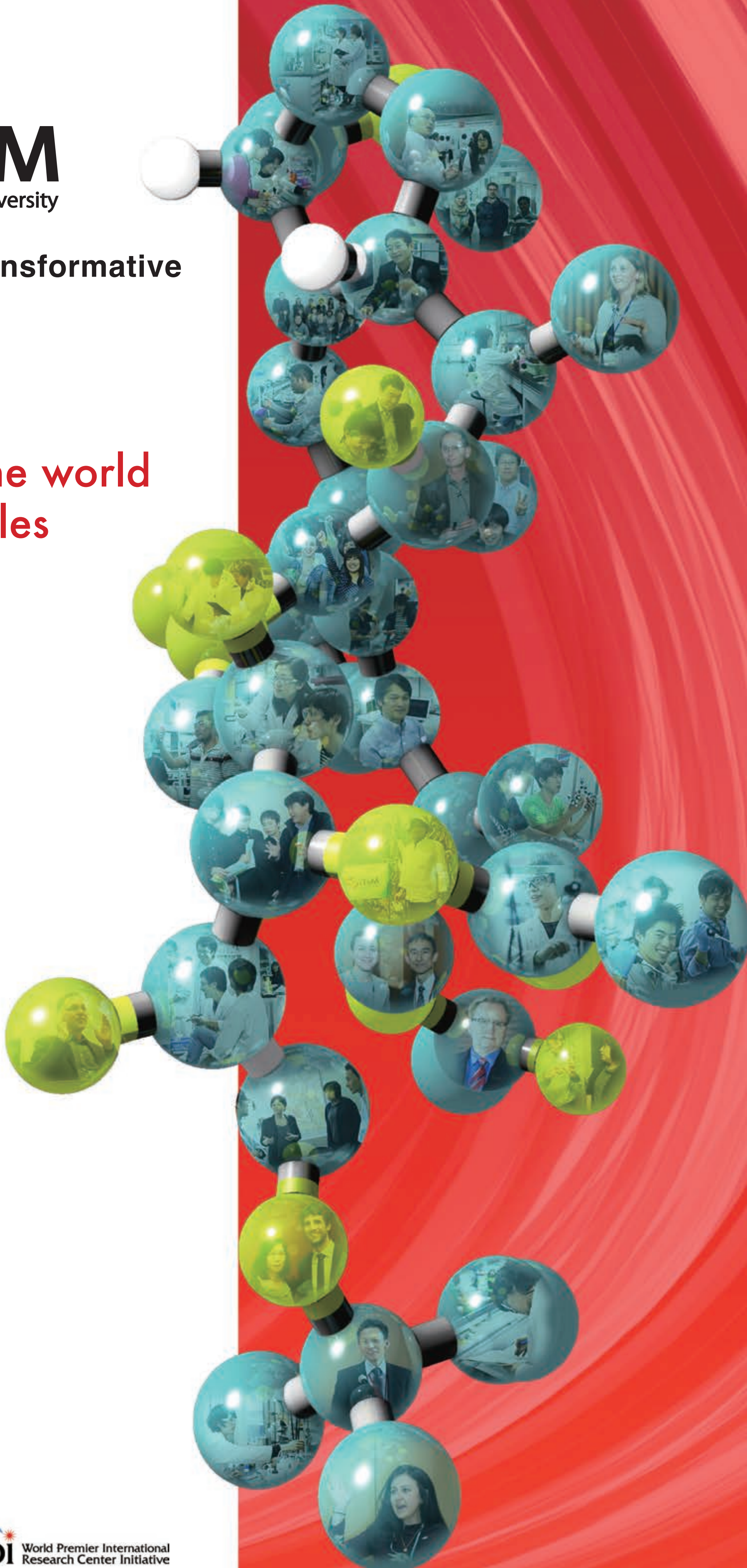
ITbM
Nagoya University

Institute of Transformative Bio-Molecules

Changing the world with molecules



NAGOYA UNIVERSITY

wpi World Premier International Research Center Initiative

ITbM's Mix Lab and Mix Office
ITbM's biologists, chemists and theoreticians work side by side in the lab and office (two-layer structure).

Contents

ITbM
Nagoya University

Connect molecules, create value, and change the world

Director's message

Changing the world with molecules

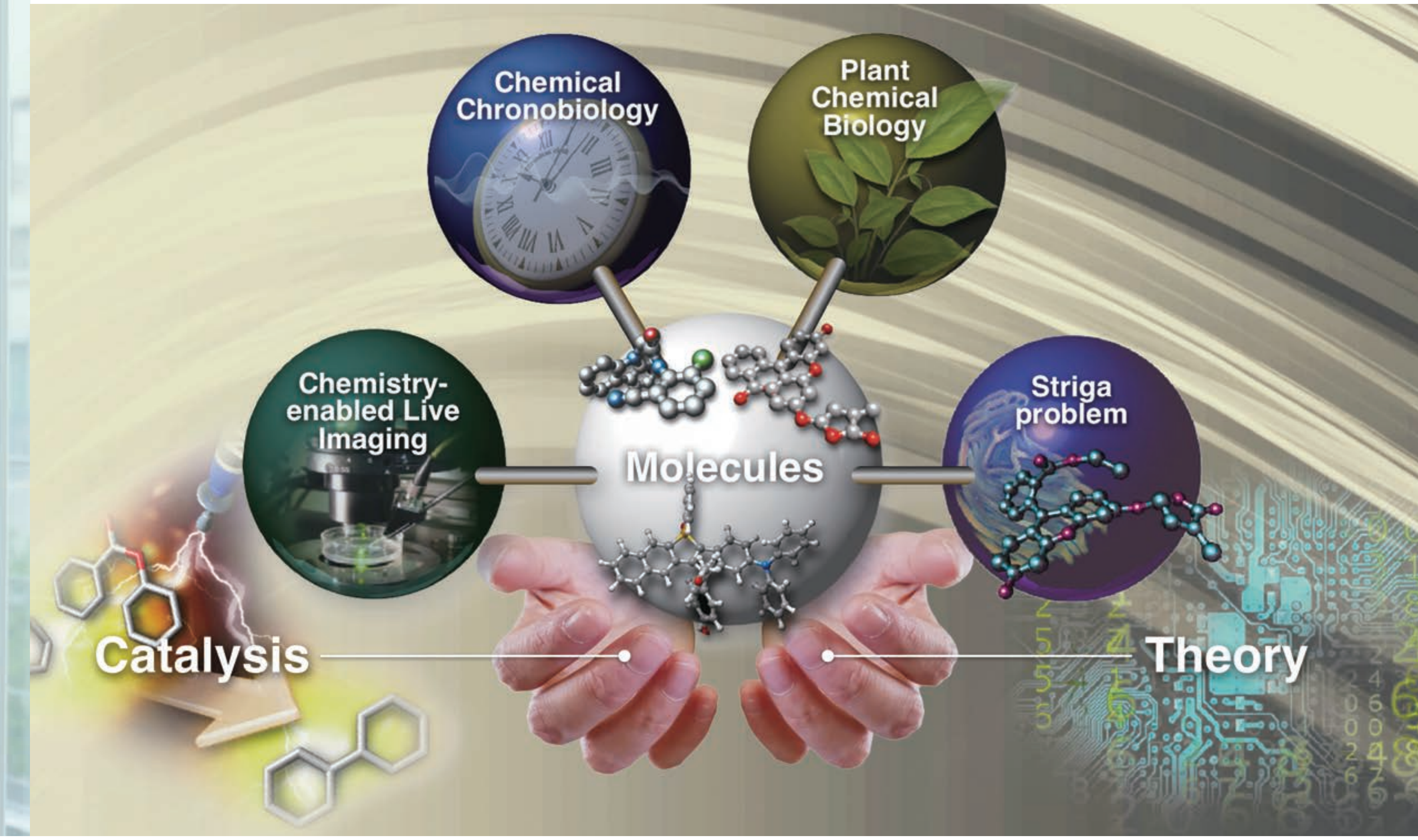
Molecules are extremely small, but they are essential to all life on the planet. They are central to the operation of all industries, including pharmaceuticals, agrochemicals, electronic materials, solar cells, displays, petrochemicals, automotive manufacturing, plastics, polymers and many other sectors. It is my strong belief that molecules have the power to change the way we do science and the way we live.

Our dream is to take advantage of the dramatic relationship between structure and function. By merging state-of-art synthetic chemistry, systems biology, and theoretical science, we aim to develop new ways of creating design-based bioactive molecules with targeted properties. These new synthetic paradigms will allow the design and synthesis of bioactive molecules both inside the flask and inside living organisms. Most importantly, our ultimate goal is to solve urgent problems in science and technology that have a significant impact on society.

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

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

Institute of Transformative Bio-Molecules
Director, Kenichiro Itami



ITbM at a glance

Interdisiciplinary research between chemistry and biology

The Institute of Transformative Bio-Molecules (ITbM) at Nagoya University in Japan, is an international research institute that conducts interdisciplinary research between chemistry and biology. ITbM was selected in October 2012 as one of the centers of the World Premier International Research Center Initiative (WPI), a ten-year program funded by the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT). ITbM officially launched in April 2013.

The objective of ITbM is to create a new interdisciplinary field of research through the collaboration of cutting-edge synthetic chemistry, animal/plant biology, and theoretical science, as well as to deliver bio-molecules that change the way we do science and we live, i.e. “transformative bio-molecules”.

Many transformative bio-molecules have been developed up to now, such as the discovery of penicillin, and the development of the highly effective anti-influenza drug, Tamiflu.

At ITbM, chemists, biologists and theoreticians are collaborating by working side by side to design and synthesize new transformative bio-molecules, and to generate a new research area on the boundaries of chemistry and biology. These endeavors will address various social issues regarding the environment, food production, and medical technology.

ITbM has defined the following four flagship research areas as the main focus of the institute: “Chemistry- enabled Live Imaging”, “Chemical Chronobiology”, “Plant Chemical Biology”, and “The Striga Problem”. By exploring a new integrative field between chemistry and biology, ITbM aims to create transformative bio-molecules through carrying out chemical biology research to “understand”, “see” and “regulate” living organisms.

ITbM researchers

An international mixture of leading scientists

ITbM is an international research institute with 13 principal investigators (PIs), including five overseas PIs, who concurrently hold posts at ITbM and their own institutions. Cooperative PIs (Co-PIs) have been appointed to oversee satellite groups at ITbM, and to maintain close contact with the PIs through e-mails and regular online meetings. The majority of postdoctoral researchers at ITbM are from overseas, and conduct research with graduate students of Nagoya University. This enables researchers to integrate with Japanese students, and also have the opportunity to learn different cultures while being in Japan.

ITbM in numbers: *As of April 2019

13 principal investigators:

8 from Nagoya University, 5 from overseas institutions

5 chemists, 6 biologists, 2 theoreticians

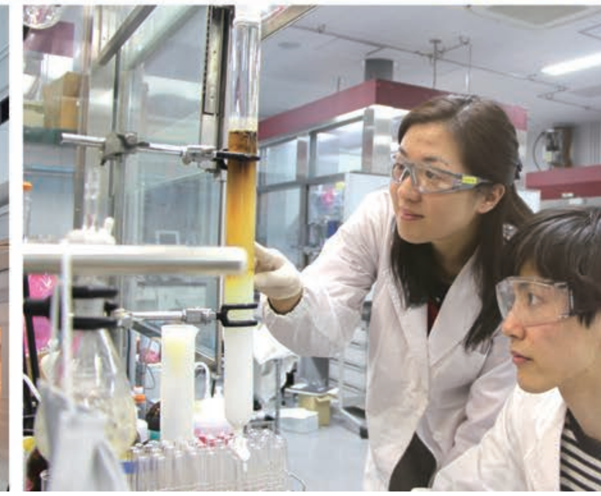
30 faculty members, 2 invited faculty members

32 postdoctoral researchers

34% international researchers

14 countries:

Canada, China, France, Germany, Hungary, India, Italy, Japan, Korea, Poland, Switzerland, Taiwan, UK, USA



Research environment

Promoting "mixing" of different fields

ITbM has set up Mix Labs to remove the physical barriers between research groups and to enhance interdisciplinary research across various fields and groups. Unlike traditional labs, where the labs are usually separated according to research groups, the Mix Labs incorporate large spaces, where researchers and students from different backgrounds share the same space and can have discussions on a daily basis. Each PI is in charge of their own research group. Nevertheless, the flexible interaction that exists between different research groups enables dynamic mixing of research that goes beyond the boundaries of conventional frameworks. Using "molecules" as the common keyword has advanced the understanding between different disciplines.

