Theoretical chemistry, computatoinal quantum chemistry	90	from April 1st 2018	usually stays at the center	

*Percentage of time that the principal investigator devotes to his/her work for the center vis-à-vis his/her total working hours.

Principal investigators unable to participate in project in FY 2018

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken
N/A				

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age)

Takeshi Yanai (44)

Affiliation and position (Position title, department, organization, etc.)

Professor, Institute of Transformative Bio-Molecules
JST PREST researcher

Academic degree and specialty

Academic degree; Dr.Eng, Specialties: theoretical chemistry, computational quantum chemistry

Effort **90%**

* Percentage of time that the principal investigator will devote to working for the center vis-à-vis his/her total working hours.

Research and education history

Professional experience

1999-2002	JSPS Research Fellow DC1; University of Tokyo
2002-2003	JSPS Research Fellow PD; Pacific Northwest National Laboratory and Oak Ridge National Laboratory, USA
2003-2005	Postdoctoral fellow; Oak Ridge National Laboratory, USA
2005-2006	Postdoctoral fellow; Chemistry and Chemical Biology, Cornell University, USA
2007-2018	Associate Professor; Department of Theoretical and Computational Molecular Science, Institute for Molecular Science, National Institutes of Natural Sciences, Japan
2017-present	JST PRESTO Researcher
2018-present	Professor; WPI-ITbM, Nagoya University

Education

1997	B.S.; University of Tokyo (Applied Chemistry)
1999	M.S.; University of Tokyo (Applied Chemistry)
2001	Dr. Eng.; University of Tokyo (Applied Chemistry)

Achievements and highlights of past research activities

Dr. Yanai has been carrying out theoretical research in such a way to expand the domain of applications of quantum chemistry calculations by developing efficient algorithms and cutting-edge theories and by making the best use of state-of-the-art computer techniques. Using these methods, he achieved unconventional electronic structure calculations for the challenging molecular systems with and without experimental collaborations. The marked achievements are (1) the establishment of the advanced QC methods using an efficient quantum many-body algorithm for high-accuracy wave function calculations; (2) its applications to multi-nuclear transition metal complexes for achieving highly-reliable characterization of their electronic states and reactivity; (3) applications to electronic excited states of photofunctional π conjugated systems; and (4) the development of the DFT functional, CAM-B3LYP, for rectifying a critical failure of DFT calculations for charge-transfer states.

Fast quantum many-body algorithm and its large-scale molecular calculations Dr. Yanai has developed an efficient quantum chemical scheme using a new class of quantum many-body algorithm, referred to as density matrix renormalization group (DMRG) theory. He showed that his method delivers an efficient numeric procedure to describe complex electronic structures of multi-nuclear coordination systems, reactive intermediates, excited states, etc, while it can avoid the combinatorial complexity of the computation. Using the DMRG-based algorithm, his group achieved the unprecedented computation of near-exact many-electron wave function of tetranuclear Mn cluster, a catalytic core of the photosynthetic water-splitting metalloenzyme in photosystem II (Nature Chem 2013). His approach enabled the construction of valence-electron wave function with 10^{18} dimensional configuration space, which is impossible for the conventional methods to describe. His interest was turned to the determination of the oxidation states of the Mn_4CaO_5 cluster. This study was highly evaluated not only because of these findings but also because it is the first computational work that provides many-electron picture of the multi-nuclear transition metal complex beyond the conventional mean-field one-electron picture. In addition, the use of the quantum many-body approach enabled him to perform

quantum many-body calculations on long-chain π conjugated systems, such as excited states of β-carotene, oligoacene, radical (or magnetic) states of carbene chains, graphene nanoribbons, and photochromic and photofunctioning molecules, and many others

Development of DFT functional: CAM-B3LYP Dr. Yanai proposed a hybrid exchange-correlation functional, designated CAM-B3LYP, which incorporates long-range properties from Coulomb attenuation (range separation) into B3LYP functional. It significantly improved the performance of DFT calculations of polarizability of conjugated chain molecules, and most importantly, charge transfer excitations. Because of its remarkable performance, it has been implemented into several prominent QC software packages, such as GAUSSIAN, etc. This functional is considered to be one of the most popular functionals. This work has been cited over 5000 times, and won "Chemical Physics Letters Most Cited Paper 2003-2007 Award." Furthermore, using DFT, he made essential computational contributions to the collaborative work with experimentalists developing a synthetic water-oxidation catalyst (pentanuclear Fe complex), which was published in Nature.

Achievements

(1) International influence * Describe the kind of attributes listed below.

a) Recipient of international awards

- Chemical Physics Letters Most Cited Paper 2003-2007 Award
- The Wiley-International Journal of Quantum Chemistry Young Investigator Award (The 49th Sanibel Symposium, 2009)
- Laureate, International Academy of Quantum Molecular Science Medal (2013)
- The 2017 Pople Medal of Asia-Pacific Conference of Theoretical and Computational Chemistry (2017)

b) Member of a scholarly academy in a major country

N/A

c) Guest speaker or chair of related international conference and/or director or honorary chairman of a major international academic society in the subject field

Guest speaker

1. T. Yanai, San Diego, USA (Mar 13-17, 2016); The 251th ACS meeting, "Recent progress in multireference dynamic correlation methods based on density matrix renormalization group." (Invited)
2. T. Yanai, Seattle, USA (Aug 28-Sep 2, 2016); Theory and Applications of Computational Chemistry 2016, "Multireference theory based on density matrix renormalization group" (Invited)
3. T. Yanai, Telluride, CO, USA (June 20-24, 2017); New Frontiers in Electron Correlation, "Projector Augmented Wave Method Incorporated into Gauss-type Atomic Orbital Based Density Functional Theory" (Invited)
4. T. Yanai, Munich, Germany (Aug 27-Sep 1, 2017); The 11th Triennial Congress of the World Association of Theoretical and Computational Chemists, "Projector Augmented Wave Method Incorporated into Gauss-type Atomic Orbital Based Density Functional Theory" (Invited).
5. T. Yanai, Toulouse, France (Jun. 13-15, 2018); ICQC 2018 Satellite Meeting, Theoretical Studies of Magnetic Systems; "DMRG-based Multistate Multireference Perturbation Theory."

Preliminary lecture

1. T. Yanai, Boulder, CO, USA (June 29, 2012); The XIVth International Congress of Quantum Chemistry, "Density Matrix Renormalization Group and Associated Dynamic Correlation Methods: Theory and Applications" (Preliminary lecture)
2. T. Yanai, Uppsala, Sweden (Jun 26-Jul 1, 2016); The 8th Molecular Quantum Mechanics, "CASPT2 theory with DMRG reference wavefunction" (Preliminary lecture)
3. T. Yanai, Mumbai, India (Dec. 15-17, 2017); The 8th Asia-Pacific Conference of Theoretical and Computational Chemistry; "Advanced Multireference Electronic Structure Theory with ab initio Density Matrix Renormalization Group" (Preliminary lecture).

d) Editor of an international academic journal

N/A

e) Peer reviewer for an overseas competitive research program (etc.)

1. Czech Science Foundation, project proposals (2015-2017)

(2) Receipt of major large-scale competitive funds (over the past 5 years)

- FY2013 – FY2015 KAKENHI Grant-in-Aid for Scientific Research (B) PI, "Theory and Its Applications Based on Density Matrix Renormalization Group for Multi-Electronic-State Chemical Processes," Grant Amount: 18,720K Yen
- FY2015 – FY2016 KAKENHI Grant-in-Aid for Scientific Research on Innovative Areas "Application of Cooperative Excitation into Innovative Molecular Systems with High-Order Photofunctions" PI of Publicly Invited Research, "Advancing electronic structure theory for high accuracy prediction of higher excited states and its application to photochemical molecules," Grant Amount: 5,070K Yen
- FY2016 – FY2018 KAKENHI Grant-in-Aid for Scientific Research (B) PI, "Elucidation of Reactivity of Metalloenzymes and Molecular Catalysts using Magnetic Spectroscopic Simulations Based on High-Accuracy Electronic Structure Theory, " Grant Amount: 14,200K Yen
- FY2017 – FY2018 KAKENHI Grant-in-Aid for Scientific Research on Innovative Areas "Application of Cooperative Excitation into Innovative Molecular Systems with High-Order Photofunctions" PI of Publicly Invited Research, "Advancing electronic structure theory for high accuracy prediction of higher excited states and its application to photochromic molecules," Grant Amount: 4,940K Yen
- FY2017-FY2020 PREST Materials Informatics, "Development of quantum simulator based on artificial neural network theory," Grant Amount 36,000 Yen
- FY2018 STINT Sweden-Japan 150 Anniversary Grants, "Breaking barriers in X-ray simulations," Grant Amount 147 200 SEK for two Swedish PIs (M. Lundberg and M. Odelius) and one Japanese PI (Yanai)

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)

1. T. Yanai, D. P. Tew, and N. C. Handy, "A new hybrid exchange-correlation functional using the Coulomb-Attenuating Method (CAM-B3LYP)," Chem. Phys. Lett. 393, 51-57 (2004). [5,622 times cited]
2. H. Iikura, T. Tsuneda, T. Yanai, and K. Hirao, "A long-range correction scheme for generalized-gradient-approximation exchange functionals," J. Chem. Phys. 115, 3540-3544 (2001). [1,572 times cited]
3. Y. Tawada, T. Tsuneda, S. Yanagisawa, T. Yanai, and K. Hirao, "A long-range-corrected time-dependent density functional theory," J. Chem. Phys. 120, 8425-8433 (2004). [1,347 times cited]
4. R. J. Harrison, G. I. Fann, T. Yanai, Z. Gan, and G. Beylkin, "Multiresolution quantum chemistry: Basic theory and initial applications," J. Chem. Phys. 121, 11587-11598 (2004). [221 times cited]
5. D. Ghosh, J. Hachmann, T. Yanai and G. K-L. Chan, "Orbital Optimization in Density Matrix Renormalization Group, with applications to polyenes and β-carotene," J. Chem. Phys. 128, 144117 (2008). [181 times cited]
6. T. Yanai and G. K-L. Chan, "Canonical transformation theory for multireference problems", J. Chem. Phys. 124, 194106 (2006) (16 pages). [153 times cited]
7. Y. Kurashige, G. K-L. Chan, and T. Yanai, "Entangled quantum electronic wavefunctions of the Mn4CaO5 cluster in photosystem II," Nature Chem. 5, 660-666 (2013). [151 times cited]
8. Y. Kurashige and T. Yanai, "High-performance ab initio density matrix renormalization group method: Applicability to large-scale multireference problems for metal compounds," J. Chem. Phys. 130, 234114 (2009). [144 times cited]
9. Y. Kurashige and T. Yanai, "Second-order perturbation theory with a DMRG self-consistent field reference function: Theory and application to the study of chromium dimer," J. Chem. Phys. 135, 094104 (2011). [136 times cited]
10. T. Yanai, Y. Kurashige, E. Neuscamman, G. K-L. Chan, "Multireference quantum chemistry through a joint density matrix renormalisation group and canonical transformation theory," J. Chem. Phys. 132, 024105 (2010) [112 times cited]

(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)

Appendix 3-1 FY 2018 Records of Center Activities

1. Researchers and other center staffs, satellites, partner institutions

1-1. Number of researchers and other center staffs

* Fill in the number of researchers and other center staffs in the table blow.
* Describe the final goals for achieving these numbers and dates when they will be achieved described in the last "center project."

a) Principal Investigators

(full professors, associate professors or other researchers of comparable standing)

(number of persons)

