World Premier International Research Center Initiative (WPI)
FY 2020 WPI Project Progress Report

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Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2021) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.
➢ Prepare this report within 10-20 pages (excluding the appendices, and including Summary of State of WPI Center Project Progress (within 2 pages)).

Summary of State of WPI Center Project Progress (write within **2 pages**)

1. Advancing Research of the Highest Global Level

The center's mission is not to leave the discovery and design of chemical reactions to serendipity or experience-guided intuition, but to purposefully create chemical reactions. The key to achieving center's mission is the development of computational and informatics techniques for predicting chemical reactions. Since the center aims at developing the "chemical reaction design and discovery" strategies for diverse application fields, the experimental team covers organic synthesis, material development, and diagnosis method development. The research progresses are reported in the following four sections: (1) Development and integration of state-of-the-art computational & informatics techniques, (2) Design and discovery of new synthesis methods, (3) Design and discovery of new materials, and (4) Creation of innovative measurement and diagnosis methods. We tackle the development of the "chemical reaction design and discovery" strategies for diverse application fields through high-level fusion researches combining various computational, informatics, and experimental techniques that these unique teams have. Through these efforts, the center will revolutionize Chemical Reaction Design and Discovery (the center's slogan).

The achievements for FY2020 are as follows: 148 papers were published in peer-reviewed journals (19 papers in journals with an IF > 10). One paper was published in *Science* (IF: 41.845), one in Nature Nanotechnology (33.407) and two in *Advanced Materials* (IF: 27.398). The center members have presented their researches in 15 invited lectures at international conferences and 10 awards have been granted. The total amount of research funding was 934 million JPY. Representative grants are JST-ERATO, JST-CREST, AMED-P-CREATE, etc.

2. Generating Fused Disciplines

To realize the center's vision and mission, we ensured maximum opportunities for researchers from different fields to exchange with each other. The specific activities are as follows.

(1) **Incubation space for fusion researches**: Establishment of mix-office, mix-labs, analytical instrument and data analysis rooms, and PI office (1,200 m^2 increased in FY2020).

(2) **ICReDD seminar system**: Seminar system toward fusion researches (20 seminars, via Zoom). Special Seminar (1, Prof. Iwata): Seminar to share the advanced researches with the center members; Stirring Seminar (2): Cross-disciplinary exchange seminar for researchers from different fields to understand their researches; Tutorial Seminar (1, AFIR tutorial seminar via hybrid): Learning seminars in which researchers from different disciplines explain the basics of each other's areas of expertise; Seeds/Needs seminar (15): seminar series by young researchers towards collaborations with researchers in different fields; Skill-up seminar (1): improving skills of oral/poster presentations and preparation for presentation materials.

(3) **Interdisciplinary research start-up support**: 7 research projects in total 13.15 million JPY were supported as challenging bottom-up fusion projects. These projects led to the increase of the number and amounts of newly granted Grant-in-Aid for Scientific Research.

(4) **Promotion of fusion researches**: Under the direction of the Director, Research Strategy Unit (RSU) Manager, Senior Research Manager (RM) from the Research Development Section and Executive Director (ED) discussed with all PIs to promote new fusion researches.

(5) **Support for obtaining funding for fusion research**: We introduced a pre-checking system for the application of Grant-in-Aid for Scientific Research, etc. The number and amounts of the granted funds were successfully increased, compared with those of the last year.

3. Realizing an International Research Environment

(1) Active recruitments of foreign and female researchers: In FY2020, 13 researchers were newly hired (9 foreigners, one female). 24 of 66 researchers are foreign nationals and 7 are female.

(2) Domestic and international collaborations: We concluded the Memorandum of Understanding

with leading domestic and international research institutions (3 institutions).

(3) International symposium (internationalization of young researchers): The 3rd international symposium was held online due to COVID-19, but nearly 300 researchers including graduate students and postdocs were participated.

(4) Suzuki Akira Award and ICReDD Award: The distinguished researchers have already been selected and the award ceremony will be held in FY2021 if possible.

(5) MANABIYA system (internationalization of young researchers): We received 22 applications including young researchers from abroad, but only two oversea and five domestic young researchers were accepted due to COVID-19.

