

## Application for Academy Center Certification World Premier International Research Center Initiative (WPI)

Host Institution	Tokai National Higher Education and Research System, Nagoya University
Research Center	Institute of Transformative Bio-Molecules
Host Institution Head	Seiichi Matsuo
Center Director	Takashi Yoshimura
Administrative Director	Tsuyoshi Matsumoto

Please prepare this application based on the content of your Center's progress report and the progress plan you submitted for the Center's final evaluation. Summarize the Center's future plans with regard to the following 8 items **within five A-4 pages**. (Also fill out the appendices at the end of this form.)

### 1. Overall Image of Your Center

\* Describe the Center's overall image including its identity.

ITbM is an international research institute established at Nagoya University (NU) to develop "transformative bio-molecules" that make a marked change in the form and nature of biological science and technology. ITbM gathers world-leading researchers in the fields of synthetic chemistry, biology, and theoretical science and they work together to conduct interdisciplinary research. ITbM established the Mix Lab and Mix Office where researchers and students from different fields are sitting side-by-side and naturally have discussions based on a flat relationship irrespective of their titles. ITbM implements measures to promote bottom-up collaboration, such as the ITbM Research Award. ITbM also starts "Chalk Talk" which provides opportunities for researchers to present their unique ideas. ITbM extends its global network to further advance its interdisciplinary research via extensive collaboration. 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 in NU, and has been inducing system reforms of NU. In 2018, a new graduate program "Graduate Program of Transformative Chem-Bio Research (GTR)" was established as a MEXT "Doctoral Program for World-leading Innovative & Smart Education (WISE)" having ITbM as its core. The Graduate School of Science makes a system reform and officially allocates PhD students also to ITbM's overseas PI groups from FY2022. ITbM will work proactively in nurturing PhD students who can pioneer new science at the interface of multiple disciplines. ITbM will also actively engage in societal implementation of research results. As represented by the development of parasitic plant striga eradication molecules, a number of socially implementable results have emerged regarding environmental adaptation in plants. ITbM will continue and accelerate these researches. Meanwhile, under the new Director Yoshimura, ITbM implements new research initiatives that contribute to improving human health, such as overcoming health hazards associated with climate change and animal-borne infectious diseases. ITbM launched a membership discussion forum "ITbM Consortium" in 2017 to provide matching opportunities with industries, which was revamped in 2020 as "ITbM/GTR Consortium" and incorporated a wider range of researchers who engage in the GTR program. ITbM has now become a truly exciting and internationally visible institute where new interdisciplinary research fields emerge and new molecules are born every day. Meanwhile, we sincerely examined the recent case of the research misconduct, and took measures to ensure to prevent any research misconduct. We will also take this as an opportunity to further develop our research, and expand ITbM's unique "Mix" by integrating a wider range of disciplines. ITbM's unique "Mix" culture has led researchers from different fields to work together and think/act differently, thereby finding unique problems and solutions, discovering something new, and providing unique solutions to key global problems.

## 2. Mid- to Long-term Research Objectives and Strategies

\* Describe new challenges in the Center's research objectives and plans after FY2022.

In April 2022, Dr. Yoshimura assumed the ITbM director's post. With the slogan of "openness, transparency, and inclusion," ITbM made organizational reforms under the leadership of the new Director in cooperation with NU to ensure that research misconduct will never occur. ITbM takes this as a good opportunity for further development of ITbM by expanding interdisciplinary research and enhancing our research capabilities.