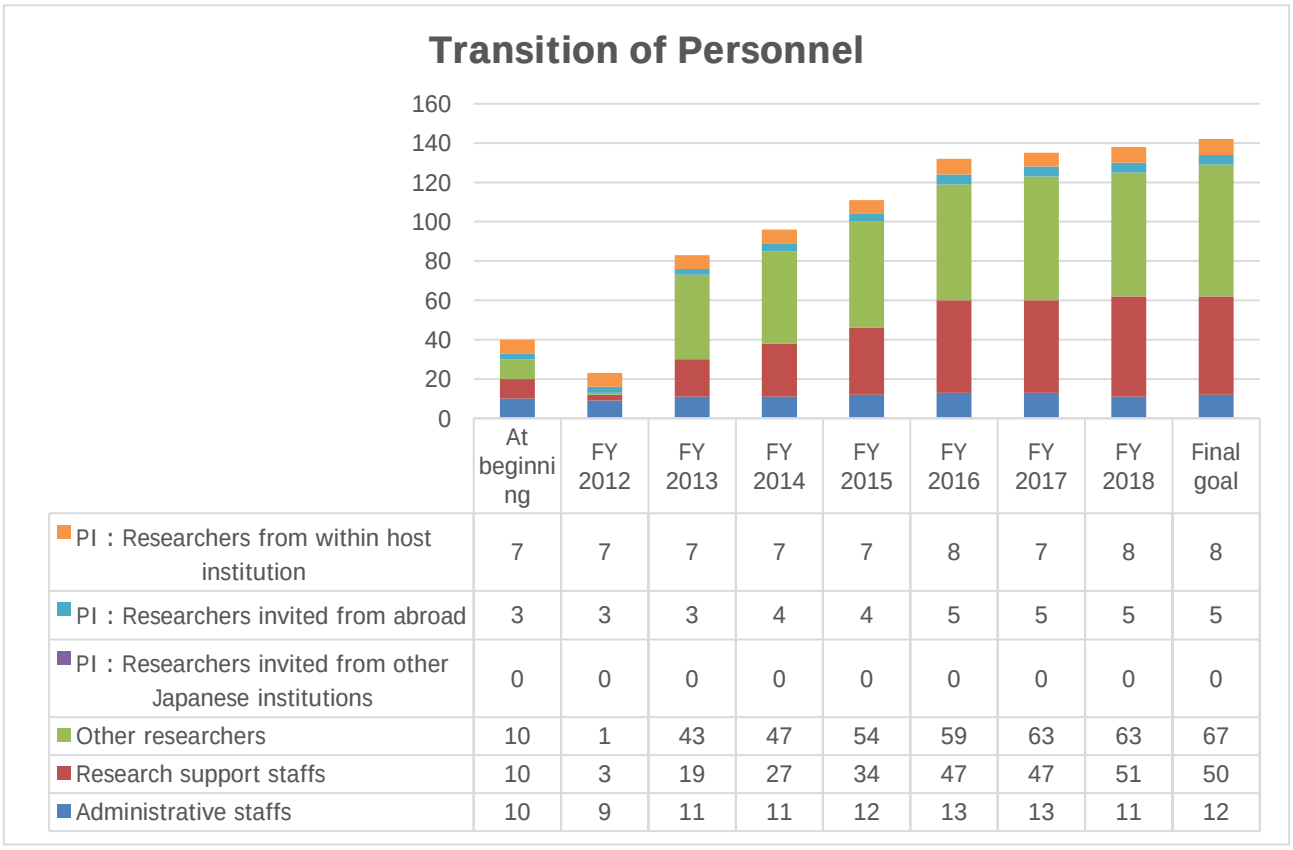
	At the beginning of project	At the end of FY 2018	Final goal (Date: March, 2022)
Researchers from within the host institution	7	8	8
Researchers invited from abroad	3	5	5
Researchers invited from other Japanese institutions	0	0	0
Total principal investigators	10	13	13

b) Total members

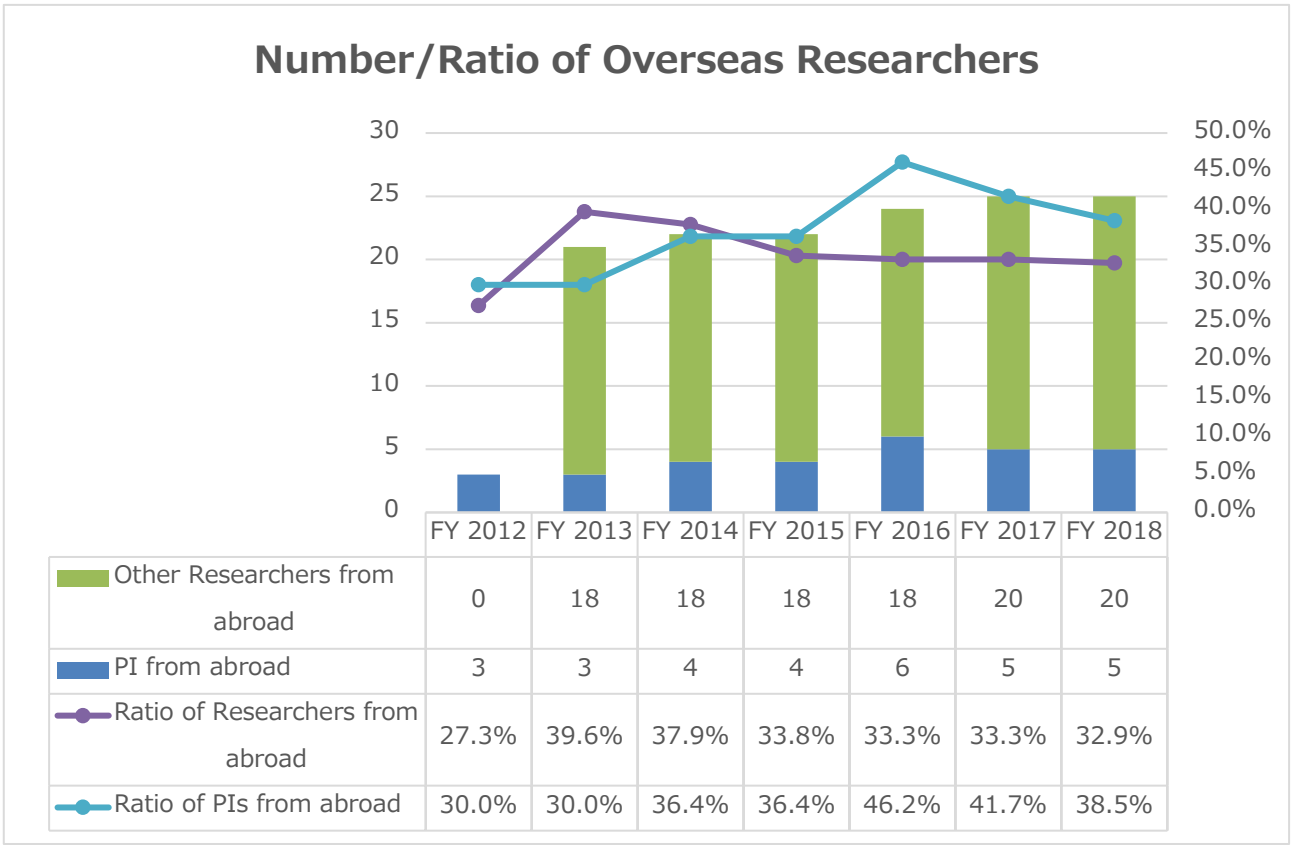
	At the beginning of project		At the end of FY2018		Final goal (Date: March, 2022)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	20		76		80	
Overseas researchers	5	25	25	33	27	34
Female researchers	4	20	19	25	21	26
Principal investigators	10		13		13	
Overseas PIs	3	30	5	38	6	46
Female PIs	2	20	3	23	3	23
Other researchers	10		63		67	
Overseas researchers	2	20	20	32	21	31
Female researchers	2	20	16	25	18	27
Research support staffs	10		51		50	
Administrative staffs	10		11		12	
Total number of people who form the "core" of the research center	40		138		142	

Appendix 3-2　Annual Transition in the Number of Center Personnel

*Make a graph of the annual transition in the number of center personnel since the start of project.

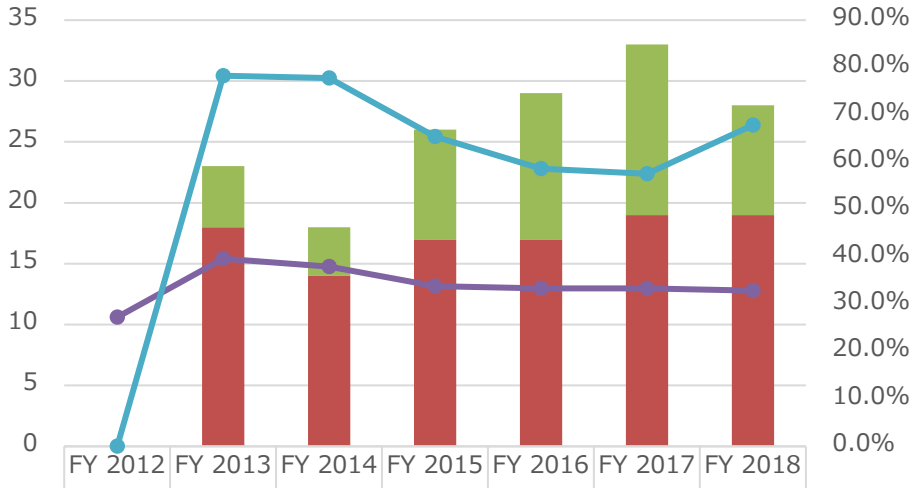


	At beginning	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018	Final goal
PI : Researchers from within host institution	7	7	7	7	7	8	7	8	8
PI : Researchers invited from abroad	3	3	3	4	4	5	5	5	5
PI : Researchers invited from other Japanese institutions	0	0	0	0	0	0	0	0	0
Other researchers	10	1	43	47	54	59	63	63	67
Research support staffs	10	3	19	27	34	47	47	51	50
Administrative staffs	10	9	11	11	12	13	13	11	12



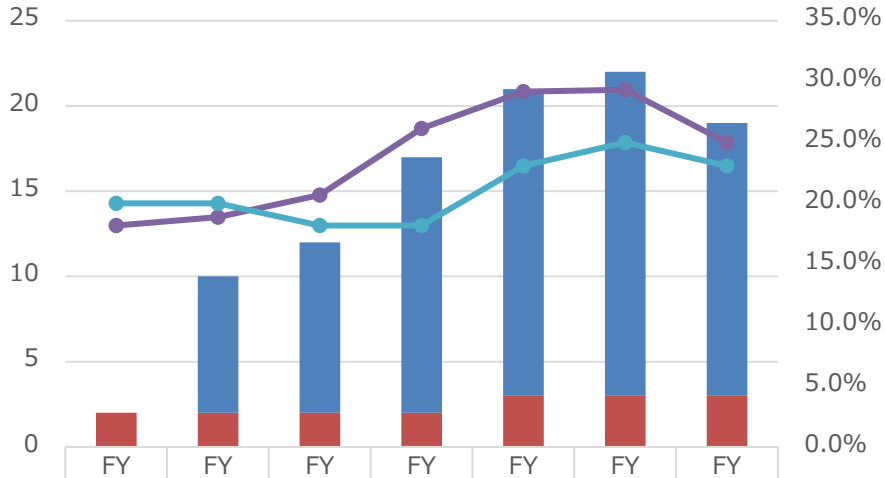
	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Other Researchers from abroad	0	18	18	18	18	20	20
PI from abroad	3	3	4	4	6	5	5
Ratio of Researchers from abroad	27.3%	39.6%	37.9%	33.8%	33.3%	33.3%	32.9%
Ratio of PIs from abroad	30.0%	30.0%	36.4%	36.4%	46.2%	41.7%	38.5%

Number/Ratio of Overseas Postdoc



	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Japanese Postdoc	0	5	4	9	12	14	9
Overseas Postdoc	0	18	14	17	17	19	19
Ratio of Researchers from abroad	27.3%	39.6%	37.9%	33.8%	33.3%	33.3%	32.9%
Ratio of Overseas Postdoc	0%	78%	78%	65%	59%	58%	68%

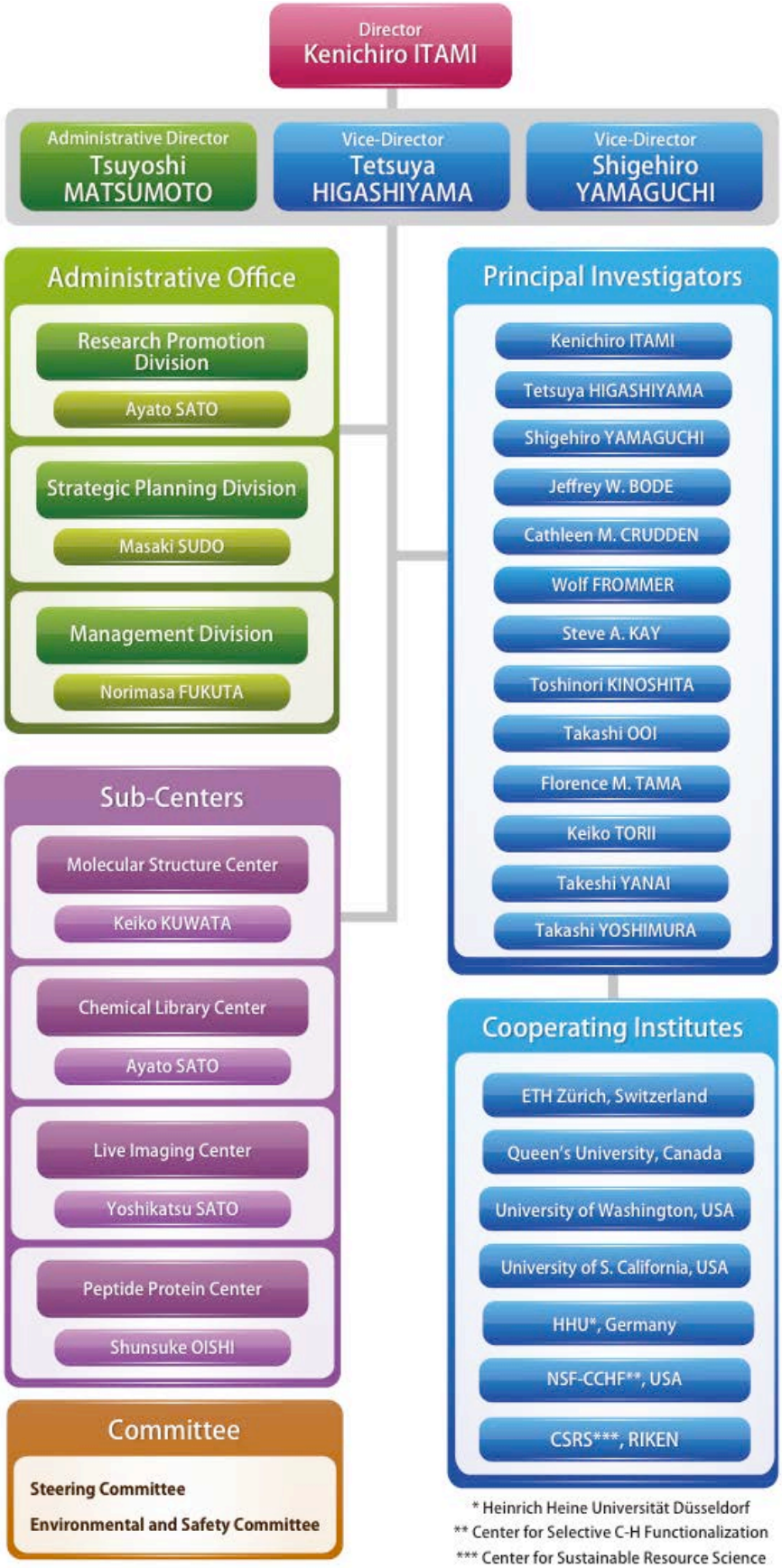
Number/Ratio of Female Researchers



	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Other Female Researchers	0	8	10	15	18	19	16
Female PI	2	2	2	2	3	3	3
Ratio of Female Researchers	18.2%	18.9%	20.7%	26.2%	29.2%	29.3%	25.0%
Ratio of Female PI	20.0%	20.0%	18.2%	18.2%	23.1%	25.0%	23.1%

