April 13, 2023

Summary of Research Center Project

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Center name: Institute for Chemical Reaction Design and Discovery (ICReDD)

Host institution: Hokkaido University

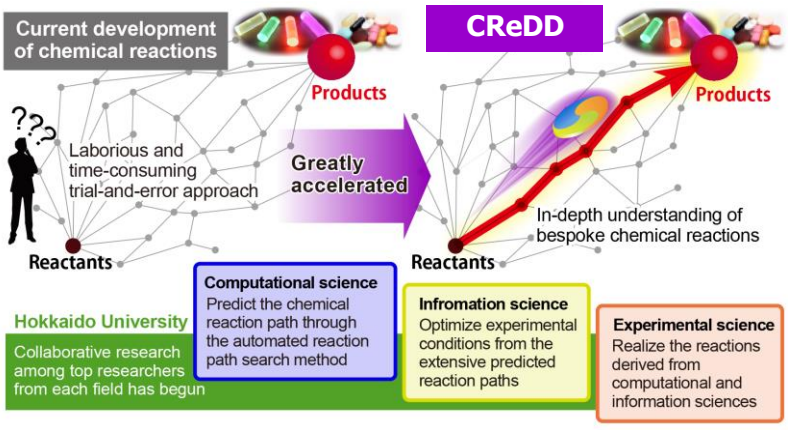
Head of host institution: Kiyohiro Houkin (President)

Center director: Satoshi Maeda, Professor, Faculty of Science

Administrative director: Koichiro Ishimori (Vice President)

1) Overall Framework of the Center Project

The ultimate goal of the Institute for Chemical Reaction Design and Discovery (ICReDD) is to acquire an in-depth understanding of chemical reactions by analyzing complex networks of chemical reaction paths in order to accelerate the efficiency of the development of new chemical reactions. These new chemical reactions will generate advanced materials and reduce the use of energy and natural resources, which is indispensable for a prosperous and sustainable future of humanity. **We aim to accomplish this objective in a research environment that integrates computational, information, and experimental sciences.** Considering that the current trial-and-error approach to the development of new chemical reactions is time-consuming and inefficient, new methods for the development of bespoke chemical reactions should be a key factor toward revolutionizing the entire field of science. By using state-of-the-art reaction path search methods based on quantum chemical calculations and collaborating with information and experimental scientists, we establish the new academic field "Chemical Reaction Design and Discovery (CReDD)", which provides substantial knowledge on chemical reactions that allows efficiently developing of advanced chemical reactions and materials.



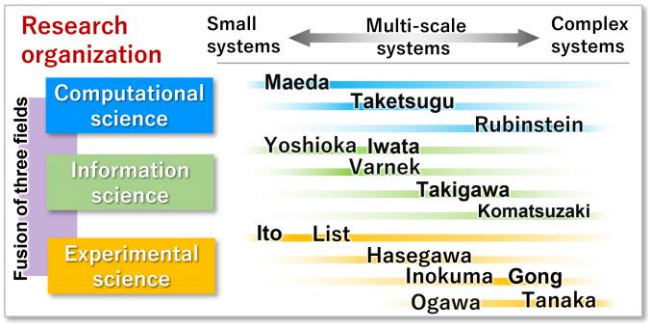
2) Content of Research

The development of new reactions by CReDD can be subdivided into three categories, depending on the size of the target molecules. The 1st category creates reactions that add high value to abundant and/or inexpensive resources (small molecules; ~100 atoms), e.g. synthesis of amino acids from CO_2. The 2nd category is concerned with the synthesis of high-tech materials (macromolecules; ~10,000 atoms), e.g. synthesis of highly efficient light-emitting materials and ultrahigh-strength carbon materials for space elevators. In the 3rd category, CReDD is used to investigate cellular and biochemical reactions, and some of the materials developed in the 2nd category are used in advanced medical care (complex molecules; > 10,000 atoms), e.g. for the establishment of new diagnostic tools and treatment strategies. In collaboration with information science, Prof. Maeda's automated reaction path search method (AFIR) is used to identify optimal synthetic paths to target structures. The real material that is significantly important and desired by human society is synthesized by experimental scientists on the basis of the theoretical prediction.

3) Interdisciplinary Research

AFIR allows the extraction of the molecular behavior that is crucial for chemical reactions. Still, when AFIR is applied to more realistic systems, the time required to carry out the necessary complex calculations is relatively long. This obstacle can be circumvented using established methods in information science (e.g.

high-speed algorithms), which dramatically reduce the time and cost for these calculations. Subsequently, experimental scientists carry out the practical verification of the proposed reactions, and the experimental results are analyzed and used as data feedback for the information scientists to extract new insights and apply these to the chemical reaction design. The success of CReDD would not only benefit areas that are directly related to the chemical industry, but also the global environment, life sciences, and society in general. The ICReDD should thus act as an initiator and incubator for rapid, productive, and innovative research based on chemical reactions that affect all aspects of society.



To advance fusion research practically, we have established several flagship and bottom-up projects that are being pursued by teams comprising multiple groups. Ideas of bottom-up projects are created by young researchers in ICReDD. Tackling these projects will enable us to continuously deliver high-impact outcomes featuring our young researchers.

In addition, we have launched three new initiatives aimed at improving the international recognition of the center and facilitating the quick implementation of our research outputs. These initiatives are the List Collaboration Platform, led by Professor List, the Mitsui Chemicals-ICReDD Innovative Chemical Reaction Design Laboratory, and the Clinical Platform for Chemical Reaction Collaboration, developed in partnership with the School of Medical Science.

4) International Research Environment

Three world-leading researchers from foreign research institutes have been invited to participate in the ICReDD. Research groups have been established for foreign PIs, and **Co-PIs** and research staff have been employed to support and manage the research groups in close collaboration with the foreign PIs, given that the latter also serves at their home institutions. Recruitment at the ICReDD has been based on a competitive, international selection process, and the goal of **~30% of the researchers being foreign has been met**. We have established an international hospitality support system for foreign researchers. **We have established the MANABIYA (an old Japanese word for "school") system** in the ICReDD to educate young researchers and graduate students on collaborative research that integrates computational, information, and experimental sciences in order to realize a global circulation system for world-class scientists in the integrative research area CReDD. We have built a broad collaboration network through the ICReDD research.

5) Center Management and System Reform

Project management: The director, Prof. Maeda, will serve for a minimum of 10 years, seconded by the vice director, Prof. Ito. Decision-making rights regarding central matters of institute management (e.g. recruitment and budgetary discretion) rests exclusively with the director of the ICReDD. Depending on the progress of research, the roles of each PI are reviewed and evaluated periodically by the director, and appropriate incentives and/or replacements are implemented. In order to strengthen cooperation with the University Executive Office and to ensure that decisions made by the University are promptly reflected at ICReDD, the Vice President was appointed as the Administrative Director. Monthly meetings are held with the President to discuss management, including future plans. The research support department creates a research environment that allows researchers and students to engage in their research without administrative interruptions.

In order to prevent research misconducts, in addition to thorough ethics education within ICReDD, a new department will be established to manage experimental data, and efforts will be made to make the center a global standard in terms of research transparency.

Research environments and establishing an independent research center: A collaborative research space including the MANABIYA system and the Inter-science Salon space have been installed in

the Creative Research Institution building (CRIS). The CRIS Global Facility Center manages instruments purchased at the ICReDD. Using the support system of each PI's affiliated department reduces the burden of administrative work for the PIs and ensures that research and education is their prime concern. At the launch, the ICReDD has secured operational funding from the university that is at least equivalent to the WPI grant. CReDD and MANABIYA will eventually be transformed into **the new "Graduate School of Chemical Reaction Design and Discovery"**. We will also create a permanent organization for the acquisition of private funding by e.g. hosting researchers from industry and establishing research consortia. To maintain a consistently high level of scientific excellence, ICReDD will establish a dynamic personnel appointment system that allows distinguished researchers to lead a second group within ICReDD while also periodically assessing and refreshing the composition of research teams as needed. The ICReDD will incorporate research areas beyond its three core fields, such as humanities and social sciences, which are required for the promotion of research and the reformation of CRIS. By sharing new management systems acquired through the WPI, the ICReDD will finally contribute to the reorganization of the University.

October 2024 revised

Research Center Project

* Compile in English within 20 A4 pages.

Center name: Institute for Chemical Reaction Design and Discovery (ICReDD)

Host institution: Hokkaido University

Head of host institution: Kiyohiro Houkin (President)

Center director: Satoshi Maeda, Professor, Faculty of Science

Administrative director: Koichiro Ishimori (Vice President)

1) Overall Framework of the Center Project

* Cleary and concisely describe your center's mission statement as a WPI center, its identity, and its goals toward achieving the objectives of the WPI program.

[Summary of the Research Center]

The ultimate goal of the Institute for Chemical Reaction Design and Discovery (ICReDD) is to "revolutionize chemical reaction design and discovery" by acquiring an in-depth understanding of chemical reactions by analyzing complex networks of chemical reaction paths in order to accelerate the efficiency of the development of new chemical reactions. These new chemical reactions will generate advanced materials and help to reduce the use of energy and natural resources, which is indispensable for a prosperous and sustainable future of humanity. We aim to accomplish this objective via the **establishment of a research environment that integrates computational, information, and experimental sciences.**

Considering that the current trial-and-error approach to the development of new chemical reactions is time-consuming and highly inefficient, developing methods for the controlled development of bespoke chemical reactions should be a key factor toward revolutionizing the entire field of science. Using state-of-the-art reaction path search methods based on quantum chemical calculations and collaborating with information and experimental scientists, we are establishing the new academic field "Chemical Reaction Design and Discovery (CReDD)", which enables us to acquire substantial knowledge on chemical reactions and efficiently develop advanced chemical reactions and materials. Moreover, we **establish the MANABIYA (an old Japanese word for "school") system in the ICReDD to educate young researchers and graduate students on collaborative research** that integrates computational, information, and experimental sciences in order to realize a global circulation system for world-class scientists in the integrative research area CReDD.

[The Necessity of Establishing the Research Center]

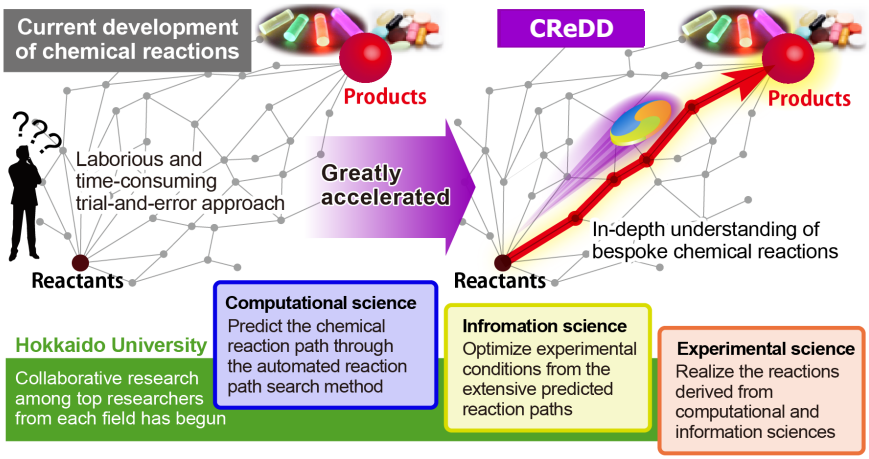
Chemical reactions provide access to the multitude of chemical compounds (e.g. agrochemicals, pharmaceuticals, and materials) that have allowed humanity to prosper. However, the development of new chemical reactions is usually time-consuming and laborious, while the probability of success is uncertain at best. In order to shorten the development period, many studies have until recently applied theoretical and computational science in an attempt to better understand chemical reactions and to design new reactions. However, it remains incredibly complicated to understand the fundamental aspects of chemical reactions based on the quantum dynamic behavior of atoms and molecules. Furthermore, conventional quantum chemical calculations occupy vast amounts of computation resources, rendering this approach less than efficient. Yet, the demand for new chemical reactions has never been higher in the context of e.g. the chemical industry, global resource exploitation, the environment, and human

healthcare. **Unless significantly more efficient methods for the development of new chemical reactions are established, it will be difficult to maintain the current growth of humanity while maintaining or increasing the current standard of living.**

[Strategy to Establish the Research Center and Specific Goals]

To solve these problems, we are establishing the new field "Chemical Reaction Design and Discovery (CReDD)" in order to efficiently develop and understand new chemical reactions by combining computational, information, and experimental sciences. By establishing the Institute for Chemical Reaction Design and Discovery (ICReDD), which is the first of its kind, we are promoting cutting-edge, integrated collaborative research, and establishing a new era of research on chemical reactions. The development of chemical reactions based on experimental trial-and-error typically requires several decades in order to develop a single new chemical reaction. To circumvent this obstacle, Prof. Maeda, the director of the ICReDD, has developed the "automated reaction path search (AFIR)" as a new method for the computational search of chemical reactions. Although this method is highly innovative and predicts the desired chemical reactions with high precision, it still requires vast amounts of computation resources. To address this issue, we use information science and the expertise from international leading researchers hosted by Hokkaido University in order to identify important reaction paths in a manner that allows high-speed calculations. Internationally leading experimental scientists at Hokkaido University (e.g. authors of top 1% paper(s) in high-impact journals and/or highly cited authors) carry out the experimental validation of the chemical reaction development.

The experimental scientists also provide feedback for the computational and information scientists, which help to improve the understanding of the reaction network. Via the integrated method described above, it becomes possible to identify promising experiments in advance, i.e., the exploration of the reaction path network can be prioritized according to the predictions. The time required for the development of new reactions can thus be reduced substantially compared to conventional methods that rely on trial and error. Additionally, with this method, it should be possible to understand the complicated transformation of many substances, which is relevant for other academic fields related to chemical reactions. Especially for the three core areas of research (computational, information, and experimental sciences), Hokkaido University has already established itself as a prominent global institution that provides a strong foundation on which the goals of CReDD can be achieved. At the ICReDD, we further establish the MANABIYA system, which is a crucial strategic aspect in order to ensure the development of world-class human resources. **Via the MANABIYA fostering system, the ICReDD establishes national and international collaborations with other research centers by i) developing a new area of research (CReDD), ii) restructuring the organization of Hokkaido University, and iii) establishing the new graduate school "School of Chemical Reaction Design and Discovery".** The integrated research on CReDD has led to the development of highly efficient



chemical reactions that can afford high-value-added chemicals with applications in agro- and environmental chemistry, pharmaceutical and materials science, medical technology, as well as energy and resource management. The target reactions and molecules are carefully selected based on the impact to the society through discussion among broad research communities and with many companies.