The mission of ITbM has been to conduct 'needs-inspired' basic research while developing transformative bio-molecules that make a marked change in the form and nature of biological science and technology. By marrying state-of-the-art synthetic chemistry, catalytic chemistry, plant biology, animal biology, live imaging, and theoretical science, ITbM has advanced new research areas of "plant chemical biology", "chemical chronobiology", and "chemistry-enabled live imaging". This exciting endeavor has resulted in the development of a range of promising bio-functional molecules, many of which have been commercialized, and the discovery of molecular mechanisms of important biological events. All of these tour-de-force achievements have led scientists in the world to place ITbM as an enabling institute where new bioactive molecules with targeted properties can be rapidly discovered, designed, and synthesized. ITbM continues to promote research aimed at the development of transformative biomolecules and to open up new research fields through interdisciplinary collaboration. Whereas advancing the research on animal/plant science that has been promoted so far, under the initiative of the new Director, ITbM will work on the research that contributes to human health with a view of the recent global climate changes. For this purpose, ITbM adds data science as its fourth pillar. Data science will also make a significant contribution to the research that ITbM has been working on. Keeping in mind the promotion of diversity, ITbM appointed a new PI and two junior PIs who are necessary to tackle this research area (see Section 3), and will take on the challenges listed below for the next 5-10 years. Through their achievement, ITbM will be further recognized as a world-leading research institute.

**(1) Parasitic Plants:** Based on our discovery of significant potential molecules for combatting the parasitic plant *Striga*, ITbM will make efforts to provide molecular solutions to the food security issues, especially focusing on Africa. For this purpose, we have initiated a collaboration with Kenya Agricultural & Livestock Research Organization (KALRO) and the International Center for Research and Education (ICREA) of NU. We are confident that our molecular approach can be used to combat other parasitic plants causing huge damage in other regions.

**(2) Chemistry-enabled plant adaptation:** Plants have inherent stress tolerance systems that enable them to adapt to environmental changes and survive under stressful conditions that are essential functions due to their inability to move. However, recent global climate change exceeds the tolerance of the current abiotic stress response of plants, and they often face serious situations such as failing to fertilize, failing to develop, and eventual death. We aim to develop such environmental stress-overcoming molecules to maximize the adaptive power of plants via an interdisciplinary approach.

**(3) Chemistry-enabled bioimaging:** Bioimaging is one of the indispensable techniques in current biology. We have developed a series of new fluorescent dyes. Their outstanding photostability enabled acquiring not only 3-D structures of cytoskeletons, but also mitochondrial inner-membrane dynamics in the living cells by conducting STED imaging. Near-infrared (NIR) fluorescent dyes are the other target molecules in our research, which have several advantages, such as diminishing photo-damage to bio-samples, minimal interference from cell autofluorescence, and deep penetration in biological tissues. With these sophisticated dyes in hand, together with state-of-the-art imaging instrumentations, we will make full use of these cutting-edge discoveries to understand and control biological systems, and also contribute to the advancement of medical diagnosis.

**(4) Nanocarbon chemistry and biology:** While it is important to strengthen fundamental technologies such as molecular synthesis, it is also important to create molecules with new structures and clarify their properties in order to maximize the potential of molecules. On the other hand, it is also important to create molecules with new structures and clarify their properties in order to maximize their potential. To this end, we will apply molecular nanocarbons as new molecular entities in biology and explore "nanocarbon biology" as a new scientific field. All the findings will be applied to other projects at ITbM, adding a new dimension to biological science and technology.

**(5) Clock-disease:** Disturbances in the circadian system have a profound impact on health, and they have been linked to several pathologies, including obesity, psychiatric disorders, cardiovascular

disease, and even cancer. ITbM has developed a number of molecules, such as circadian clock regulators with anti-cancer properties, that have been shown to reduce jet-lag. The human menstrual cycle, sleep-wake cycle, and manic-depressive cycle are all influenced by the phases of the moon. In traditional agriculture, the phases of the moon were also used for planting and harvesting. In the animal kingdom, lunar phases are widely used for migration, mating, and predator avoidance. Thus, it is clear that lunar influences are involved in life functions and human health. ITbM tackles to elucidate the molecular mechanisms of these effects via collaborative approach.