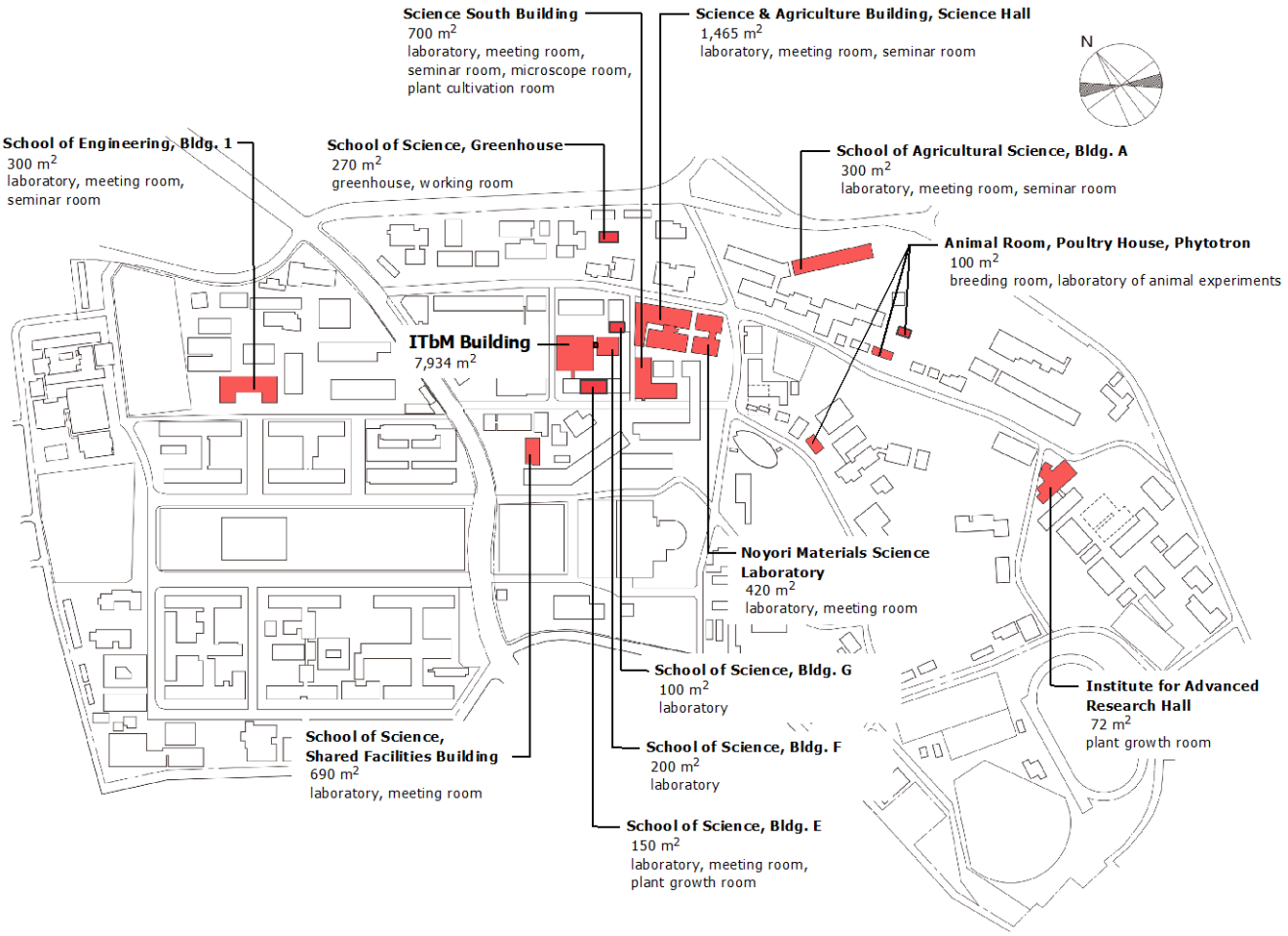
Appendix 3-3 Diagram of Management System

- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such as the center director, administrative director, head of host institution, and officer(s) in charge at the host institution (e.g., executive vice president for research).



Appendix 3-4 Campus Map

- Draw a simple map of the campus showing where the main office and principal investigator(s) are located.



Appendix 3-5 Project Expenditures in FY2018

1) Overall project funding

* In the “Total costs” column, enter the total amount of funding required to implement the project, without dividing it into funding sources.
* In the “Amount covered by WPI funding” column, enter the amount covered by WPI within the total amount.
* In the “Personnel,” “Project activities,” “Travel,” and “Equipment” blocks, the items of the "Details" culumn may be changed to coincide with the project’s actual content.

(Million yens)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center director and administrative director	32	18
	Principal investigators (no. of persons):12	101	18
	Other researchers (no. of persons):57	293	239
	Research support staffs (no. of persons):32	51	51
	Administrative staffs (no. of persons):24	88	60
	Subtotal	565	386
Project activities	Cost of dispatching scientists (no. of persons):1	3	3
	Research startup cost (no. of persons):6	8	8
	Cost of international symposiums (no. of symposiums):5	1	1
	Rental fees for facilities	23	3
	Cost of consumables	24	23
	Cost of utilities	64	63
	Other costs	85	75
	Subtotal	208	176
Travel	Domestic travel costs	4	4
	Overseas travel costs	15	14
	Travel and accommodations cost for invited scientists	6	6
	(no. of domestic scientists):10		
	(no. of overseas scientists):11		
	Travel cost for scientists on transfer	1	1
	(no. of domestic scientists):4		
	(no. of overseas scientists):1		
	Subtotal	26	25
Equipment	Depreciation of buildings	37	7
	Depreciation of equipment	149	99
	Subtotal	186	106
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	253	
	KAKENHI	365	
	Commissioned research projects, etc.	481	
	Joint research projects	32	
	Ohers (donations, etc.)	32	
	Subtotal	1163	0
Total		2148	693

Costs (Million yens)

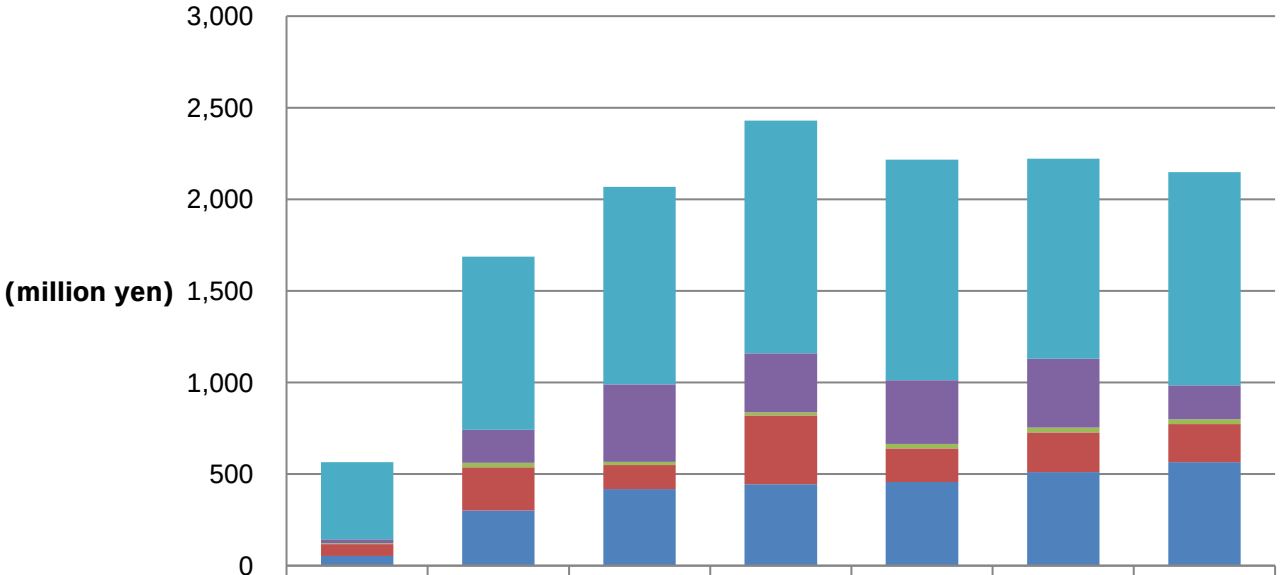
WPI grant in FY 2018	693
Costs of establishing and maintaining	0
Costs of equipment procured	106
Name of equipment:Automated Pipetting System Number of units: 1 Set	30
Name of equipment:Multi-angle Light Scattering Detector Number of units: 1 Set	13
Name of equipment:Prominence gel permeation chromatography system Number of units: 1 Set	8
Name of equipment:Highly Sensitive Hybrid Detector Number of units: 1 Set	7
Name of equipment:Confocal and Stimulated Emission Depletion Microscope FALCON Number of units: 1 Set	6
Others	42

*1. Funding sources that include government subsidies (including Enhancements promotion expenses (機能強化促進経費), National university reform reinforcement promotion subsidy (国立大学改革強化推進補助金) etc.), indirect funding, and allocations from the university's own resources.
*2 When personnel, travel, equipment (etc.) expenses are covered by KAKENHI or under commissioned research projects or joint research projects, the amounts should be entered in the “Research projects” block.

Appendix 3-6　Annual Transition in the Amounts of Project Funding

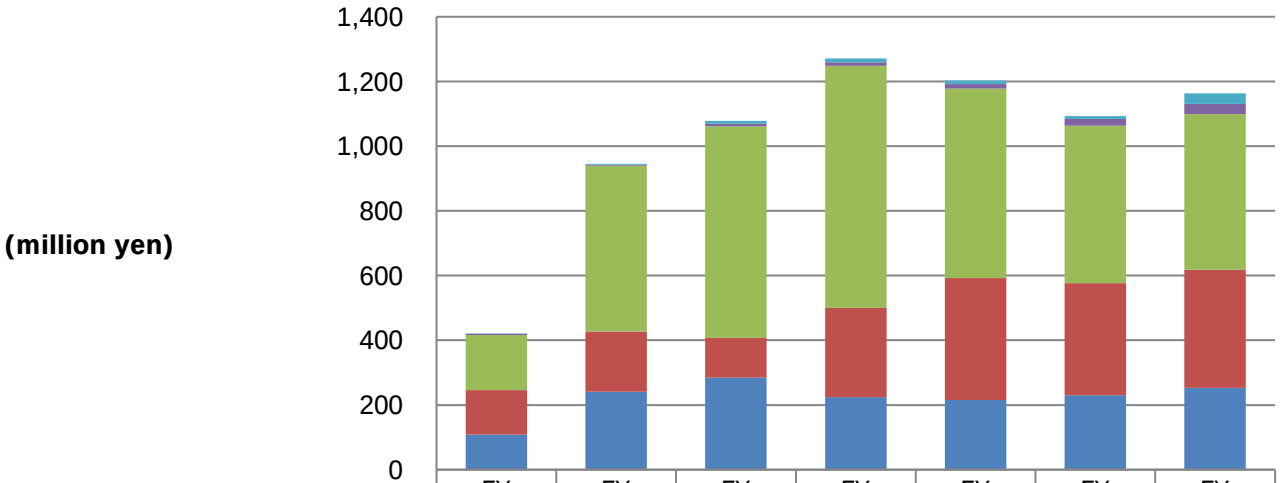
*Make a graph of the transition in the number of overall project funding.

Transition of Project Expenditures



	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Research Projects	421	946	1,078	1,271	1,203	1,093	1,163
Equipment	22	180	423	322	348	376	186
Travel	4	25	18	17	25	26	26
Project Activities	65	236	130	375	183	216	208
Personnel	53	301	419	445	457	511	565

Transition of Research Project Expenditures



	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018
Ohers (donations, etc.)	1	3	9	12	11	9	32
Joint research projects	4	3	8	11	14	21	32
Commissioned research projects, etc.	170	512	654	748	586	486	481
KAKENHI	138	187	122	276	377	347	365
Project supported by other government subsidies, etc. *1	108	241	285	224	215	230	253

*1 Definition is as shown in Appendix 3-5 (Project Expenditures)

Appendix 4-1 FY 2018 Status of Collaboration with Overseas Satellites

- If satellite and partner institutions have been established, fill in required items of the form below.

1. Satellites and partner institutions

- List the satellite and partner institutions in the table below (including the domestic satellite institutes).
- Indicate newly added and deleted institutions in the "Notes" column.