2) Content of Research

2) -1 Research fields

* Write in your target research field(s)
* Describe the importance of the target research field(s), including the domestic and international R&D trends in that research domain and neighboring field(s), and describe the scientific and/or social significance of the field(s).
* Describe the value of carrying out research in the field(s) as a WPI center (e.g., Japan's advantages in the subject fields, the project's international appeal as an initiative that challenges world-level science issues, and the future prospects of the research)
* List up to 5 centers either in Japan or overseas that are advancing research in fields similar to the center's field(s), and evaluate research levels between your center and those centers.

[Establishment of the Research Field Chemical Reaction Design and Discovery]

The objective of our institute is to "revolutionize chemical reaction design and discovery" through establishing the new research field "Chemical Reaction Design and Discovery (CReDD)" in order to gain a fundamental understanding of the intricacies of chemical reactions, which represent very complicated quantum dynamical phenomena, and to develop new chemical reactions at high speed. The development of chemical reactions may help to alleviate serious social problems such as increasing industrial waste and food shortages and contribute to a more sustainable future society. **For that purpose, we are integrating computational, information, and experimental sciences. Among these three scientific areas, collaborations between two of these three fields is relatively common, while collaborations between all three areas remain elusive.** The ICReDD is designed to fully integrate world-leading research at Hokkaido University on reaction path search (computational science), mathematical and statistical modeling (information science), and cutting-edge experimental verification of the proposed models and pathways in order to realize a prediction-based design and rapid development of bespoke chemical reactions.

The ICReDD also plays a central role in the development of world-leading young researchers who master techniques in computational, information, and experimental sciences. **In the ICReDD, all reaction paths for the synthesis of target compounds from feedstock chemicals are systematically investigated *de novo*. This is an unprecedented approach that stands in sharp contrast to existing informatics projects.** Materials informatics and chemoinformatics projects such as the materials genome initiative in the USA, the materials research by information integration initiative of the National Institute for Materials Science (NIMS) and the Novel Materials Discovery (NOMAD) laboratory in the EU generally design target materials rather than reactions, which is similar to the operational principle of AIMR (Tohoku WPI). Literature-based projects such as PubChem in the USA, Reaxys (Elsevier), and SciFinder (American Chemical Society) search for *known* reactions.

In contrast, the focus of the ICReDD is placed on *discovering a variety of unknown reactions*, which fundamentally changes the system of field integration and collaborative research. Although several established WPIs, such as the ITbM (Nagoya WPI) and the MANA (NIMS WPI) continuously develop new purpose-orientated molecules and materials using chemical reactions, these are obtained using classical trial-and-error approaches. In contrast, the integrated approach of the ICReDD leads to numerous new reactions, each of which should efficiently generate bespoke chemicals and materials. **The potential of this approach to deliver successful collaborative research is highly promising. The ICReDD**

should therefore become a benchmark for rapid, productive, and innovative research on new chemical reactions. The ICReDD also plays a crucial role to promote these innovative and integrative research methods to a higher level by disseminating the results beyond immediate institutional boarders.

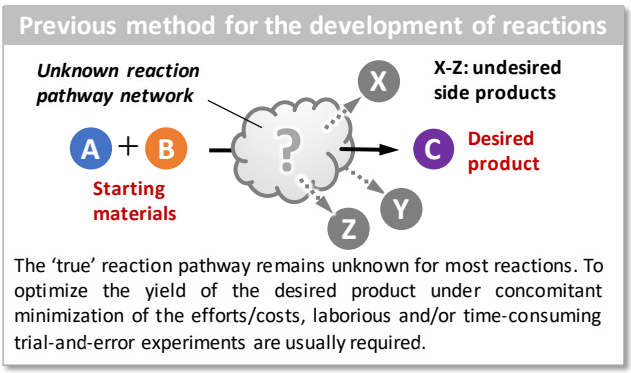
2)-2 Research Objectives and Plans

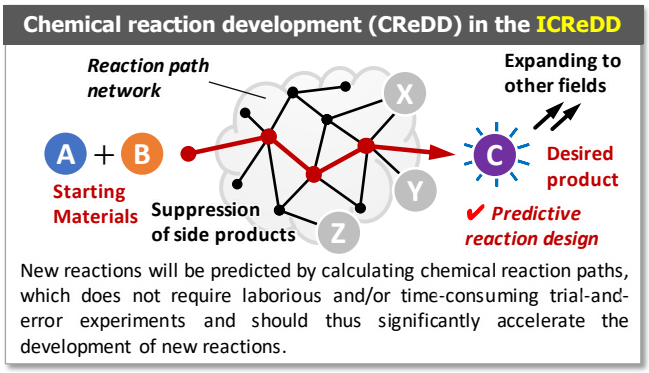
* Describe in a clear and easy-to-understand manner by the general public the research objectives that your project seeks to achieve by the end of its grant period (in 5 years). In that process, what world-level scientific and/or technological issues are you seeking to solve? What will be the expected impact of the scientific advances you aim to achieve on society in the future?
* Describe concretely your research plan to achieve these objectives and any past achievements related to your application.

[Objectives of Chemical Reaction Design and Discovery (CReDD)]

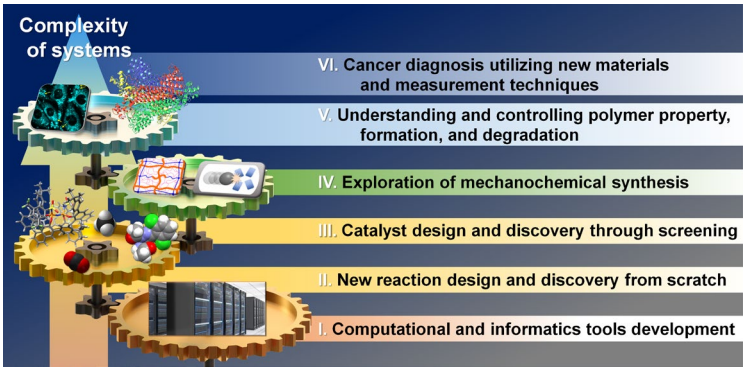
The extremely advanced materials that propel modern societies cannot be obtained for free, as they always represent the product of chemical processes that turn bulk and/or feedstock chemicals into value-added compounds using chemical reactions as tools. The objective of CReDD is the development of new chemical reactions that allow the effective synthesis of target compounds under concomitant minimization of the use of exhaustible resources (materials and energy). **The development of new reactions in the context of CReDD can be subdivided into three categories, depending on the size of the target molecules.** In the first category CReDD aims to create reactions that add high value to abundant resources and/or low-value substances (**small molecules of ~100 atoms**), while the second category is concerned with the synthesis of high-tech materials (**macromolecules of ~10,000 atoms**). The third category is concerned with the use of CReDD for cellular and biochemical reactions, whereby some of the materials developed in category 2 are applied to advanced medical care **(complex molecules > 10,000 atoms**). **In the early stage of the ICReDD, we select model reactions for proof of concept. Then, in the middle to the later stage, reactions that have a significant impact on the society are carefully selected based on the discussion with the broad scientific community members and companies.**

The key technique used in the CReDD is the automated reaction path search method (AFIR) that has been developed by Prof. Maeda, who is the director of the ICReDD. AFIR allows the accurate prediction of various reaction pathways to produce value-added target molecules from simpler starting materials. In order to apply this method effectively to relatively large molecules, which would conventionally incur prohibitively high costs for calculations and produce extremely complex experimental data, suitable information science tools (e.g. mathematical models and statistical analysis techniques) are developed and applied. As the complexity of such models and techniques increases with increasing size of the target molecules, CReDD is initially concerned with relatively simple molecular systems (category 1) and before subsequently advancing to more complex systems (categories 2 and 3).





To advance the actual research in ICReDD based on the aforementioned fusion concept, we have continuously worked on several flagship projects. As for FY2022, six projects shown in the figure below are running in parallel. Among the six projects, Project-I is special and serves as the foundation of ICReDD. All computational and informatics PIs collaborate with Project-I and provide feedback on the application of their tools to other projects. Project-I is closely related to all the other projects and provides computer-aided acceleration tools for them. During the monthly meetings, all computational and information sciences groups come together to share successful and unsuccessful cases based on their contributions to the other flagship projects. This feedback loop allows us to stay updated with the latest state-of-the-art computational and informatics tools used in these projects, and helps us to further advance these tools. The other projects exhibit a hierarchical complexity, where the complexity increases in the order of the project number. In other words, the number of atoms involved in the reaction treated in each project increases in this order. Tackling these projects with varying complexities simultaneously will enable us to establish a comprehensive set of tools that can be applied to a wide range of problems in chemical and materials sciences. Below, the six flagship projects are described in brief:



Project-I: Computational and informatics tools development. Project-I shares successful and unsuccessful cases of applications of computational and informatics tools to other projects and discusses ideas on their further development. This feedback loop between Project-I and the other projects strengthens our foundation and helps accelerate all our projects. Such an effort will create a range of computation-aided reaction design strategies that can be tailored to individual cases. In the first half of the WPI period, Project I contributed to the development of the QCaRA/AFIR approach, which combines the AFIR method with a graph-theory-based method for calculating reaction yields, leading to the first-principle discovery of previously unexplored chemical reactions. In addition, a cheminformatics-based approach to predicting the enantioselectivity of organocatalysis has contributed to the discovery of new catalysis.

In the second half of the WPI period, we will continue these efforts. Specific methods that we will develop are an integrated computational-informatics method for designing an appropriate organometallic catalyst for a given chemical transformation (related to project-II), an integrated computational-informatics method for designing a high performance organocatalyst that achieves asymmetric activation of unfunctionalized molecules (related to project-III), a simulation method for identifying unknown intermediates generated in a ball mill reaction environment (related to project-IV), a theory for modeling the influences of mechanical impacts (related to project-IV), a simulation method for studying the behavior of radical flagments formed by mechanical stretching force (related to project-V), and an informatics method for accelerating drug discovery for eradicating cancer stem cells (related to project-VI).

Project-II: New reaction design and discovery from scratch. This project tackles the highly ambitious objective of predicting new reactions from scratch using quantum chemical calculations. So far, we have demonstrated multiple successful examples of (non-catalytic) small molecule synthesis.

In the second half of the WPI period, we will focus our efforts on the discovery of catalysis. This can

be done in part on the basis of the achievements in non-catalytic reactions made in the first half of the WPI period, but is a much more complex matter requiring the further development of computational and informatics tools. The goal of this project is to establish a systematic design flamework for discovering a organometallic catalyst that can achieve previously unexplored chemical transformations.

Project-III: Catalyst design and discovery through screening. This project entails finding the optimal substituents for a catalyst through a computational screening process. To date, we have demonstrated a successful example of improving to enhance the enantioselectivity of List's IDPi catalyst for a known chemical transformation by using an informatics approach to screen and optimize the catalytic conditions.

The goal of this project is to achieve an asymmetric activation of unfunctionalized molecules using a computational and informatics approach. Such a transformation is highly ambitious for an organocatalyst and may be an appropriate goal for the second half of the WPI period.

Project-IV: Exploration of mechanochemical synthesis. This project focuses on mechanochemical synthesis using ball mills. This synthetic method has emerged as a highly promising tool in organic synthesis. However, our understanding of the process and its applicability is not yet sufficient.

The goal of this project is to broaden its applicability, elucidate unexpected species unique to this synthesis, and construct a theory for modeling the influences of mechanical impacts. In the first half of the WPI period, we have investigated novel types of ball mill reactions such as the cross-coupling of solid materials and synthesis of new organometallic reagents like the solid-state Grignard reagents. In the second half, based on the rational design of mechanochemical reactions, we will further expand its applicability and achieve solid-state photoredox reactions, synthesis of new organometallic reagents such as solid-state organocalcium compounds, decomposition and recycling of polymer materials, and highly efficient organocatalytic reactions in a ball mill.

Project-V: Understanding and controlling polymer properties, formation, and degradation. The project involves the design of polymer properties through simulation, visualization of polymer mechanoradicals, utilization of polymer mechanoradicals, the design of polymer sequences to maximize desired properties, and more. To date, we have established a computational method to identify radical fragments formed by mechanical stretching force and applied it to generic polymers and double network hydrogel polymers.

In the second half of the WPI period, we will find a design principle to maximize the performance of muscle-like double-network hydrogels. This will be done by studying the behavior of radical fragments formed by mechanical stretching force using both experimental measurement techniques and computational reaction pathway exploration. These measurement and pathway exploration tools will be used in another application that degrades polymeric materials in plastics by mechanical impact and uses them to synthesize useful materials.

Project-VI: Cancer diagnosis utilizing new materials and measurement techniques. In the first half of our WPI period, we have discovered the hydrogel-activated reprogramming phenomenon (HARP). This has been achieved utilizing the double-network hydrogel material developed by our PI. In collaboration with Dr. Mano, Director of the National Cancer Center, the effectiveness of the rapid cancer stem cell generation method using HARP was confirmed. The results confirmed that cancer stem cells obtained by this method have the same profile as those obtained by conventional methods. In FY2022, we have launched a consortium called the "Clinical Platform for Chemical Reaction Collaboration" in partnership with the School of Medical Science. Through this consortium, we aim to accelerate the

utilization of our chemical products in medical diagnosis and treatment. In order to further accelerate fusion research between chemistry and clinical medicine, the center has changed experimental science PIs from Prof. Sawamura to Prof. Ogawa (Chemical Biology) in FY2023 to realize efficient cancer treatment methods based on detailed chemical manipulations.

There are two directions in this project: one is to understand HARP properly and another is to achieve its clinical application. In the second half of our WPI project, we will address both of these topics simultaneously, through a fusion team among chemical biologists, materials scientists, informaticians, tumor pathologists, clinicians, and medical doctors.

Bottom-up project: Additionally, we have called ideas from young researchers every year and launched them as bottom-up projects. Based on their outcomes, successful bottom-up projects are promoted to flagship projects, while underperforming flagship projects are evaluated and may be discontinued. This approach allows us to consistently deliver high-impact outcomes featuring our young researchers.