**(6) Climate change resilience:** Global climatic and environmental changes are exceeding the adaptive capacity of not only plants but also animals including humans. Due to global warming, the number of heat stroke patients and deaths is on the rise, and health hazards caused by heat waves are serious worldwide. In addition, animal-borne infectious diseases such as dengue fever and Zika fever are on the rise. Heat stress also reduces the reproductive efficiency and growth of livestock, poultry, fish and shellfish. Using data science, we will elucidate the mechanisms of environmental adaptation in animals and promote the development of molecules that control environmental adaptation. We will also contribute to the improvement of human health by tackling animal-borne infectious diseases such as dengue fever and Zika fever through the power of molecules.

### 3. Management System of the Research Organization

\* Describe the system of organizational management via which the center will execute the above-described research strategy and plan.

\* In Appendix 1-3, list the Principal Investigators, enter the number of center personnel (researchers, research-support staff, and administrative staff), and provide a diagram of the Center's organizational management system.

**Prevention of research misconduct:** ITbM sincerely examined the recent case of research misconduct, and took all measures to ensure to prevent any research misconduct. We will also take this as an opportunity to further develop our research through organizational reforms. ITbM has operated under a top-down management system from the start, and the Director has the authority to make final decisions over all matters concerning the operation and management of ITbM. This approach has eliminated bureaucratic processes and enabled ITbM to make quick and flexible decisions. On the other hand, the hierarchical organizational management could have contributed to trigger research misconduct. Therefore, under the initiative of the new center director, the organization was reformed to a **flat structure with "openness", "transparency", and "inclusion"** as keywords. While eliminating the bureaucracy, we will foster a culture in which opinions can be exchanged regardless of his/her title. Actually, **all members of ITbM will be addressed as "##-san (e.g., Yoshimura-san)," each other.** The **ITbM Steering Committee meeting, which had mostly been led by PIs, was changed to a system that allows all ITbM faculty members to participate.** This change brought about remarkable changes within just a few months; as they were able to share various issues, young researchers became more proactive to improve ITbM, and the ITbM's research activities were significantly revitalized.

Another initiative to prevent research misconduct is a **double-mentoring system**. The system has been applied to the students of the WISE program GTR (see Section 2-2). The open educational system urges students to communicate with a second mentor from other laboratories. Accordingly, the students naturally tend to consult with their double mentors when they have any problems. This system is also effective to create new collaborative research via scientific talks with the second mentor. We also strongly encourage students to study abroad by all means such as the travel support of the graduate program GTR.

It is also important to re-enforce **education on research ethics** to prevent research misconduct. We have shared the common notion that research failure is quite common even at the highly productive ITbM and is an inevitable process to success, and that research misconduct is totally meaningless. Whereas we established **the rule to store lab-notebooks and save original data**, we are preparing the system to **save the original data on the cloud to prevent intentional data falsification** by researchers. **Open science**, in which original data is made public through databases and other means, should also be actively promoted to make reproducible and transparent results a common property of humankind, thereby contributing to the acceleration of research worldwide and the return of research outcomes to society.

**Research Organization Management:** ITbM has been recognized as an essential research institute for NU to become a world-leading research university and was assigned as a permanent organization in March 2022. We recognize that diversity and organizational rejuvenation are important for the sustainable development of ITbM. Following discussions at the WPI Program Committee, ITbM assigned one female PI and two junior PIs (one female and one non-Japanese). ITbM continues to recruit junior PIs strategically, in view of nurturing young researchers and enhancing diversity.

Despite the unique independence of ITbM, ITbM's Director and core members are having close contact with the Chancellor, President, Trustee, and the related departments. While PhD students and

undergraduate students have been allocated to NU PI groups and several overseas PI groups, the Graduate School of Science has made a system reform to officially allocate more PhD students, especially to ITbM's overseas PI groups from FY2022. We will further strengthen ties with the departments of NU and actively contribute to the education of PhD students.

#### 4. Plan for Promoting the International Circulation of World's Best Brains

\* Describe your policy and concrete plan for promoting the international circulation of the world's best brains, which is an important function of the WPI Academy.