<Satellite institutions>

Institution name	Principal Investigator(s), if any	Notes
N/A	N/A	

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
ETH Zurich	Jeffrey W. BODE	
Queen's University	Cathleen M. CRUDDEN	
University of Washington	Keiko TORII	
University of Southern California	Steve A. KAY	
Heinrich Heine University Düsseldorf	Wolf B. FROMMER	
NSF Center for Selective C-H Functionalization	N/A	
University of Freiburg	N/A	
RIKEN Center for Sustainable Resource Science (CSRS)	N/A	
Institute of Chemistry (IoC), Academia Sinica	N/A	

- If overseas satellite institutions have been established, fill in required items on the form below. If overseas satellite institutions have not been established, it is not necessary to complete the form.

2. Coauthored Papers

- List the refereed papers published in FY 2018 that were coauthored between the center's researcher(s) in domestic institution(s) (include satellite institutions) and overseas satellite institution(s). List them by overseas satellite institution in the below blocks.
- Transcribe data in same format as in Appendix 1-4. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1-4 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2019 and not described in Appendix 1-4.

Overseas Satellite 1 Name (Total: OO papers)

1) N/A
2) N/A
3) N/A
4) N/A

Overseas Satellite 2 Name (Total: OO papers)

1) N/A
2) N/A
3) N/A
4) N/A

3. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2018. Enter by institution and length of exchange.
- Write the number of principal investigator visits in the top of each space and the number of other researchers in the bottom.

Overseas Satellite 1:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2018	N/A	N/A	N/A	N/A	N/A

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2018	N/A	N/A	N/A	N/A	N/A

Overseas Satellite 2:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2018	N/A	N/A	N/A	N/A	N/A

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2018	N/A	N/A	N/A	N/A	N/A

Appendix 4-2 FY 2018 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.

Total: 51

	Name	Age	Affiliation (Position title, department, organization)	Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
1	Cathleen Crudden	52	Principal Investigator, ITbM / Professor, Department of Chemistry, Queens University	Ph.D. Chemistry	・Arthur C. Cope Scholar Award (2019) ・IPMI Carol Tyler Award (2018) ・The Aldrich Lecture Award (2014) ・Clara Benson Award, CSC (2011) ・Catalysis Lectureship Award, Catalysis Society (2010)	6 weeks	・participation as principal investigator
2	Keiko Torii	53	Principal Investigator, ITbM / Professor, Department of Biology, Washington University	Ph.D. Biochemistry	・Clayton Person Lecture (Department of Botany, University of British Columbia, Canada) (2018) ・Distinguished Lecture, Institute of Plant Molecular Biology, Academia Sinica, Taipei (2016) ・35th Saruhashi Award (2015) ・2015 ASPB Fellow Award, American Society of Plant Biologists (2015) ・Fellow, AAAS (2012) ・JSPS Prize (2008) ・SJWS Award (2006)	1 month	・participation as principal investigator
3	Jeffrey W. Bode	45	Principal Investigator, ITbM / Professor, Department of Chemistry and Applied Bioscience, ETH Zurich	Dok. Nat. Sci.	・Mukaiyama Award (2018) ・E.J.Corey Award (2011) ・Novartis Lectureship (2010) ・6th Yoshimasa Hirata Memorial Lecuture (2010)	2 weeks	・participation as principal investigator
4	Wolf B. Frommer	61	Professor Heinrich Heine University Dü sseldorf and Max Planck Institute for Breeding Research, Germany	Dr. rer. Nat	・ Member, German Academy of Sciences, Leopoldina (2015) ・ Laurence Bogorad Award for Excellence in Plant Biology Research, American Society of Plant Biology (2012) ・ Fellow, American Association for the Advancement of Science (2003) ・ European Science Award, Körber Foundation (2001) ・ Gottfried-Wilhelm-Leibniz Preis, German Research Foundation (DFG) (1998) ・ Young investigator Award, German Federal Ministry for Science and Technology (1992)	3 weeks	・participation as principal investigator
5	Michael Feldbrügge	52	Professor, Heinrich-Heine University Düsseldorf	Ph.D. for Plant Breeding	・Postdoctoral Fellowship of the German Science Foundation (DFG)	2 days	・lecture @ ITbM seminar ・research discussion
6	Eric Meggers	50	Professor, Philipps-Universität Marburg	Ph.D. in Chemistry	・Novartis Synthetic Organic Chemistry Lecureship (The University of Texas at Austin, USA) (2017) ・Zasshi-kai Lectureship 2017 (The University of Tokyo, Japan) (2017) ・IOCF Yoshida Lectureship (Kyoto and Osaka University, Japan) (2016) ・Novartis Chemistry Lectureship Award (2009-2010) ・Camille Dreyfus Teacher-Scholar Award, USA (2006) ・Thieme Chemistry Journal Award (2003)	3 days	・lecture @ ITbM seminar ・research discussion
7	Satoshi Fujita	32	Postdoctoral Fellow, Department of Plant Molecular Biology, University of Lausanne	Ph.D. in Biological Science	・Overseas research fellowship from the Japan Society for the Promotion of Science (2016-2018) ・Inoue Research Award for Young Scientists (2014) ・Research Felloships of the Japan Society for the Promotion of Science for Young Scientists (2010-2012) ・Research Fellowships of Plant Education Unit in NAIST (2008-2009)	1 day	・lecture @ ITbM seminar ・research discussion
8	Anna Koltunow	59	Team Leader, CSIRO, Australia	Ph.D. in Biochemistry	・Director of 2 New Zealand Crown Research Institutes and 2 additional research companies ・Fellow of the Australian Academy of Science (2016) ・Senior CSIRO leadership as Program Leader and Deputy Chief at CSIRO Plant Industry (2001-2006; 2013-2014) ・President and Past-President of the International Society for Plant Reproduction Society (2002-2006; 2006-2010) ・Australian Research Council 5-year Fellow (1991-1995)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research
9	Anja Geitmann	48	Professor, Department of Plant Science, Faculty of Agricultural and Environmental Sciences, McGill University	Dottore di Recerca in Biologia (Ph.D.)	・Fellow of the American Society of Plant Biologists (2017) ・Prix d'excellence en enseignement (Teaching award), Faculté des arts et des sciences, Université de Montréal (2012) ・Nouveau chercheur, Fonds pour la Fromation de Chercheurs et l'Aide à la Recherche (FCAR) (2001-2006) ・Marie Curie Fellowship for Postdoctoral Studies, European Union (1998-2001)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research
10	Dolf Weijers	43	Professor, Wageningen University	Ph.D. Biochemistry / Biotechnology	・"Teacher of the Year 2013" at Wageningen University ・Annual award of the Netherlands Society for Biochemistry and Molecular Biology ・NWO ALW VIDI Grant (2006-2011) ・EMBO Long-term fellowship (2001-2002)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research
11	Mark A.Johnson	48	Associate Professor, Department of Molecular Biology, Cell Biology, and Biochemistry, Brown University	Ph.D. Microbiology and Cellular and Molecular Biology	・Richard B. Salomon Faculty Research Award (2007) ・NIH Ruth L. Kirschstein National Research Service Award (2002-2004)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research
12	Alice Y. Cheung	63	Professor, Department of Biochemistry and Molecular Biology, University of Massachusetts	Ph.D. Molecular Biophysics and Biochemistry	・Conti Faculty Fellowship, University of UMass, Amherst (2018) ・Distinguished Faculty Lecturer and Recipient of UMass, Amherst Chancellor's Medal (2014) ・Outstanding Research Award College of Natural Sciences (CNS), UMass, Amherst (2012) ・Mellon Mutual Mentoring Award, Senior faculty member (2012) ・Research Leadership in Action Award, UMass, Amherst (2010) ・American Society of Plant Biologists Fellows Award (2010) ・Yale University Junior Faculty Fellowship (1991) ・Rockefeller Foundation Postdoctoral Fellowship and Research Award (1982-1986) ・University Fellowships, Yale University Graduate School (1976-1980)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research
13	Stefanie Sprunck	47	Assistant Professor, Institute of Plant Science, University of Regensburg	Ph.D. Molecular Biology	・HIRASE award ofJapanese Society of Plant Morphology (2009)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research
14	Arp Schnittger	48	Professor, University of Hamburg	Dr. rer. nat. habil.	・ERC award for young investigators (ERC starting grant) (2008) ・European molecular biology organization award for young investigators (EMBO YIP) (2007)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research
15	Rita Gross-Hardt	48	Professor, University of Bremen	Ph.D. in Developmental Genetics	・ERC Consolidator Grant (2014) ・EMBO Long-Term Fellowship (2002-2004)	2 days	・invited lecture @ International Symposium on Frontiers and Future of Plant Reproduction Research

16	Wei-Cai Yang	55	Professor, IGDB, Chinese Academy of Sciences	Ph.D. Molecular Biology	・Outstanding Service Award (2008)	2 days	・research discussion
17	Noni Franklin-Tong	58	Emeritus Professor, University of Birmingham	Ph.D. Genetics	・BBSRC Advanced Research Fellowship (1992)	2 days	・research discussion
18	Li-Jia Qu	40	Professor, Peking University	M.S. & Ph.D.	・Changjiang Scholar, MOE (2008) ・China Youth Science and Technology Award (2007) ・Excellence Youth Grant, NSFC (2006)	2 days	・research discussion
19	Daphne Goring	55	Professor, University of Toronto	Ph.D. Medical Genetics	・AAAS Fellow (2012) ・C.D. Nelson Award (2001) ・NSERC scholarships and awards ・Premier's Research Excellence Award in Ontario	2 days	・research discussion
20	Scott Russell	66	Professor, University of Oklahoma	Ph.D. in Botany	・Centennial Award for contributions to the plant sciences (2006) ・Merit Award, Botanical Society of America (2005) ・George Lynn Cross Research Professorship, University of Oklahoma (2000) ・Special Service Award, Botanical Society of America (1998) ・Regents' Award for Superior Research and Creative Activity, University of Oklahoma (1994) ・Jeanette Siron Pelton award, Botanical Society of America (1988) ・OU Associates Distinguished Lecturer (1986-87) ・University of Alberta Dissertation Fellowship (1980-81)	2 days	・research discussion
21	Bo Liu	54	Professor, University of California at Davis	Ph.D. Botany	N/A	2 days	・research discussion
22	Jörg D. Becker	49	FCT Investigator, Instituto Gulbenkian de Ciência	Ph.D. Biology	N/A	2 days	・research discussion
23	Hen-Ming Wu	68	Professor, University of Massachusetts	Ph.D. Chemistry / Biophysics	・The National Science Foundation's Division of Integrative and Organismal Systems and Division of Molecular and Cellular Biosciences (2017)	2 days	・research discussion
24	Roger Linington	44	Associate Professor, Department of Chemistry, Simon Fraser University	Ph.D. Chemistry	・Tier II Canada Research Chair in High-Throughput Screening and Chemical Biology (2015) ・American Society of Pharmacognosy Matt Suffness Young Inverstigator award (2014) ・Stevenson College Favorite award (2013)	12 days	・invited lecture @ 6th International Symposium on Transformative Bio-Molecules (ISTbM-6)
25	Ruben Martin	42	Professor, Institute of Chemical Research of Catalonia	Ph.D.	・ParazaPharma Lectureship Award (2019) ・MIT-Merck Lectureship Award (2019) ・Hirata Award (2018) ・Novartis Chemistry Award (2018) ・ChemSocRev Pioneering Investigator Lectureship Award (2018)	7 days	・invited lecture @ 6th International Symposium on Transformative Bio-Molecules (ISTbM-6)
26	Satchidananda Panda	47	Professor, Salk Institute for Biological Studies	Ph.D.	・The Julie Martin Mid-Career Award in Aging Research (2014) ・Pew Scholar in Biomedical Research (2006) ・Dana Foundation Award in Brain and Immune System Imaging (2006)	6 days	・invited lecture @ 6th International Symposium on Transformative Bio-Molecules (ISTbM-6)
27	Christopher S. Jeffrey	38	Associate Professor, University of Nevada, Reno	Ph.D.	・Outstanding Undergraduate Reasearch Mentor Award (2018) ・CNPq Science Without Borders Award (2013-2017) ・Westfall Scholar Mentor (2013 and 2017) ・Mousel-Feltner award for excellence in research (2015) ・Senior Scholar Mentorship Award (2013)	3 weeks	・invited lecture @ 6th International Symposium on Transformative Bio-Molecules (ISTbM-6)
28	Cyril Zipfel	40	Professor, Institute of Plant and Microbial Biology, University of Zürich	Ph.D.	・Tsuneko and Reikji 'Okazaki Award' (2018) ・European Research Council (ERC) Consolidator Grant (2018) ・ASPB Charles Albert Shull Award (2015) ・ERC Starting Grant (2012) ・Ed Fischer Prize from the Friedrich Miescher Institute (2006)	5 days	・invited lecture @ 6th International Symposium on Transformative Bio-Molecules (ISTbM-6)
29	Bin Liu	45	Professor, National University of Singapore	Ph.D. Chemistry	・Micro-Nano Letters Researcher Award (2018) ・Asian Scientist 100 list (2017) ・President's Science and Technology Awards (2016) ・Singapore National Institute of Chemistry (SNIC) -BASF Materials Award (2014)	3 days	・invited lecture @ 6th International Symposium on Transformative Bio-Molecules (ISTbM-6)
30	Holger Braunschweig	57	Professor, Institute of Inorganic Chemistry, University of Wuerzburg	Ph.D. Science	・Alfred Stock Memorial Prize of the GDCh (2016) ・RSC Main Group Award, Royal Society of Chemistry (2014) ・Gottfried Wilhelm Leibniz Prize of the DFG (2009)	2 weeks	・JSPS invitation fellowship
31	John Dayton Tovar	43	Professor, Department of Chemistry, Johns Hopkins University	Ph.D. Organic Chemistry	・Journal of Physical Organic Chemistry "Early Excellence" profilee (2012) ・Thieme Chemistry Journal Award (2010) ・NSF CAREER Award (2007) ・Princeton Applied Research New Young Investigator Award (2004) ・Baxter-IBNAM Early Career Development Award, Northwestern (2003)	3 weeks	・JSPS invitation fellowship
32	David W. C. MacMillan	51	Professor, Princeton University	Ph.D. Chemistry	・Gabor A. Somorjai Award for Creative Research in Catalysis (2018) ・Ryoji Noyori Prize (2017) ・Max Tishler Prize (2016) ・Ernst Schering Prize (2015)	4 days	・invited lecture @ 24th Nagoya Medal Seminar of Organic Chemistry
33	James E. Petersson	40	Associate professor, Department of Chemistry, University of Pennsylvania	Ph.D.	・Award for Early Excellence in Physical Organic Chemistry (2013) ・Sloan Research Fellow (2012) ・NSF CAREER Award (2012) ・Searle Scholar (2010)	2 days	・lecture @ ITbM seminar ・research discussion
34	Christian Hackenberger	43	Leibins-Humboldt-Professor (W3) for Chemical Biology Humboldt Universitätat zu Berlin and FMP	Ph.D.	・Leonidas Zervas Award of the European Peptide Society (2018) ・Leibniz Gründerpreis for the foundation of Tubulis Technologies (2018) ・Fellow of the Royal Society of Chemistry (2016) ・ORCHEM-Award of the GDCh for junior investigators (2012) ・Heinz-Maier-Leibnitz-Award of the DFG (2011)	2 days	・research discussion
35	Julian I. Schroeder	60	Professor, University of California San Diego	Ph.D. Physics/Biophysics	・Elected Member Leopoldina The German National Academy of Sciences (2017) ・Elected Member of the U.S. National Academy of Sciences (2015) ・Cozzarelli Prize Natl. Acad. of Sciences to authors of Song et al. (2010) ・Highly Cited Researcher, Animal and Plant Science, Inst.f.Sci. Information (isiHighlycited.com) (2002) ・Novartis Professor in Plant Sciences, UCSD (2001-) ・Blasker Award in Environmental Science and Engineering, S.D. Foundation (2001) ・Charles Albert Shull Award, American Society of Plant Biologists (1997)	6 days	・invited lecture @ Japan-Taiwan Plant Biology 2019 ・research discussion