The Mix Labs have played an immense role in advancing collaborative interdisciplinary research at ITbM, as the faculty, postdoctoral researchers and students are able to communicate across different fields and put their research proposals immediately into action. Over 20 interdisciplinary research themes have emerged from young researchers in the Mix Labs, and some of the research outcomes have already been released as patents and publications, as well as commercialization of reagents through technology transfer to industries.

The ITbM Research Award was established to promote interdisciplinary research proposed by young researchers working in the Mix Lab. The award provides start-up funding and is granted to outstanding collaborative research projects that are proposed by a team of researchers from different fields, which consist of at least one ITbM researcher (non-PIs). Many of the selected proposals have become representative projects at ITbM.

ITbM's new research building that reflects the Mix Lab concept was completed in March 2015. The building's whole area space is 7,934 m^2 and is a 6-storied building that consists of two sets of Mix Labs and Mix Offices. The labs and offices make up a 2-layer structure, where the Mix Offices are an open space over the windows that has a good view of the Mix Labs situated below.

The center is also equipped with a kids' room to assist researchers with children, as well as refresh spaces, and a wooden deck in order to enable interactions between members. ITbM Tea break Meetings are held weekly to facilitate communication between members of the institute.

International Symposium on Transformative Bio-Molecules (ISTbM)

Hirata Award

Tsuneko & Reiji Okazaki Award

Nagoya Medal of Organic Chemistry

Towards globalization

International symposia and awards

ITbM is organizing a number of international symposia and awards each year. Through these international events, ITbM is establishing a strong network with leading researchers in the fields of synthetic chemistry, animal/plant biology and theoretical sciences. These activities are part of ITbM's globalization strategy, which aims to enhance globalization.

International Symposium on Transformative Bio-Molecules (ISTbM)

ITbM organizes its international symposium each year in Nagoya by inviting world-leading researchers who carry out research in ITbM's related fields. ISTbM contributes to the establishment of ITbM's international network and promotes international research collaborations.

Hirata Award

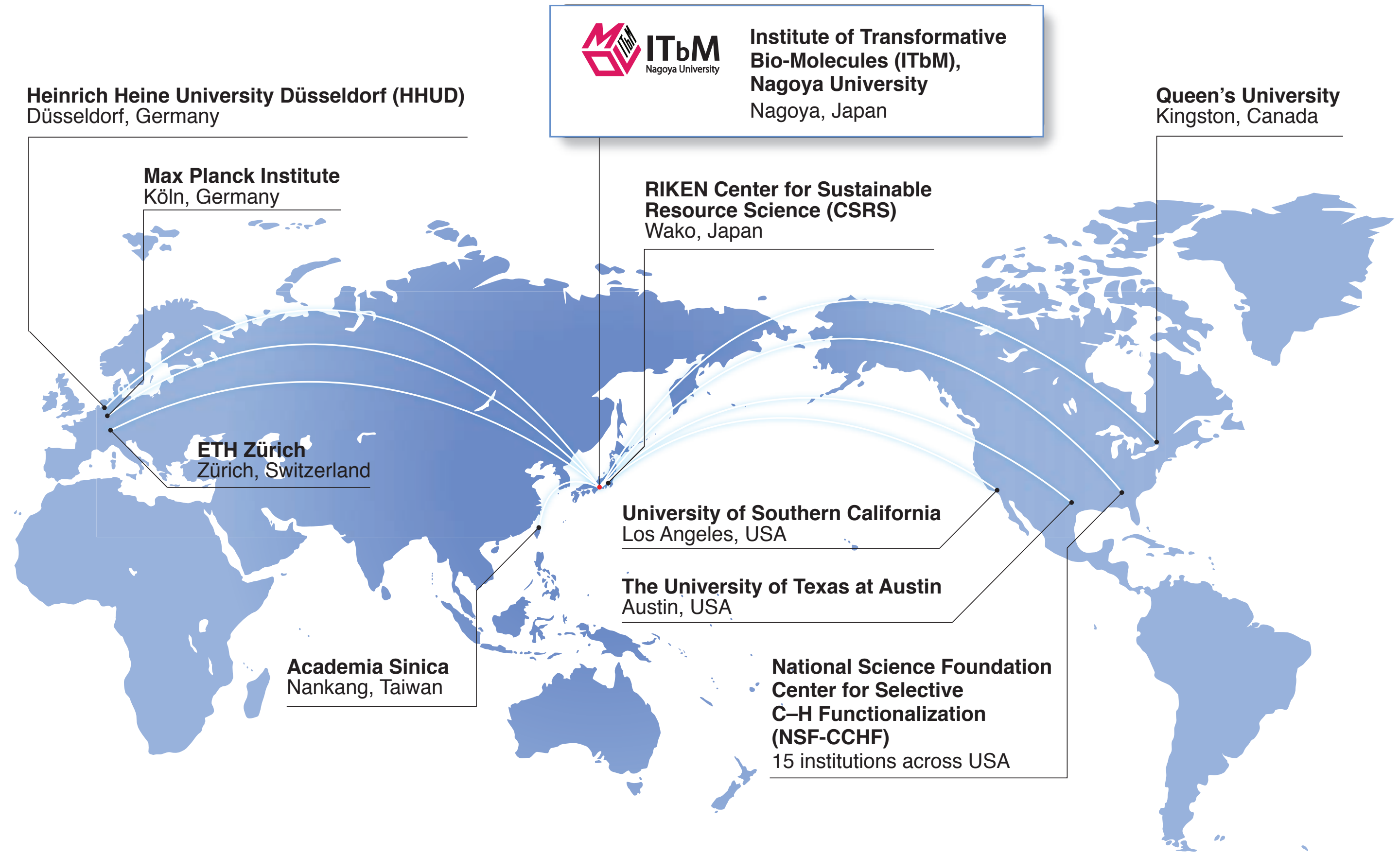
The Hirata Memorial Lecture started in 2005 at Nagoya University and is an international award granted each year to a rising star in the field of organic chemistry. This award was established in memory of the great achievements of the late Dr. Yoshimasa Hirata, Honorary Professor of Nagoya University. Dr. Hirata is known for the discovery of many natural products, including tetrodotoxin, a neurotoxin found in puffer fish, and greatly contributed to the advancement of natural product chemistry. Throughout the years, the Hirata Memorial Lecture has been given by many distinguished young chemists and has grown to become an internationally recognized honor in organic chemistry. From 2015, the Lecture has changed its name to the "Hirata Award" and is organized by ITbM.

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, Special Professor of Nagoya University and the late Dr. Reiji Okazaki, Honorary Professor of Nagoya University. Drs. Okazaki are known for their discovery of the Okazaki Fragments, which are short DNA fragments that are formed during DNA replication, and have contributed to advancing the field of molecular biology. Their efforts have also inspired subsequent generations of researchers. The Okazaki Award is an international award that is presented each year to a young leading scientist, who has made significant contributions in the field of life sciences through unique approaches and techniques.

Nagoya Medal of Organic Chemistry

The Nagoya Medal of Organic Chemistry is an international award that was established in 1995 by Dr. Ryoji Noyori, Special Professor of Nagoya University, and Dr. Hisashi Yamamoto, Honorary Professor of Nagoya University, under the support of the MSD Life Science Foundation (previously known as the Banyu Life Science Foundation International). Every year, the Nagoya Gold Medal is awarded to an organic chemist who has made significant original contributions to the field in its broadest sense, and the Silver Medal is presented to a promising scientist based in Japan, whose research has had a major impact on the field of synthetic organic chemistry. From 2014, ITbM's director, Dr. Kenichiro Itami, assumed the role of chairman of the Nagoya Medal, thus ITbM became the organizer of this award.



Partnerships and global networks

ITbM has collaborations with institutions worldwide. In addition to the universities/institutes where the overseas PIs hold posts (ETH Zürich, Queen's University, The University of Texas at Austin, University of Southern California, Heinrich Heine University Düsseldorf, and Max Planck Institute), ITbM is collaborating closely with the National Science Foundation Center for Selective C–H Functionalization (NSF-CCHF, Center Director: Dr. Huw Davies, Emory University), the RIKEN Center for Sustainable Resource Science (RIKEN CSRS, Center Director: Dr. Kazuo Shinozaki) and Institute of Chemistry, Academia Sinica (Director: Dr. Yu-Ju Chen). Joint workshops are held with these collaborating institutes. In addition, student and faculty exchanges are ongoing between ITbM and CCHF.

Researchers at Nagoya University who carry out research related to ITbM's are also involved as collaborators.

Academia Sinica
Nankang, Taiwan

Faculty members:
Kei Murakami
Hideto Ito
Akiko Yagi
Kazuma Amaike

Shinya Hagihara
(Affiliated researcher)

Itami Group

Professor Kenichiro Itami

Position — Grad. Sch. of Science, Nagoya Univ.
E-mail — itami@chem.nagoya-u.ac.jp
Education — 1998 Dr. Eng.; Kyoto Univ.
Research interests — synthetic chemistry, catalytic chemistry, materials chemistry
Hobbies — sports, ramen, hot spring, Jaguar F-TYPE British Design Edition
Favorite molecule — benzene
Place of birth — Pennsylvania, USA

Research overview: The ultimate goal of the Itami group is to develop “transformative molecules”, innovative functional molecules that make a marked change in the form and nature of science and technology. With such a goal in mind, the work of the Itami group has centered on catalyst-enabling synthetic chemistry with broad directions. The emphasis is on the development of new catalysts for solving challenging synthetic problems, for realizing super-efficient chemical syntheses, for high demand molecule activations, and for producing as-yet unexplored molecules of significant interest in various fields.

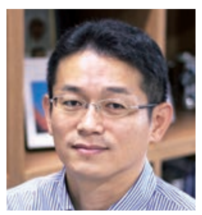
Faculty members:
Kohsuke Ohmatsu
Daisuke Uraguchi
Yoshitaka Aramaki
Ken Yamanomoto

Ooi Group

Professor Takashi Ooi

Position — Grad. Sch. of Eng., Nagoya Univ.
E-mail — tooi@chembio.nagoya-u.ac.jp
Education — 1994 Dr. Eng.; Nagoya Univ.
Research interests — organic synthesis and catalysis
Place of birth — Aichi, Japan

Research overview: We have been creating a bold stream of research on the molecular design of various organic ion pairs and their rational structural modifications for eliciting unique functions as molecular catalysts, providing a solid basis for the safe and sustainable supply of useful organic compounds. At ITbM, we develop innovative molecular catalysts that can revolutionize organic reactions and chemical syntheses in order to not only provide sustainable chemical processes, but also accelerate the discovery of transformative bio-molecules as a reliable means for solving problems of fundamental biological significance.



Faculty members:
Masayasu Taki
Masahito Murai
Soichiro Ogi
Naoki Ando

Aiko Fukazawa
(Affiliated researcher)

Yamaguchi Group

Professor Shigehiro Yamaguchi

Position — Grad. Sch. of Science, Nagoya Univ.
E-mail — yamaguchi@chem.nagoya-u.ac.jp
Education — 1997 Dr. Eng.; Kyoto Univ.
Research interests — physical organic chemistry, fluorescent molecules

Research overview: We work on a variety of topics in the fields of main group chemistry and physical organic chemistry. In particular, the emphasis is placed on the construction of new π-conjugated scaffolds, which is crucial for pursuing photo/electronic functions of organic molecules. At ITbM, we are pursuing the challenge of designing and synthesizing transformative fluorescent π-conjugated molecules for bioimaging applications. A number of fascinating fluorescent molecules have been developed so far, not only for optoelectronic applications like OLEDs (organic light emitting diodes), but also for biological applications such as fluorescent probes.

Faculty member:
Shunsuke Oishi
(Co-PI)

Bode Group

Professor Jeffrey Bode

Position — ETH Zürich, Switzerland
E-mail — bode@itbm.nagoya-u.ac.jp
Education — 2001 Dok. Nat. Sci.; ETH Zürich, Switzerland
Research interests — synthetic chemistry, protein synthesis, chemical biology
Place of birth — California, USA

Research overview: The chemical synthesis of proteins can be accomplished by peptide ligation reactions. In our own research, we have developed a new amide-forming reaction of α-ketoacids and hydroxylamines (KAHA ligation) that allows the synthesis of proteins by combining peptide segments under aqueous conditions without coupling reagents or side chain protecting groups. Rendering the synthesis of proteins – including highly modified derivatives and covalent protein–protein conjugates – as routine and convenient as bacterial protein expression is the long term goal of our research program.