We believe the strong relationships between ITbM and external organizations are also quite important. We will strengthen our international collaborative relationships with existing partners such as NSF-CCHF (US), RIKEN CSRS (Japan), Academia Sinica (Taiwan), and KALRO (Kenya). ITbM's 5 world-leading overseas PIs are also active to promote the internationalization of ITbM. They are sending a few researchers from his/her institutes to ITbM every year and will continue this activity. In addition, the overseas PI groups will be involved in the PhD course education from FY2022, which will attract PhD students from abroad and accelerate internationalization.

ITbM recognizes the importance of fostering young researchers with an international perspective and has been providing PhD students with research opportunities overseas. ITbM will continue this initiative more actively by utilizing such as the Graduate Program WISE and the Joint Degree Programs.

ITbM will continue to host annual international symposia (ISTbM) and three international awards (Hirata Award, Tsuneko & Reiji Okazaki Award, and Nagoya Medal of Organic Chemistry).

#### 5. Plan for Disseminating the WPI Program Achievements

\* Describe your policy and concrete plan for disseminating WPI center achievements both within the host institution and to other universities, especially their experience and know-how accumulated on establishing top world research institutes and advancing system reforms.

As a Designated National University, NU continues to pursue system reforms to become a world-class research university in line with President Matsuo's goal of "NU MIRAI 2020". In this context, ITbM is positioned as NU's flagship research institute, and contributes to achieving the goal.

**Establishment of measures to prevent research misconduct:** In response to our case of research misconduct at ITbM, ITbM and NU have worked together to take thorough measures to prevent research misconduct, establish a concrete action plan, and horizontally deploy it throughout NU. The measures will be regularly discussed and revised as necessary. Through this endeavor, ITbM and NU will protect researchers from research misconduct, and as a result, the research activities of ITbM and NU will be promoted.

**Establishment of the International Advanced Research Organization:** NU established the Nagoya University Institute for Advanced Research (NAIAS) to further strengthen its world-leading basic research, and placed ITbM under its umbrella. The Institute for Advanced Research (IAR), which implements next-generation research support programs such as WPI-next, was also placed under NAIAS, and the know-how accumulated at ITbM is horizontally deployed.

**Spread of the Mix Lab concept to promote interdisciplinary research:** The ITbM Mix Lab concept is being widely recognized at many institutions inside and outside of NU through the following graduate program GTR, because of its high success in encouraging unexplored interdisciplinary research. We will also communicate with other departments and spread our Mix Lab as good practices.

**Establishment of a new graduate program with ITbM at its core:** NU recognizes the significance of the Mix Lab concept and plans to extensively involve ITbM in the evolution of graduate schools. NU and ITbM have put together a proposal for a program entitled "Graduate Program of Transformative Chem-Bio Research (GTR)", as an application to the *Doctoral Program for World-leading Innovative & Smart Education (WISE Program)* of MEXT, and was successfully selected in late 2018. In GTR, ITbM is positioned as a hub for promoting interdisciplinary research in the field of natural sciences, and the designated faculty members of ITbM will be engaged in the education of PhD students through supervising collaborative research. An important aspect of this program is its ripple effect. Through discussions to prepare the concrete plan, the ITbM spirit of Mix was widely shared among the cooperating institutes and firms, spreading to the researchers on site. The GTR installed three Mix Labs so far to ensure the success of the program. On the other hand, we also recognize that barriers still exist in organizational structures in NU. We will continue to work with NU headquarters and the related departments to improve graduate education at NU.

**Establishment of an effective public relations system in NU:** In cooperation with other WPI institutes, ITbM has been engaged in various public relations and outreach activities. By sharing the expertise and experience of ITbM, NU now has a system to send out international press releases

highlighting the research accomplishments of the entire university. ITbM will further cooperate with NU to establish a more efficient public relations system and organize outreach activities as a whole. It is also notable that ITbM has established strong ties with high schools, particularly in the Tokai area. Many of the researchers at ITbM have given lectures at high schools through this program. As a result, our cutting-edge science attracts many high school students, and more importantly, many high school teachers. The WPI Science Symposium in 2018 organized by ITbM was a focal point for these interactions. We will share this experience with NU to continue improving our strategy to attract and encourage top students.