36	Jen Sheen	N/A	Professor, Harvard Medical School	Ph.D. Cellular and Developmental Biology	・The Shang-Fa Yang Lecturer/Award, Academia Sinica, Taipei, Taiwan (2015) ・Martin Gibbs Medal, ASPB (2013) ・Plenary Speaker at the International Congress on MPMI, Kyoto, Japan (2012) ・The NSF Achievement-Based Award (2009-2014) ・The NSF Achievement-Based Award (2002-2007) ・Presidential Seminars at NAIST, Japan (2000) ・The Japanese RITE International Award (1997-1998)	4 days	・invited lecture @ Japan-Taiwan Plant Biology 2019 ・research discussion
37	Michael Cowley	38	Chancellor's Fellow, School of Chemistry, University of Edinburgh, U.K.	Ph.D. Chemistry	・ERC Starting Grant	1 day	・lecture @ ITbM seminar ・research discussion
38	Noah Z. Burns	45	Assistant Professor, Stanford University, Stanford CA, U.S.A.	Ph.D. Chemistry	・Kavli Fellow (2018) ・Dean's Award for First Years of Teaching at Stanford (2017) ・Amgen Young Investigator Award (2017) ・Stanford Terman Fellow (2013–present) ・Thieme Chemistry Journal Award (2012) ・Roche Excellence in Chemistry Award (2006)	1 day	・lecture @ ITbM seminar ・research discussion
39	Lawrence T. Scott	74	Professor, Department of Chemistry, Boston College Adjunct Visiting Professor Department of Chemistry, University of Nevada, Reno, U.S.A.	Ph.D. Chemistry	・Cope Scholar Award (2016) ・American Chemical Society George A. Olah Award for Hydrocarbon Chemistry (2011) ・Research Achievement Award, International Society for Polycyclic Aromatic Compounds (2009) ・Distinguished Research Award, Boston College (2003) ・Japan Society for the Promotion of Science Senior Scientist Fellowship (1985 and 2003) ・Alexander von Humboldt Foundation Senior Scientist Award (1999)	2 days	・invited lecture @ International ERATO Itami Molecular Nanocarbon Symposium 2019 ・research discussion
40	Rainer Streubel	60	Professor, Institute for Inorganic Chemistry University of Bonn	Dr. rer. nat. in Chemistry	・Japan Society for the Promotion of Science Visiting Research Fellowship (2016) ・Honorary professor of Chemistry at the University of St Andrews/Edinburgh, UK (since 05/2010) ・Japan Society for the Promotion of Science Lecture Ship Award (2004) ・Heinrich-Büssing-Award der Stiftung zur Förderung der Wissenschaften an der Technischen Universität Braunschweig (1998)	1 day	・lecture @ ITbM-IGER-RCMS seminar ・research discussion
41	Jerome Lacour	55	Professor, University of Geneva	Ph.D. in Chemistry	・International Organic Chemistry Foundation (IOCF) lectureship, Japan (2014) ・Chimia, Editor-in Chief (2011-2014) ・Geneva Chemical Society, President (2010-2013) ・Grammaticakis-Neuman Prize, French Academy of Sciences (2005) ・Werner Prize and Medal, Swiss Chemical Society (2002)	1 day	・lecture @ ITbM-IGER-RCMS seminar ・research discussion
42	Martin Oestreich	46	Professor, Technische Universität Berlin	Ph.D. in Chemistry	・45th IOCF Lectureship (2018) ・JSPS Invitational Fellowship for Research in Japan (2018) ・David Ginsburg Memorial Lecture, Technion, Haifa/Israel (2015) ・Steinhofer Lecture, Albert-Ludwigs-Universität Freiburg, Freiburg im Breisgau/Germany (2013) ・"Goldener Brendel" Wanderpreis für hervorragende Lehre, Westfälische Wilhelms-Universität Münster/Germany ・ORCHEM-Preis für Naturwissenschaftler, Liebig-Vereinigung der GDCh	1 day	・lecture @ GTR-ITbM-IGER-RCMS seminar ・research discussion
43	Philippa Ross	32	Executive Editor, the Royal Society of Chemistry	BSc Hons in Medicinal Biochemistry	N/A	1 day	・lecture @ Meet the Editor (hosted by the Royal Society of Chemistry) ・research discussion
44	Douglas Stephan	66	Professor, University of Toronto	Ph.D. in Chemistry	・Einstein Visiting Fellow, TU Berlin (2016) ・Thomson Reuters Highly Cited Researcher (2015) ・Applied Catalysis Award (Royal Society of Chemistry, UK) (2014) ・Canadian Green Chemistry and Engineering Award (2014) ・CIC Medal (Chemical Institute of Canada) (2014)	1 day	・lecture @ Meet the Editor (hosted by the Royal Society of Chemistry) ・research discussion
45	Carlos Romero Nieto	37	Assistant Professor, University of Heidelberg	Ph. D. in Organic Chemisty	・Frontiers grant (Excellence Initiative, University of Heidelberg) (2017) ・Hengstberger Award from the University of Heidelberg (2016) ・Liebig Fellowship from the 'Fonds der Chemischen Industrie' (German Chemical Industry Association) (2013)	1 day	・lecture @ GTR-ITbM-IGER-RCMS seminar ・research discussion
46	Simon Rüdiger	57	Professor, Head of Biology Department, Heinrich Heine University	Ph.D.	・Electedhead of Department of Biology, Heinrich Heine University (2010-2012) ・Speaker of the Center for Advanced Imaging at the HHU Marie-Curie Fellow (2010-) ・Marie-Curie Fellow (1991-1993)	3 days	・invited lecture @ 6th International Symposium on Transformative Bio-Molecules (ISTbM-6)
47	Ueli Grossniklaus	55	Professor, Institute of Plant Biology, University of Zürich	Ph.D.	・Thomson Reuters Highly Cited Researcher in Plant and Animal Science (2014) ・Member of Leopoldina, the German National Academy of Sciences (2011) ・Awardee of an Advanced Grant from the European Research Council (ERC) (2009) ・Member of the European Molecular Biology Organization (EMBO) (2007)	3 days	・lecture @ ITbM seminar ・research discussion
48	Mickaël Delcey	N/A	Postdoctoral Researcher, Uppsala University	Ph.D.	N/A	12 days	・research discussion
49	Kwan Yin Cheung	28	Research Assistant, Chinese University of Hong Kong	Ph.D. Chemistry	・Lau Oi Wah Memorial Award for Scholastic Excellence (2012) ・Chung Chi Scholarships for Excellence (2012) ・Dr. Wong Kam Han Memorial Prizes (2011)	12 months	・collaborative research
50	Hai-Dong Ding	39	Associate Professor, College of Bioscience and Biotechnology, Yangzhou University	Ph.D. Botany	N/A	4 months	・collaborative research
51	Michael Menaker	84	Commonwealth Professor of Biology Department of Biology University of Virginia, USA	Ph.D.	・ Society for the Study of Biological Rhythms (SRBR) Directors' Award for Mentoring (2016) ・University of Virginia Distinguished Scientist Award (2009) ・University of Groningen Honorary Doctorate (2009) ・Honma Life Science Foundation, Sapporo, Japan, Aschoff-Honma Prize (2009) ・Peter C. Farrell Prize in Sleep Medicine, Harvard Medical School Division of Sleep Medicine (2007)	2 days	・lecture @ ITbM seminar ・research discussion

Appendix4-3 Postdoctoral Positions through Open International Solicitations

* In the column of number of applications and number of selection, put the total number (upper), the number and percentage of overseas researchers in the < > brackets (lower).

Fiscal year	number of applications	number of selection
FY2012	0	0
	< 0, 0%>	< 0, 0%>
FY2013	141	16
	< 138, 98%>	< 15, 94%>
FY2014	5	5
	< 4, 80%>	< 4, 80%>
FY2015	24	9
	< 24, 100%>	< 9, 100%>
FY2016	7	7
	< 5, 71%>	< 5, 71%>
FY2017	18	13
	< 10, 56%>	< 10, 77%>
FY2018	11	8
	< 8, 73%>	< 8, 100%>

Appendix4-4 Status of Employment of Postdoctoral Researchers

* Prepare the information below during the period from the start of the center through March 2019.

* List each researcher in 1 line. If the list exceeds this form, add extra pages.

Japanese Postdocs

Period of project participation	Previous affiliation, position title (Country)	Next affiliation, position title (Country)
Apr. 1, 2013 -Nov. 30, 2013	Nagoya University Postdoc（Japan）	Nagoya University Designated Associate Professor（Japan）
Apr. 1, 2013 -Mar. 31, 2014	Nagoya University Postdoc（Japan）	Nagoya University Designated Assistant Professor（Japan）
Apr. 1, 2013 -May. 31, 2015	Nagoya University Postdoc（Japan）	University of Geneva Postdoc（Switzerland）
Sep. 1, 2013 -Jun. 15, 2017	California State University Student（USA）	SOKENDAI (The Graduate University for Advanced Studies) Doctoral Student（Japan）
Oct. 1, 2013 -Feb. 28, 2017	National Institute for Basic Biology Doctoral Student（Japan）	Yokohama City University Designated Assistant Professor（Japan）
Apr. 1, 2014 -Mar. 31, 2017	Monash University HFSP Postdoc（Australia）	Gakushuin University Assistant Professor（Japan）
Nov. 1, 2014 -Present	University of Toronto Postdoctoral Fellow（Canada）	Nagoya University Designated Associate Professor（Japan）
Apr. 1, 2015 -Mar. 31, 2016	Nagoya University Postdoc（Japan）	Nagoya University Postdoc（Japan）
Apr. 1, 2015 -Mar. 31, 2017	Nagoya University Postdoc（Japan）	Chuo University Assistant Professor（Japan）
Apr. 1, 2015 -Mar. 31, 2018	Nagoya University Technical Assistant（Japan）	Suntory Flowers Ltd. （Japan）
Apr. 1, 2015 -Mar. 31, 2018	Kyushu University Postdoc（Japan）	Nagoya University Postdoc（Japan）
Apr. 1, 2015 -Mar. 31, 2019	The University of Tokyo Postdoc（Japan）	Ritsumeikan University Assistant Professor（Japan）
Oct. 1, 2015 -Mar. 31, 2016	Nagoya University Postdoc（Japan）	Waseda University Lecturer（Japan）
Feb. 1, 2016 -Mar. 31, 2016	Kyoto University Postdoc（Japan）	Nagoya University Assistant Professor（Japan）
Apr. 1, 2016 -Jun. 18, 2017	Kyoto University Doctoral Student（Japan）	Kochi University of Technology Assistant Professor（Japan）
Apr. 1, 2016 -Mar. 31, 2019	The Technical University of Munich Postdoc（Germany）	National Institute for Basic Biology Assistant Professor（Japan）
Apr. 1, 2016 -Mar. 31, 2019	Kyoto University Doctoral Student（Japan）	NUProtein Co., Ltd. （Japan）
Apr. 1, 2016 -Present	Chubu University Postdoc（Japan）	(Currently at ITbM)
Dec. 1, 2016 -Present	Nara Institute of Science and Technology Post-doctoral Position（Japan）	(Currently at ITbM)
Jan. 1, 2017 -Present	Chinese Academy of Sciences(PSC) Associate Specialist（Chinese）	(Currently at ITbM)
Feb. 1, 2017 -Mar. 31, 2017	Nagoya University Postdoc（Japan）	Kyoto University Postdoc（Japan）