Strategies of industry-academia collaboration for implementing research results in society: To make the latest computational methods developed at ICReDD widely available to society, "GRRM20" was launched from HPC Systems, Inc. in 2021 under a program license agreement with the University, in which the latest features of the AFIR method are available. GRRM20 is a "technology needed in society" that companies also need, and selling it is one of the center's contributions to society. The center already established a system for the use of this program in MANABIYA (INDUSTRY) for joint research with companies. With the aim of further implementing research results in society, the center will accelerate its industry-academia collaboration in the second half of the grant period by utilizing the industry-academia collaborative research space in the new building. The results have already materialized as new industry-academia collaborations in ICReDD. From FY2023, "Mitsui Chemicals-ICReDD Laboratory" as one of the Industry Creation Laboratories will be launched for joint research focused on the swift, high-precision design of new reactions that will contribute to the development of high-performance materials and the creation of a recycling-oriented society, based on ICReDD's strength in chemical reaction design and discovery, which integrates the three fields of computational science, information science, and experimental science, and Mitsui Chemicals' knowledge of materials development. Another company is considering establishing a similar industry creation laboratory. Additionally, efforts will focus on achieving further advances in chemical reaction design and discovery via research and development of new computational science and information science technologies. These initiatives will lead to the rapid implementation of our research outputs in social and industrial applications.

2)-3 System for advancing the research

* Describe the center's research organization (including its research, support and administrative components) and your concept for building and staffing the organization.
* Describe your concrete plan for achieving the center's final staffing goal, including steps and timetables.
* Describe your concrete plans (steps and timetables) for achieving the center's gender-balance plan. When describing the plan, the following should be noted:
  1. Concrete plans should be divided into the following two categories and each plan should be described.
     a. plans at the executive level including the center director and administrative director
     b. plans among principal investigators (professors, associate professors) and other researchers
  2. In addition to the above 1, describe the following plans:
     a. plans for fostering researchers with a view to achieving gender plans
     b. plans for domestic and international promotion activities to attract female researchers to the center
* If the center will form linkage with other institutions, domestic and/or foreign, *by establishing satellite functions*, provide the name(s) of the partner institution(s), and describe their roles, personnel composition and structure, and the collaborative framework with the

center project (e.g., contracts to be concluded, schemes for resource transfer).

* If the center will form linkage with other institutions, domestic and/or foreign, *without establishing satellite functions*, provide the names of the partner institutions and describe their roles and linkages within the center project.
* Appendix: "List of Principal Investigators" (to be attached)
* Appendix: "Composition of personnel in center" (to be attached)

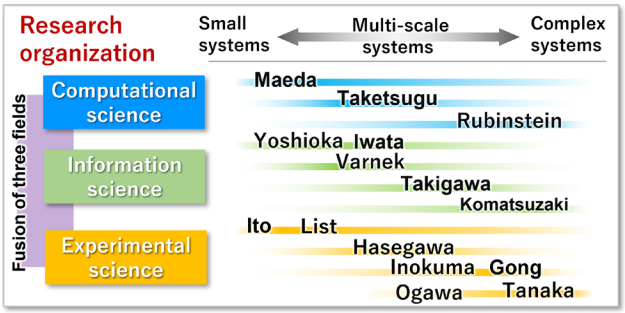
[Research Organization]

Computational Science: The director of the ICReDD, **Prof. Maeda**, heads an internationally leading research group concerned with computational chemistry; Prof. Maeda has developed the automated reaction path search method (AFIR) (*PCCP* **2013**; top 1% paper), which is used to **predict reaction path networks for various chemical reactions.** The establishment of the reaction path network is crucial for the integrated nature of this initiative. In cases where reactions involve an excited state, **Prof. Taketsugu**, who has extensive experience in calculating photoreaction processes, performs high-precision calculations. **Prof. Rubinstein (Duke University)**, a specialist in the computational science of polymer models, examines complex reaction systems including macromolecules (polymers and gels). In addition to these PIs, we appoint associate professors and (post)doctoral research fellows who are familiar with computational science in order to model macromolecules and complex systems based on the results from the high-precision calculations on reactions involving small molecules.

Information Science: As chemical reactions have far-reaching implications at the micro, meso, and macro level, information science uses statistical and mathematical models to analyze and unveil complex multi-layer hierarchical systems with cross-layer coordination. This should **allow bridging the gap between different hierarchical layers (from quantum and physical chemistry to biophysics to cell biology)** and also disentangling the complex nature of chemical reaction networks that has been exposed by Prof. Maeda's research. **Prof. Arimura** (data mining), who is a world-leading expert on scalable data mining, led the design of efficient algorithms for the discovery of knowledge in the computational and experimental data that has been accumulated in the ICReDD's cross-sectional research. In FY2019, we changed information science PIs from Prof. Arimura to **Prof. Yoshioka** (Knowledge Engineering) (Director of Global Stations for Big Data and Cybersecurity, GI-CoRE) to realize an efficient information retrieval from experimental databases and literature. Prof. Iwata (Mathematical Engineering) from the Graduate School of Information Science and Technology at the University of Tokyo joined as a PI in FY2020. **Prof. Iwata** develop an informatics tool to extract useful information for chemical reaction design and discovery from the AFIR reaction path map database (AFIR3M-DB) used at ICReDD, supporting the development of an efficient database. **Prof. Varnek (chemoinformatics, University of Strasbourg)** integrates computational and experimental sciences in category 1 using state-of-the-art chemoinformatics methods for molecular screening and reaction design. **Prof. Komatsuzaki** (mathematical science), who is experienced in the analysis of chemical reaction networks, works on the mathematical modeling of macromolecules and complex systems. **Prof. Takigawa**, an expert in machine learning, establishes data-driven predictive models based on machine learning and data science to extract maximum information from the diverse kinds of available data. This approach provides a rational strategy for the optimal design of experiments as well as the design and discovery of bespoke functional materials and life-science-related molecules.

Experimental Science: Experimental scientists **create the CReDD output via the implementation of reactions at various hierarchical levels.** For the development of high-value-added reactions (category 1), we target a broad variety of molecules that range from pharmaceuticals to functional materials. **Vice Director Prof. Ito** (synthetic chemistry) and **Prof. Sawamura** (catalysis)

address transition-metal-catalyzed reactions, while **Prof. List (reaction design, Max Planck Institute for Coal Chemistry)**, who is a world-renowned expert on reaction design, investigates catalytic organic reactions for the efficient development of reactions without having to rely on trial-and-error methods. In category 2, **Prof. Hasegawa** (optical material science) develops high-performance light-emitting materials based on the predictions of the excited-state calculations performed by Prof. Taketsugu, while **Prof. Gong** (polymer science), who is a gel materials expert, creates stimuli-responsive materials that e.g. toughen upon exposure to mechanical stimuli and that can decompose or deteriorate in a controlled manner. **Prof. Inokuma** (structural chemistry) performs structural analyses of the obtained macromolecules and provides feedback for the collaborators concerned with information science. The thus obtained experimental information helps to the reduce the calculation costs in category 2. During the experimental verification of category 3, In order to accelerate fusion research between chemistry and clinical medicine, we have changed experimental science PIs from Prof. Sawamura to **Prof. Ogawa** (Chemical Biology) in FY2023 to realize efficient cancer treatment methods based on detailed chemical manipulations. **Prof. Tanaka** (tumor pathology), who is an expert in disease-function analysis, investigates complex cell responses using the new materials obtained in category 2. In collaboration with information science researchers, he aims to effectively find hidden biochemical reaction systems that are hampered by diseases. The experimental researchers then develop innovative regenerative medical strategies that do not require genetic engineering, novel diagnostic tools for cancer to overcome cell variation, and biocompatible materials that can control cellular responses.



Integrated Research Center and Collaboration Organizations: The ICReDD hosts ~100 members, which includes ~30 coordinators and support staff. We invite foreign PIs using a cross-appointment system and encourage the creation of sub-research groups that host full-time Co-PIs and (post)doctoral research fellows at Hokkaido University, which provide significant valuable leadership training for younger researchers. PIs invite and host foreign researchers in order to further their professional development in the three core areas of CReDD, and to promote human-resource development and collaborative research. **In order to disseminate CReDD internationally, we are implementing the MANABIYA system, which consists of a continuous cycle of short-term visitors comprising approx. 20 foreign researchers and graduate students**. Since we can lead and accelerate research in other institutes, we invite researchers (*without satellite functions*) from other WPI centers such as the ITbM (Nagoya University) and the MANA (NIMS), as well as from other foreign research institutes and companies to practically experience CReDD. We also consult with Prof. Minato (Kyoto University), who is familiar with this area of research, to ensure that these collaborations proceed efficiently. **By focusing on the accelerated collaborative research, the ICReDD will hopefully become the premier international center of integrated computational, information, and experimental researches on chemical reactions.**

List-Platform: From 2023, the ICReDD will establish an international collaboration research platform to promote the next generation organocatalytic chemistry with digital transformation (DX), which will accelerate new developments in research originating from ICReDD. This research platform, called "List-Platform", will be headed by Professor List, a Nobel laureate, and will promote next generation

organocatalytic chemistry that integrates computational science with DX technologies such as robotics, machine learning, and artificial intelligence by applying the advanced technologies of ICReDD, which combine computational science, information science, and experimental science. This List-Platform will establish five research groups, starting with basic theoretical research and extending to catalyst development, evaluation and optimization, drug discovery and materials development, and synthetic process development, and will mobilize the collective efforts of top-level researchers inside and outside the university. Furthermore, we will invite world-class researchers from Japan and abroad as fellows to provide advice on research and share research results widely, aiming to become a leading international research exchange center for sustainable DX organocatalytic chemistry research.

The center's gender-balance plan: The center will take various measures to ensure the diversity of its members, especially to achieve an appropriate gender balance. As of March 31, 2024, the number of PIs was 15 including 3 foreign PIs, 48% of all researchers were foreign nationals, and 19% were female researchers (total of 84 researchers, including 40 foreign nationals and 16 female researchers. These researchers are split between the fields of Computation (16 researchers, 19%), Information (19 researchers, 23%), and Experiment (49 researchers, 58%). Achieving an appropriate gender balance at the center is one of our top priorities, and we will make our utmost efforts to achieve at least 25% female researchers at the center as soon as possible. The total goal of 25% female researchers is broken down into specific goals for different seniority levels, with a goal of 20% females at the executive level (center director, administrative director, etc), 13% at the principal investigator level (professors and associate professors) and 27% among other researchers. To achieve this goal, all PI-groups are asked to have at least one female researcher. ICReDD has already secured positions for a female assistant professor and a tenure-track associate professor. In the future, the center plans to recruit several open positions for female-only faculty members. Through these positions, a career path system for female researchers from student, postdoctoral researcher, assistant professor, and associate professor (Jr. PI) to professor (PI), can be expected to function as a role model for and attract more attention from female researchers. Finally, they will be established as PIs of the center and inject a fresh, young perspective into the center’s research direction and leadership. The center periodically conducts seminars and other events that contribute to the promotion of diversity, equity, inclusion, and gender balance for members of faculty, staff, students, etc. The center will also actively recruit female faculty members and students using the University Accelerated Gender Balance Action Plan and the University Fellowship System, and establish a strong, collaborative relationship with the Office of Diversity, Equity, and Inclusion.

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

* Paste onto table a) in Appendix: personnel_in_the_center.

	At beginning of project	At end of FY 2023	Final goal (March 2028)
Researches from within the host institution	11	12	12
Foreign researchers invited from abroad	3	3	3
Researchers invited from other Japanese institutions	0	0	0
Total principal investigators	14	15	15

b) Total number of members

* Paste onto table b) in Appendix: personnel_in_the_center.

			At beginning of project		At end of FY 2023		Final goal (March 2028)	
			Number of persons	%	Number of persons	%	Number of persons	%
Researchers			14		84		85	
	Overseas researchers		3	21	40	48	38	45
	Female researchers		1	7	16	19	21	25
	Principal investigators		14		15		15	
		Overseas PIs	3	21	3	20	7	47
		Female PIs	1	7	2	13	2	13
	Other researchers		0		69		70	
		Overseas researchers	0	0	37	54	31	44
		Female researchers	0	0	14	20	19	27
Research support staffs			0		3		4	
Administrative staffs			6		20		19	
Total number of people			20		107		108	

		At beginning of project		At end of FY 2023		Final goal (March 2028)	
		Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students		67		64		80	
	Employed	17	25	16	25	48	60

※b) The number of doctoral students in the lower table can be duplicated in the upper table of overall composition.

Chemical reaction design and discovery

Computational science

● Director **MAEDA, Satoshi** (computational science)
Development of automated reaction path search methods
The Japan Society for the Promotion of Science (JSPS) Award, Banyu Chemist Award, Principle Investigator of Core Research Evolutional Science and Technology (CREST)
Publications: e.g. *Science*, *JACS*, and *Angew. Chem.*

● **TAKETSUGU, Tetsuya** (quantum chemistry)
Development of light-emitting materials by calculation of excited states
NIMS Global Research Center for Environment and Energy Based on Nanomaterials Science (GREEN)
Publications: e.g. *Science*, *JACS*, and *Adv. Mater.*

● **RUBINSTEIN, Michael** (polymer physics)
Duke University and Hokkaido University Distinguished Professor, Co-chair Gordon Research Conference
Modeling of various polymeric systems
Advisory Board member of *Soft Matter*
Publications: e.g. *Nature*, *Nature Materials*, and *Science*.