## **6. Plan for Sustaining the WPI Brand**

\* Describe your plan for sustaining and enhancing the WPI brand.

ITbM will sustain the WPI brand by further advancing our research activities as a top-level research center. Based on the tight bond of chemistry, biology, and theoretical science built over the past 10 years, we will add data science as a new pillar to explore new frontiers under the new director. We will involve new researchers with diversity and generational change in mind, and establish a research hub that is even more recognized worldwide. We also recognize that outreach activities are keys to raising the value of the center and the WPI brand. We will further promote public relations activities and attract researchers from around the world. Expanding ITbM's network will also contribute to building the WPI brand. So far 99 ITbM researchers/PhD students have been promoted to faculty positions in academia, and act as ITbM supporters. ITbM's international symposia and awards will significantly contribute to increasing ITbM's international visibility to attract overseas researchers and PhD students as denoted above, which will also contribute to the recognition of the WPI brand.

## **7. Support by Host institution**

\* Describe measures that the host institution will take to support and sustain your Center.

ITbM is positioned as a flagship research institute in President Matsuo's initiative NU MIRAI 2020 and the NU's "Designated National University" concept. To secure the employment of ITbM's faculty and staff members, NU has launched the Nagoya University Institute for Advanced Study (NAIAS), and positioned ITbM under this umbrella. Even under this new structure, the Director of ITbM retains the authority to make decisions for matters regarding ITbM. NU and ITbM have undertaken the reorganization, conscious of maintaining the good relationships already established between ITbM with other departments/faculties at NU. Eight NU PIs will continue their cooperation with their original faculties, and the students are allocated. While students were not allocated to the overseas PI groups at the beginning, it became possible from FY2022.

## **8. Resource Allocation Plan**

\* Describe your plans over a 5-year period for allocating resources acquired from both the host institution (e.g., financial resources and positions) and from external research funding to execute the Center's functions and activities described above.

\* In Appendix 4, enter concrete numbers in the Resource Allocation Plan.

At its inception, ITbM had 8 PI positions transferred to it from NU. In 2019, 7 more faculty positions for ITbM were officially secured by the President-Management Point System and allocated to ITbM as tenure positions. Since 2018, NU has been requesting to MEXT the budget (Gaisan Yokyu) with the highest priority to strengthening ITbM, and so far 6 faculty positions have been allocated.

From FY2022, NU increases the support to secure additional 8 faculty positions and the selected postdocs/staff who are essential to run ITbM. In addition, NU supports a junior PI position to promote the internationalization and diversity of ITbM.

ITbM promotes industry-academia collaboration with the full cooperation of NU. In 2020, the ITbM Consortium was renewed as the "ITbM / GTR Consortium" with the participation of researchers engaging in chemistry & life science in the above-mentioned GTR program, and the ITbM's research is expanding. This consortium provides for the member-companies the latest unpublished achievements and also a place for exchanging information among the companies and recruiting excellent students, thus functioning as a place for discovering joint research between industry and academia.

ITbM will also promote the acquisition of diverse funds such as large competitive funds and fundraising activities through the Nagoya University Foundation.

## Appendix 1 List of Principal Investigators (Application for Academy Center Certification)

\* If the number of principal investigators exceeds 10, add rows as appropriate.

\* Give age as of 1 April 2022

\* For investigators who cannot participate in the center project from FY 2022, indicate the time that their participation will start in the "Notes" column.

\* Enter the host institution name and the center name in the footer.