Apr. 1, 2017 -Oct. 31, 2018	Nagoya University Postdoc（Japan）	K.K.Air Liquide Laboratories （Japan）
Sep. 1, 2017 -Present	Osaka Prefecture University Postdoctoral Researcher （Japan）	(Currently at ITbM)
Dec. 1, 2017 -Present	Tokyo University of Science Post-doctoral Researcher（Japan）	(Currently at ITbM)
Apr. 1, 2018 -Apr. 30, 2018	Nagoya University Doctoral Student（Japan）	ETH-Zürich Postodoctoral Researcher（Switzerland）
Apr. 1, 2018 -Jun. 30, 2018	Kyoto University Doctoral Student（Japan）	The University of Tokyo Assistant Professor（Japan）
Apr. 1, 2018 -Mar. 31, 2019	Tokyo Institute of Technology Doctoral Student（Japan）	Kyushu University Assistant Professor（Japan）
Apr. 1, 2018 -Present	Nagoya University Postdoc（Japan）	(Currently at ITbM)

Overseas Postdocs

Period of project participation	Previous affiliation, position title (Country)	Next affiliation, position title (Country)	Nationality
Apr. 1, 2013 -Nov. 14, 2013	Nagoya University Postdoc（Japan）	Nagoya University Postdoc（Japan）	Taiwanese
Apr. 1, 2013 -Apr. 7, 2014	Nagoya University Postdoc（Japan）	Western Washington University Assistant Professor (USA)	USA
Apr. 1, 2013 -Apr. 30, 2015	Nagoya University Doctoral Student（Japan）	Indian Institute of Science Education and Research Assistant Professor（India）	Indian
Apr. 1, 2013 -Mar. 31, 2019	The University of Tokyo Postdoctoral Fellow（Japan）	Peking University Professor（China）	Chinese
Jun. 1, 2013 -Mar. 31, 2014	RIKEN Post-doctoral Position（Japan）	Sygnature Discovery Senior Research Scientist (UK)	French
Jun. 1, 2013 -May. 31, 2014	Interdisciplinary Research Centre in Biomedical Materials, COMSATS Institute of Information Technology Assistant Professor（Pakistan）	Interdisciplinary Research Centre in Biomedical Materials, COMSATS Institute of Information Technology Assistant Professor（Pakistan）	Pakistani
Jun. 1, 2013 -Aug. 31, 2015	Max-Planck-Institut Post-Doc Research Fellow（Germany）	Max-Planck-Institut Post-Doc Research Fellow（Germany）	Chinese
Jun. 1, 2013 -Nov. 30, 2015	University of South Florida Doctoral Student（USA）	The University of Sydney Postdoctoral Research Associate （Australia）	Indian
Jun. 16, 2013 -Jan. 31, 2016	AstraZeneca India Pvt Ltd （India）	Nagoya University Designated Assistant Professor (Japan)	Indian
Jul. 5, 2013 -Jul. 31, 2014	University College Dublin CSCB Doctoral Student（Ireland）	Universidad Nacional Autonoma de Mexico Senior Postdoc（Mexico）	Mexican
Oct. 1, 2013 -Jul. 31, 2015	Nagoya University Doctoral Student（Japan）	Nanchang University Associate Professor（China）	Chinese
Oct. 1, 2013 -Dec. 31, 2015	Indian Institute of Technology Madras Doctoral Student（India）	Anthem Bioscience, Pvt. Ltd. (India)	Indian
Nov. 1, 2013 -Aug. 31, 2016	Okayama University Postdoc Research Fellow（Japan）	Xi'an Jiaotong University Lecturer（China）	Chinese
Jan. 1, 2014 -Feb. 29, 2016	University of North Carolina Doctoral Student（USA）	Amgen Inc. （USA）	USA

Jan. 16, 2014 -Mar. 14, 2016	Heinrich-Heine-Universität Düsseldorf Research Assistant (Postdoc)（Germany）	Next Move KK （Japan）	German
Apr. 16, 2014 -Present	University of British Columbia Doctoral Student（Canada）	(Currently at ITbM)	Canadian
May. 1, 2014 -Jan. 31, 2015	University of Amsterdam Postdoc（Netherlands）	Institut des Sciences Chimiques de Rennes CNRS Research Associate （France）	Spanish
Sep. 1, 2014 -Dec. 19, 2014	Queen's University Postdoctoral Fellow（Canada）	Queen's University Postdoctoral Fellow（Canada）	Swedish
Dec. 16, 2014 -Jun. 30, 2017	University Rovira I Virgili Doctoral Student（Spain）	Nagoya University Designated Assistant Professor（Japan）	Swedish
Apr. 16, 2015 -Present	University of British Columbia Doctoral Student（Canada）	(Currently at ITbM)	Canadian
May. 16, 2015 -May. 15, 2017	University of Jyväskylä Post-doctoral Research Scientist （Finland）	Neste Corporation Inc. (Finland)	Finnish
Jun. 1, 2015 -Apr. 30, 2017	Karlsruhe Institute of Technology Postdoctoral Research Fellow（Germany）	Schrödinger, Inc. （Germany）	German
Nov. 1, 2015 -Present	University of Hong Kong Doctoral Student（Hong Kong）	(Currently at ITbM)	Chinese
Mar. 1, 2016 -Aug. 31, 2017	Indian Institute of Science Doctoral Student（India）	Central Drug Research Institute Scientist（India）	Indian
Apr. 1, 2016 -Present	Nagoya University Postdoc（Japan）	(Currently at ITbM)	Indian
May. 16, 2016 -Dec. 31, 2016	ETH-Zürich Master's Student（Switzerland）	Siegfried AG (Switzerland)	Swedish
Oct. 1, 2016 -Oct. 31, 2017	Free University of Berlin Postdoctoral Research Associate （Germany）	Kyoto University Program-Specific Senior Lecturer （Japan）	German
Jan. 1, 2017 -Dec. 31, 2017	University of Washington Postdoctoral Fellow（USA）	Central Drug Research Institute Assistant Professor（India）	Indian
Jan. 1, 2017 -Present	Indian Institute of Technology Tirupati Project Officcer（India）	(Currently at ITbM)	Indian
Jan. 16, 2017 -Aug. 31, 2018	University of Manchester Doctoral Student（UK）	University of Manchester Fixed-Term Lecturer（UK）	UK
Apr. 1, 2017 -Feb. 16, 2019	Nagoya University Postdoc（Japan）	Shanghai Jiao Tong University Assistant Professor（Chinese）	Chinese
Jun. 1, 2017 -Present	Academia Sinica Postdoctoral Fellow（Taiwan）	(Currently at ITbM)	Taiwanese
Jun. 1, 2017 -Present	University of Münster Doctoral Student（Germany）	(Currently at ITbM)	Chinese
Aug. 1, 2017 -Feb. 28, 2019	University of Calabria Doctoral Student（Italy）	Hokkaido University Postdoctoral Researcher（Japan）	Italian
Aug. 1, 2017 -Present	University of Edinburgh Doctoral Student（UK）	(Currently at ITbM)	Chinese
Aug. 1, 2017 -Present	Indian Institute of Technology Madras Research Associate（India）	(Currently at ITbM)	Indian

Sep. 1, 2017 -Aug. 31, 2018	Polish Academy of Sciences Postdoctoral Researcher（Poland）	Polish Academy of Sciences Research Fellow（Poland）	Polish
Sep. 1, 2017 -Mar. 31, 2019	ENS Paris-Saclay Postdoc（France）	Institut Curie Researcher (France)	Hungarian
Oct. 15, 2017 -Present	Polish Academy of Sciences Assistant（Poland）	(Currently at ITbM)	Polish
Nov. 1, 2017 -Present	Sun Yat-sen University Doctoral Student（China）	(Currently at ITbM)	Chinese
Nov. 16, 2017 -Present	University of Toronto Postdoctoral Fellow（Canada）	(Currently at ITbM)	Canadian
Nov. 18, 2017 -Jan. 31, 2018	University of Calgary Doctoral Student（Canada）	Cold Spring Harbor Laboratory Post-doctoral -Researcher（USA）	Indian
Apr. 1, 2018 -Dec. 31, 2018	Institute for Molecular Science Researcher（Japan）	Sun Yat-sen University Associate Professor（China）	Chinese
Oct. 1, 2018 -Present	University of California, Berkeley Master's Student（USA）	(Currently at ITbM)	Swedish
Oct. 1, 2018 -Present	National University of Singapore Doctoral Student（Singapore）	(Currently at ITbM)	Chinese
Nov. 1, 2018 -Present	Stockholm University Postdoc（Sweden）	(Currently at ITbM)	Spanish
Jan. 1, 2019 -Present	High Energy Accelerator Research Organization Postdoctoral Scientist（Japan）	(Currently at ITbM)	UK
Jan. 16, 2019 -Present	KU Leuven Postdoctoral Researcher（Belgium）	(Currently at ITbM)	Vietnamese

Appendix4-5 List of the Cooperative Research Agreements with Overseas Institutions

*Prepare the information below during the period from the beginning of the Center through March 2019.

1. Name of an Agreement : Memorandum of Understanding
   Dates of an Agreement : April 1, 2013
   Counterpart of an Agreement : Queen's University
   Summary of an Agreement : The MOU is to affiliate Dr. Cathleen M. Crudden (Queen's Univ) to NU with the position of Overseas Principal Investigator to be engaged in collaborative research at NU. The MOU includes relationship, commitment, MTA, IP, publications and so on.

2. Name of an Agreement : Memorandum of Understanding
   Dates of an Agreement : April 1, 2013
   Counterpart of an Agreement : University of Washington and Howard Hughes Medical Institute
   Summary of an Agreement : The MOU is to affiliate Dr. Keiko Torii (University of Washington, Howard Hughes Medical Institute) to NU with the position of Overseas Principal Investigator to be engaged in collaborative research at NU. The MOU includes relationship, commitment, MTA, IP, publications and so on.

3. Name of an Agreement : Memorandum of Understanding
   Dates of an Agreement : September 1, 2013
   Counterpart of an Agreement : ETH Zurich
   Summary of an Agreement : The MOU is to affiliate Dr. Jeffrey Bode (ETH Zurich) to NU with the position of Overseas Principal Investigator to be engaged in collaborative research at NU. The MOU includes relationship, commitment, MTA, IP, publications and so on.

4. Name of an Agreement : The Memorandum of Understanding on the promotion and collaborations
   Dates of an Agreement : March 18, 2014
   Counterpart of an Agreement : Albert-Ludwigs-Universität Freiburg
   Summary of an Agreement : This MOU is to enable mutual exchange of students and researches and to promote joint research in such as medical sciences, chemistry and life sciences, and Institute for advanced studies and research.

5. Name of an Agreement : Memorandum of Understanding on collaboration and cooperation
   Dates of an Agreement : January 7, 2015
   Counterpart of an Agreement : The RIKEN Center for Sustainable Resource Science (CSRS)
   Summary of an Agreement : This MOU is to promote researches in biology, chemistry, and their interdisciplinary fields under collaboration and cooperation.

6. Name of an Agreement : Memorandum of Understanding on Joint Workshop
   Dates of an Agreement : January 7, 2015
   Counterpart of an Agreement : The RIKEN Center for Sustainable Resource Science (CSRS)
   Summary of an Agreement : The MOU is to hold Joint-Workshop under non-disclosure agreement.

7. Name of an Agreement : Agreement concerning joint activities between FRIAS/University of Freiburg and Nagoya IAR/Nagoya University
   Dates of an Agreement : May 14, 2015
   Counterpart of an Agreement : The Freiburg Institute for Advanced Study, Albert-Ludwigs-Universität Freiburg
   Summary of an Agreement : The agreement is to deepen the collaboration and contribute to strategic partnership. The Institutes will call for joint research groups and jointly fund to the groups selected in a joint FRIAS-Nagoya IAR call.

8. Name of an Agreement: Memorandum of Understanding
   Dates of an Agreement : April 1, 2017
   Counterpart of an Agreement : Heinrich Heine University Düesseldorf
   Summary of an Agreement : The MOU is to affiliate Dr. Wolf B. Frommer (Heinrich Heine University Düesseldorf) to NU with the position of Overseas Principal Investigator to be engaged in collaborative research at NU. The MOU includes relationship, commitment, MTA, IP, publications and so on.

9. Name of an Agreement: Agreement for Academic Exchange and Cooperation
   Dates of an Agreement: Sep. 7, 2017
   Counterpart of an Agreement: Institute of Chemistry, Academia Sinica
   Summary of an Agreement: The agreement is to develop academic exchange and cooperation in education and research between two institutes, including exchange of students and faculty, exchange of scientific materials, publications and information, and joint research and other activities within the range of interest of both Institutes.

10. Name of an Agreement : Memorandum of Understanding on collaboration and cooperation
    Dates of an Agreement : October 2, 2017
    Counterpart of an Agreement : Graduate School of Nanobioscience, Yokohama City University
    Summary of an Agreement : This MOU is to promote researches in biology, chemistry, and their interdisciplinary fields under collaboration and cooperation.