Information science

● **YOSHIOKA, Masaharu** (knowledge engineering)
Efficient information retrieval from experimental databases and literature
Director of Global Stations for Big Data and Cybersecurity, GI-CoRE

● **IWATA, Satoru** (mathematical engineering)
Development of informatics tool to extract useful information for chemical reaction design and discovery from the AFIR reaction path map database
Principle Investigator of CREST and ERATO

● **VARNEK, Alexandre** (chemoinformatics) University of Strasbourg
Reaction databases and molecular screening
Vice-president of the French Society of Chemoinformatics
Publications: e.g. *JACS*

● **TAKIGAWA, Ichigaku** (machine learning)
Reaction network modeling and data-driven predictions
Principle Investigator of Precursory Research for Embryonic Science and Technology (PRESTO)
Publications: e.g. *Nature Comm.*

● **KOMATSUZAKI, Tamiki** (mathematical science)
Mathematical modeling of macromolecule systems and data-driven science
Editorial Board member of *Sci. Rep.*, Director of CREST
Publications: e.g. *PRL*, *PNAS*, *Nature Comm.*, and *Nature Chem. Bio.*

Experimental science

● Vice Director **ITO, Hajime** (synthetic chemistry)
Development of new reactions including multi-element reactions and small molecules
CSJ Award for Creative Work, Principle Investigator of PRESTO, Funding Program for Next Generation World-Leading Researchers (NEXT)
Publications: e.g. *Nature Chem.*, *Nature Comm.*, *JACS*, and *Angew. Chemie.*

● **LIST, Benjamin** (reaction design) Max-Planck Institute for Coal Chemistry
Development of new reactions with organocatalysts and/or small molecules
Thomson Reuters Highly Cited Researcher, Editorial Advisory Panel member of *Nature Comm.*, Editor-in-Chief of *Synlett*
Publications: e.g. *Nature*, *Science*, *Nature Chem.*, *Chem. Rev.*, and *JACS.*

● **HASEGAWA, Yasuchika** (optical materials science)
Development of light-emitting materials with high brightness and high durability, macromolecules
CSJ Award for Creative Work, Prizes for Science and Technology from the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT)
Publications: e.g. *JACS*, *Sci. Rep.*, and *Angew. Chem.*

● **INOKUMA, Yasuhide** (structural chemistry)
Development of functional crystalline and polymer materials, macromolecules
Nagase Special Prize, The Young Scientists' Prize by MEXT, Principle Investigator of PRESTO
Publications: e.g. *Nature*, *Nature Chem.*, *JACS*, and *Angew. Chem.*

● **GONG, Jing-Ping** (polymer chemistry) Hokkaido University, Distinguished Professor
Development of biocompatible/Self-evolving gels, and macromolecules
RSC Fellow, CSJ Award for Creative Work, Award of the Japanese Society of Polymer Science, Grants-in-Aid for Scientific Research (S), Grants-in-Aid for Specially Promoted Research, Principal Investigator, Editorial Board member of *Macromolecules*, *Polymer*, *Soft Matter*
Publications: e.g. *Science*, *Nature Mater.*, and *Nature Comm.*

● **OGAWA, Mikako** (chemical biology)
Development of efficient cancer treatment methods based on detailed chemical manipulations
American Journal of Nuclear Medicine and Molecular Imaging, Senior Editorial Board
Publications: e.g. *Nature Medicine*, *Nature Comm.*

● **TANAKA, Shinya** (tumor pathology)
Cell control by new material(s), machine learning, and complex molecules
Director of the Japanese Society of Pathology, Incitement Award of the Japanese Cancer Association, Incitement Award of the Japanese Society of Pathology, Associate Editor of *Brain Tumor Pathol.*
Publications: e.g. *Nature Str. Mol. Biol.*

Advisor and collaborative researcher

MINATO, Shin-ichi (information science) Kyoto University
Research Director of ERATO, Visiting Professor at Hokkaido University

2)-4 Securing research funding

Past record

* Give the total amount of research funding (e.g., competitive funding) secured by the principal investigators who will join the center project. Itemize by fiscal year (FY2018-2022).

Past record of the total amount of research funding acquired by the PIs between FY2018 and FY2022:

¥197,667,491 (FY2018 (half-year)); ¥590,484,235 (FY2019); ¥605,345,001 (FY2020); ¥406,725,491 (FY2021); ¥555,375,511 (FY2022); ¥2,355,597,729 (Total FY2018-FY2022).

Funding prospects after the establishment of the center

* Based on the past record, describe your concrete prospects for securing resources that match or exceed the WPI grant (FY2023-2027).
* Calculate the total amount of research funding (e.g., competitive funding) based on the amount of funding that the researchers will allocate to the center project. Be sure that the funding prospects are realistically based on the past record.

ICReDD PIs receive about 510 million yen in research funding per year. The total annual amount of research funds obtained by young researchers in the PIs' laboratories and the four Jr-PIs hired with the support of the university in FY2022 is expected to be about 640 million yen, which will be sufficient to promote their research activities. In order to support young researchers in obtaining research funding in the fields of chemistry and informatics, ICReDD has established a system to brush up their application documents for competitive funding. Based on this, it is expected that the success rate of research fund applications will be improved and that continuous research funding will be secured. In addition, in FY2023, a five-year large-scale joint research project (250 million yen in total) with a company will be launched. We plan to continue to actively acquire private sector funds in cooperation with the Institute for the Promotion of Business-Regional Collaboration. These research funds, together with commitments of financial support from our host institution, will secure resources equivalent to or greater than WPI grants.

3) Interdisciplinary Research

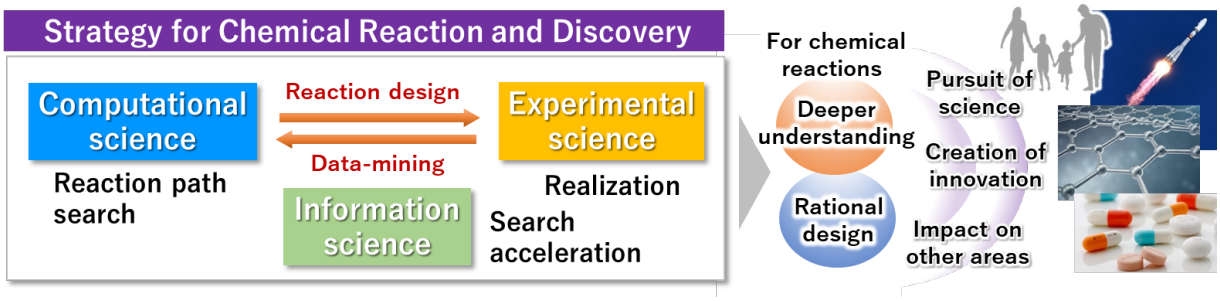
* Describe the fused research domains, why interdisciplinary research is necessary and important in the target field(s), and what new field(s) can be expected to be created by way of this project. Describe your concrete strategy for fusing different research domains and creating new field(s) by the fusion.

[Necessity and Significance of Integrated Research]

Given their particular importance for human activity and sustenance, it is hardly surprising that industry branches related to chemical reactions have a combined annual impact of 500 trillion yen (4 trillion USD). The rational design of chemical reactions based on a better understanding of how they procced should allow carrying out these operations more efficiently. **However, using quantum chemistry to examine chemical reactions is very expensive and time-consuming as the numerous combinations of possible chemical reaction patterns usually require prolonged calculations.** Prof. Maeda's automated reaction path search method allows calculating virtual forces between molecules that are next to each other or separated (artificial force-induced reaction; AFIR), which enables the extraction of the molecular behavior that is crucial for chemical reactions. Still, when this method is applied to more complex 'realistic' systems, the time required to carry out the necessary complex calculations is relatively long. This obstacle could potentially be circumvented by taking advantage of established methods in information science such as high-speed algorithms and pattern calculations, which should dramatically reduce the calculations. Subsequently, experimental scientists carry out the practical verification of the proposed

reactions in collaboration with the computational and information scientists. In addition, experimental results are analyzed and used as data feedback for the information scientists to extract new insights and apply these to the chemical reaction design.

The academic field of "Chemical Reaction Design and Discovery (CReDD)" aims to understand and design bespoke chemical reactions by integrating three different areas of research. The success of CReDD would not only benefit areas that are directly related to chemical reactions, but also the global environment, life sciences, and society in general, as most industrial productions depend on substances obtained from chemical reactions. The creation of CReDD as an academic research area and the foundation of a WPI dedicated to CReDD should thus act as an initiator and incubator for ripple effects that affect all aspects of society. Collaborative research of PIs for the ICReDD at Hokkaido University has already produced significant preliminary results that have become the foundation of ICReDD.



For example, Profs. Maeda (computational science) and Ito (experimental science), the director and vice director of ICReDD, have already discovered new reaction mechanisms for highly complex reactions using the AFIR method (JACS **2015**). Prof. Taketsugu (computational science) has already developed new functional materials in collaboration with Profs. Ito (experimental science) and Hasegawa (experimental science; JACS **2017**). Prof. Takigawa (information science) is a world leader in the development of new catalytic reactions using computational science and machine learning in collaboration with experimental scientists at Hokkaido University (RSC Advances **2016**). However, to truly integrate these three areas of research and to firmly establish CReDD, the collaborating scientists must work together in a research center in order to foster cross-fertilization and maximize synergistic effects. At this integrative research institute, we not only accomplish groundbreaking research, but also train and educate a future generation of internationally oriented researchers that are experts in all three research areas.

[Strategies for Advancing Integrated Research]

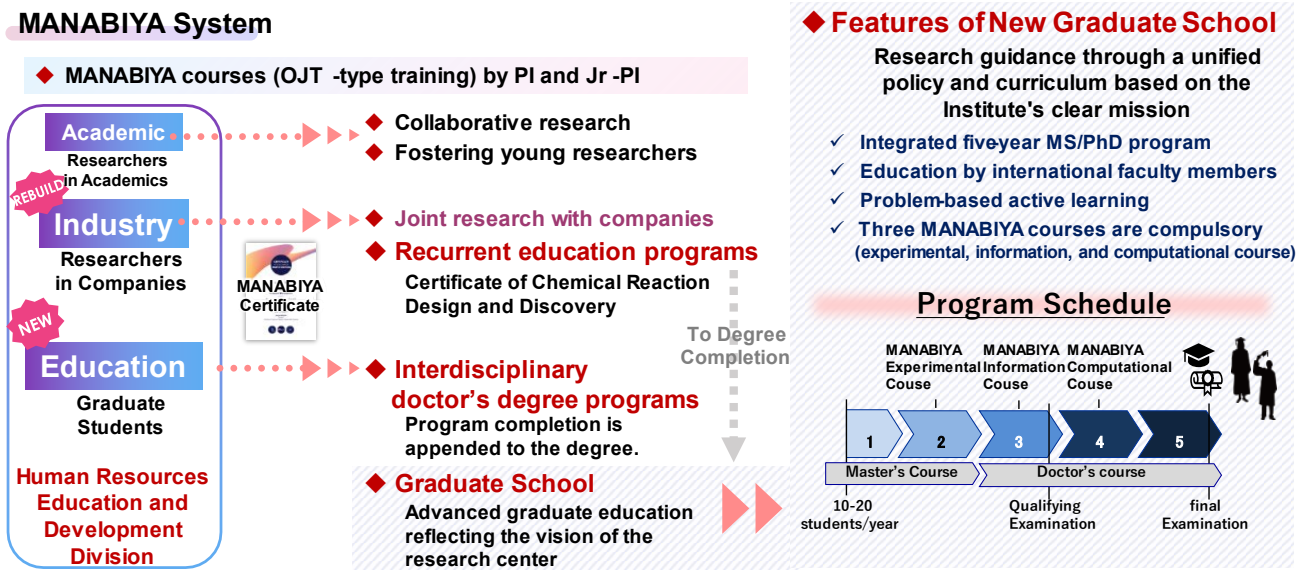
Research activities take place at the **"Hokkaido University Creative Research Institution (CRIS) Building,"** and the close proximity of researchers results in frequent information exchange and collaboration. We invite young researchers from national and international institutes for periods of 1-3 months in order to familiarize them with this new collaborative approach to develop new reactions. This **MANABIYA system invites approximately 20 foreign researchers and graduate students (MANABIYANs) per year.** These researchers are trained in the new collaborative methods and they return to their home institutions to apply them there. **After 10 years, the MANABIYAN network should comprise >200 researchers** in a balanced mixture of experienced global leaders and young researchers, which should support the further development of this new field. Additionally, we also provide

high-quality video conference systems that are continuously connected in order to facilitate exchange and collaboration with foreign satellite institutes.

Until now, the purpose of MANABIYA (ACADEMIC and INDUSTRY) was to promote collaborative research, foster young researchers, and promote research in collaboration with companies. From FY2023, ICReDD will establish "MANABIYA (EDUCATION)" as an education curriculum for graduate students. This MANABIYA (EDUCATION) will serve as the core of two main educational systems that ICReDD will be established. One of the education systems is an interdisciplinary degree program open to all graduate students in the University. In this program, by completing a variety of curricula centered on on-the-job training at the multiple MANABIYAs, participating graduate students are expected to acquire the skills and knowledge of ICReDD researchers and apply them to their own research. Graduate students who complete "MANABIYA (EDUCATION)" will receive a certificate of completion issued by ICReDD and graduate credits.

Another educational system is ICReDD's own graduate school. Based on MANABIYA (EDUCATION), we are aiming to establish a graduate school that reflects the philosophy and vision of ICReDD. The graduate school is designed to be an integrated five-year program, and enrolled graduate students will take three MANABIYA (EDUCATION) courses in different fields (experimental, computational and information science) over the five years. In addition, they will receive an interdisciplinary and international education through a combination of PBL-type lectures in English by ICReDD's international researchers and short-term study abroad programs. This graduate school is expected to foster human resources who can share ICReDD's vision and lead the society of Society 5.0 in the future.

To establish and effectively operate the MANABIYA system, including the new MANABIYA (EDUCATION) as well as other MANABIYAs, ICReDD will establish the "Human Resource Development Unit" in 2023, which is in charge of fostering researchers, graduate students, and industrial researchers using the MANABIYA system, as well as creating strategies and roadmaps for the center's graduate and recurrent education. "Chemical Reaction Design and Discovery" and "MANABIYA" will also be firmly rooted in the university's organizational structure via the establishment of the "Graduate School of Chemical Reaction Design and Discovery".



As described above, we work on several flagship projects. Each project involves groups from two or more disciplines. Setting and working on such flagship projects together have been a strong driving force to promote interdisciplinary fusion in ICReDD. In addition, we call ideas from young researchers in ICReDD and provide them an opportunity to lead a bottom-up project. These flagship and bottom-up projects are evaluated yearly. Then, promising ones are expanded or promoted from bottom-up to flagship. Conversely, ones that are not proceeding well are terminated or restarted as a bottom-up project. These projects are carried out under the director's initiative. To do that, we set a position called fusion research coordinator. The fusion research coordinator joins periodic meetings of all these projects and reports their progress to the director. If necessary, the fusion research coordinator by himself participates in a project and leads the project together with project's leader. Moreover, all researchers in ICReDD have a formal opportunity to report their progress twice every year to the director, the administrative director, and the fusion research coordinator.