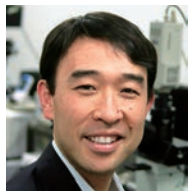
Faculty member:
Masakazu Nambo
(Co-PI)

Crudden Group

Professor Cathleen Crudden

Position — Queen's Univ., Canada
E-mail — cruddenc@chem.queensu.ca
Education — 1994 Ph.D.; Univ. of Ottawa, Canada
Research interests — asymmetric synthesis, organometallic catalysis, nano materials
Hobbies — swimming, cycling, heavy metal
Favorite molecule — BINAP (chiral ligand)
Place of birth — Belfast, North Ireland

Research overview: Research in the Crudden group focuses on catalysis and materials chemistry. We are interested in developing new reactions to prepare interesting organic molecules, in particular reactions that are enantioselective or enantiospecific. With our collaborators at ITbM, we aim to investigate the biological activity of these molecules for applications in the pharmaceutical and agricultural industries. We are also interested in the use of carbon–based molecules as ligands for metal surfaces and nanomaterials comprised of gold and other metals. With our collaborators at ITbM and other institutions across the world, we aim to investigate the applications of these materials in various fields, including catalysis and biological imaging.



Faculty members:
Minako Ueda
Narie Sasaki
Masahiro M. Kanaoka
Daisuke Kurihara
Hidenori Takeuchi
Yoko Mizuta

Michitaka Notaguchi
(Affiliated researcher)

Higashiyama Group

Professor Tetsuya Higashiyama

Position —— Grad. Sch. of Science, Nagoya Univ. and The Univ. of Tokyo
E-mail —— higashi@bio.nagoya-u.ac.jp
Education —— 1999 Dr. Sci.; The Univ. of Tokyo
Research interests —— plant reproduction, peptides, live cell imaging
Hobbies —— driving the car with the family, traveling
Favorite molecule —— LURE, AMOR
Place of birth —— Yamagata, Japan

Research overview: At ITbM, we strive to produce novel and useful hybrid plants through combination of our unique live cell biology and synthetic chemistry to generate key molecules responsible for plant reproduction. We have also been a leader in advancing development of relevant molecules and technology for innovative bioimaging, and have succeeded in establishing a system for live imaging of early plant embryogenesis. We're working towards development of ideal fluorescent molecules suitable for *in vivo* labeling of specific components, which allows directly visualization of the dynamics of these signaling molecules deep in the whole tissue using two-photon microscopes.

Faculty members:
Naoyuki Uchida
(Co-PI)
Soon-Ki Han

Torii Group

Professor Keiko Torii

Position —— The Univ. of Texas at Austin and Howard Hughes Medical Institute, USA
E-mail —— torii@itbm.nagoya-u.ac.jp
Education —— 1993 Ph.D.; Univ. of Tsukuba
Research interests —— plant development, cell-cell communication, peptides
Hobbies —— art (illustration), music (choir and orchestra)
Favorite molecule —— LRR-RLK (plant kinase receptor), caffeine
Place of birth —— Tokyo, Japan

Research overview: In the Torii-Uchida group, we strive to probe signaling dynamics and manipulate plant development via integrated approaches of synthetic cell biology, chemical biology and molecular genetics. Fully leveraged on ITbM's core strengths and ambitious mission to fuse catalysis chemistry and plant & animal biology, we aim to: (i) design small molecules to highjack inter- and intra-cellular signaling networks; and develop fluorescent probes to visualize signaling dynamics (synthetic cell biology); (ii) design and screen for small molecules to manipulate plant growth (chemical biology); and (iii) elucidate the functions of ligand-receptor pairs in plant development, with a specific focus on the EPF-peptides and ERECTA family receptors (developmental genetics).

Faculty member:
Masayoshi Nakamura
(Co-PI)

Frommer Group

Professor Wolf B. Frommer

Position —— Heinrich Heine Universität Düsseldorf and Max Planck Institute for Breeding Research, Germany
E-mail —— wfrommer@itbm.nagoya-u.ac.jp
Education —— 1987 Dr. rer. nat.; University of Köln, Germany
Research interests —— molecular biology, biochemistry, chemical genomics
Hobbies —— traveling to Japan, motorcycle riding, skiing, martial arts, sweets
Favorite molecule —— isorhamnetin-3-O-β-D-glucopyranoside
Place of birth —— somewhere in Germany

Research overview: The research in the Frommer group at ITbM is carried out in the following four areas: (i) engineering of genetically encoded biosensors and sponges for *in vivo* biochemistry; (ii) characterization of the determinants of interactions between small molecules and transporters to help identifying novel drugs and agrochemicals; (iii) search for yet unidentified receptors for small molecules; and (iv) chemical genomics and imaging of processes related to cellular growth and dynamics.

Faculty members:
Norihito Nakamichi
Yuichiro Tsuchiya
Koji Takahashi
Yin Wang
Mizuho Ichinose
Yosuke Toda

Kinoshita Group

Professor Toshinori Kinoshita

Position —— Grad. Sch. of Science, Nagoya Univ.
E-mail —— kinoshita@bio.nagoya-u.ac.jp
Education —— 1994 Dr. Sci.; Kyushu University
Research interests —— plant molecular biology
Hobbies —— observing & raising living organisms

Research overview: Our research focuses on understanding the mechanism of how plants adapt and respond to ever-changing environmental signal. Stomata is the key in this process - since the pair of guard cells surrounding stomatal pores regulate CO_2 uptake for photosynthesis and water loss from leaves in response to environmental signals. We have been studying signaling pathways responsible of stomatal opening and closing, and have identified the key components that regulate this behavior. To elucidate the full signaling pathway of stomatal opening and closing, we are using genetic, biochemical and physiological approaches to uncover the full mechanism. Our discovery will allow generation of plants with high productivity and drought tolerance, simply through the regulation of stomatal openings.

Faculty members:
Taeko Ohkawa
Yusuke Nakane

Yoshimura Group

Professor Takashi Yoshimura

Position —— Grad. Sch. of Bioagricultural Sciences, Nagoya Univ.
E-mail —— takashiy@agr.nagoya-u.ac.jp
Education —— 1996 Dr. Agr.; Nagoya Univ.
Research interests —— animal integrative physiology, chronobiology, systems biology
Hobbies —— traveling, visiting museums, sports
Favorite molecule —— DHEA (anti-aging supplement)
Place of birth —— Shiga, Japan

Research overview: Cyclic environmental changes such as day-night and seasonal cycles control all organisms on earth. To better adapt to these cyclic events, organisms have developed internal biological clocks during the evolutionary process. To understand animals' clever adaptation strategies to environmental changes, we apply interdisciplinary approaches to various animals that have highly sophisticated mechanisms. Our findings are currently fueling development of transformative bio-molecules that will improve animal production and human health.

Faculty member:
Tsuyoshi Hirota
(Co-PI)

Kay Group

Professor Steve Kay

Position —— Univ. of Southern California, USA
E-mail —— kay@itbm.nagoya-u.ac.jp
Education —— 1984 Ph.D., Univ. of Bristol, UK
Research interests —— chronobiology, chemical biology
Hobbies —— tuna fishing
Place of birth —— Jersey, UK

Research overview: By using the resources of clock modifying compounds and genes in combination with state-of-the-art technologies at ITbM, the Kay-Hirota group aims to discover "transformative bio-molecules" that will revolutionize clock research and ultimately benefit human health. A unique combination of molecular, genetic, genomic, biochemical, and chemical biology approaches will allow us to reveal key regulatory processes of the circadian clock and define molecular links between the clock and rhythmic regulation of physiology and behavior. Proof-of-concept chemical probes will provide useful tools to control clock function in a conditional manner and also act as starting points for developing therapeutics for circadian clock-related disorders.

Research groups: Theory

Calculating and analyzing molecules

Tama Group

Professor Florence Tama

Position — Grad. Sch. of Science, Nagoya Univ.
E-mail — florence.tama@nagoya-u.ac.jp
Education — 2000 Ph.D.; Univ. Paul Sabatier, France
Research interests — computational biophysics
Hobbies — traveling, movies
Place of birth — Carmaux, France

Research overview: Research in the Tama group focuses on the computational studies of structures and functions of large macromolecular assemblies. Dysfunctions of these bio-molecules may result in severe diseases, and in order to understand such diseases and develop treatments, the functional mechanisms of these bio-molecules need to be elucidated. To this goal, Tama's group 1) develops new computational techniques to determine 3D structures and dynamics of biological complexes; and 2) works in collaboration with experimental groups to elucidate functions of bio-molecules of interest.

Faculty members:
Kazuhiro Fujimoto
Masaaki Saitow

Yanai Group

Professor Takeshi Yanai

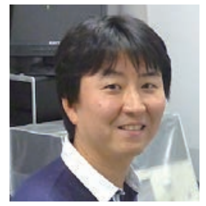
Position — Grad. Sch. of Science, Nagoya Univ.
E-mail — yanait@chem.nagoya-u.ac.jp
Education — 2001 Dr. Eng.; The Univ. of Tokyo
Research interests — computational quantum chemistry
Hobbies — programming, starbucksing, camping
Favorite molecules — Nitrogen molecule and chromium dimer
Place of birth — Shimane, Japan

Research overview: The heart of chemistry lies in the transformation of molecules. In the Yanai group, we investigate transformations of molecular systems through theoretical and quantum chemistry computational methods. The prime goal of our research is to elucidate the principals and mechanisms guiding chemical transformations, while recognizing the importance of the role of electrons in these systems.

Centers

Accelerating ITbM's interdisciplinary research

Live Imaging Center



Designated Associate Professor
Yoshikatsu Sato

E-mail:
sato-yoshikatsu@i.mbox.nagoya-u.ac.jp

Center overview: The Live-imaging Center provides access of advanced optical microscopes to everyone–from ITbM members to researchers worldwide. We have many cutting-edge microscopes and equipments, including; (1) multifunctional laser scanning system for spectral imaging with ultimate sensitivity, multi-photon imaging, and high speed imaging; (2) laser microdissection; (3) optical tweezers; (4) Infrared evoked gene operation system (IR-LEGO) equipped with (5) laser thermal micro-injector and (6) pico-pipette for collecting small volumes; (7) light sheet microscope; (8) STED superresolution system equipped with (9) fluorescence lifetime imaging. In addition to the supporting activities for our users, our mission is developing transformative bioimaging molecules by collaborating with Yamaguchi, Itami, and Higashiyama group. Furthermore, we also study our own research about the plant cell physiology in response to the environmental stimuli.

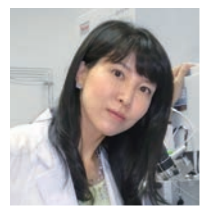
Chemical Library Center

Designated Associate Professor
Ayato Sato

E-mail: ayato-sato@itbm.nagoya-u.ac.jp

Center overview: Focusing on creating bioactive hit molecules for specific biological phenomena. The Chemical Library Center is the pioneer of collaborative research at ITbM. With approximately 70,000 compounds available, the center expanding the unique libraries with selected natural products, pharmaceuticals drugs, and novel synthetic compounds. The center is equipped with an automated chemical dispensing machine, clean bench, incubators and high performance liquid chromatography-mass spectrometer, which are relevant to conduct chemical biology research. It works as a hub where synthetic chemists bring the molecules that they have designed and synthesized and the biologists use the molecules for their assays. Up to now, the center has been providing over 1,200,000 compounds to over 85 collaborators. A new style of an interdisciplinary research is recently arising, where the chemists propose novel biological assay methods using the small molecules that they have designed based on feedback from the biologists.

Molecular Structure Center



Designated Assistant Professor
Keiko Kuwata

E-mail: kuwata@itbm.nagoya-u.ac.jp

Center overview: The Molecular Structure Center is equipped with cutting-edge machines for structural determination of organic and biological molecules synthesized by members of ITbM. Numerous top-notch machines are available to facilitate members of ITbM: (1) X-ray diffractometer with a Super Bright X-ray generator; (2) Super high resolution NMR machine equipped with a probe that can be cooled to the temperature of liquid helium and nitrogen (UltraCOOL-, SuperCOOL-NMR); (3) High performance liquid chromatography mass spectrometer equipped with a nanospray unit for proteomics analysis (nanoLC-MS/MS); (4) High performance liquid chromatography-mass spectrometer equipped with an electric field Fourier transformation spectrometer for high accuracy metabolomics analysis (LC-MS); (5) MALDI imaging spectrometer (MALDI-TOF/TOF); and (6) Hydrogen/deuterium exchange mass spectrometer for protein interaction analysis (HDX-MS).

Peptide Protein Center

Designated Assistant Professor
Shunsuke Oishi

E-mail: oishi@itbm.nagoya-u.ac.jp

Center overview: The Peptide Protein Center provides tailor-made peptides and proteins to ITbM's biology groups. Using ligation chemistry developed by ITbM's Bode group, we can prepare linear peptides, cyclic peptides, and synthetic proteins. The peptides and proteins prepared can be tailored to suit different needs; We have successfully incorporated novel fluorescent molecules developed the Yamaguchi group, and unnatural amino acids synthesized by the Ooi group into synthetic peptides and proteins. We envision that these unique compounds would be transformative for the biological studies in ITbM.