	Name	Current affiliation (position title, organization, department)	Academic degree and current specialties	Effort(%)*	Notes (Enter "new" or "ongoing")
1	Takashi YOSHIMURA*	Director, Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Agriculture Specialties: Animal Physiology, Systems Biology, Neuroendocrinology	80	ongoing
2	Jeffrey W. BODE*	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 Bioconjugation	21	ongoing
3	Cathleen M. CRUDDEN*	Professor Department of Chemistry, Queen's University, Canada	Ph.D Specialities: Catalysis, Organic Synthesis, Materials Chemistry,	21	ongoing
4	Kenichiro ITAMI*	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Engineering Specialties: Organic Synthesis, Catalysis, Pharmaceuti-cal Science, Nanocarbon Chemistry	70	ongoing
5	Toshinori KINOSHITA*	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Science Specialities: Plant Molecular Physiology	70	ongoing
6	Takashi OOI*	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Engineering Specialties: Organic Synthesis, Catalysis, Molecular Recognition	70	ongoing
7	Keiko TORII*	Professor College of Natural Sciences The University of Texas at Austin Investigator Howard Hughes Medical Institute	Ph.D. Specialties: Plant Development, Signal Transduction, Stem Cell Maintenance/Differentiati-on in Plants	21	ongoing
8	Shigehiro YAMAGUCHI*	Vice-Director, Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Engineering Specialties: Main Group Chemistry, Physical Organic Chemistry	70	ongoing

9	Steve A. KAY*	University and Provost Professor of Neurology, Biomedical Engineering and Biological Sciences, Director of Convergent Bioscience Co-Director of the USC Norris Center for Cancer Drug Development, Keck School of Medicine. University	Ph.D. Specialties: Chronobiology, Genetics, Biochemistry, Systems Biology	10	ongoing
10	Florence TAMA*	Professor Institute of Transformative Bio-Molecules / Department of Physics, Graduate School of Science, Nagoya University	Ph.D Specialties: Computational Biophysics	50	ongoing
11	Wolf B. FROMMER*	Professor, Heinrich Heine University Düsseldorf and Max Planck Institute for Breeding Research	Dr. rer. nat. Specialties: Biology	21	ongoing
12	Takeshi YANAI*	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Engineering Specialties: Theoretical Chemistry, Computatoinal Quantum Chemistry	70	ongoing
13	Yuichiro TSUCHIYA*	Designated Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Agriculture Specialties: Plant Genetics, Chemical Biology	70	new
14	Azusa KAMIKOUCHI	Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Pharmaceutical Sciences Specialities: Neuroscience	50	new
15	Anuphon LAOHAVISIT	Designated Associate Professor Institute of Transformative Bio-Molecules, Nagoya University	Ph.D. Specialties: Plant Signaling, Plant Physiology, Chemical Biology	80	new
16	Quan PHUNG	Associate Professor Institute of Transformative Bio-Molecules / Graduate School of Science. Nagoya University	Ph.D. Specialties: Data Science, Theoretical Science	50	new
17	Yoko MIZUTA	Designated Assitant Professor Institute of Transformative Bio-Molecules, Nagoya University	Dr. Science Specialities: Plant Molecular Physiology	80	new

**World Premier International Research Center Initiative (WPI)**  
**Number of Center Personnel**

		FY2022	
		Number of persons	%
	Researchers	63	/
	Overseas researchers	20	31.7
	Female researchers	20	31.7
	Principal investigators (PIs)	17	/
	Overseas PIs	7	41.2
	Female PIs	5	29.4
	Other researchers	27	/
	Overseas researchers	2	7.41
	Female researchers	7	25.9
	Postdocs	19	/
	Overseas Postdocs	11	57.9
	Female Postdocs	8	42.1
	Research support staffs	47	/
	Administrative staffs	7	/
	<b>TOTAL</b>	<b>117</b>	<b>/</b>

Tokai National Higher Education and Research System, Nagoya University

Institute of Transformative Bio-Molecules



## World Premier International Research Center Initiative (WPI) Diagram of Organizational Management System

- Diagram the Center's organizational management system and its position within the host institution in an easily understood manner.