Regarding results, we have published 547 papers in the first half of the WPI period, of which 160 are from fusion research involving contributions from two or more research groups in ICReDD. For example, Maeda-group (computation) together with Mita (experimental lab-chief) published multiple papers on the development of new synthetic methods utilizing quantum chemical reaction path networks (*Chem. Sci.* **2020**, *Nat. Synth.* **2022**, *Nat. Commun.* **2022**). Iwata-group (information) together with Maeda-group (computation) developed a combinatorial optimization approach to tackle the huge diversity of chemical space (*Sci. Rep.* **2021**). List-group (experiment) and Varnek-group (information) achieved an informatics-driven discovery of new organocatalysis (*Angew. Chem.* **2023**). Ito-group (experiment) together with Maeda-group (computation) discovered a mechanochemical Grignard reagent and investigated its structure (*Nat. Commun.* **2021**). Gong-group (experiment, material), Ito-group (experiment, organic), and Maeda-group (computation) developed a fluorescence probe to rapidly detect mechanoradicals in hydro-gel materials (*J. Am. Chem. Soc.* **2023**). Gong-group (experiment, material) and Tanaka-group (experiment, medical) discovered the hydrogel-activated reprogramming phenomenon (HARP) which could potentially revolutionize cancer diagnosis (*Nat. Biomed. Eng.* **2021**). These outputs evidence the effectiveness of our strategy and prove that the strategy would work well for achieving our goal of "revolutionizing chemical reaction design and discovery".

4) International Research Environment

4)-1 System for advancing international research

* Describe your concrete plan for building an international research center including the makeup of its foreign researchers, establishment of oversea satellites, or similar functions. Include a time schedule for the plan.

* Describe concretely your strategy for staffing foreign researchers (e.g., postdoc positions) through open international solicitations. Describe the procedures you will use to do so.

We have invited three world-leading researchers from foreign research institutes to participate in the ICReDD. Prof. Rubinstein (Duke University, USA) is a globally acclaimed researcher in theoretical polymer physics. Since 2016, he has worked as a visiting professor at the Global Institute for Collaborative Research and Education (GI-CoRE; Hokkaido University), where he has recently been appointed as Distinguished Professor. Currently, he is in the process of developing collaborative research related to soft matter. Prof. Varnek (University of Strasbourg, France) is a world-renowned researcher in chemoinformatics, who also focuses on the dissemination and education of chemical informatics. Prof. List (Max Planck Institute for Coal Research, Germany) is a leading experimental scientist in reaction design, especially in the context of organic catalysts.

Foreign PIs stay in ICReDD for a sufficient period, e. g. two months, to contribute to the fusion research in cooperation with Co-PIs by frequently using TV-conference to increase the percentage of time they spend on site. Since foreign PIs simultaneously serve at their home institutions and the ICReDD, **we have established research groups for foreign PIs within our center and employed Co-PIs and research staff** (i.e., specially appointed associate and assistant professors as well as postdoctoral fellows) to support and manage the research groups in close collaboration with the foreign PIs. All specially appointed associate/assistant professors and postdoctoral fellows employed at the ICReDD are selected through a competitive, international recruitment process, and **>40% of these researchers are foreign.** The aforementioned Co-PI system has had great success at the WPI of Nagoya University (ITbM), and a similar scheme was used in the SMART program between the Massachusetts Institute of Technology and the National University of Singapore. With this system, world-renowned foreign PIs have established research teams at the ICReDD in collaboration with Co-PIs, creating outstanding research environments that promote interdisciplinary interaction. Such an inspirational environment should allow the continuous fostering of young researchers, who represent the future of the scientific community and technology development. Foreign PIs also invite young foreign researchers to participate in the ICReDD via the aforementioned MANABIYA system.

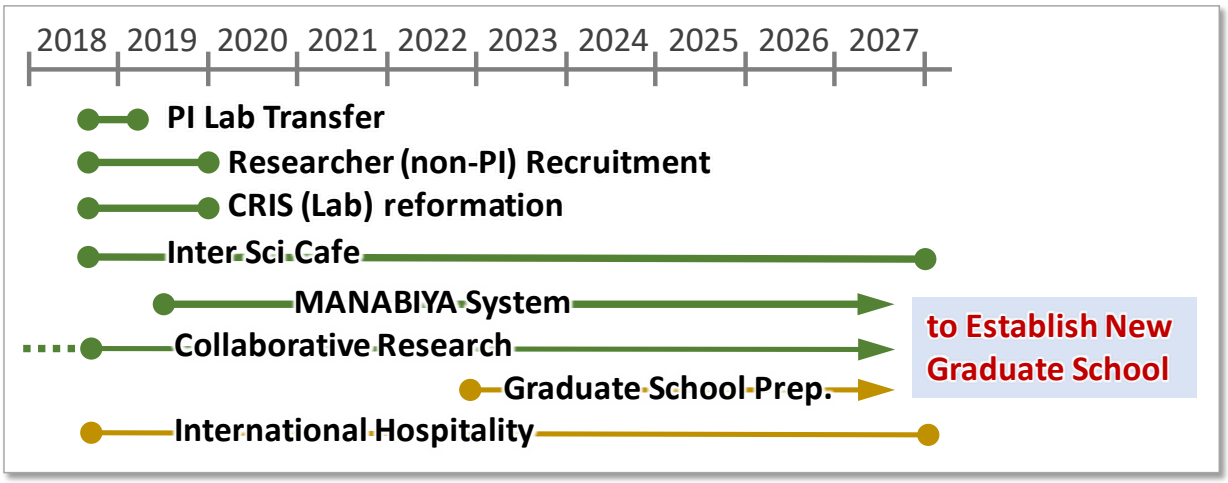
In 2014, as part of its mid-to-long-term strategy, Hokkaido University has established **the Global Institution for Collaborative Research and Education (GI-CoRE)**, with a faculty organization scheme that is under the direct control of the president of the university. This institution has launched six GI-CoRE centers in research fields that are considered to be the strengths of the university and promoted organized international collaborative research with voluntary funding. Among these centers, especially the Soft Matter GI-CoRE and the Information Science GI-CoRE are currently used as centers of collaborative research that would be connected to the ICReDD. **These GI-CoRE centers are carefully incorporated into the ICReDD as key sub-organizations.** In the Soft Matter GI-CoRE, Prof. Gong serves as a representative to promote strong collaborative research. Furthermore, we continue to promote and support systematic collaboration with Duke University (Soft Matter GI-CoRE) and the University of Massachusetts Amherst (Information Science GI-CoRE). We also collaborate closely with Emory University (computational chemistry), the Swiss Federal Institute of Technology in Zurich (ETH Zurich; experimental science), Peking University (experimental science), and Stockholm University (experimental science) through collaborative research and the MANABIYA system, thus generating an environment that encourages international collaboration while promoting interactions among researchers. We try to expand the collaboration network further by actively interacting with researchers both in Japan and abroad. To compensate for the decrease in face-to-face communication, we regularly hold online meetings using zoom to maintain an environment that allows us freely to communicate, chat, and discuss research topics.

Agreements are in place with the Max Planck Institute, the University of Strasbourg, the University of Tokyo, and Chubu University. Furthermore, Duke University, Peking University, Stockholm University, University of Oslo, Queen's University, and ICIQ (Institut Català d'Investigació Química (Institute of Chemical Research of Catalonia)) were strong collaborative institutions. We plan to continue to collaborate with these research institutions and conclude exchanges and agreements in a planned and concrete manner in cooperation with the University's International Cooperation Organization.

To expand the scope of ICReDD's research both inside and outside the University and serve as an incubation system for next PIs, ICReDD will establish a new position called the ICReDD fellow from FY2023. ICReDD provides ICReDD fellows invited from Japan and overseas with our resources and collaborate with

them.

Collaborating international institutes	Country	MANABIYA	Collaborative research	Official inter-university agreement
University of Strasbourg [Foreign PI]	France	✔	✔	✔
Max Planck Institute for Coal Research [Foreign PI]	Germany	✔	✔	✔
Duke University [Foreign PI]	U.S.A.	✔	✔	✔ Soft Matter GI-CoRE
ESPCI	France	✔	✔	✔ Soft Matter GI-CoRE
University of Massachusetts Amherst	U.S.A.	✔	✔	✔ Information Science GI-CoRE
Swiss Federal Institute of Technology in Zurich (ETH)	Switzerland	✔	✔	✔
Stockholm University	Sweden	✔	✔	✔
Emory University	U.S.A.	✔	✔	
Peking University	China	✔	✔	✔



4) -2 Establishment of international research environment

* Describe your concrete strategy for establishing an international research environment, administration system, and support system (e.g., appointment of staff and provision of startup funding) to accommodate researchers from overseas.
* Concretely describe how the center will provide an environment in which researchers can work comfortably on their research by being exempted from duties other than research and related educational activities, and how they will be provided adequate staff support to handle paperwork and other administrative functions. Include your procedure and time schedule.
* Describe your strategy, procedure and timing for periodically holding international research conferences or symposiums (at least once a year).

Start-up research funds are provided for the foundation of the research groups of the foreign PIs to establish research environments that allow a start of the research activity that is as frictionless as possible. As **English is the working language in the ICReDD**, all members of staffs that are endowed with management tasks and the operation of the ICReDD must be fluent in English in order to ensure sufficient support for research activities, collaborations, publications, and administrative work. The already established GI-CoRE and the associated centers at Hokkaido University have thereby provided support for foreign researchers. Furthermore, we have established **an international hospitality support system** that provides assistance for foreign PIs and their families regarding non-research-oriented issues such as visas and housing in order to ease the transition and promote research efficiency. This system utilizes the

resources of the already established GI-CoRE and the Institute for International Collaboration at Hokkaido University. We have also implemented **an international promotion program** to enable effective collaboration between foreign researchers and Japanese researchers and their students. We frequently invite world-class researchers to the ICReDD and host **annual international symposia**. Part of the **MANABIYA system** works as a short-term exchange program between young foreign researchers and Japanese graduate students in order to promote diversification within the ICReDD and to establish and nurture an international network.

5) Center Management and System Reform

5) -1 Project management

* Describe the role of the center director and the administrative director.
* Concretely describe your concept for establishing an administrative organization, the center's decision-making system and how authority is allocated between the center director and the host institution.
* Concretely describe how the center will adopt a rigorous system for evaluating research and will introduce a system for merit-based compensation (e.g., annual salary scheme). Describe your procedures and timing for operationalizing these systems.

The goals and concepts of the ICReDD with the WPI program at its core will be consistently developed by the director, Prof. Maeda, who is despite his youth a world-leading computational scientist. Prof. Maeda will serve for a period of at least 10 years, seconded by Prof. Ito, a world-renowned experimental scientist with extensive experience in organizational operations, who serves as the vice director. The ICReDD has been established within the Creative Research Institution (CRIS) building and formed a center dedicated to the fusion of globally leading computational, information, and experimental sciences in order create an internationally competitive research/education environment. **Decision-making rights regarding central matters of institute management such as recruitment of personnel and budgetary discretion rest exclusively with the director of the ICReDD, who also presides over a university-allocated budget of at least 10 million yen per year that can be freely used by the director.** Upon the launch of the program, we have built a co-management system to support the ICReDD's young director based on the extensive experience of the vice director. In the medium-to-long term, the director will establish a system of top-down decision-making. **To support the decision-making process of the director, a steering committee, composed of the vice director, the administrative director, and the university research administrators (URAs), has been established.** The attendance of PIs at steering committee meetings is not required so that the PIs can focus exclusively on research. However, PIs may directly advise the director about any concerns if and when necessary. Based on the performance-evaluation system that has already been introduced at Hokkaido University, **we have constructed a salary scheme that is centered on research performance and ability. Depending on the progress of research, the roles of each PI will be reviewed and evaluated periodically by the director, and appropriate incentives and/or replacements will be implemented.**

[Research Support Department]

In order to strengthen cooperation with the University Executive Office and to ensure that decisions made by the University are promptly reflected at ICReDD, the Vice President was appointed as the Administrative Director. Monthly meetings are held with the President to discuss management, including future plans. We have also established a section for WPI procedures employing full-time staff members to provide a smooth transition during the program's initial stages and to support continued research activities. We have established an "International Planning Section" to support foreign PIs, researchers, students, and

to organize international symposia. The "Public Relations Section" provides services and support for the management of e.g. websites and the organization of events, while a "Research Promotion Section" selects researchers and students, and organizes collaborative work between industrial partners, the government, and the university. The research support department ensures that the research environment is suitable for researchers and students to comfortably engage in their research without administrative interruptions.

5) -2 Research environment

* Concretely describe how equipment and facilities, including laboratory space, will be provided in a manner appropriate for a "world premier international center." Include your procedure and timing.
* Concretely describe how the center will consider to arrange for its researchers to participate in the education of graduate students.
* Concretely describe the plans by the host institution to provide a support system and to work toward improving the environment for achieving gender balance.
* Describe your measures other than the above to ensure that world's top researchers from around the world can comfortably devote themselves to their research within an international and competitive environment at the center.