State-of-the-art equipment are available in all centers. External access to the four centers can be arranged upon request.

Research achievements

1 Combating the plant parasite, *Striga*

1 Sphinx molecule to rescue African farmers from witchweed

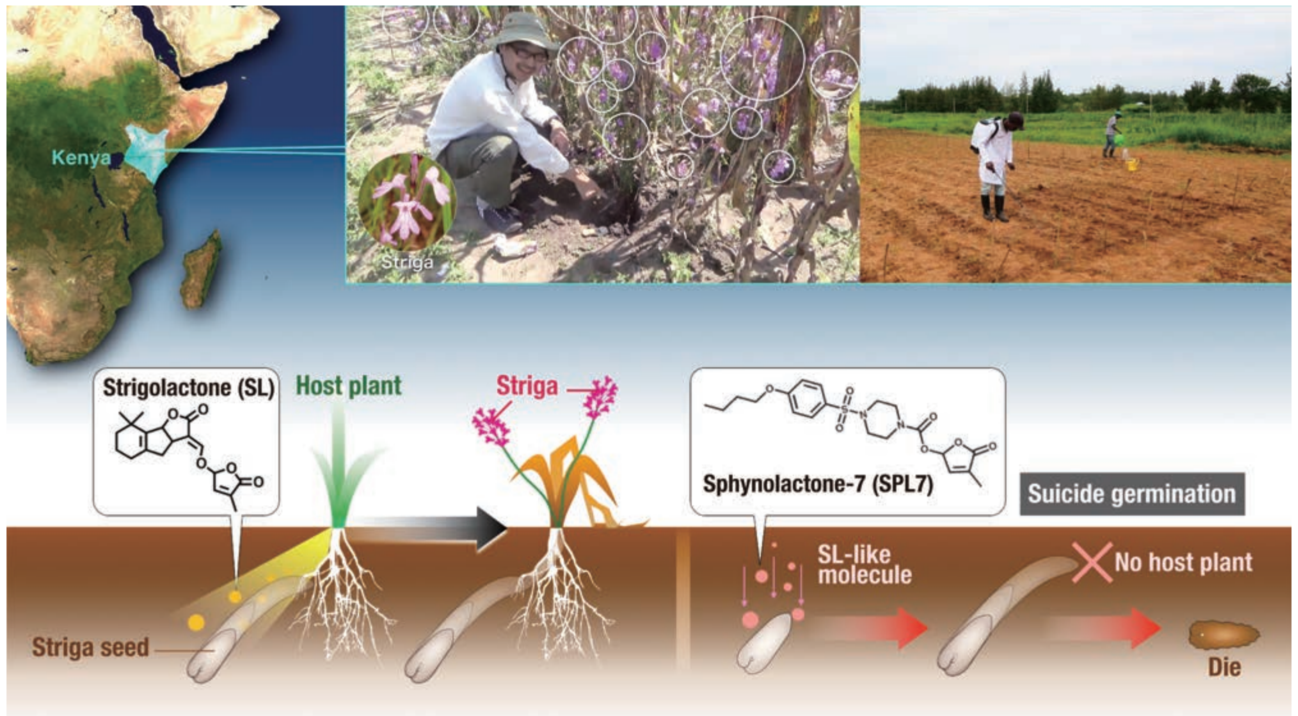
Despite its beautiful purple-pink flowering, Striga is a major threat for food crops affecting global food security. Striga is a parasitic plant that mainly affects Africa, where its roots deprive host crop plants (rice and corn) from their nutrients. The host plant eventually withers, leading to yield losses in approximately 40 million hectares of land, worth over 10 billion U.S. dollars, which affects over 100 million people. Yet, the full mechanism on how Striga detects the presence of the host plants has been unclear and efforts are being made to develop new methods to combat Striga.

Dr. Daisuke Uraguchi (Ooi Group), Dr. Yuichiro Tsuchiya (Kinoshita Group), and their groups have come together to develop a molecule, SPL7, that forcibly germinates Striga seeds at extremely low concentration. SPL stimulates Striga germination at femtomolar (10^{-15} M) range, yet only bound to the strigolactone receptor in Striga. The potency is on par with natural strigolactone, 5-deoxystriogl, which is the strongest germination stimulant to Striga among all commercially available compounds.

Field trials of SPL7 to control Striga growth in a field located in Kenya are ongoing.

Reference:

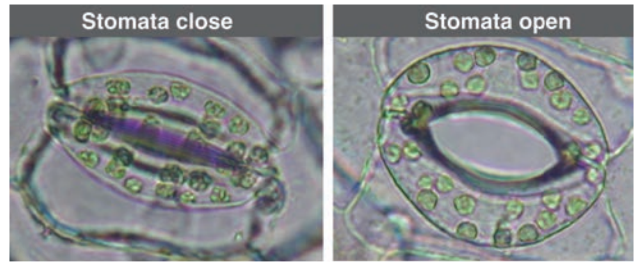
"A femto-molar range suicide germination stimulant for the parasitic plant *Striga hermonthica*" by Daisuke Uraguchi, Keiko Kuwata, Yuh Hijikata, Rie Yamaguchi, Hanae Imaizumi, Sathiyanarayanan AM, Christin Rakers, Narumi Mori, Kohki Akiyama, Stephan Irle, Peter McCourt, Toshinori Kinoshita, Takashi Ooi, Yuichiro Tsuchiya, *Science* **2018**, 362, 6420. DOI:



SL-like molecules work as inducers of suicidal germination to purge the soil of viable Striga seeds before planting the crop seed.

2 Stomata for plant growth and development

1 Enhancement of photosynthesis and plant growth through the promotion of stomatal opening: A step forward towards improving crop production and reducing atmospheric CO_2



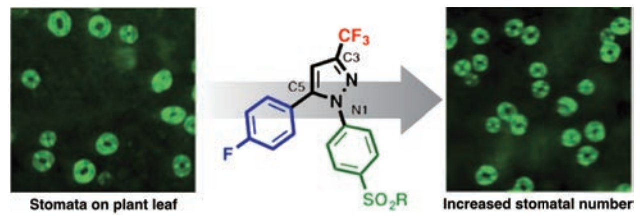
By determining the key factor in regulating photosynthesis and plant growth, Professor Toshinori Kinoshita and his group have succeeded in developing a method to increase photosynthesis (CO_2 uptake) and plant growth through the promotion of stomatal opening in the model plant, *Arabidopsis thaliana*. Enhanced stomatal opening was achieved by overexpressing the plasma membrane H^+-ATPase (enzyme) in guard cells surrounding the stomata. The study is expected to contribute to the promotion of plant production and towards the development of a sustainable low carbon society.

References:

"Overexpression of plasma membrane H^+-ATPase in guard cells promotes light-induced stomatal opening and enhances plant growth" by Yin Wang, Ko Noguchi, Natsuko Ono, Shin-ichiro Inoue, Ichiro Terashima, and Toshinori Kinoshita, *PNAS* **2013**, 111, 533. DOI: 10.1073/pnas.1305438111

"A Raf-like protein kinase BHP mediates blue light-dependent stomatal opening" by Maki Hayashi, Shin-ichiro Inoue, Yoshihisa Ueno, and Toshinori Kinoshita, *Sci. Rep.* **2017**, 7, 45586. DOI: 10.1038/srep45586

2 More mouths can be fed by boosting number of plant pores: Discovery of small molecules that increases the number of stomata on plant leaves

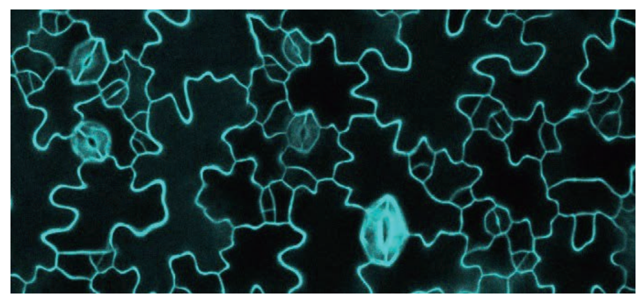


Professors Keiko Torii, Kenichiro Itami and their groups have synthesized a new bioactive small molecule that has the ability to increase stomata numbers on flowering plants (*Arabidopsis*) without stunting their growth. Molecules were synthesized using a rapid palladium-catalyzed C–H arylation methodology developed by the Itami group. The team's new discovery could help elucidate the stomatal development mechanism in plants.

References:

"Discovery of synthetic small molecules that enhance the number of stomata: C–H functionalization chemistry for plant biology" by Asraa Ziadi, Naoyuki Uchida, Hiroe Kato, Rina Hisamatsu, Ayato Sato, Shinya Hagihara, Kenichiro Itami and Keiko U. Torii, *Chem. Commun.* **2017**, 53, 9632. DOI: 10.1039/C7CC04526C

3 Scientists reveal why plant stomata has its particular lip shape: Stomata's master regulator gene MUTE demonstrates how organisms develop their shape

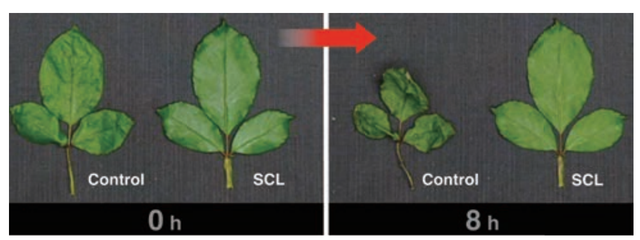


Professor Keiko Torii and her collaborators have revealed the mechanism on how stomata in land plants are formed through a single symmetric cell division. The scientists discovered that a gene in plants known as MUTE orchestrates stomatal development. As the regulation style by the MUTE gene can be observed in a similar manner in the gene expression mechanism of animals and enzymes, this research provides insight to how various organisms have developed their shape. Developmental regulation of the stomata is expected to contribute towards crop improvement.

References:

"MUTE Directly Orchestrates Cell-State Switch and the Single Symmetric Division to Create Stomata" by Soon-Ki Han, Xingyun Qi, Kei Sugihara, Jonathan H. Dang, Takaho A. Endo, Kristen L. Miller, Eun-Deok Kim, Takashi Miura, Keiko U. Torii, *Dev. Cell* **2018**, 45, 303. DOI: 10.1016/j.devcel.2018.04.010

4 Discovery of compounds that keep plants fresh: Controlling plant pore openings for drought tolerance and delay in leaf withering



Rose leaves sprayed with stomata closing compound (SCL) withered less compared to rose leaves without spraying (control) after 8 hours.

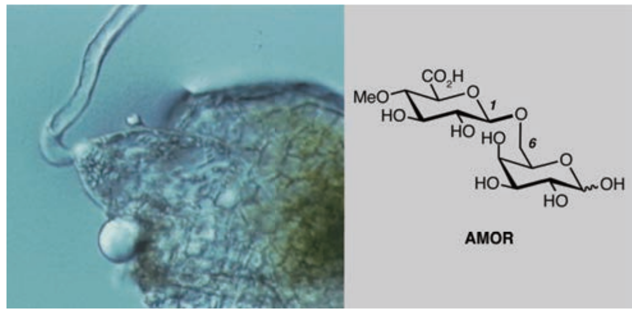
Professor Toshinori Kinoshita and his team have discovered new compounds that can control stomatal movements in plants. Some of the compounds have shown to prevent leaves from drying up and suppress withering when sprayed onto rose and oat leaves. Further investigation could lead to the development of new compounds that can be used to extend the freshness of cut flowers and flower bouquets.

References:

"Identification and Characterization of Compounds that Affect Stomatal Movements" by Shigeo Toh, Shinpei Inoue, Yosuke Toda, Takahiro Yuki, Kyota Suzuki, Shin Hamamoto, Kohei Fukatsu, Saya Aoki, Mami Uchida, Eri Asai, Nobuyuki Uzumi, Ayato Sato and Toshinori Kinoshita, *Plant Cell Physiol.* **2018**, 59, 1568. DOI: 10.1093/pcp/pcy061

3 Pollen tube attraction and fertilization

1 AMOR, a love potion for plant fertilization: Discovery and synthesis of AMOR sugar chains that activate pollen tube



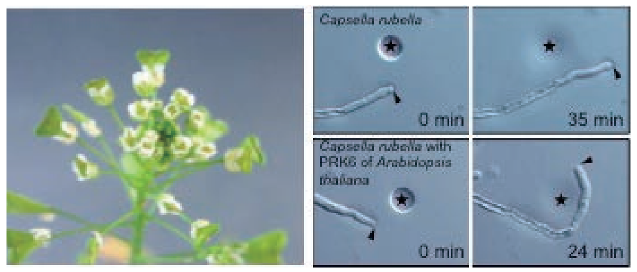
Left: Pollen tube activation with AMOR (in *Torenia fournieri*)
Right: Structure of AMOR disaccharide

Professor Tetsuya Higashiyama and his group have succeeded in discovering AMOR (**A**ctivation **Mo**lecule for **R**esponse-Capability), a sugar chain molecule that increases the fertilization efficiency in *Torenia fournieri* plants. AMOR was found to be responsible for activating pollen tubes leading to fertilization. The word AMOR is taken from the Latin word for "love" and "cupid", thus illustrating its function of bringing female and male organs together. Through collaboration with Professor Kenichiro Itami's group, the team has synthesized a disaccharide, i.e. a double sugar, which exhibits the same properties as AMOR. This discovery is expected to lead to advances in improving plant fertilization efficiency as well as open new doors in carbohydrate chemistry for applications in plant science.