4. Making Organizational Reforms

(1) Improvement of management structure: To ensure the center's research policy, personal interviews of all the center researchers with the Director and ED were set immediately after newly hired and before the contract renewal. To support the leadership of the Director, RM joined the administrative meetings. To secure the sustainable development of the center, monthly meetings with the President were scheduled.

(2) Revision of organizational structure: To improve the center's management and accelerate the research projects, three working groups (WG), Future Planning WG, New Building Preparation WG, Equipment Installation Management WG, were established.

5. Efforts to Secure the Center's Future Development over the Mid- to Long-term

(1) Composition of researchers, and final composition of personnel
- Currently, 47% computational/information and 53% experimental scientists.
- At the end of March 2021/2023, 24/34 of 66/75 researchers (36/45%) were foreign nationals and 7/12 (11/16%) were female (15/15 PIs, 27/28 faculty members, 14/21 researchers, and 10/11 research collaborators).

(2) Buildings and facilities
- In addition to 1,400 m^2 of CRIS building renovation, we received additional 1,200 m^2 of research space. The new building (5,500m^2) was decided to build and will be completed in FY2022. The design work for the new building have already started in October 2020.The new building will provide "*Super Mix-lab*" so that researchers of three fields (75 researchers) can interact on a daily basis to accelerate fusion research further.

(3) Form of organization
- Future Planning WG discussed the organizational structure, financial plans, and the budget requests during and after the subsidy period. The organization of the new graduate school was also discussed in this WG.

(4) Finance (external funds, joint research funds with companies)
- In FY2020, we received 454 million JPY in University Top-down Financial Support and 934 million JPY in External Funds.
- Future Planning WG estimated amounts of the indirect cost to maintain the research activities as 100 million JPY, corresponding to 600 million JPY for Grants-in-Aid for Scientific Research, etc. and 100 million JPY for corporate joint researches.

(5) Human resources development
- For the further internationalization and diversity, the university allowed us to hire three tenure-track professors (Junior PIs) from abroad in FY2021. We are planning to hire at least one female researcher as the professor.
- By utilizing MANABIYA, we conducted joint researches with 3 students and 2 young researchers from other institutions and fostered them. The "Advanced Computational Chemistry" course was also held at the Hokkaido Summer Institute (53 students took the course).
- We started the joint symposium with other faculties in Hokkaido University to promote the personnel exchange and to explore further fusion researches. The first joint symposium was held with Faculty of Science (Dec. 2020), and nearly 100 researchers were participated. The joint symposium with Faculty of Engineering is scheduled in April 2021.

(6) Graduate school
- The concept of the new graduate school (15 to 20 students per year) based on MANABIYA was discussed with the Dean of Graduate School of Chemical Sciences and Engineering and the University Headquarters.
- We decided to install educational facilities such as "MANABIYA server" for State-of-the-art theoretical computing and information science and designed the room for computation practice in the new building.
- We started discussion to link the new graduate school to the advanced graduate education system of the university, the SMatS Program, "Advanced Training Course for Smart Materials Science".

6. Others

(1) Press release: 10 press releases; 1 press conference was hosted.

(2) Outreach activities: We participated in 4 events, gave one general public lecture, one lecture for elementary, junior high and high school students, and two joint symposia with other faculties in Hokkaido University. In addition to enhancing the website and SNS, we have published Monthly News Postcards (since Jun. in 2020) to convey research highlights, Quaternary News Posters (since Aug. in 2020) to convey research contents in an easy-to-understand manner, and Annual Reports (Aug. 2020) to widely disseminate information both domestically and internationally.

＊ Describe clearly and concisely the progress being made by the WPI center project from the viewpoints below.
- In addressing the below-listed 1-6 viewpoints, place emphasis on the following:
(1) Whether research is being carried out at a top world-level (including whether research advances are being made by fusingdisciplines).
(2) Whether a proactive effort continues to be made to establish itself as a “truly” world premier international research center.
(3) Whether a steadfast effort is being made to secure the center’s future development over the mid- to long-term.

1. Advancing Research of the Highest Global Level

＊ Among the research results achieved by the center, concretely describe those that are at the world’s highest level. In Appendix 1, list the center’s research papers published in 2020.
＊ Regarding the criteria used when evaluating the world level of center, note any updated results using your previous evaluation criteria and methods or any improvements you have made to those criteria and methods.