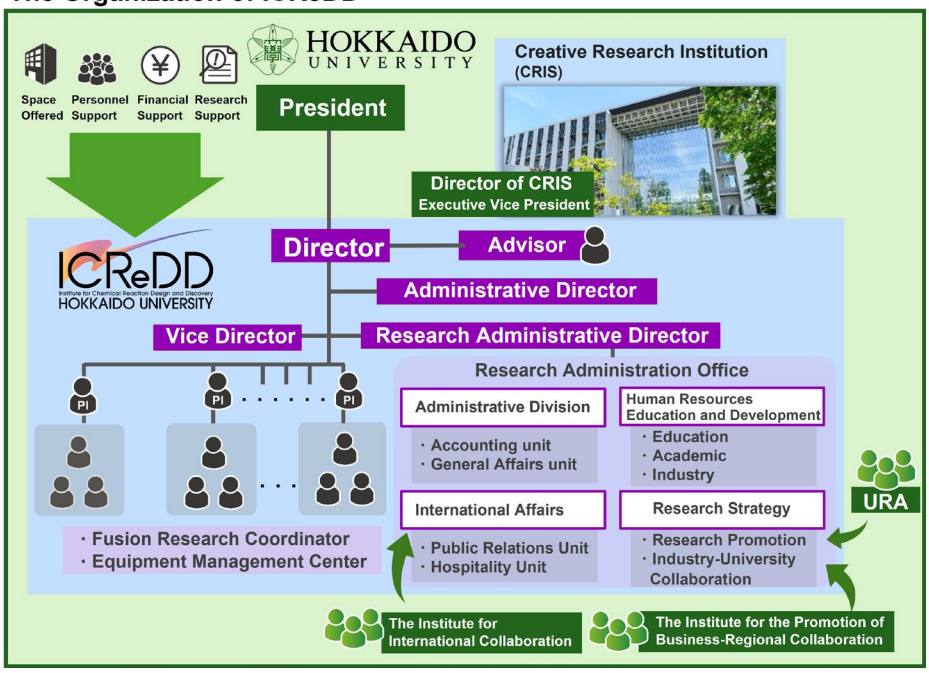
The university already provided 2,600 m^2 of ICReDD space in the CRIS building and pays for the use of the space, including utilities. The center's research space was expanded from 2,600m^2 to 8,100m^2 in February 2023.The University provided land on the north side of the campus, where the CRIS building and industry-academia collaboration research facilities are concentrated, and a new research building (4 floors, 5,500 m^2) was completed, creating an environment where a total of over 100 researchers can conduct research under one roof. This includes an animal laboratory, an industry-academia collaboration laboratory and a fusion research office where 90 researchers can research in a single space. In order to realize the director's vision in which researchers and graduate students gather from all over the world, synergistically integrate knowledge that is beyond their respective disciplines, engage in collaborative research, and thus establish a world-leading research institute, we have implemented the "MANABIYA" system and the "Inter-science Salon" space. **PIs and researchers educate graduate students, who are invited to the "MANABIYA" from the PI's laboratories and other national and international institutes for periods of 1-3 months, to master the new reaction development methods established in the ICReDD.** We aim to have a continuous cycle of short-term visitors that comprises approximately 20 foreign researchers and graduate students per year, and to establish a new graduate school that provides intellectual resources based on the discoveries of the ICReDD. The "Inter-science Salon" serves as a space for researchers to casually gather in a relaxed environment in order to promote interdisciplinary discussions. The director thus spearheads the development of an internationally leading research institute that continually exchanges researchers. The MANABIYA system promotes diversification within the ICReDD and establishes an international network. The international hospitality support system, by utilizing the resources of the already established GI-CoRE and the Institute for International Collaboration at Hokkaido University, provides assistance for the foreign PIs and their families regarding non-research-oriented issues such as visas and housing to ease the transition. As a result, the foreign PIs are disengaged from the affairs of daily life and it promotes the efficiency of their research activities. The outstanding researchers at the ICReDD are appointed following a competitive selection process and offered tenured faculty positions in order to ensure the continuation of internationally leading education and research at Hokkaido University (*cf.* form 5-4-2). In addition to the use of shared instruments [currently there are ~160 cutting-edge instruments at the CRIS Global Facility Center (GFC)] and financial support from the university regarding analytical fees, **the GFC maintains and manages analytical instruments purchased at the institute, which allows the PIs to focus exclusively on research.** The Institute for International Collaboration prepares and supports the living environment for foreign researchers employed at the center

and their family members.

Support system and environmental improvement for achieving gender balance: The university developed a policy for improving gender balance (Ratio of female faculty members: 23% by 2028) based on the university's program "Accelerate Ambitious of All", adopted as part of the MEXT subsidy program "The Initiative for Realizing Diversity in the Research Environment (leadership training for women)" (FY2023-FY2028). Aiming to accelerate the increase of the ratio of women in upper-level and managerial positions, the University has established the "Support for Female Students and Graduate Students Entering Doctoral Programs," "Support for Invitation of Female Researchers," "Support for the Employment of Technical Assistants over Life Events," "Mentoring & Job Shadowing Training Support Program for Female Researchers Pursuing Higher Positions," and "Support for Female Researchers to be Hired and to be Proactively Assigned to Upper-Level Positions." The university established the "Accelerated Action Plan to Promote Recruitment and Active Promotion of Female Researchers to Higher Positions" to promote 25 female associate professors to professorships in FY2023. 34 applications were received, and a total of 25 professors (17 in Natural Sciences and 8 in Humanities and Social Sciences) were promoted. As a result, the percentage of female professors increased from 7.4% to 10.4%. The university set a target of 20% female professors by FY2028. At ICReDD, one female researcher took advantage of "Support for the Employment of Technical Assistants over Life Events" and a research assistant staff was hired during her childcare leave (FY2021), which led to a smooth return to research activities after she returned to work. The university also established the "Yoshie Katsurada Award," named after Hokkaido University's first female professor, to honor female faculty members who have developed outstanding academic research and are expected to be active in the next generation of management positions, and in FY2023, four female researchers, including one PI, received this award. Also, the temporary childcare space have been set up in the CRIS Building and ICReDD building in FY2023, providing a space that ICReDD researchers can also use for care for their children.

Prevention of research misconduct: We recognize that ICReDD bears a serious responsibility for managing the research misconduct committed by one of its past researchers. In the second half of the WPI funding period, researchers at the center are required to attend ICReDD's own research ethics seminars at the time of hiring and periodically thereafter on an annual basis in addition to the usual research ethics education training provided by the University. For the purpose of preventing paper fraud and proper data management in the center, the Equipment Management Center was established by hiring a researcher holding a PhD with expertise in the field to manage data on equipment at the center and to check all figures for submission against the raw data. The common database for computational and information science was established within the center to enhance its transparency and promote the information sharing. These efforts will be made to make the center a global standard in terms of research transparency. Furthermore, by facilitating an environment in which research results can be openly discussed, we will prevent misconduct and further accelerate fusion research.

The Organization of ICReDD



5) -3 Establishing an independent research center in sync with reorganizing the host institution

* Concretely describe how your proposal seeks to establish a new center that will achieve independence within 10 years and how the project will advance synchronization between WPI center support and reform of the host institution's existing organization?

* With prior consent from the host institution, describe concretely the host institution's mid-to-long-term plan and schedule for achieving the center's independent operation within the host institution, including adjustments to the existing organization and/or acquisition of external funding.

The ICReDD will be established as a permanent organization in collaboration with the university administration. For that purpose, we will use the organizational reform of the "Creative Research Institution (CRIS, established in 2002)", which is a university-wide organization that supervises cross-departmental research in order to integrate the ICReDD as an independent institute within the university organization in the future. **After the sixth year, with sufficient progress of the collaborative research to carry out social implementations, we will i) incorporate research fields beyond the ICReDD's core areas (computational, information and experimental sciences) in order to further promote and develop CReDD, and ii) start reforming the CRIS.** The results obtained from research in the ICReDD should also inspire related research in humanities and social sciences, especially in the context of life ethics and public policy, given that the research activities in the ICReDD will be connected to a wide variety of pressing social issues in today's changing society. **This cross-fertilization should directly lead to the reorganization of Hokkaido University through the integration of humanities and social sciences with science and engineering, which concerns aspects of e.g. intellectual property, safety evaluations, science and technology ethics, and international operation standards of technology.** Using the support system of each PI's affiliated department reduces the burden of administrative work for the PIs and ensures that research and education is their prime concern. The ICReDD secures operational funding (including laboratory costs for PIs and research space) from the university that is at least equivalent to the WPI grant. By increasing the ratio of the voluntary expenses of the university after the sixth year, the ICReDD will gradually become independent and secure ongoing research activities (*cf.* form 5: Host Institution's Commitment). The reorganization

and integration of existing graduate schools in order to establish of **the graduate school of "Chemical Reaction Design and Discovery"** will be implemented from FY2023, with plans to cement "the Chemical Reaction Design and Discovery" and newly established "MANABIYA education program for graduate students" as educational organizations of the university. In order to incorporate the world's most advanced research back into educational programs, we plan to establish a system for cross-disciplinary and interdisciplinary education that is not bound by the framework of existing research institutes and graduate schools. We established the "Human Resource Development Unit" which is in charge of fostering researchers, graduate students, and industrial researchers using MANABIYA, as well as creating strategies and roadmaps for the center's graduate and recurrent education. We already hired a full professor and specialized faculty with extensive teaching and research experience for this unit. No other international research institute in the university has a human resource development Unit, and this organizational reform will lead to ICReDD's further development as a research center and its contribution to the entire university. **We also will create a permanent organization for the acquisition of private funding by e.g. hosting researchers from industry and establishing research consortia with industrial partners.** Concretely, managers at Institute for the Promotion of Business-Regional Collaboration, Hokkaido University, will mediate between researchers at ICReDD and corporation members of the research consortia to promote research collaboration. (*cf.* form 5-9-2).

After the funding period from WPI, ICReDD will be established as a permanent research institute at Hokkaido University. Ten senior PI's laboratories will be created in ICReDD, and one regular associate professors and one post-doctoral researcher will be assigned to each senior PI by personnel expenses funded by the University. These ten senior PIs are top-level researchers who undergo annual evaluations and may be replaced based on their performance to ensure that the center maintains the highest level of excellence. In addition, we plan to establish six junior PI (Jr. PI) groups, led by rising stars in related fields. These junior PIs will be recruited from top institutes abroad and appointed as tenure-track associate professors. The center has already secured four tenure-track associate professors (Jr. PI) and one assistant professor to ICReDD as of April 2022. Additional two Jr. PI will be hired in FY2023. Six young PIs will be assigned one postdoctoral researcher each by covering the costs at the university's expense. The University plans to gradually switch the associate professors and postdoctoral researchers who are currently employed by the WPI grant to employment at the University's employment expense starting in FY2023, with a view to staffing the center after its permanent establishment. Ultimately, ICReDD will consist of 10 PI and 6 Jr. PI research groups, which is a structure that can sustain research capacity during the grant period. Although the PIs will be employed at the expense of their home departments, the university will employ at its own expense 6 Jr. PIs, 10 associate professors in the PI groups, and one postdoctoral researcher in each research group (a total of 16 postdoctoral researchers). The University will also employ at its own expense a Fusion Research Coordinator, faculties in charge of Human Resource Development Units, and other research support personnel. If the progress of future research at the center necessitates the replacement or addition of a PI, it is envisioned that a new PI will be appointed from among the ICReDD fellows. With this dynamic personnel circulation system, ICReDD will maintain the highest level of scientific excellence always.

ICReDD is the flagship project for realizing the University's near-future strategy of becoming a "Global Brain Circulation Center for World-Class Research," and is the core of the University's fourth mid-term objectives and mid-term plan. Going forward, ICReDD will continue to be the driving force behind the transformation of Hokkaido University into a truly international center of education and research.

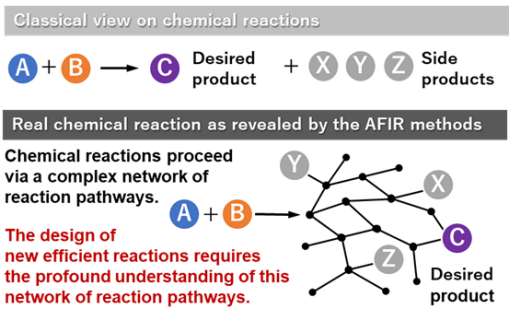
Center Director's Vision

Hokkaido University Prof. Satoshi Maeda

The development of new chemical reactions is intrinsically entangled with the prosperity of humanity and the preservation of the environment. One of the most notable chemical reactions discovered in the last century was the Haber-Bosch process, which catalytically synthesizes ammonia (NH_3) from nitrogen (N_2) and hydrogen (H_2). Also known as "the reaction that turns air into bread," the Haber-Bosch process enables the mass production of fertilizer, which helped with overcoming the global food shortages at the beginning of the 20th century. A more recent example of such transformative chemical reactions with profound impact is cross-coupling reactions, the discovery of which was awarded the 2010 Nobel Prize in Chemistry. These reactions are used to produce approximately 20% of all medicinal reagents, and almost all liquid crystalline and organic electroluminescent materials. The industrial use of these chemical reactions contributes ~60 trillion yen per annum to the global economy. **The development of new chemical reactions thus significantly affects the evolution of society.** However, the currently used methods for the design and development of bespoke chemical reactions are highly inefficient. Usually, these methods are based on trial and error, which is not only very laborious and time-consuming, but the discovery of truly innovative reactions is relatively rare. **As the development and implementation of new chemical reactions often take decades in reality, fundamentally new scientific approaches are required.**

The goal of this initiative is to establish the scientific field of "Chemical Reaction Design and Discovery (CReDD)", which should allow the efficient development of chemical reactions through a combination of computational, information, and experimental sciences. CReDD elevates the state-of-the-art methods for the development of chemical reactions to the next level by (1) establishing design guidelines for chemical reactions based on quantum-chemical calculations, (2) understanding the complexity of chemical reactions and designing new reactions via informatics methods, and (3) experimentally validating the theoretically proposed reactions. Quantum-chemical calculations that are implemented at the Institute for Chemical Reaction Design and Discovery (ICReDD) are different from previous approaches that have been employed to verify *known* reaction mechanisms. Quantum-chemical calculations that are capable of unveiling *unknown* pathways should represent a scientific advancement of substantial magnitude. A key technology that enables such calculations is the "automated reaction path search (AFIR) method" developed by Prof. Maeda, the director of the institute, who is an internationally renowned pioneer in this area. Merely 20 years ago, automatic searches for chemical reaction paths based on quantum-chemical calculations were considered impossible. However, Prof. Maeda proposed the idea of applying a virtual mechanical force to reaction systems in order to unveil potential pathways. Based on this idea, he developed the world's first general method to systematically predict *unknown* reaction paths. This method is not only of academic interest, and several companies are currently conducting collaborative research with Prof. Maeda.

It is highly remarkable that when the AFIR method is used for the analysis of chemical reactions, the results often show that these reactions proceed via paths that are very different from those initially anticipated. Simple chemical formulae reveal a large volume of uncharted **reaction path networks**, which show all possible pathways from the reactants to the major product and minor byproducts. Understanding reaction path networks ultimately allows discovering unknown pathways to targeted products and blocking those to undesired byproducts. For the bespoke design of chemical reactions, **it is thus inevitable to study reaction path networks and identify controllable reaction pathways.**



In addition, the AFIR method also addresses the considerable challenge of 'complexity'. Even simple reactions that include only a few atoms may exhibit very complicated reaction-path networks, rendering the differentiation between significant and insignificant reaction paths highly difficult. Thus, the aid of information science is essential in order to identify promising reaction paths. The faculty at Hokkaido University hosts numerous internationally renowned researchers in e.g. path enumeration, data mining, and machine learning, who could help analyze such complex networks. By including the knowledge of information scientists, this initiative aims to understand intricate reaction-path networks and extract important factors that should be considered prior to the experimental stage. Simultaneously, large volumes of previously obtained experimental data are examined and meaningful data are forwarded to computational scientists in order to simplify the calculations required to obtain the reaction-path networks.