References:

"The AMOR arabinogalactan sugar chain induces pollen-tube competency to respond to ovular guidance" by Akane G. Mizukami, Rie Inatsugi, Jiao Jiao, Toshihisa Kotake, Keiko Kuwata, Kento Ootani, Satohiro Okuda, Subramanian Sankaranarayanan, Yoshikatsu Sato, Daisuke Maruyama, Hiroaki Iwai, Estelle Garénaux, Chihiro Sato, Ken Kitajima, Yoichi Tsumuraya, Hitoshi Mori, Junichiro Yamaguchi, Kenichiro Itami, Narie Sasaki and Tetsuya Higashiyama, *Curr. Biol.* **2016**, 26, 1091. DOI: 10.1016/j.cub.2016.02.040

2 Where males sense females in plants: Unraveling the unknown receptors and mechanism for fertilization in plants



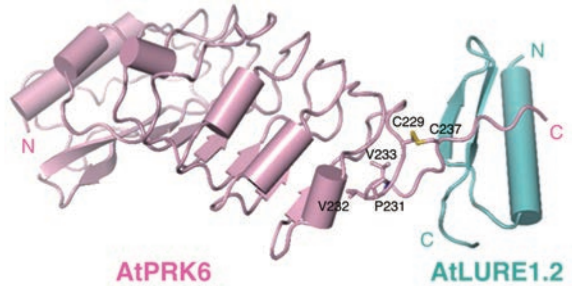
Left: *Capsella rubella*
Right: *C. rubella* pollen tube attraction to *Arabidopsis thaliana* LURE before (top) and after (bottom) introducing *A. thaliana* PRK6

Pollen tubes are attracted by LURE peptides, which are produced from ovules, to bring about fertilization. Dr. Hidenori Takeuchi and Professor Tetsuya Higashiyama have now revealed for the first time, the receptor in pollen tubes that is required to detect LURE in the model plant, *Arabidopsis thaliana*. The discovery of this unknown mechanism of plant fertilization may allow for improvements in the efficiency of pollen tube growth to be made, resulting in an increased success rate of fertilization. In addition, this study may also generate new methods to enable cross-fertilization between different plant species to generate new crops.

References:

"Tip-localized receptors control pollen tube growth and LURE sensing in *Arabidopsis*" by Hidenori Takeuchi and Tetsuya Higashiyama, *Nature* **2016**, 531, 245. DOI: 10.1038/nature17413

3 Unlocking the mystery of pollen tube guidance: Solving the cocrystal structure of a pollen tube attractant and its receptor



Crystal structure of LURE bound to its receptor protein PRK6 (in *Arabidopsis thaliana*)

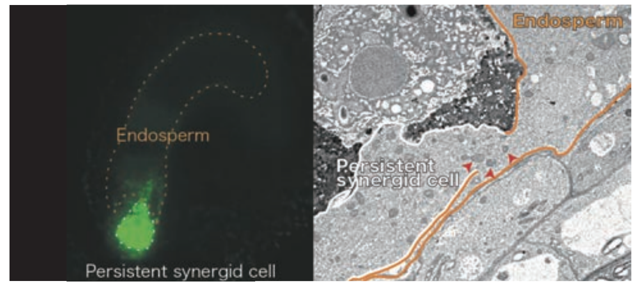
Pollen tube guidance towards the ovule is an important step for fertilization in flowering plants. In order for this to happen, a pollen tube attractant peptide LURE guides the pollen tube precisely to the ovule. Professor Tetsuya Higashiyama and his international colleagues have succeeded in analyzing for the first time, the crystal structure of LURE (key) bound to its receptor protein PRK6 (**p**ollen **r**eceptor-like **k**inase 6; lock). This unique binding scheme between LURE and PRK6 appears to be involved in the precise control mechanism for the direction of pollen tube growth. Further elucidation of this key and lock mechanism may lead to applications in generating useful hybrid plant species.

References:

"Structural basis for receptor recognition of pollen tube attraction peptides" by Xiaoxiao Zhang, Weijia Liu, Takuya T. Nagae, Hidenori Takeuchi, Heqiao Zhang, Zhifu Han, Tetsuya Higashiyama and Jijie Chai, *Nat. Commun.* **2017**, 8, 1331. DOI: 10.1038/s41467-017-01323-8

4 Plant growth and morphology

1 Cell fusion 'eats up' the 'attractive cell' in flowering plants: Solving the mystery of the progression of fertilization in *Arabidopsis* by live cell imaging



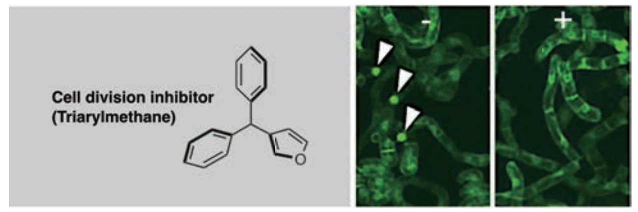
A novel cell to cell fusion in a fertilized ovule in *Arabidopsis thaliana*

Flowering plants naturally know when they need to spare or eliminate their cells. An international team led by Dr. Daisuke Maruyama and Professor Tetsuya Higashiyama, has examined plant cells of the ovule by live imaging to reveal a novel cell-elimination system based on an unusual cell fusion, thereby uncovering the mechanism by which flowering plants prevent further attraction of multiple pollen tubes after successful fertilization.

References:

"Rapid elimination of the persistent synergid through a cell fusion mechanism" by Daisuke Maruyama, Ronny Völz, Hidenori Takeuchi, Toshiyuki Mori, Tomoko Igawa, Daisuke Kurihara, Tomokazu Kawashima, Minako Ueda, Masaki Itoh, Masaaki Umeda, Shuh-ichi Nishikawa, Rita Groß-Hardt and Tetsuya Higashiyama, *Cell* **2015**, 161, 907. DOI: 10.1016/j.cell.2015.03.018

2 Three rings stop cell division in plants: Development of a triarylmethane compound for possible control of plant growth



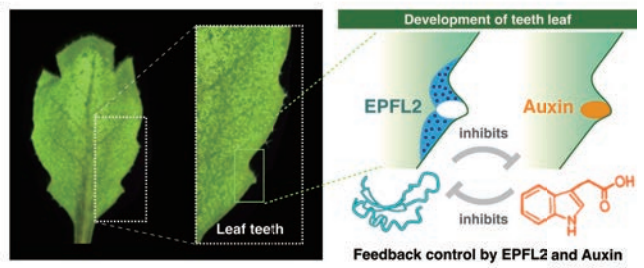
Structure of a cell division inhibitor (triarylmethane) and images of cell division activity in plant cells. Arrows show cells arising from cell division. (-): Cells without the addition of the inhibitor ; (+): Cells with addition of the inhibitor

Drs. Minako Ueda and Masakazu Nambo and their team have succeeded in developing a new compound, a triarylmethane, that can rapidly inhibit cell division in plants. This compound was found to selectively inhibit cell division in plant cells versus animal cells, and shows reversible inhibitory properties. This triarylmethane could therefore be a potential candidate for developing into an agrochemical for the selective control of plant growth..

References:

"Combination of Synthetic Chemistry and Live-Cell Imaging Identified a Rapid Cell Division Inhibitor in Tobacco and *Arabidopsis thaliana*" by Masakazu Nambo, Daisuke Kurihara, Tomomi Yamada, Taeko Nishiwaki-Ohkawa, Naoya Kadofusa, Yusuke Kimata, Keiko Kuwata, Masaki Umeda and Minako Ueda, *Plant Cell Physiol.* **2016**, 57, 2255. DOI: 10.1093/pcp/pcw140

3 Unlocking the mystery on how plant leaves grow their teeth: Discovery of EPFL2 peptide (key) and its receptor (lock) that make zigzag edges on leaves

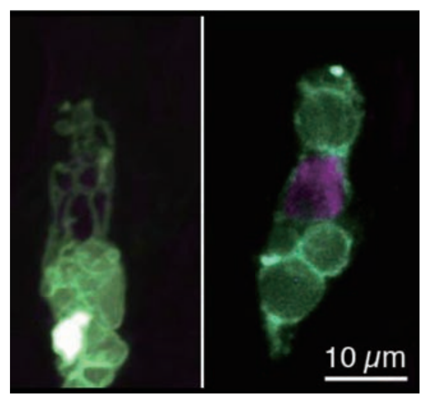


Dr. Naoyuki Uchida, Professor Keiko Torii and their group have discovered the key element, an EPFL2 peptide, that is responsible for creating the teeth-like shapes on plant leaves. The zigzag edges of leaves, so-called leaf teeth, are important for making the characteristic shapes of each leaf. This study illustrates the unexplored mechanism of leaf teeth formation and will shed light on how leaves have developed to become the shapes that they are today.

References:

"A secreted peptide and its receptors shape the auxin response pattern and leaf margin morphogenesis" by Toshiaki Tameshige, Satoshi Okamoto, Jin Suk Lee, Mitsuhiro Aida, Masao Tasaka, Keiko U. Torii and Naoyuki Uchida, *Curr. Biol.* **2016**, 26, 2478. DOI: 10.1016/j.cub.2016.07.014

4 Vacuole dynamics in zygotes revealed with a powerful live imaging system: The importance of vacuole migration towards healthy plant development



Vacuole and nucleus in *Arabidopsis* zygotes. The wild type (left) properly polarized the zygote, but a vacuole mutant (right) failed and thus formed a more symmetric zygote.

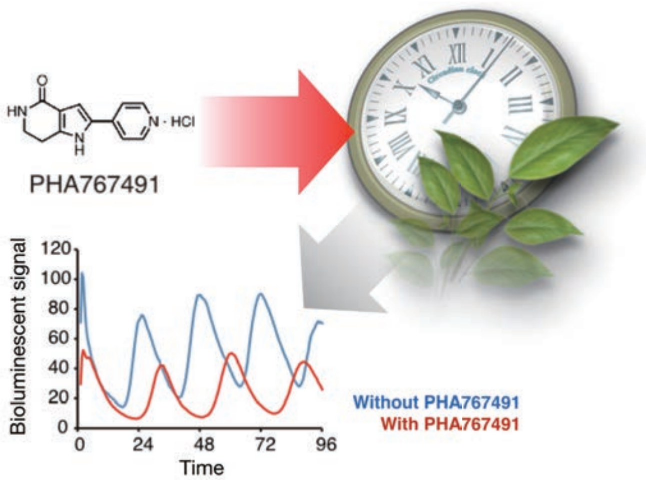
Dr. Minako Ueda, Professor Tetsuya Higashiyama and their team have discovered that the movement of vacuoles is involved in the asymmetry of plants fertilized eggs. As a result of observing the movement of a vacuole in a fertilized egg in real time, the research team observed that when fertilization occurs the vacuole rapidly dehydrates and becomes smaller and the vacuole moves in a specific direction while dynamically changing its shape. Moreover, if this mechanism is lost, not only can the zygotes no be divided asymmetrically, but the final shape of the plant becomes abnormal; therefore, the importance of the dynamic movement of the vacuole has become clear. This discovery is expected to help clarify the mechanism of plant formation in the future.