I. The center’s scientific mission

For the achievement of sustainable development goals through realization of Society 5.0, new chemical reactions are required for creation of novel functional molecules and high-performance materials, and even for medical treatments for intractable diseases. However, the design and discovery of new chemical reactions have depended on serendipity or experience-guided intuition, which was a bottleneck in the innovation for the new society. The center’s mission is to establish the “chemical reaction design and discovery” strategies and to enable humanity to purposefully create chemical reactions without relying on serendipity or experience-guided intuition. The center combines computational science, information science, and experimental science to develop new synthesis methods, new materials, and new applications across all fields in our society. In the center, the computational research team capable of simulations of chemical reactions of various types tackles the development of practically useful chemical reaction design techniques through close cooperation with information and experimental teams. In order to tackle various issues in highly complex chemical processes, the information team covering diverse fields ranging from chemo- and materials-informatics to combinatorial optimization, knowledge engineering, and mathematical modeling has been established by gathering top information scientists in these fields. The experimental team also consists of top scientists having diverse backgrounds, i.e., organic synthesis, materials chemistry and polymer physics, and medical science. In the center, we tackle the development of “chemical reaction design and discovery” strategies for diverse application fields through high-level fusion researches combining computational, informatics, and experimental techniques own by these teams. Through these efforts, the center will revolutionize chemical reaction design and discovery.

II. Overview of the center’s research

The key to achieving the center’s mission is the development of computational and informatics techniques for predicting chemical reactions. Since the center aims at developing “chemical reaction design and discovery” strategies for diverse application fields, the experimental team covers organic synthesis, material development, and diagnosis method development. Therefore, the center tackles the following four targets hierarchically: (1) Development and integration of state-of-the-art computational & informatics techniques, (2) Design and discovery of new synthesis methods, (3) Design and discovery of new materials, and (4) Creation of innovative measurement and diagnosis methods. These four have different complexity, and by tackling them, it is expected that a series of strategies for different complexities can hierarchically be constructed.

In order to accelerate the project, we have launched the seven flagship projects as illustrated in the below figure. The project I, the center’s heart and fundamentals, corresponds to the above target (1). The projects II, III, IV, and V, related to the target (2), are hot topics in organic synthesis. The project VI aiming at environmental contribution is related to the target (3). The project VII tackles one of the most significant medical subject, i.e., cancer diagnosis, as the flagship of the target (4). These all are of high-impact and also challenging. In FY2020, we have kick started all the seven flagship projects and proceeded them actively.

In addition, we called for bottom-up projects in early FY2020, with establishing the fusion research start-up grant. Using the grant, young researchers in the center launched several new fusion

research projects. In this report, preliminary results from such projects are described in **2-5** and **4-1**. We have also conducted collaborative researches with groups outside the center, by calling for MANABIYA-academic researcher applications in early FY2020. In this report, two of outcomes from MANABIYA are presented in **2-9** and **2-10**.

III. Achievements and progress on the center research

Below, preliminary reports and interdisciplinary collaborations are marked as follows.

* Preliminary report (confidential)

† Interdisciplinary collaboration within the center

‡ Interdisciplinary collaboration with groups outside the center

The seven flagship projects are indicated by **#PJ-I#**, **#PJ-II#**, **#PJ-III#**, **#PJ-IV#**, **#PJ-V#**, **#PJ-VI#**, or **#PJ-VII#**

Also, research outcomes created by the MANABIYA system are indicated by **#MANABIYA#**

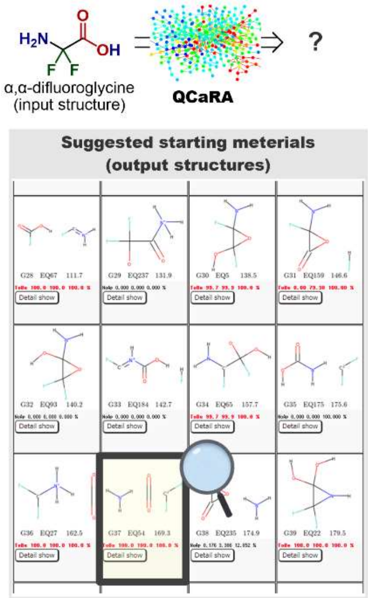
(1) Development and integration of state-of-the-art computational & informatics techniques

The development and integration of fundamental computational and informatics methods are key issues in creating strategies for the computation- and informatics-driven chemical reaction design and discovery. This subsection describes achievements in FY2020 concerning the flagship project I "Integration of theory-driven and data-driven reaction prediction".