Theoretical predictions become meaningful only after they have been experimentally proven, however. In this initiative, we aim to merge experimental science with computational and information sciences on a globally leading

level. The hitherto insufficient conceptual understanding that chemical reactions proceed via an extensive network of chemical reaction paths has left experimental scientists with no other alternative but to continue the laborious, expensive, and inefficient processes of trial and error. In contrast, CReDD (1) uses the AFIR method to calculate chemical reaction-path networks, and (2) applies concepts of information science in order to extract meaningful information for experiments, thus narrowing down optimal experimental conditions. This approach enables "pinpointing" promising experiments, which considerably shortens the time required to develop chemical reactions. As the majority of the experimental scientists who joined this initiative have already collaborated with computational or information scientists, synergy among scientists from different backgrounds has been attained. In addition, information science provides a feedback loop, in which data obtained by the experimental scientists is circulated back to the computational scientists; the synergetic effects from the combination of three fields have led to the improvement and refinement of CReDD.

The development of CReDD enables the discovery of reactions that afford (1) high-value-added chemicals (small to medium-size molecules), (2) new materials (macromolecules), and (3) state-of-the-art medical technology (complex systems). Reactions of the type (1) create useful chemical agents from low-value materials, e.g. via the synthesis of biologically relevant molecules from CO_2. Reactions of the type (2) produce materials with advanced functionality, e.g. highly luminescent or stimuli-responsive materials. Finally, reactions of the type (3) afford advanced materials for applications in a clinical context, e.g. improved biomedical materials leading to reagents for regenerative medicine and diagnosis. These reactions vary widely in complexity and in the environments for the reacting molecule(s). To cover this broad scope, we have strategically assembled a team of researchers from different disciplines.

To advance fusion research practically, we have established several flagship projects that are being pursued by teams comprising multiple groups. As for FY2022, six such projects are being run in parallel. Project-I holds a special position among these projects as it serves as the foundation of ICReDD. All computational and informatics groups collaborate with Project-I and provide feedback on the application of their computational and informatics tools to other projects. The remaining projects are focused on addressing practical chemical targets exhibiting a hierarchical complexity ranging from small molecule synthesis to polymer material control and cancer diagnosis. Simultaneously tackling these projects with varying complexities will enable us to establish a comprehensive set of tools that can be applied to a broad range of problems in chemical and materials sciences. Additionally, we invite ideas from young researchers every year and launch them as bottom-up projects. Successful bottom-up projects are promoted to flagship projects, while underperforming flagship projects are evaluated and may be discontinued. This approach allows us to consistently deliver high-impact outcomes featuring our young researchers.

ICReDD has steadily achieved results in line with the vision set forth in ICReDD's initial WPI application. In addition to the discovery of new reactions using the AFIR method described above, ICReDD's achievements include catalyst optimization using quantum chemical calculations, the discovery of new catalysts using chemoinformatics and robotic synthesis, and the development of functional gels using quantum chemical calculations. Also worthy of special mention are the innovative research developments by ICReDD PIs concerning mechanochemical synthesis using mechanical stimulation as a new means of molecular activation, as well as the cancer stem cell reprogramming technology using hydrogels. Another item of particular note is the Nobel Prize in Chemistry being awarded to Professor Benjamin List, one of ICReDD's PIs. During the second half of ICReDD's WPI funding, we will add ICReDD's fusion research perspective to these efforts to develop research from a broader perspective. Specifically, we will accelerate the application of computational science and information science to complex systems, such as solid-phase synthesis and synthesis of materials with applications in medicine. In addition, we have launched three new initiatives aimed at improving the international recognition of the center and facilitating the quick implementation of our research outputs. These initiatives are the List Collaboration Platform, led by Professor List, the Mitsui Chemicals-ICReDD Innovative Chemical Reaction Design Laboratory, and the Clinical Platform for Chemical Reaction Collaboration, developed in partnership with the School of Medical Science.

Another goal of this initiative is to generate, nurture, and train a new generation of researchers who master all three subjects, i.e. computational, information, and experimental sciences, so that CReDD can be developed further in the future. **The continued relevance of CReDD is ensured by sharing the results of this initiative with the world via the foundation of the MANABIYA (Japanese for 'school') system, where researchers from outside the center have the opportunity to collaborate and benefit from the innovative technology and knowledge developed there.** Specifically, foreign experimental researchers have the opportunity to join MANABIYA and learn about e.g. the AFIR method and machine learning by collaborating with ICReDD. These researchers use the knowledge and techniques acquired at ICReDD upon returning to their home institutes. Through MANABIYA, ICReDD is becoming a global research hub that continuously welcomes researchers from all over the world. This allows ICReDD to not only thrive, but also to contribute to the research of other universities, research institutes, and companies that develop chemical reactions. **In the future, the MANABIYA system will evolve into the new "Graduate School of Chemical Reaction Design and Discovery". Furthermore, by sharing the management system of excellence acquired through the WPI, ICReDD will reform Hokkaido University.**

After the funding period from WPI, ICReDD will be established as a permanent research institute at Hokkaido University. Unlike conventional research institutes, ICReDD will implement a dynamic personnel appointment system. This system invites top researchers from the other departments of Hokkaido University or from top institutes outside of Hokkaido University, and provides them with an opportunity to have an additional laboratory in ICReDD

by providing them with enough resources and budget. These researchers will undergo annual evaluations and may be replaced based on their performance to ensure that the center maintains the highest level of excellence. In addition, we will provide young prominent researchers with an opportunity to have their own groups as junior PIs. With such a dynamic personnel circulation, ICReDD will maintain the highest level of scientific excellence always.

On the other hand, we recognize that ICReDD bears a serious responsibility for managing the research misconduct committed by one of its past researchers. In the second half of the WPI funding period, in addition to thorough ethics education within ICReDD, a new department will be established to manage experimental data, and efforts will be made to make the center a global standard in terms of research transparency. Furthermore, by facilitating an environment in which research results can be openly discussed, we will prevent misconduct and further accelerate fusion research.

Reaction development that relies solely on the trial-and-error approach is too time-consuming to solve current global problems that include pollution as well as the scarcity of energy and resources. CReDD is revolutionizing the traditional approach to developing reactions by fusing computational, information, and experimental sciences. We strive to spread the benefits of this approach by establishing a global WPI and integrating other disciplines. Our sincere hope is that our WPI may contribute to a brighter and more prosperous future for all of humanity.

Host Institution's Commitment

May 12, 2023

To MEXT

National University Corporation Hokkaido University
Kiyohiro Houkin, President

I confirm that the measures listed below will be carried out faithfully and concretely as follows regarding "Institute for Chemical Reaction Design and Discovery (ICReDD)"

Concrete Measures

・Describe the concrete measures that the host institution will take to satisfy the following requirements.

1) For the center to become a truly "world premier international research center" and independent by the time WPI support ends, the host institution must clearly define the center's role within its own mid-to-long-term strategy and provide its comprehensive support from the time that the funded project starts.

※Describe the center's role within host institution's own mid-to-long-term strategy.

The mid-to-long-term strategy of Hokkaido University is based on several progressive schemes related to research and education towards the internationalization of the university. In 2002, the Creative Research Institution (CRIS) was established to promote interdisciplinary research under a trans-departmental scheme. In 2014, Hokkaido University defined its vision for the near future, i.e., until its 150th anniversary in 2026, as contributing to the resolution of pressing global issues, which are outlined in the 'Future Strategy for the 150th Anniversary of Hokkaido University'. For that purpose, Hokkaido University established "Institute for Chemical Reaction Design and Discovery (ICReDD)" as a flagship initiative to substantially improve the research performance of Hokkaido University with the support of the WPI project of the MEXT and to provide maximum research support to achieve its near-future vision. The ICReDD is incorporated into the CRIS framework and thus be able to make full use of already established infrastructure and resources to promote the WPI center.

ICReDD will play a central role in the university's fourth mid-term objectives and mid-term plan as the flagship research project to achieve the university's near-future strategy of establishing a "global brain circulation center for world-class research".

Excerpt from Medium-term Goals and Plans (FY2022-FY2026)

Medium-term Goals

Strategically define areas of international presence to become a world-class research university. Establish an education and research environment (special research funds, special salary system, etc.) that will attract excellent researchers and students from Japan and abroad. Build a world-class institute with an accumulation of the most advanced education and research facilities, including data infrastructures, and accumulation of intellectual assets, including an international network and hub function that transcends industry-academia-government collaboration.

Medium-term plan

Attract excellent researchers from Japan and abroad, based on the core functions and the international collaborative research utilizing the unique characteristics of the university, such as the "Institute for

Chemical Reaction Design and Discovery (ICReDD)", which aims to form a world-class research center or research on zoonosis. Furthermore, establish a world-class research center linked to education by implementing graduate school education that reflects the cutting-edge research of the center in the curriculum.

2) Providing a mid-to-long-term policy for amending the plan on the direction of the host institution's organization and operation, one that includes the reform of the institution's existing organization in ways that will achieve the center's independence and create a permanent place for it within the organization. A concrete plan and schedule must be set and carried out for restructuring the host institution's organization.

※Describe both a mid-to-long-term policy for amending the plan on the direction of the host institution's organization and operation and provide a concrete plan and schedule.

Hokkaido University established the ICReDD within the CRIS framework to provide maximum support for this international research center. In order to become a world-leading research center and generate results that may change the future of humanity, this WPI advances the research implementation and involves further research collaborations outside the ICReDD's core areas (computational, information, and experimental sciences).

1. Since the establishment of ICReDD, the university has strongly supported ICReDD and has secured funds equal to or more than the WPI grant for its operation (FY2018: 358 million yen, FY2019: 1,026 million yen, FY2020: 1,388 million yen, FY2021: 1,904 million yen, FY2022: 2,657 million yen). From FY2023, ICReDD plans to gradually become independent and secure continuous research activities by increasing the proportion of the university's voluntary cost burden.
2. In order to ensure that the ICReDD sustainably continues its research activities independently, the university provided financial support starting for tenure positions that were offered to outstanding WPI researchers. These were appointed following a rigorous selection process based on research activities such as high-impact publications and receipt of competitive funds. Based on this plan, 4 tenure-track associate professors and 1 assistant professor have already been assigned to ICReDD as of April 2022, and the university plans to ensure ICReDD's permanence by providing the required positions by the end of the grant period in FY2027. The university also provides the ICReDD with full access to its financial infrastructure, i.e., the opportunity to request budget estimates and to apply for competitive cross-departmental funding.
3. From FY2023, the reorganization and integration of existing graduate schools in order to establish of the graduate school of "Chemical Reaction Design and Discovery" will be implemented, with plans to cement "Chemical Reaction Design and Discovery" and "MANABIYA" as educational organizations of the university. In order to incorporate the world's most advanced research back into educational programs, the university plans to establish a system for cross-disciplinary and interdisciplinary education that is not bound by the framework of existing research institutes and graduate schools. The ICReDD establishes the "ICReDD Human Resource Development Unit" to design a human resource development framework that will function as a model case for next-generation higher education through a multilateral approach for students and working people, regardless of national or international affiliation. No other international research institute in the university has such a human resource development unit, and this organizational reform will also lead to ICReDD's further development as a research center to foster young researchers, which would contribute to the reformation of the entire university.
4. The university supports the formation of consortia that involve companies that collaborate with the ICReDD in order to promote industrial collaborations and establishes a system to attract independent funding for the ICReDD. From FY2023, a five-year large-scale joint research project with a company was launched. The ICReDD will conduct recurrent education by using MANABIYA (INDUSTRY) to attract companies in related fields and expand its network in order to best match ICReDD research with these industries.

5. After ten years, the ICReDD will become a permanent independent research organization within the university. The university's evaluation committee will assess the ICReDD's approach and reapply successful systems and methods, such as research and education systems, to other departments of the university. ICReDD established "human resource development unit" with a view to establishing a graduate school in the future. "Chemical Reaction Design and Discovery" and "MANABIYA" will also be firmly rooted in the university's organizational structure via the establishment of the "Graduate School of Chemical Reaction Design and Discovery". Since the center will have its own graduate school, which is different from current graduate school, ICReDD graduate school will have an influence on the development of young researchers at other research institutes, etc., and add new and attractive contents such as MANABIYA, which is a laboratory visit in a different field, to the regular graduate school curriculum.

3) Provide sufficient support for carrying out the center's operation and research activities, including necessary personnel, financial, and system support.

The university provided physical and financial support that is at least equal to that of the WPI grant via the following measures.

1. To strengthen the research support system, the management organization was reorganized into the Research Support Division to better clarify research support and administration. The Executive Director was newly appointed as the Administrative Director to ensure stronger cooperation with the university Executive Office and to ensure that decisions made by the university are promptly reflected in the center's projects. The Research Support Division was reorganized into the following four units: the "Administrative Affairs Unit", which is responsible for general affairs and accounting; the "International Planning Unit", which invites outstanding overseas researchers and students and conducts international outreach beyond the academic community in cooperation with the Institute for International Collaboration; the "Research Strategy Unit", which works with the URA and the Institute for the Promotion of Business-Regional Collaboration to obtain large-scale funds, promotes collaboration agreements with other institutions, and to establish joint research projects with companies; and the "Human Resource Development Unit", which is in charge of fostering researchers, graduate students, and industrial researchers using MANABIYA, as well as creating strategies and roadmaps for ICReDD's graduate and recurrent education. Additionally, the "Fusion Research Coordinator" and "Equipment Management Center" is directly connected to the research division, so that the Center Director's policies are managed, and progress is monitored in close concert with researchers. In this way, the ICReDD plans to secure the personnel necessary to establish ICReDD as a permanent research institution. In order to guarantee smooth program management, and given the international orientation of the ICReDD, the university already hired full-time clerical employees who are fluent in English for the ICReDD, and, from 2023, a full professor and specialized faculty with extensive teaching and research experience for the ICReDD Human Resource Development Unit.
2. The university has provided ICReDD space 2,600 m^2 in the Creative Research Institution Building and space charges including utility costs, etc. Moreover, the university completed the "International Research Center for Chemical Reaction Design and Discovery" (new building, 4 floors above ground, 5,500 m^2) by the end of FY2022, which was requested to the MEXT a portion of the building cost for the improvement of facilities for national universities, and president's discretionary expense covered half of the construction cost. The university plans to permanently establish ICReDD as a dynamic research center that always promotes cutting-edge, world-class research based on a new adaptive research strategy involving periodically changing researchers and research themes.
3. To reduce the educational and administrative burden on the departments of each PI, the university take measures to provide labor costs (~50 million yen per year) for the corresponding departments as a form of compensation.