References:

"Polar vacuolar distribution is essential for accurate asymmetric division of *Arabidopsis* zygotes" by Yusuke Kimata, Takehide Kato, Takumi Higaki, Daisuke Kurihara, Tomomi Yamada, Shoji Segami, Miyo Terao Morita, Masayoshi Maeshima, Seiichiro Hasezawa, Tetsuya Higashiyama, Masao Tasaka and Minako Ueda, *PNAS* **2019**, 116, 2338. DOI: 10.1073/pnas.1814160116

5 Body clocks of animals and plants

1 Casein kinase 1 family regulates PRR5 and TOC1 in the *Arabidopsis* circadian clock

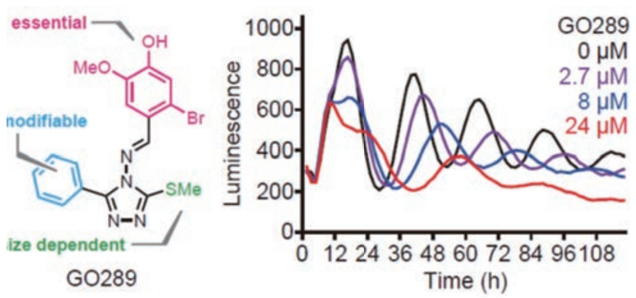


Using small molecules, an international team led by Dr. Norihito Nakamichi and Professor Toshinori Kinoshita have revealed the mechanism of *Arabidopsis* circadian clock. Organisms have acquired a genetically integrated circadian clock to adapt to day-night and seasonal changes. However, the mechanism of the circadian clock of land plants was not deciphered until now, due to presence of a large number of paralogous genes from whole-genome duplication processes during evolution. The research group has proved that multiple members of the casein kinase I (CK1) family is involved in *Arabidopsis* circadian clock, by using a molecular probe of the small molecule that lengthens period of the circadian clock. In addition, substrate proteins of CK1 for period lengthening was identified. Given that plant circadian clock controls many physiological processes including flowering time regulation, further discovery of molecules modulating circadian clock has profound implication of plant improvement, which is important as one of our adaptation strategies to global environmental change.

References:

"Casein kinase 1 family regulates PRR5 and TOC1 in the *Arabidopsis* circadian clock" by Takahiro N Uehara, Yoshiyuki Mizutani, Keiko Kuwata, Tsuyoshi Hirota, Ayato Sato, Junya Mizoi, Saori Takao, Hiromi Matsuo, Takamasa Suzuki, Shogo Ito, Ami N Saito, Taeko Nishiwaki-Ohkawa, Kazuka Yamaguchi-Shinozaki, Takashi Yoshimura, Steve Kay, Kenichiro Itami, Toshinori Kinoshita, Junichiro Yamaguchi, Norihito Nakamichi, *PNAS* **2019**, 116, 11528. DOI: 10.1073/pnas.1903357116

2 Discover new compound that changes the speed of the body clock: Suppresing the grwoth of cultured acute myeloid leukemia cells

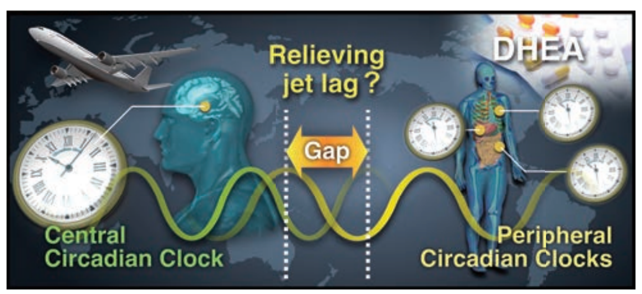


Our biological circadian clock regulates various daily rhythms, such as sleep/wake rhythm, body temperature, and metabolism. Disruption of the circadian rhythm is linked with sleep disorders, cancer and other diseases. The groups led by Dr. Tsuyoshi Hirota and Professor Kenichiro Itami have successfully identified GO289, which greatly lengthened circadian period. Found using a cell-based phenotypic screen, the new compound is a potent and selective inhibitor of casein kinase 2 (CK2). Furthermore, GO289 exhibited cell type–dependent inhibition of cancer cell growth that correlated with cellular clock function. This research open doors to molecule-based solutions for circadian-related diseases.

References:

"Cell-based screen identifies a new potent and highly selective CK2 inhibitor for modulation of circadian rhythms and cancer cell growth" by Tsuyoshi Oshima, Yoshimi Niwa, Keiko Kuwata, Ashutosh Srivastava, Tomoko Hyoda, Yoshiki Tsuchiya, Megumi Kumagai, Masato Tsuyuguchi, Teruya Tamaru, Akiko Sugiyama, Natsuko Ono, Norjin Zolboot, Yoshiki Aikawa, Shunsuke Oishi, Atsushi Nonami, Fumio Arai, Shinya Hagihara, Junichiro Yamaguchi, Florence Tama, Yuya Kunisaki, Kazuhiro Yagita, Masaaki Ikeda, Takayoshi Kinoshita, Steve A. Kay, Kenichiro Itami, Tsuyoshi Hirota, *Science Advances*, **2019**, 5, eaau9060, DOI: 10.1126/sciadv.aau9060

3 Revisiting existing drugs finds molecules that control body clocks: Discovery of an anti-aging supplement that reduces jet lag in mice



Molecules for entrainment of central and peripheral circadian clocks may lead to the future drugs for circadian rhythms disorders and symptoms such as jet lag.

Through drug repurposing, a team of researchers led by Professor Takashi Yoshimura has discovered compounds that can either shorten or lengthen the circadian rhythm in human cells. They identified that DHEA (dehydroepiandrosterone), one of the most abundant hormones in humans, also known as a common anti-aging supplement demonstrated period shortening in cells and phase shifting activities in vivo. When it 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 rhythm disorders.

References:

"Identification of circadian clock modulators from existing drugs" by T. Katherine Tamai, Yusuke Nakane, Wataru Ota, Akane Kobayashi, Masateru Ishiguro, Naoya Kadofusa, Keisuke Ikegami, Kazuhiro Yagita, Yasufumi Shigeyoshi, Masaki Sudo, Taeko Nishiwaki-Ohkawa, Ayato Sato, and Takashi Yoshimura, *EMBO Mol. Med.* **2018**, 10, e8724. DOI: 10.15252/emmm.201708724

6 Animal behavior and seasonality

1 Bossy rooster takes the lead vocal of cock-a-doodle-doo: Social ranking in roosters affects order of crowing

From ancient times, people have been aware of the rooster's "cock-a-doodle-doo" that marks the break of dawn, but has anyone wondered who crows first? Professor Takashi Yoshimura and his group have revealed that there is actually a systematic rule based on social ranking that determines the order of crowing in roosters. They have also found that a rooster's circadian clock is involved in their crowing at dawn.

References:

"The highest-ranking rooster has priority to announce the break of dawn" by Tsuyoshi Shimmura, Shosei Ohashi, and Takashi Yoshimura, *Sci. Rep.* **2015**, 5, 11683. DOI: 10.1038/srep11683

"Circadian clock determines the timing of rooster crowing" by Tsuyoshi Shimmura and Takashi Yoshimura, *Curr. Biol.* **2013**, 23, R231. DOI: 10.1016/j.cub.2013.02.015

2 Shining light on the 100-year mystery of birds sensing spring for offspring

Professor Takashi Yoshimura and his group have identified for the first time, a key photoreceptor cell deep inside the brain of birds, such as quails, which takes the role of eyes in humans by directly responding to light and regulates breeding activity according to seasonal changes. The study is expected to contribute to the improvement of production of animals as well as deepen our understanding on the evolution of eyes and photoreceptors.

References:

"Intrinsic photosensitivity of a deep brain photoreceptor" by Yusuke Nakane, Tsuyoshi Shimmura, Hideki Abe and Takashi Yoshimura, *Curr. Biol.* **2014**, 24, R596. DOI: 10.1016/j.cub.2014.05.038

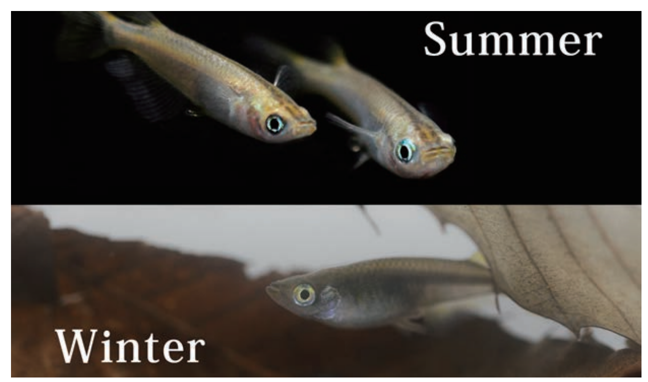
3 One hormone, two roles: Sugars differentiate seasonality and metabolism

Using mice, Professor Takashi Yoshimura and his group have discovered the mechanism on how a single hormone manages to trigger two different functions, i.e. seasonal sensing and metabolism, without any cross activity. Their studies uncovered the elegant strategy of organisms, where tissue-specific glycosylation and subsequent immune recognition is used to impart two distinctive functions on a single hormone.

References:

"Tissue-specific post-translational modification allows functional targeting of thyrotropin" by Keisuke Ikegami, Xiao-Hui Liao, Yuta Hoshino, Hiroko Ono, Wataru Ota, Yuka Ito, Taeko Nishiwaki-Ohkawa, Chihiro Sato, Ken Kitajima, Masayuki Iigo, Yasufumi Shigeyoshi, Masanobu Yamada, Yoshiharu Murata, Samuel Refetoff, Takashi Yoshimura, *Cell Rep.* **2014**, 9, 801. DOI: http://dx.doi.org/10.1016/j.celrep.2014.10.006

4 Discovery of dynamic seasonal changes in color perception: The small fish "medaka" shows large differences in color perception in summer and winter



Professor Takashi Yoshimura and his group have discovered that Japanese medaka fish show a difference in color perception according to the season. Previous studies have also reported that human color perception changes according to the season. This phenomenon of seasonal change in color perception is therefore not limited to medaka and may be a phenomenon widely preserved in various animals.

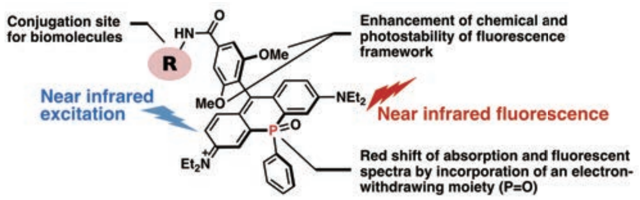
References:

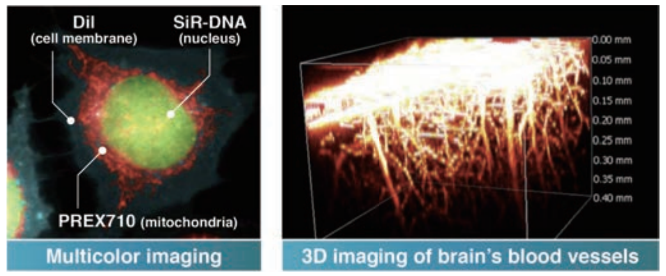
"Dynamic plasticity in phototransduction regulates seasonal changes in color perception" by Tsuyoshi Shimmura, Tomoya Nakayama, Ai Shinomiya, Shoji Fukamachi, Masaki Yasugi, Eiji Watanabe, Takayuki Shimo, Takumi Senga, Toshiya Nishimura, Minoru Tanaka, Yasuhiro Kamei, Kiyoshi Naruse and Takashi Yoshimura, *Nat. Commun.* **2017**, 8, 412. DOI: 10.1038/s41467-017-00432-8

7 Molecules for live cell imaging

1

Taking a deep look: a near infrared fluorescent dye for long term bioimaging: Promising photostable tool for single molecule tracking, in vivo deep tissue imaging, and multicolor imaging





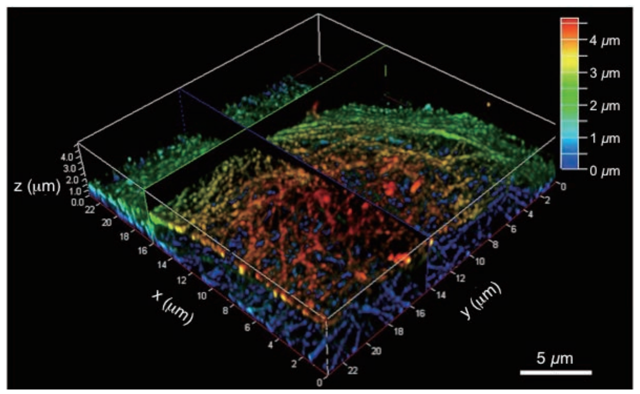
A team of researchers from ITbM (Professor Shigehiro Yamaguchi, Dr. Masayasu Taki, etc.) and RIKEN and Ehime University have succeeded in developing a photostable fluorescent dye that allows long term bioimaging of living cells in the near infrared region. In conventional fluorescence imaging of biological samples using visible light, it is difficult to observe deep blood vessels and organs due to cellular dysfunction, light irradiation, and increased noise due to autofluorescence. The joint research team succeeded in developing an extremely chemically- and photo-stable near-infrared fluorescence dye, PREX 710, by the incorporation of a phosphine oxide moiety to a rhodamine dye. This new labeling agent is useful for long-term single molecule and deep imaging of blood vessels in the brain because it has a site that can bind to biomolecules. This work has future application to life sciences and medical research.