11. Name of an Agreement: Agreement for Academic Exchange and Cooperation
    Dates of an Agreement: May 18, 2018
    Counterpart of an Agreement: Faculty of Mathematics and Natural Sciences, Heinrich Heine University Düesseldorf
    Summary of an Agreement: The agreement is to develop academic exchange and cooperation in education and research between two institutes, including exchange of students and faculty, exchange of scientific materials, publications and information, and joint research and other activities within the range of interest of both Universities.

Appendix4-6 Holding International Research Meetings

* Indicate up to ten of most representative international research conferences or symposiums held from the start of the center through March 2019 and give the number of participants using the table below.

Date	Meeting title and Place held	Number of participants
Feb. 28, 2019	The 24th Nagoya Medal of Organic Chemistry, Nagoya	From domestic institutions:320 From overseas institutions: 5
Oct. 4-5, 2018	The 6th International Symposium on Transformative Bio-Molecules (ISTbM-6), Hirata Award, Okazaki Award, Nagoya	From domestic institutions: 400 From overseas institutions: 15
June 11-16, 2018	The 25th International Congress on Sexual Plant Reproduction, Gifu	From domestic institutions: 50 From overseas institutions: 75
Dec. 22, 2017	The 23rd Nagoya Medal of Organic Chemistry, Nagoya	From domestic institutions: 370 From overseas institutions: 5
Nov. 20-21, 2017	The 5th International Symposium on Transformative Bio-Molecules (ISTbM-5), Hirata Award, Okazaki Award, Nagoya	From domestic institutions: 383 From overseas institutions: 15
Sep. 25-26, 2017	1st international symposium by ITbM and the University of Freiburg "Multicomponent Supramolecular Catalysts for Sustainable Chemical Synthesis", Freiburg, Germany	From domestic institutions: 20 From overseas institutions: 100
July 13-14, 2017	2017 IoC-IPMB-ITbM Joint Workshop on New Frontiers by Fusing Chemistry and Biology, Taipei, Taiwan	From domestic institutions: 30 From overseas institutions: 60
Nov. 16-17, 2016	2016 ITbM-IoC Joint Workshop on Biomolecules and Materials, Nagoya	From domestic institutions: 50 From overseas institutions: 20
Nov. 11, 2016	International Symposium on Biological Rhythms “Towards understanding the molecular clockwork”, Nagoya	From domestic institutions: 200 From overseas institutions: 30
June 16-17, 2016	2016 ITbM-CCHF-IBS International C-H Functionalization Workshop, Nagoya	From domestic institutions: 40 From overseas institutions: 60

Appendix 5 List of Achievements of Center's Outreach Activities between FY 2012 – 2018

* Using the table below, show the achievements of the Center's outreach activities from FY2012 through FY2018 (number of activities, times held).

*If there are any rows on activities the center didn't implement, delete that (those) row(s). If you have any activities other than the items stated below, fill in the space between parentheses after "Others" on the bottom with the name of those activities and state the numbers of activities and times held in the space on the right. A row of "Others" can be added, if needed.

Activities	FY2012 (number of activities, times held)	FY2013	FY2014	FY2015	FY2016	FY2017	FY2018
PR brochure, pamphlet	0	2	7	5	5	5	7
Lectures, seminars for the general public	0	4	4	1	7	13	4
Teaching, experiments, training for elementary, secondary and high school students	0	9	7	9	8	14	12
Science cafe	0	0	1	1	4	2	2
Open house	0	2	4	4	4	4	4
Participating, exhibiting in events	1	4	6	3	7	10	8
Press releases	2	1	12	8	17	21	22
Publications of the popular science books	0	0	0	0	0	0	0
Others（Laboratory tours ）	0	8	21	17	19	24	33

Appendix 5 List of Media Coverage of Projects Carried out between FY 2012 – 2018

* Select main items of press releases, media coverage, and reports for FY 2012-2018 (especially by overseas media)

1) Japan

No.	Date	Type of the media (e.g., newspaper, magazine, television)	Description
1	Feb. 2 - 7, 2019	Newspaper (2)	Research on "Cell-based screen identifies a new potent and highly selective CK2 inhibitor for modulation of circadian rhythms and cancer cell growth", published online in Science Advances, was featured in Kagaku Shimbun & Nikkei Shimbun. Tsuyoshi Hirota (Associate Professor, Co-PI, Kay-Hirota G) and Kenichiro Itami (Center Director)
2	Nov. 5 - 9, 2018	Newspaper (5)	Series Articles "Let's know more about plants" were published in Nikkei Shimbun. Keiko Torii (PI)
3	Oct. 18, 2018	Newspaper (1), TV (1)	Joint research on tidal power between Toyota Boshoku and ITbM was featured in Mainichi Shimbun & Tokai TV. Kenichiro Itami (Center Director)
4	May 31 - Jun. 1, 2018	Newspaper (3)	Tetsuya Higashiyama's Chunichi Cultural Award was featured in Chunichi Shimbun & Chunichi Shunju. Tetsuya Higashiyama (PI)
5	Oct. 1 2017	Magazine (1)	Kenichiro Itami's Interview was featured in Technologist's Magazine. Kenichiro Itami (Center Director)
6	Jun. 1 - Sep. 26, 2017	TV (1)	Takashi Yoshimura (animal biology), Kenichiro Itami (synthetic chemistry), Tetsuya Higashiyama's (plant biology) research was featured in a TV program series: Kagaku Michiru. Takashi Yoshimura (PI), Kenichiro Itami (Center Director) and Tetsuya Higashiyama (PI)
7	May 3 - Jun. 1, 2017	Newspaper (1)	Kenichiro Itami's Chunichi Cultural Award was featured in Chunichi Shimbun. Kenichiro Itami (Center Director)
8	Mar. 30, 2016	Web (1)	Research highlight on nanocarbons, published in Nature Review Materials, was featured in Nature Japan. Kenichiro Itami (Center Director)
9	Mar. 22, 2016	Web (1)	Research highlight on aromatic rings, published in JACS, was featured in Chemistry World (RSC). Kenichiro Itami (Center Director)
10	Jul. 10, 2015	Newspaper (7), Website (10)	Research on plant reproduction, published in Developmental Cell, was featured in Chunichi Shimbun, Asahi Shimbun, Yomiuri Shimbun, Mainichi Shimbun, Nikkei Sangyo, Nikkan Kogyo Shimbun, Yahoo, Jiji, WSJ, Nikon, etc. Tetsuya Higashiyama (PI)

11	Jul. 10, 2015	Magazine/Web(1)	Keiko Torii's comments on women in science were appeared in Science. Keiko Torii (PI)
12	May 26,2015	Newspaper (3), Web (4), TV (1)	Construction of ITbM's new building was featured in Asahi Shimbun, Yomiuri Shimbun, Chunichi Shimbun, Nikkan Kogyo, CBC News, etc.
13	Dec. 21, 2014	TV (1)	TV program focusing on ITbM's Mix Labs and Cutting Edge Research in Science was featured in NHK BS1 "Chikyu (Earth) Agora" (50 min).
14	Oct 9 - Oct 20, 2014	Web (26)	Research on Mechanistic Studies of Nickel Catalysis published in JACS (Release Title: "Chemists uncover new role of a key base in organic synthesis" by Emory University) was featured in EurekAlert!, Phys.org, Science Codex, Science Newsline, etc. Kenichiro Itami (Center Director)
15	Mar. 31 - Apr. 18, 2014	Web (52)	Research on "Carbon nanotubes grow in combustion flames" was featured in Phys.org, Science Daily, JST Science Portal, MyNavi News, etc. Stephan Irle (PI)
16	Nov. 25 - Dec. 6, 2013	Newspaper (3), TV (1)	Research on "Highly challenging construction of contiguous all-carbon quaternary stereocenters" was featured in Chunichi Shimbun, Nikkei Sangyo, Kagaku Shimbun & CBC. Kohsuke Ohmatsu (Lecturer) and Takashi Ooi (PI)
17	Jul. 15, 2013 - Feb. 15, 2014	Web (4), Magazine (1)	Research on a new form of carbon: Grossly warped "nanographene" was featured in MyNavi news, Phys.org, Chemistry World, Cutting Edge Chemistry 2013 & Newton. Kenichiro Itami (Center Director)
18	Jul. 1 - 3, 2013	Newspapers (6), Web (3), Magazine (1)	Research on the regulatory mechanism of fish seasonal responses was featured in Chunichi Shimbun, Asahi Shimbun, Nikkei Shimbun, Mainichi Shimbun, Yomiuri Shimbun, Mittwoch, Yahoo news, jijicom, CBC & milsil. This result was also highlighted in Switzerland. Takashi Yoshimura (PI)
19	Mar. 27, 2013	Newspaper (3), Web (3)	Itami's diameter selective synthesis was highlighted in Nature Nanotechnology. Itami's research results received favorable coverage in the mass media with titles such as 'Templates ring up uniform nanotubes' and 'Grown from a ring'. It was featured in Nature Nanotech- nology, Chunichi Shimbun, Yomiuri Shimbun, Tokyo Shimbun, Nikkan Kogyo web, Nanotech Japan Chemistry world (Royal Society of Chemistry). Kenichiro Itami (Center Director)
20	Mar. 18 - 22, 2013	Web (2), Newspaper (3)	Research on "How a Rooster Knows to Crow at Dawn, Elucidation how the timing of rooster crowing is determined by circadian clock" was featured in National Geographic News, Chunichi Shimbun, Nikkei Shimbun, Asahi Shimbun & NHK web. Takashi Yoshimura (PI)
21	Feb. 1, 2013	Magazine (1)	Kenichiro Itami was elected the 108 most talented people by mainstream media and intellectuals, which was featured in Bungei Shunju (politics and economics). Kenichiro Itami (Center Director)

22	Dec. 19, 2012- Jan. 22, 2013	Newspaper (4)	Research on "Elucidation of the mechanism that pollen tube discriminates conspecific species by pollen tube attractants" was featured in Chunichi Shimbun, Mainichi Shimbun, Kagaku Shimbun & Tokyo Shimbun. Tetsuya Higashiyama (PI)

2) Overseas

No.	Date	Type of the media (e.g., newspaper, magazine, television)	Description
1	Dec. 14 -17, 2018	Newspaper (5), Web (International: 6/Domestic: 9), Magazine (International:1/Domestic:1)	Research on "Sphynx molecule to rescue African farmers from witchweed", published in Science, was featured in Chunichi Shimbun, Asahi Shimbun, Nikkei Shimbun, Toyo Keizai, Monthly Chemistry magazine, FNN News, CBC TV, NHK, Nagoya TV, Fuji TV, Chemistry World, Science Magazine, etc. Yuichiro Tsuchiya (Associate Professor, Kinoshita G)
2	Apr. 18- May 24, 2018	Web(International:15/Domestic:5), TV (2)	Research on "Identification of circadian clock modulators from existing drugs", published online in EMBO Molecular Medicine, was featured in AlphaGalileo JP, EurekAlert! JP, ReserchSEA, Health Medicine Network, Science Newsline, NHK, etc. Takashi Yoshimura (PI)
3	Apr. 9-30, 2018	Newspaper (3), Web (International:12/Domestic: 12), TV (1)	Research on "Identification and Characterization of Compounds that Affect Stomatal Movements", published online in Plant & Cell Physiology, was featured in Chunichi Shimbun, Nikkei Shimbun, Nikkan Kogyo Shimbun, NHK, etc. Toshinori Kinoshita (PI)
4	Jul. 7 – 24, 2014	Magazine (1); Websites (International: 62, Domestic: 9) incl. Yahoo News and 19 Indian websites	Prof. Takashi Yoshimura's research on Internal Brain Receptors of Birds published in Current Biology Release Title: "Shining light on the 100-year mystery of birds sensing spring for offspring"
5	Jan. 26 - Feb. 8, 2018	Newspaper (5), Web (International: 13/Domestic: 10)	Research on "Zipping-up" rings to make nanographenes, published in Science, was featured in Chunichi Shimbun, Asahi Shimbun, Nikkei Shimbun, Nikkan Kogyo Shimbun, Kagaku Shimbun, C&EN News, etc. Kenichiro Itami (Center Director)
6	Sep 4 - Nov 3, 2017	Newspape (5), Web (1), TV (1), Magazine (International:1/Domestic:1)	Research on the color perception of Medaka fish, published in Nature Communications, was featured in Chunichi Shimbun, Asahi Shimbun, Yomiuri Shimbun, Nikkan Kogyo Shimbun, Nikkei Shimbun, NHK, Newton magazine, Science Daily & Science Magazine. Takashi Yoshimura (PI)
7	1-May-17	Magazine (International:1)	Research on ClearSee, a reagent to see inside plants, published in Development. was featured in National Geographic. Tetsuya Higashiyama (PI)