4. The university established an integrated technical staff organization, Office for Technical Support, to which technical staff members from various departments in the university were dually appointed, and the consolidation of the centralized administrative system within its operating structure to strengthen the support system for cross-divisional education and research activities. In response to a request from ICReDD, the Office for Technical Support dispatched technical staff, performing duties in cooperation with the equipment management faculty members to assist in the maintenance and management of ICReDD's equipment (nuclear magnetic resonance equipment) under the coordination with the Equipment Management Unit.

4) Provide necessary support to achieve the independence of the center and sustain its research at a top world level after the WPI grant period ends.

ICReDD will be maintained as a permanent organization in conjunction with the university administration. Positioned as a special research institute under the direct control of the President, ICReDD will maintain continuous research activities, and after about 10 years of research activities, it will be made permanent as a research center that constantly promotes cutting-edge, world-class research without fixing the assignment of researchers, based on a new research strategy positioned in the mid-term objectives and mid-term plan, etc.

1. The university strongly supports new developments in ICReDD's research and, in 2022, it has accepted an estimated budget request from ICReDD for "List's cooperation research platform" for further development of research and enhancement of domestic and international research hub functions, and requested a budget to the government, which was adopted and launched from FY2023.
2. The university secured four tenure-track associate professors and one assistant professor to ICReDD as of April 2022. After the end of the subsidy period, one regular associate professors and one post-doctoral researcher will be assigned to each PI of the center by personnel expenses funded by the university. Six young PIs will be assigned one post-doctoral fellow each by covering the costs at the university's expense. The university plans to gradually switch these associate professors and postdoctoral researchers who are currently employed by the WPI grant to employment at the university's employment expense starting in FY2023, with a view to staffing the center after its permanent establishment.
3. With the aim of further implementing research results in society, the center will accelerate its industry-academia collaboration in the second half of the grant period by utilizing the university's industry-academia collaborative research space in the new building. The university has also reorganized and strengthened its industry-academia collaboration system with a view to accepting researchers from industry and establishing a research consortium with industry in FY2022. From this, the system will be capable of systematically supporting ICReDD's acquisition of private funding and can be maintained and made permanent while promoting fundraising. The results have already materialized as new industry-academia collaborations in ICReDD. From FY2023, "Mitsui Chemicals-ICReDD Laboratory" will be launched for joint research focused on the swift, high-precision design of new reactions that will contribute to the development of high-performance materials and the creation of a recycling-oriented society.

5) Provide a system that will in practice allow the center director to make decisions in implementing the center project, including personnel and budgets, and that will secure the autonomy of its operation.

1. The President and the ICReDD Director hold regular monthly meetings to discuss operations, including future plans to establish ICReDD as a sustainable research center. To strengthen cooperation with the University Executive Office and to ensure that decisions made by the university are promptly reflected at ICReDD, the Executive Director was appointed as the Administrative Director. The university

authorized that the Director has the authority to make decisions over the appointment of personnel, the center's budget, and research priorities in addition to other matters. The Steering Committee authorizes the Director to make final decisions, thus it is the place for discussion and acts as an advisor to the Director.

2. The university revised the university's salary regulations to allow for higher salaries in order to hire the talented researchers. From FY2022, a new a unique and unprecedented regulation was established to provide incentives based on the research performance and evaluation of center faculty members; the determination of eligibility and the amount of the incentive are left to the discretion of the Director. Along with self-evaluations, the center director conducted interviews to determine the evaluation.
3. To acquire top-level researchers who can advance the Chemical Reaction Design and Discovery fields, the ICReDD has implemented a cross-appointment system and has utilized this to employ professors at Kyoto University and the University of Tokyo as principal investigators. In addition, an agreement was signed with the Graduate School of Information Science and Technology, the University of Tokyo, to which the principal investigator belonged, to promote research related to ICReDD.

Decision-making system

The university established the Institute rule, "Hokkaido University Institute for Chemical Reaction Design and Discovery Rules". All matters concerning the operation and management of the center fall under the purview of the Director. The university also established "Hokkaido University Institute for Chemical Reaction Design and Discovery Steering Committee Rules" to organize the system, which enables the Director to exercise strong leadership in the center concerning important matters such as personnel and execution of the budget. Furthermore, the university established discretionary funds (at least 10 million yen per year) that can be used freely by the director of the ICReDD.

6) Provide support to the center director by coordinating with other departments regarding the assigning of researchers to the center and the creating of an effective environment for the center within the host institution. Needed adjustments to do so should be made proactively while giving consideration to their effect on the educational and research activities of those departments.

The university set up an environment in which the participating PIs from each department in the ICReDD can concentrate on WPI research. Coordination with the individual departments was led by the president and the executive vice president for research.

The university and the Dean of the Department to which the ICReDD PIs affiliated have made arrangements to reduce the teaching and administrative duties of ICReDD PIs in their respective university departments. To reduce the educational and administrative burden on the departments of each PI, the university provided labor costs (50 million yen per year) for the corresponding departments as a form of compensation.

7) Offer cooperation in flexibly applying, revising, or supplementing the host institution's internal systems as needed for the center to effectively implement new management methods unfettered by conventional modes of operation (e.g. English-language environment, merit-based pay, top-down decision making, linkage to graduate school education).

The ICReDD has reviewed its research support structure for the second half of the WPI funding period, as its composition has increased, and fusion research has made steady progress since its inception in 2018. The ICReDD has actively developed international outreach activities beyond academia by strengthening cooperation with internal organizations such as the Institute for International Collaboration, Institute for the Promotion of Business-Regional Collaboration, URA, and the Office of Diversity Equity and Inclusion, and promote an effective international strategy to invite many excellent researchers and students from

abroad.

1. The university already provided the director of the ICReDD with all decision-making rights regarding important matters of institute management such as recruitment and budgetary discretion. To support the director in the decision-making process, the ICReDD has set up a Steering Committee.
2. The mission of the center is communicated to all members through interviews with researchers conducted by the Center Director. Laboratory chiefs are appointed in mixed laboratories and mixed offices, and laboratory management is conducted so that the Center Director's policies are promptly communicated. The "Fusion Research Coordinator," directly connected to the research division, actively promotes and plans fusion research based on the policies of the center director and advises on the progress of the research. Authority has been delegated to the Future Plan WG, Equipment Management WG, so that they can manage the center by the direction of the Center Director.
3. In FY2022, a new regulation was established to provide incentives based on the research performance and evaluation of center faculty members, for whom no evaluation system was previously in place. The results of the self-performance evaluation, and discretionary performance evaluation based on annual interview with director are used to determine the salary increase or decrease by one or two steps from the base annual salary for the following year, which has not yet been done in any other departments in the university.
4. The university assigned administrative staff who are capable in English and are composed of personnel with excellent ability and experience in a variety of areas. All the administrative information is provided in both English and Japanese. Interviews by the International Planning Unit staff with foreign researchers and PIs were conducted, and a one-stop support system was established. The administrative department provides a wide range of support daily by staff who can respond in both English and Japanese. Many documents related to the daily lives of foreign researchers and their families and university administrative procedures are translated into English by ICReDD's administrative department. Emphasis is placed on support for foreign researchers at the time of employment (coming to Japan) and at the time of retirement, and careful explanations are provided in English about Japanese taxes and social insurance systems. To create an environment in which foreign researchers can concentrate on their research, ICReDD provides language support for contracts and necessary living procedures when looking for private apartments and helps them to settle in Sapporo. Support for child enrollment, communication support with schools, and Japanese language courses for learning Japanese are also introduced. For preschool children, assistance is provided in guiding them through nursery school and kindergarten procedures, contacting the schools with inquiries, and so on. As for health care support for the individual and his/her family, advice on hospital selection, explanation and accompaniment to appointments, and support for pregnant women during childbirth are provided. In response to the COVID-19, the center also checked the situation in case of fever, contacts the public health center, and provides up-to-date information on vaccination.

8) Secure, provide and deliver the necessary infrastructure for the center to carry out its activities (e.g. research space, facilities, land).

Provisions for the ICReDD, such as the use of the university campus infrastructure including the CRIS building, are outlined below.

1. The university has provided ICReDD space 2,600 m^2 in the Creative Research Institution Building and space charges including utility cost, etc. The university also provided land on the north side of the campus, where industry-academia collaboration research facilities are concentrated, on which a new research building (5,500 m^2) was constructed by the end of FY2022. Thus, the university is providing ICReDD with sufficient space including the original laboratory spaces of the PIs.
2. The university provided the fees required to analyze synthesized samples in the context of the ICReDD, as well as the usage fees for the open facility system, which provides access to cutting-edge equipment such as high-resolution NMR spectrometers that are managed by the university (FY2019: 850 thousand

yen; FY2020: 1 million yen; FY2021: 2.5 million yen; FY2022: 2.3 million yen)

3. The university set up a common space (ICReDD Salon), where all WPI researchers can gather for lunch meetings every month in order to exchange ideas across different disciplines in English, whereby especially young researchers are encouraged to disseminate their research progress.

9) Provide other types of assistance to give the center maximum support in achieving its concepts and objectives and in becoming a world premier international research center in both name and deed.

Hokkaido University provides unreserved support for the implementation of the plans of the ICReDD by integrating its goals and plan into that of the fourth medium-term of the university, which should help to nurture and establish the institute as a permanent and integral part of the university.

1. In order to strengthen cooperation with the University Executive Office and to ensure that decisions made by the university are promptly reflected at ICReDD, the Vice President was appointed as the Administrative Director. Monthly meetings are held with the President to discuss management, including future plans.
2. In addition to providing access to the CRIS infrastructure, the university supports the ICReDD by providing access to resources of other relevant organizations, such as the Institute for International Collaboration (2-1) and the Institute for the Promotion of Business-Regional Collaboration (2-2).

2-1. Agreements were put in place with the Max Planck Institute, the University of Strasbourg, the University of Tokyo, and Chubu University. Furthermore, Duke University, Peking University, Stockholm University, University of Oslo, Queen's University, and ICIQ (Institut Català d'Investigació Química (Institute of Chemical Research of Catalonia)) were strong collaborative institutions. The ICReDD plans to continue to collaborate with these research institutions. The university supports exchanges and agreements in cooperation with the Institute for International Collaboration.

2-2. In June 2021, GRRM20 was launched by HPC Systems, Inc. under a program license agreement with the university, and license income has been increasing year by year. The ICReDD strengthens international public relations in collaboration with the university's Public Relations Office and launched fundraising activities, including the creation of a mechanism to obtain external funding.

10) The host institution is to self-evaluate the results of the system reforms achieved by the center and distribute the results that it evaluates highly to all of its departments.

The university highly evaluates ICReDD's achievements and plans to expand it to other departments of the university, such as a management system that clearly separates research and administrative organization, like a center director and administrative director, a careful performance evaluation system that provides incentives to faculty members, a hospitality system that supports the daily life of foreign researchers, and the assignment of faculty members specializing in fusion research (fusion research coordinator) and instrument management faculty to prevent research misconduct. The educational reform of a research institution having its own graduate school is worthy of attention not only for its impact within the university but also outside the university, and as an attempt to foster human resources to take responsibility for the world-leading-edge research. Thus, ICReDD should serve as the impulse and driving force to rebuild Hokkaido University into a truly international world-class research and education center.

11) (For host institutions that already have an existing WPI center) Fully support and sustain the existing center and advance its development as a top world-level research institute while being concurrently capable of fully supporting the new center.

Not applicable.

12) (For host institutions that already have an existing WPI center) Take the initiative to spread the existing center's good system reform results to other departments throughout the

institution and thus applied them to its own reform.

Not applicable.

Appendix

List of Principal Investigators

・If the number of principal investigators exceeds 10, add columns as appropriate.
・Place an asterisk(*) by the name of the investigators who are considered to be ranked among the world's top researchers.
・Give age as of 1 April 2023.
・For investigators who cannot participate in the center project from its beginning 1 April of 2023, indicate the time that their participation will start in the "Notes" column.
・Include principal investigators affiliated with satellite institutions. Give the name of their satellite institutions in the "Notes" column.

	Name	Current affiliation (Department/ School/Institution)・Title	Specialization	Effort * (%)	Notes
1	Center Director Satoshi MAEDA*	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Computational Chemistry	80	
2	Tetsuya TAKETSUGU*	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Quantum Chemistry	80	
3	Michael RUBINSTEIN*	Professor, Duke University	Polymer Physics	20	
4	Masaharu YOSHIOKA*	Professor, Institute for Chemical Reaction Design and Discovery / Graduate School of Information Science and Technology, Hokkaido	Knowledge Engineering	20	
5	Alexandre VARNEK*	Professor, University of Strasbourg	Chemoinformatics	20	
6	Ichigaku TAKIGAWA*	Specially Appointed Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Program-Specific Professor,Center for Innovative Research and Education in Data Science, Institute for Liberal Arts and Sciences	Machine Learning	20	
7	Tamiki KOMATSUZAKI*	Professor, Institute for Chemical Reaction Design and Discovery / Research Center of Mathematics for Social Creativity, Research Institute for Electronic Science, Hokkaido	Mathematical Science	80	
8	Satoru IWATA*	Specially Appointed Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Professor, Graduate School of Information Science and Technology, The University of Tokyo	Mathematical Engineering	20	

9	Hajime ITO*	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Synthetic Chemistry	80	
10	Mikako OGAWA*	Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University / Graduate School of Pharmaceutical Sciences, Hokkaido University	Pharmaceuticals - analytical and physicochemistry	80	
11	Benjamin LIST*	Specially Appointed Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Professor and Director, Max Planck Institute for Coal Research	Reaction Design	20	
12	Yasuchika HASEGAWA*	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Optical Materials Science	80	
13	Yasuhide INOKUMA*	Associate Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Structural Chemistry	80	
14	Jian Ping GONG*	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Advanced Life Science, Hokkaido University	Polymer Chemistry	80	
15	Shinya TANAKA*	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Medicine, Hokkaido University	Tumor Pathology	80	

* Percentage of time that the principal investigator will devote to working for the center vis-à-vis his/her total working hours. (Activities carried out using competitive funding can be included as effort as long as they correspond to the purpose of the WPI center and are conducted for the center.)