References:

"A Highly Photostable Near-Infrared Labeling Agent Based on a Phospha-rhodamine for Long-Term and Deep Imaging" by Marek Grzybowski, Masayasu Taki, Kieko Senda, Yoshikatsu Sato, Tetsuro Ariyoshi, Yasushi Okada, Ryosuke Kawakami, Takeshi Imamura, and Shigehiro Yamaguchi, *Angew. Chem. Int. Ed.* **2018**, 57, 10137. DOI: 10.1002/anie.201804731

2

Super-photostable fluorescent labeling agent for super-resolution microscopy: A powerful tool for 3D and multicolor STED imaging of cellular ultrastructure

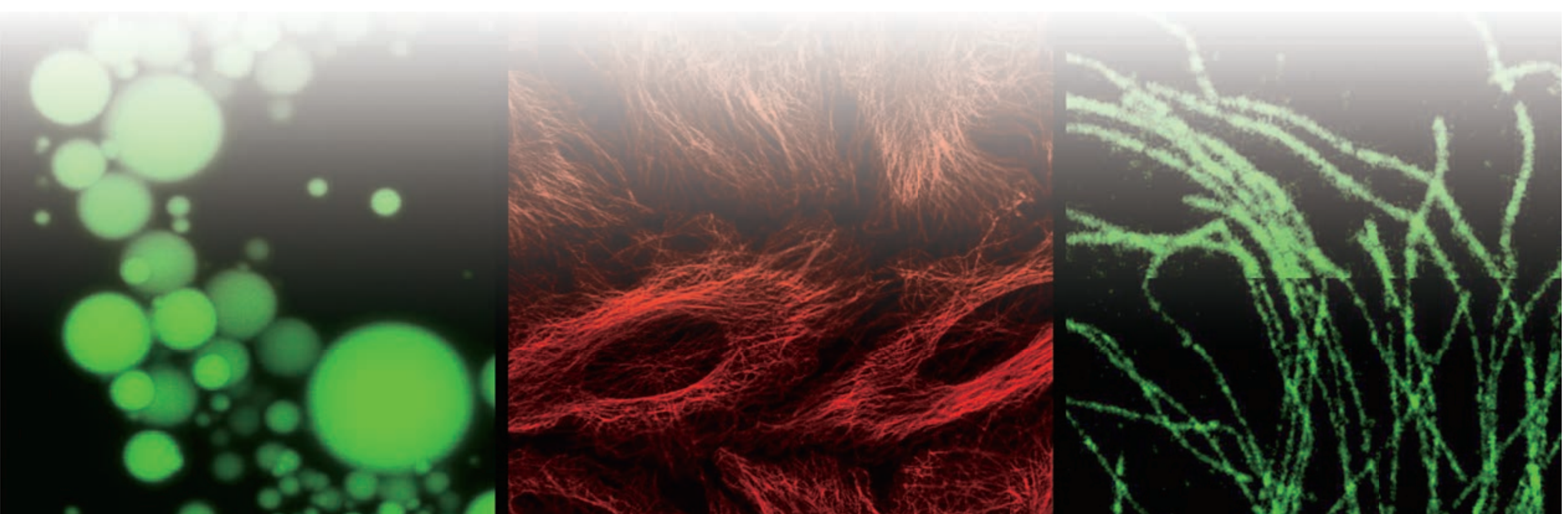


3D imaging of the cytoskeleton with PB430

Drs. Masayasu Taki, Yoshikatsu Sato (Live Imaging Center), Professors Shigehiro Yamaguchi, Tetsuya Higashiyama and their groups have developed a super-photostable fluorescent dye, PhoxBright 430 (PB430), to visualize cellular ultrastructure by super resolution microscopy. The exceptional photostability of this new dye enables continuous STED imaging. Together with its ability to fluorescently label proteins, PB430 can be used in the 3D construction and multicolor imaging of biological structures. The unique properties of PB430 make it a powerful tool to reveal the structures and functions of cells, and has the potential to be applied for prolonged visualization of the movement of organelles and molecules within cells.

References:

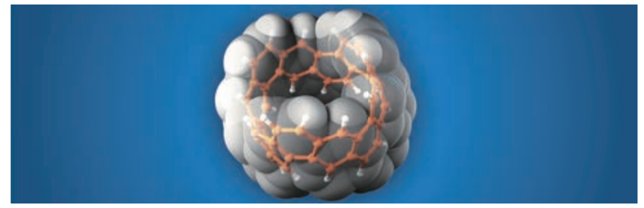
"Super-Photostable Phosphole-Based Dye for Multiple-Acquisition Stimulated Emission Depletion Imaging" by Chenguang Wang, Masayasu Taki, Yoshikatsu Sato, Aiko Fukazawa, Tetsuya Higashiyama, and Shigehiro Yamaguchi, *J. Am. Chem. Soc.* **2017**, 139, 10374. DOI: 10.1021/jacs.7b04418



8 Organic synthesis and catalysis

1

At last: beautiful, consistent carbon belts
Synthesis of a carbon nanobelt with potential applications in nanotechnology



Chemists have tried to synthesize carbon nanobelts for more than 60 years, but none have succeeded until now. Professor Kenichiro Itami and his group have reported the first total synthesis of a carbon nanobelt. Carbon nanobelts are expected to serve as a useful template for building carbon nanotubes and would open a field of nanocarbon science.

References:

"Synthesis of a Carbon Nanobelt" by Guillaume Povie, Yasutomo Segawa, Taishi Nishihara, Yuhei Miyauchi, Kenichiro Itami, *Science* **2017**, 356, 172. DOI: 10.1126/science.aam8158

2

"Zipping-up" rings to make nanographenes: A fast and efficient method for graphene nanoribbon synthesis

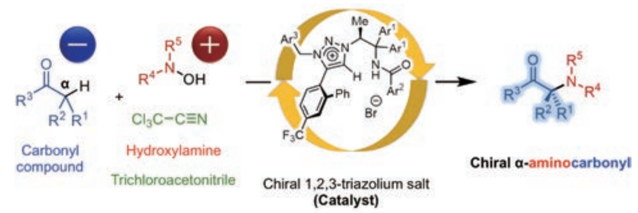
Professor Kenichiro Itami and his group have now developed a facile route to form nanographenes in a controlled fashion. This simple and powerful method for nanographene synthesis could help generate a range of novel optoelectronic materials, such as organic electroluminescent displays and solar cells.

References:

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

3

Rapid synthesis towards optically active *α*-aminocarbonyl therapeutics: New catalytic asymmetric reaction directly installs amines into carbonyl compounds



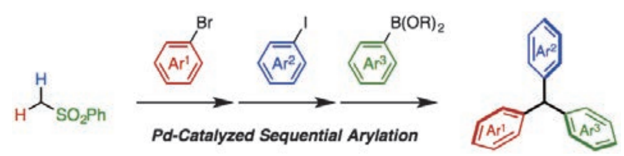
Professor Takashi Ooi and his group have developed a new reaction to directly install amines into carbonyl compounds using their unique phase-transfer catalyst. This unprecedented method leads to the rapid formation of optically active (chiral) *α*-aminocarbonyls, which are structural moieties found in many biologically active compounds and in therapeutics, such as anti-malarial and anti-HIV agents.

References:

"A Modular Strategy for the Direct Catalytic Asymmetric α-Amination of Carbonyl Compounds" by Kohsuke Ohmatsu, Yuichiro Ando, Tsubasa Nakashima, Takashi Ooi, *Chem* **2016**, 1, 802. DOI: 10.1016/j.chempr.2016.10.012

4

Efficient synthesis of triarylmethanes: Sequential incorporation of aryl rings by palladium catalysts



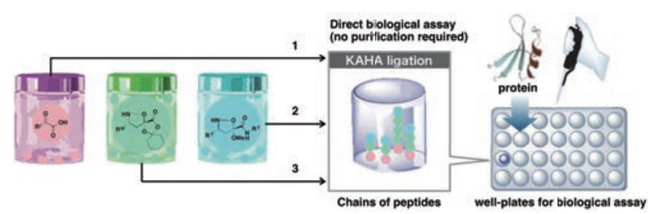
Dr. Masakazu Nambo and Professor Cathleen Crudden have synthesized unsymmetric triarylmethanes, which a privileged structure, from methyl phenyl sulfone as an inexpensive and readily available template. The three aryl groups were installed through two sequential palladium-catalyzed C–H arylation reactions, followed by an arylative desulfonation reaction.

References:

"Modular Synthesis of Triarylmethanes through Palladium-Catalyzed Sequential Arylation of Methyl Phenyl Sulfone" by Masakazu Nambo, Cathleen M. Crudden, *Angew. Chem. Int. Ed.* **2013**, 53, 742. DOI: 10.1002/anie.201307019

5

"Pick 'n' Mix" chemistry to grow cultures of bioactive molecules



Professor Jeffrey Bode and his group have developed a new method, "synthetic fermentation", to build large libraries of bioactive peptide molecules, which can be used directly for biological assays. This is achieved by simply mixing a small number of building blocks (amino acid derivatives) in water.

References:

"Synthetic fermentation of bioactive non-ribosomal peptides without organisms, enzymes or reagents" by Yi-Lin Huang and Jeffrey W. Bode, *Nature Chem.* **2014**, 6, 877. DOI: 10.1038/nchem.2048

Promoting research: ITbM administration

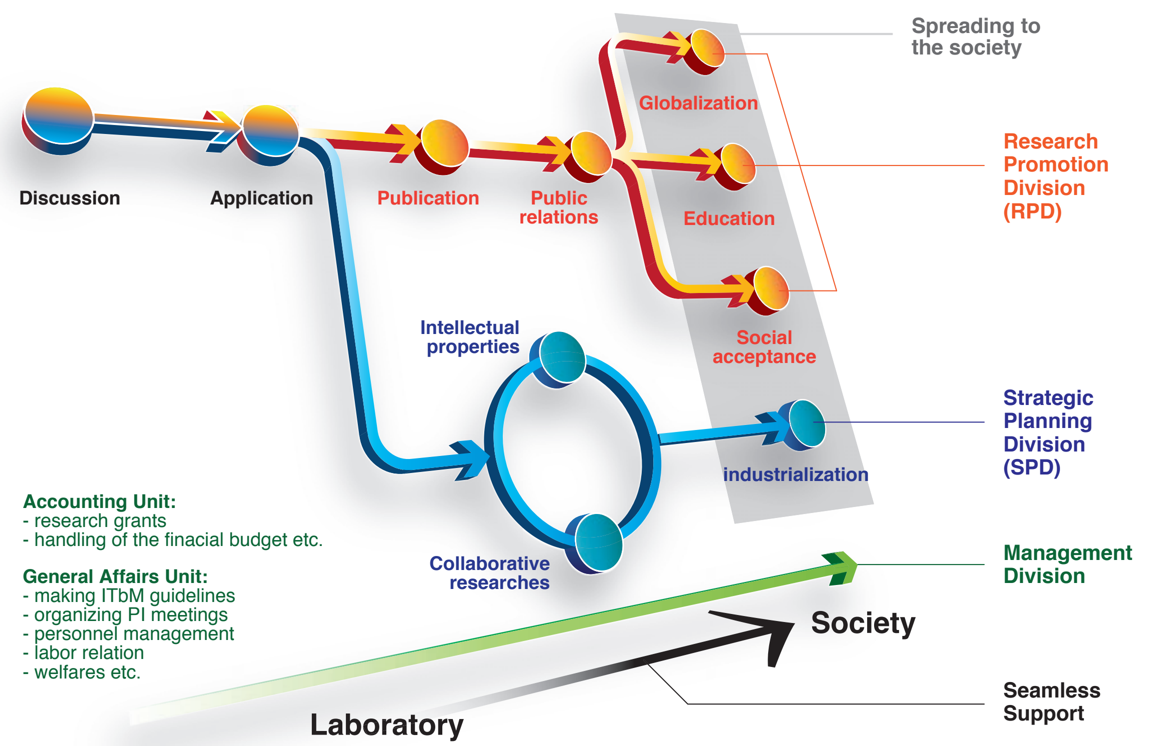
The ITbM Administrative Department plays a crucial role in supporting ITbM. Three divisions have been established: Management, Research Promotion Division (RPD) and Strategic Planning Division (SPD). The Management Division deals with general affairs and accounting; the RPD works closely alongside researchers to promote ITbM's research through public relations, outreach activities and organization of events; and the SPD is involved in intellectual properties and social implementation of ITbM's research outcomes.