8	Jan 26 - Feb 19, 2017	Newspaper (5), Web (International:4/Domestic:1)	Research on nanographene synthesis, published in Science, was featured in Chunichi Shimbun, Asahi Shimbun, Kagaku Shimbun, Nikkan Kogyo Shimbun, Nikkei Shimbun, NHK News, C&EN News, Science Daily, Phys.org, Materials Today. Kenichiro Itami (Center Director)
9	Apr. 14 - Dec. 17, 2017	Newspaper(6), TV(5), Magazine (International:2/Domestic:1)	Research on the synthesis of a carbon nanobelt, published in Science, was featured in Chunichi Shimbun, Asahi Shimbun, Mainichi Shimbun, Yomiuri Shimbun, Nikkei Shimbun, Toyo Keizai, Monthly Chemistry magazine, FNN News, CBC TV, NHK, Nagoya TV, Fuji TV, Chemistry World & Science Magazine. Kenichiro Itami (Center Director)
10	Nov 22 - Dec 19, 2016	Newspaper (4), Web (International: 15/Domestic: 13)	Research on plant cell division, published in PNAS, was featured in Asahi Shimbun, Chunichi Shimbun, Nikkei Sangyo, Mainichi Shimbun, Kyodo News, Global Plant Council. Minako Ueda (Lecturer) and Tetsuya Higashiyama (PI)
11	Nov 21 - Dec 12, 2016	Newspaper (1), Web (International: 52/Domestic: 2), Magazine (1)	Research on genetic engineering, published in Plant and Cell Physiology, was featured in Nikkei Sangyo Shimbun, Nikkei Biotech, Chinese Media, etc. Tetsuya Higashiyama (PI)
12	Sep 2 - 29, 2016	Newspaper (3), Web (International: 21/Domestic: 50), Magazine (1)	Research on the zig-zag of leaves, published in Current Biology was featured in Chunichi Shimbun, Nikkei Shimbun, Kagaku Shimbun, Kodomono Kagaku magazine, Kyodo News, Indian Media, etc. Toshiaki Tameshige (Postdoc) , Naoyuki Uchida (Associate Professor, Co-PI) and Keiko Torii (PI)
13	May 23 - Nov. 12, 2016	Web (International: 70)	Research on the biological rhythm, published in Angewandte Chemie, was featured in Huffington Post, MSN, Fox News, UK, Canadian, Indian and Dutch Media. Kenichiro Itami (Center Director) and Takashi Yoshimura (PI)
14	Apr 8 - Jun 9, 2016	Newspaper (4), Web (International: 34/Domestic: 21)	Research on "the discovery of AMOR, a sugar chain molecule that increases the fertilization efficiency in plants", published in Current Biology, was featured in Asahi Shimbun, Chunichi Shimbun, Kagaku Shimbun, Nikkei Shimbun, Kyodo News, JST Science Portal, Chinese Media, etc. Tetsuya Higashiyama (PI)
15	Aug 8 - 30, 2016	Newspaper (3), Web (International: 40/Domestic: 25)	Research on the synthesis of organic nanotubes, published in JACS was featured in Nikkei Sangyo Shimbun, Chunichi Shimbun, Kagaku Shimbun, Yahoo News, Mynavi News, Brazilian, Russian, Chinese, Spanish Media, etc. Kenichiro Itami (Center Director)
16	Mar. 23, 2016	Web (International: 19/Domestic: 3)	Research on the plant circadian clock, published in the Plant Cell, was featured in Alpha Galileo JP, EurekAlert! JP, etc. Norihito Nakamichi (Associate Professor, Kinoshita G)

17	Mar. 10, 2016	Newspaper (2), Web (International: 32/Domestic: 3), TV (1), Radio (1)	Research on plant fertilization, published in Nature, was featured in Science Daily, Global Plant Council, Chunichi, Kagaku Shimbun, Nature News & Views, NHK News, NHK Radio. Tetsuya Higashiyama (PI)
18	Aug. 21- Sep. 28, 2015	Newspaper (5), Web (International: 34/Domestic: 7)	Interdisciplinary research on "the development of a molecule to probe the growth of parasitic plants", published in Science, was featured in Chunichi Shimbun, Nikkei Sangyo Shimbun, Kagaku Shimbun, Yomiuri Shimbun, Science Daily, Nature Chemical Biology, Science. Shinya Hagihara (Associate Professor, Itami G), Yuichiro Tsuchiya (Associate Professor, Kinoshita G)
19	May 9 - Jun. 19, 2015	Newspaper (1); Web (International: 53/Domestic: 7); Magazine (2)	Interdisciplinary research on "molecules that can change the circadian rhythm", published in Angewandte Chemie, was featured in Chunichi Shimbun, Science Daily, Chemisch2Weekblad (Dutch), Social News (Spanish), Yahoo, Chemistry, etc. Kenichiro Itami (Center Director), Takashi Yoshimura (PI), Stephan Irle (PI) and Steve A. Kay (PI)
20	Feb. 27, 2015	Magazine (1)	Takashi Yoshimura, Stephan Irle and Jeffrey Bode's research was highlighted in Asia Research News 2015, the online and paper-based magazine focusing on Asian research. Takashi Yoshimura (PI), Stephan Irle (PI) and Jeffrey Bode (PI)
21	Jul. 7 - 24, 2014	Web (International: 62/ Domestic: 9), Magazine (1)	Research on Internal Brain Receptors of Birds published in Current Biology (Release Title: "Shining light on the 100-year mystery of birds sensing spring for offspring") was featured in incl. Yahoo News and 19 Indian websites. Takashi Yoshimura (PI)
22	May 27 - Jul. 25, 2014	Newspaper (2), Web (International: 39/Domestic: 2), TV (International: 1), Magazine (1)	Research on Nickel Catalysis published in Angewandte Chemie International Edition (Release Title: "A novel "Kabuto-like" nickel catalyst forms bioactive frameworks from low-cost phenol derivatives") was featured in incl. BBC. Kenichiro Itami (Center Director)
23	Apr. 1- 18, 2014	Magazine (1); Web (International: 45/Domestic: 8)	Research on Carbon Nanotubes published in Carbon (Release Title: "Carbon nanotubes grow in combustion flames") was featured in incl. Science Daily, Phys.org, Chem Europe. Kenichiro Itami (Center Director)
24	Dec. 24, 2013 - Apr. 2, 2014	Newspaper (4), Web (85), Magazine (1), TV (1)	Research on "Enhanced plant growth through promotion of stomatal opening" was featured in Asahi Shimbun, Shinano Mainichi Shimbun, Mainichi Shimbun, Kagaku Shimbun, Asahi, Chunichi, Nikkei, Phys.org, Science Daily, International Daily News, milsil, JST Science Channel, etc. Toshinori Kinoshita (PI)

Appendix6-1 Host Institution's Commitment (Fund, Personnel)

1. Contributions from host institution

(1) Fund, Personnel

* Regarding "Fund" entry, describe with reference to the items in the Progress Report (Jisseki-hokoku-sho) based on Article 12 of the Grant Guidelines (Kofu-yoko).

* Don't include competitive funding obtained by researchers (used as research project funding)

(FY 2012-2018)

<Fund> **(million yen)**

Fiscal Year	2012	2013	2014	2015	2016	2017	2018
Personnel	44	129	152	158	157	163	178
Faculty members	31	101	110	111	120	118	128
Full-time	31	78	81	85	94	85	96
Concurrent	0	23	29	26	26	33	32
Postdocs			13	13	6	13	19
RA etc.							
Research support staffs	3	3	3	3	1	2	3
Administrative staffs	10	25	26	31	30	30	28
Full-time	10	25	26	31	30	30	28
Concurrent							
Project activities	22	19	22	173	22	22	31
Travel					1		1
Equipment	1		2801		1		
Research projects							
Total	67	148	2975	331	181	185	210

<Personnel> **(person)**

Fiscal Year	2012	2013	2014	2015	2016	2017	2018
Personnel	18	18	21	20	21	21	23
Faculty members	13	13	14	13	15	14	15
Full-time	6	6	7	7	8	7	8
Concurrent	7	7	7	6	7	7	7
Postdocs			2	2	1	2	3
RA etc.							
Research support staffs	1	1	1	1	1	1	1
Administrative staffs	4	4	4	4	4	4	4
Full-time	4	4	4	4	4	4	4
Concurrent							

Appendix6-1 Host Institution's Commitment

1. Contributions from host institution

(2) Provision of land and/or building(s), lab space, etc.

Laboratory space
Nagoya University (NU) is providing 5,357 m^2 plus an additional 463 m^2 of an old building to be incorporated in ITbM's new building, adding to a total of 5,820 m^2 research space (including 4,166 m^2 provided complimentarily) in addition to the ITbM's new building.

Personnels
NU has been covering salaries of
1) 8 PIs of NU.
2) 7 designated associate professors who take charge of education in each department to relieve the PIs of this responsibility. The 7 positions will be allocated to ITbM as tenure positions in 2019.
3) 4 administrative staff + 1 URA through assignment from the University's human resource.

As of April 2019, 2 more positions are newly allocated to ITbM through the NU's request to MEXT with the highest priority to strengthen ITbM's activity.

Financial support toward construction of ITbM's new building
NU provided the financial support toward construction of ITbM's new building.

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

Decision making system
NU established the Institute rule, "Nagoya University Institute of Transformative Bio-Molecules Rules", to limit the role of the President of NU only to the appointment of the Director. All matters concerning operation and management of the Center fall under the purview of the Director.
NU also established "Nagoya University Institute of Transformative Bio-Molecules Steering Committee Rules" to organize the system, which enables the Director to exercise strong leadership in the Center concerning important matters such as personnel and execution of the budget.

Decision supporting system
Steering Committee meeting is held once a month to provide advice to the Director about the management of ITbM. Informal PI meetings are also held when necessary to discuss details such as research progress and lab management. Accordingly, the Director makes decisions on the allocation of personnel and facilities by consulting the Administrative Director who handles the budget.

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

Employment of 7 associate professors
NU has employed 7 associate professors to carry out educational activities and those of entrance examinations to allow NU PIs to concentrate on their research at ITbM.

Students allocation
All the 8 NU PIs are holding strong ties with their original departments, and undergraduate and graduate students are assigned in the same way before starting ITbM. Three overseas PIs in biology were assigned as a collaborating researcher in the Graduate School of Science, and a few PhD students have been allocated to the groups every year.

4. Revamping host institution's internal systems to allow introducing of new management methods

(e.g., English-language environment, merit-based pay, cross appointment, top-down decision making unfettered by conventional modes

of operation)

As denoted in **2**, it was authorized by NU that the Director has the authority to make decisions over the appointment of personnel, the Center's budget, and research priorities in addition to other matters as they arise. The Steering Committee authorizes the Director to make final decisions, thus it is the place for discussion and acts as an advisor to the 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 bonus to the Director, the Vice Director, PIs, and the Administrative Director based on their performance and evaluations, the determination of eligible persons and the amount of bonus is left to the discretion of the Director. The Executive Board of NU determines the special bonus of the Director.
NU assigned administrative staff who are eligible in English. Thus, the Administrative Department is composed of personnel with excellent ability, experience in a variety of areas, and a good command of English. All the administrative information is provided in both English and Japanese. The Steering Committee meetings are also conducted in English.

5. Utilities and other infrastructure support provided by host institution

(*In addition to those listed in the item 1. "Contributions from host institution")

As denoted in **1**, NU is providing ITbM with sufficient space including the original laboratory spaces that the NU PIs have been allocated even after establishment of the new building.
NU is very well equipped with top-level major instruments necessary for ITbM's research. The quality and number of these instruments rivals the best institutions in the world. These instruments can be used by all ITbM members.

NU revised the rule of the use of halls of residence to provide ITbM's foreign researchers to reside, and to extend the possible duration from one to two years.

6. Support for other types of assistance

In order to promote efficient use of intellectual properties and research outcomes from ITbM and other NU institutes, NU conducted the organizational reform of research supporting units to establish the "Department for Academic Research & Industry-Academia-Government Collaboration". ITbM's activities are strongly supported by this department particularly related to collaboration and technology transfer to industries through business matching.

Most tasks to operate the new building have been supported by the Graduate School of Science to reduce the burden of ITbM. The guard system, fire alarm system, door-access control system, security camera system at ITbM are operated through the resources of the Graduate School of Science.

Appendix6-2 The Host Institution's Mid-term Plan

* Excerpt the places in the host institution's "Mid-term objectives" and/or "Mid-term plan" that clearly show the positioning of the WPI center within its organization.

Medium-term Goal and Plan of National University Corporation Nagoya University

Phase Two (April 1, 2010 – March 31, 2016)

- Goal regarding research; Goal regarding research level and results and implementation system
  - Proceed with international-level research based on the Nagoya University Research Plan (M4)

- Actions to be taken to achieve goals regarding research; Actions to be taken to achieve goals regarding research level and results and implementation system
  - 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)" (K10)

Phase Three (April 1, 2016 – March 31, 2022)

- Goal regarding education; Goal regarding education content and results
  - We will provide high quality education focusing on internationally accepted level to develop global-scale human resources with logical thought and imagination (M1)
- Goal regarding research; Goal regarding research level and results and implementation system
  - To produce the intellectuals as the comprehensive university that conducts world-leading researches (M5)

- Actions to be taken to achieve goals regarding education; Actions to be taken to achieve goals regarding education content and results
  - Based on admissions, curriculi, and diploma policies for education courses in the graduate school, NU will further improve education content by promoting international standardization (e.g. using syllabus written in both Japanese and English and developing the course numbering system), expanding common courses, developing and implementing the personnel training program in cooperation between the industry and universities, leading education and research across specialized fields and providing transferable skills training. NU will improve its international compatibilities by developing joint degree programs with world class partner universities. NU will provide the education program in the doctoral course integrated with the advanced researches conducted in various NU institutes such as the Institute of Transformative Bio-Molecules (ITbM) to attract capable doctoral candidates (K2).
- Actions to be taken to achieve goals regarding research; Actions to be taken to achieve goals regarding research level and results and implementation system
  - NU will promote the world-leading fundamental research and establish an international and original research center engaged in cross-section study, international collaborative study, and comprehensive study by promoting "World Premier International Research Center Initiative," "Center of Innovation (COI) Program," and "The Program for Promoting the Enhancement of Research Universities" (K11).