1-1) Integration of theory-driven and data-driven reaction prediction **#PJ-I#**

This project is the center's heart. Especially, the further development of an automated reaction path search method called artificial force induced reaction (AFIR) method (a), the construction of a computational reaction path database recording those obtained by AFIR were done (b, c, and d). Apart from AFIR-related developments, various informatics tools for accelerating chemical reaction discovery were also developed through close collaborations between information scientists and computational/experimental scientists (e, f, g, and h).

†a) Generalization of quantum chemistry aided retrosynthetic analysis (QCaRA)



The **Maeda group** proposed the "Quantum Chemistry-aided Retrosynthetic Analysis" (QCaRA) to realize the automated synthetic path prediction. QCaRA applies the AFIR method to search systematically for the decomposition paths of a target molecule and suggests a synthesis method corresponding to the reverse reaction of the obtained path. Previously, QCaRA was successfully used to discover a novel three-component coupling reaction affording α,α-difluoroglycine derivative (***Chem. Sci.*** 2020).

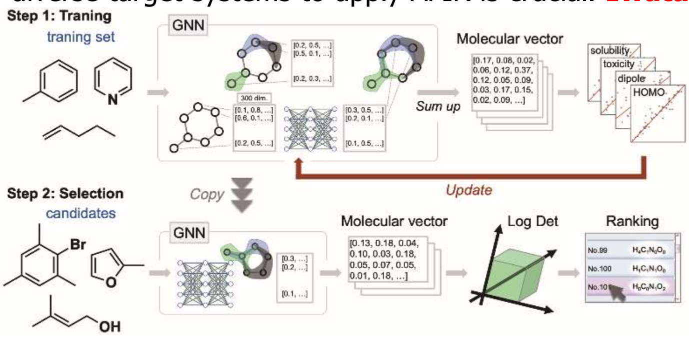
However, QCaRA was applicable only to one-step reactions, not to multistep reactions. In FY2020, **Maeda group** generalized QCaRA by combining AFIR with a graph-theoretical/kinetics method called rate constant matrix contraction (RCMC) method, which enabled its application to multistep cases. The QCaRA/AFIR-RCMC method provided a reaction path network consisting of ~20000 paths and predicted ~1000 chemical reactions affording α-acyloxyamide. It is emphasized that the calculation did not require any information on the predicted chemical reactions except for the target product. Therefore, we succeeded in establishing the automated prediction method for chemical reactions of desired products (***ChemRxiv*** 2021). Because its computational cost is huge in large systems and currently applicable to small systems (<30 atoms), the further development is under progress.

*†b) QCaRA reaction path database

Maeda group has developed a computational chemical reaction database using QCaRA/AFIR-RCMC, which promotes utilization of the reaction path network and the tool development to analyze it. The database contains reaction path networks generated by QCaRA/AFIR-RCMC and lists many known and unknown chemical reactions. We have completed the search in ~60 systems and obtained ~1,000,000 paths and ~120,000 chemical reactions. Currently, the database has been open to **Taketsugu group**, **Varnek group**, **Takigawa group**, **Yoshioka group**, and **Komatsuzaki group**, and various theoretical/informatics approaches analyzing/utilizing the data has been under development.

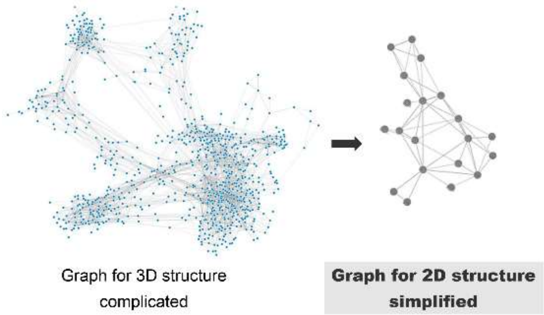
†c) Selection strategy of diverse molecules for exploring chemical space

As mentioned in **1-1-b**, we started to create the database of chemical reaction path network. While expanding the database, selection of diverse target systems to apply AFIR is crucial. **Iwata group** and **Maeda group** have investigated a systematic method to select diverse molecules using supervised learning and submodular optimization. Based on structures and properties of candidate molecules, we constructed spherical vector representations of molecules so that a variety of physical quantities can be predicted. We then utilized these vector representations to select a diverse set of molecules so that the volume of the parallelopiped spanned by the selected molecules should be maximized approximately (***Sci. Rep.*** 2022). The method helps generating an effective database which covers diverse transformations and would be useful in the new reaction discovery.