The Management Division is composed of the general affairs unit and the accounting unit, both of which carry out duties equivalent to university administration. The general affairs unit is responsible for making ITbM's guidelines, organizing PI meetings, personnel management and labor relation, as well as welfares. The accounting unit is in charge of matters related to research grants, as well as the handling of financial budgets that includes personnel expenses, honorariums, travel expenses and supplies.

The goal of the RPD is to create a bridge between researchers and university administration, and is involved in a wide range of activities. This includes support in the discovery of new seeds for collaborative research and obtaining research grants, support for overseas researchers' everyday life in Japan, and overall promotion of the institute through the organization of various events, such as symposia, seminars, workshops and meetings, along with internal/external communication.

In order to promote social implementation of the technologies developed at ITbM, the SPD was established in May 2016. SPD plays a role in contributing to society by feeding research outcomes into society. This division supports evaluation of inventions, patent applications, collaborative researches with domestic and overseas companies, license agreements, strategic construction of partnerships with companies aiming for industrialization/commercialization, running the ITbM Consortium and establishment of venture business, etc. Both RPD and SPD consisting of members who hold advanced degrees in science/engineering, support and promote ITbM research activities from basic to social stage consistently and seamlessly, cooperating with each other and using the expertise, resources and skills, to receive international recognition as a research center that conducts interdisciplinary research between chemistry and biology.

The ITbM Administrative Department provides both English and Japanese support to all ITbM members, both overseas and Japanese researchers. This Institute aims to create an international atmosphere, where researchers are comfortable and able to fully focus on their research.



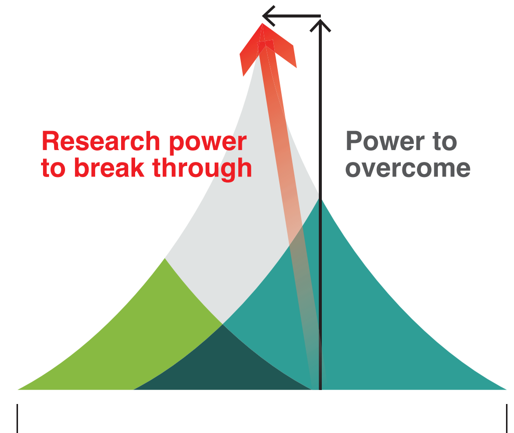
GTR
Transformative Chem-Bio Research
Nagoya University

Graduate Program of Transformative Chem-Bio Research

The best way to acquire real research power is to accumulate experience with promoting and accomplishing exciting high-quality research on your own initiative

Our new graduate program, GTR (Graduate Program of Transformative Chem-Bio Research), aims to train scholars who will pioneer interdisciplinary frontiers in the areas of chemistry and life science. In order to achieve sustainable development of society, many challenges must be overcome, including environmental and energy problems, stable food production, the development of materials leading to industrial and technological innovations, and life science research that contributes to health. To address these issues faced by science and society, the roles of chemistry and life science research are becoming increasingly important. To break through these issues, both advances in research in each field and promotion of interdisciplinary research are necessary.

To bridge the gaps between traditional disciplines, we need outstanding "research power to break through," which consists of two elements: "the power to overcome" and "the power to connect." The former is based on experience, confidence, and solid practical knowledge and skills that can be fostered through promoting and accomplishing high-quality research on important topics. On the other hand, the latter leads to the creation of innovative ideas through free and vigorous discussions across research fields.
The GTR program provides a practical course for acquiring these important research capabilities through challenge to exciting interdisciplinary research in diverse research environments in which each student benefits from the guidance of two mentors.



Nagoya University:
Institute of Transformative Bio-Molecules (ITbM); Graduate School of Science; Graduate School of Engineering; Graduate School of Bioagricultural Sciences; Graduate School of Pharmaceutical Sciences

Cooperative Institutions:
RIKEN, Institute for Molecular Science, National Institute for Basic Biology (Graduate University for Advances Studies); Kaneka Corp.; Konica Minolta Inc.; Japan Tobacco Inc., Plant Innovation Center;
ITbM consortium (16 companies, 2019)

http://gtr.itbm.nagoya-u.ac.jp/en/index.html

Accomplishments: Awards and Honors

Keiko Torii
Saruhashi Award

Kenichiro Itami
Arthur C. Cope Scholar Award

Wolf Frommer
Tsuming Tu Award

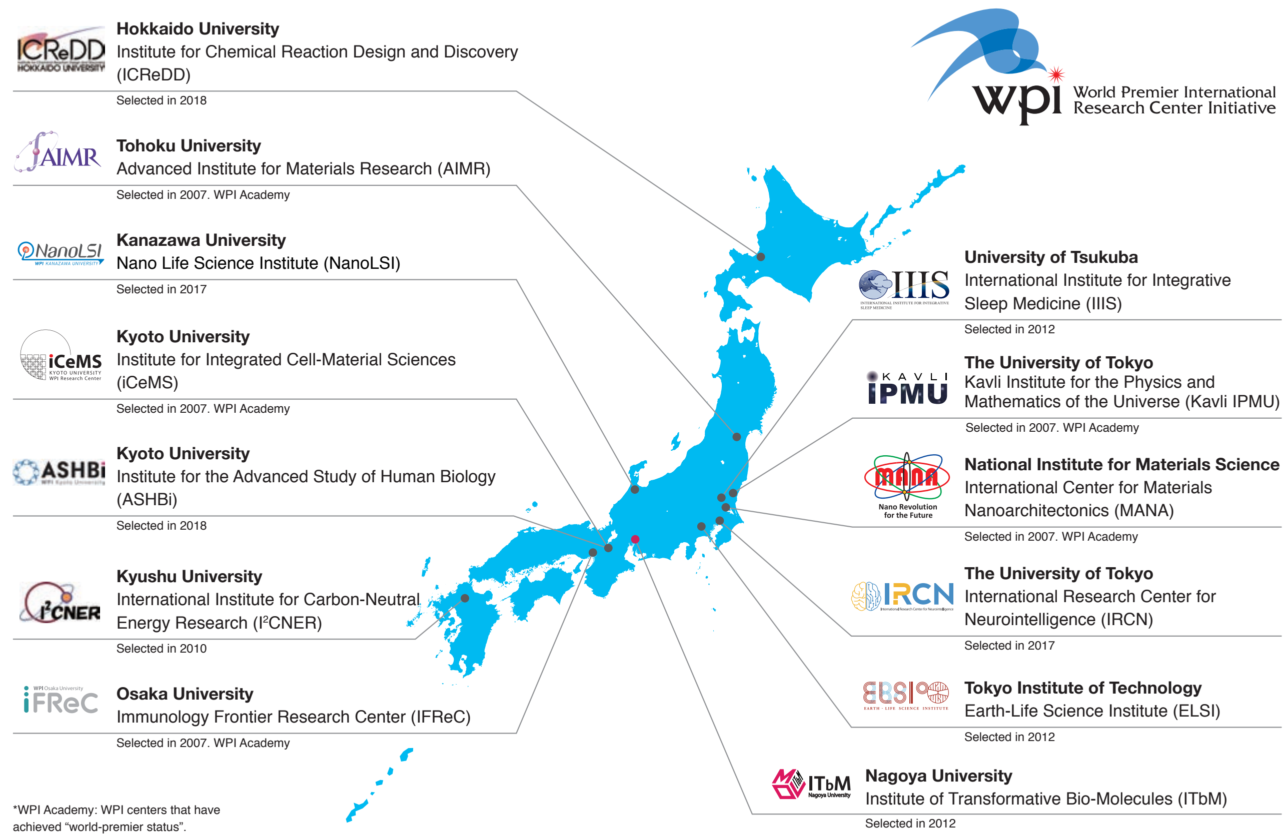
Year	Award / Honor	Awardees
2019	Arthur C. Cope Scholar Award	Cathleen Crudden
2019	Humboldt Research Award	Shigehiro Yamaguchi
2019	Special Award of The Botanical Society of Japan	Live Imaging Center
2018	JSPS Prize	Takeshi Yanai
2018	The Netherlands Scholar Award for Supramoleculer Chemistry	Kenichiro Itami
2018	Highly Cited Researchers 2018	Wolf Frommer, Kenichiro Itami, Steve Kay
2018	Academic Award of The Botanical Society of Japan	Tetsuya Higashiyama
2018	Chunichi Cultural Award	Tetsuya Higashiyama
2018	Ichimura Prize in Science for Distinguished Achievement	Shigehiro Yamaguchi
2018	IPMI Carol Tyler Award	Cathleen Crudden
2018	MEXT Minister's Young Scientist Award	Hidenori Takeuchi
2018	Mukaiyama Award	Jeffrey Bode
2018	Tsungming Tu Award	Wolf Frommer
2017	Alexander von Humboldt Professorship	Wolf Frommer
2017	Chunichi Cultural Award	Kenichiro Itami
2017	CSJ Award for Creative Research, Chemical Society of Japan	Kenichiro Itami
2017	CSJ Award for Young Chemists, Chemical Society of Japan	Daisuke Yokogawa
2017	HFSP Career Development Award (CDA)	Masayoshi Nakamura
2017	Highly Cited Researcher 2017	Wolf Frommer, Kenichiro Itami, Steve Kay
2017	Inoue Prize for Science	Tetsuya Higashiyama
2017	MEXT Minister's Young Scientist Award	Norihito Nakamichi, Kohsuke Ohmatsu
2017	R. U. Lemieux Award, Canadian Society for Chemistry	Cathleen Crudden
2017	SYNLETT Best Paper Award	Cathleen Crudden, Masakazu Nambo
2017	Yomiuri Techno Forum Gold Medal Prize	Kenichiro Itami
2016	CFT (Concrete-Filled Steel Tube) Award	ITbM building
2016	Nagase Prize	Kenichiro Itami
2016	SYNLETT Best Paper Award	Kenichiro Itami
2015	Arthur C. Cope Scholar Award, American Chemical Society	Kenichiro Itami
2015	CSJ Award for Creative Research, Chemical Society of Japan	Shigehiro Yamaguchi
2015	CSJ Award for Young Chemists, Chemical Society of Japan	Kohsuke Ohmatsu
2015	Fellow of ASPB (American Society of Plant Biologists) Award	Keiko Torii
2015	Killam Research Fellowship	Cathleen Crudden
2015	Mukaiyama Award	Shigehiro Yamaguchi
2015	Saruhashi Award	Keiko Torii
2015	Van Meter Award, American Thyroid Association	Takashi Yoshimura
2014	Fellowship in the Chemical Institute of Canada (FCIC)	Cathleen Crudden
2014	Fellow of the Royal Society of Chemistry, UK	Takashi Ooi
2014	Highly Cited Researcher 2014	Steve Kay
2014	Inoue Prize for Science	Keiko Torii
2014	NISTEP Nice Step Researcher	Tetsuya Higashiyama
2014	Yomiuri Techno Forum Gold Medal Prize	Tetsuya Higashiyama
2013	Fellow of the Royal Society of Chemistry, UK	Jeffrey Bode
2013	Inoue Prize for Science	Takashi Ooi
2013	JSPS Prize	Kenichiro Itami
2013	Mukaiyama Award	Kenichiro Itami
2012	JSPS Prize	Shigehiro Yamaguchi

Support and sustainability

About WPI

The World Premier International Research Center Initiative (WPI) was launched in 2007 by the Japanese government's Ministry of Education, Culture, Sports, Science and Technology (MEXT). This is a ten-year funding program that aims to build globally visible research centers in Japan that each have a very high research standard and an outstanding research environment, which will attract frontline researchers from around the world to come to work in these centers.

A total of 13 WPI centers have been selected across Japan up to now. Each center is being developed under the strong leadership of the center director for implementing the following 4 basic objectives set by the WPI program: (1) Science: advancing leading-edge research; (2) Fusion: creating interdisciplinary research domains; (3) Globalization: establishing international research environments; and (4) Reform: improving research organization.



Supporting ITbM

ITbM will continue to conduct basic research to contribute in solving major challenges in the global society. In order to offer placement to talented personnel, secure intellectual properties, and to continue to generate advancing results in research and technology transfer, action is needed after the ten-year support from the WPI program finishes at the end of March 2022. Donations to ITbM will help ensure that ITbM will still be able to respond to social challenges in the future and flourish.

Donation

NAGOYA UNIVERSITY
Foundation page

Contact

Administrative Department
Institute of Transformative Bio-Molecules (ITbM),
Nagoya University
Furo-cho, Chikusa-ku, Nagoya 464-8601, Japan
TEL: +81-52-747-6843 FAX: +81-52-789-3240
E-mail: office@itbm.nagoya-u.ac.jp

URL: http://www.itbm.nagoya-u.ac.jp

Issued: September 2019