†d) RePathDB – a comprehensive database and navigation system for large arrays of data generated in quantum chemical calculations

Varnek group and **Maeda group** have developed software tools for handling and modeling the geometry and energy data generated with the AFIR method, because AFIR generates huge arrays and the manual analysis of these data may become cumbersome if the pathway only on 3D structures are considered, which prevents smooth discovery of new chemical reactions. Our RePathDB library introduces a unique combined relational/graph architecture that relates 3D structures to their corresponding 2D molecular graphs, which reduces the reaction pathway graph and thus accelerates the search for important pathways (***J. Chem. Inf. Model.*** 2021).



†e) Artificial intelligence framework of reaction generation (AI FoRGe)

Varnek group worked on the development of approaches of novel reaction generation by machine learning and artificial intelligence to predict novel chemical reaction for desired properties. We have trained a deep neural network on a dataset of reactions extracted from US patents to generate SMILES for reactions similar to Suzuki-Miyaura coupling as an example. Suzuki-Miyaura coupling is focused because it is widely used in organic synthesis and is the most prominent reaction discovered in Hokkaido University. From the generated database, we selected the most relevant chemical reactions by applying a series of special chemical filters (AI filters): 1) chemical validity; 2) "novelty filter" which determines if the reaction is known; 3) structure simplification to avoid irrelevant substituents that do not influence the reaction itself; 4) fast DFT calculations to ensure the feasibility of the reactions. Valid and novel reactions were cross-referenced in the literature, and 5 out of 13 suggested reaction centers have been found in recent publications or patents (***Sci. Rep.*** 2021), which means our developed approach can predict valid and feasible chemical reactions.

In addition, Nagata (experimental scientist) of **Maeda group** has selected some of the suggested reactions for the further experimental validation together with the development of new catalysts (under progress). Although the US patent database was used in this study, any chemical reaction database can be used in principle. Therefore, applying it to the computational chemical reaction database in SCAN (a unique database created by the center) is also under progress.

f) Molecular graph autocompletion by graph neural networks

A tool for enumerating/suggesting possible molecular structures assists designing drag-like molecules. **Takigawa group** proposed to use a generative model to grow novel molecules on a given subgraph in this purpose. Such a subgraph query is usually called a scaffold (i.e., privileged or bioactive scaffold) in the drug discovery, and performs as a core structure in the molecule to preserve the preferable bioactivity properties. Fixing the scaffold usually dramatically reduces the search space of the desired drug. The group designed a system which allows users to edit the intermediate graph candidates during the molecule design process in multiple steps. Moreover, the edit operation to predict the user's real intention to improve effectiveness was also introduced to reach the desired drug straightforwardly (***Proceedings of DEIM 2021***).

***†g) Extraction of chemical reaction related metadata from chemical paper database**

Registered data of chemical reaction in literatures and reaction databases are usually inconsistent, which prevents the use of known knowledge to develop new chemical reactions. To revamp this problem, **Yoshioka group** and **Maeda group** worked on extraction of chemical reaction related metadata from chemical papers using natural language processing (NLP) technology.

Two tasks were set: making a corpus using chemical compounds database that covers wide varieties of chemical compounds description (***Proceedings of SCIDOCA 2020***) and constructing corpus by making alignment between research papers and chemical reaction database. We have conducted experimental analysis using *Organic Syntheses* as a target journal and Reaxys as a target chemical reaction database. This alignment is not simple because extraction of such information from the paper is not consistent, which requires experimental scientists to check experimental result in the journal. Accordingly, we have started to contact with an editorial member of *Organic Syntheses* to discuss this issue. We have also started to construct corpus using this experimental result. With such approaches, not only the center but also researchers in the world will be able to access newly constructed consistent database enabling further development of chemical reactions.

†h) Informatics acceleration of exploring chemical and parameter spaces

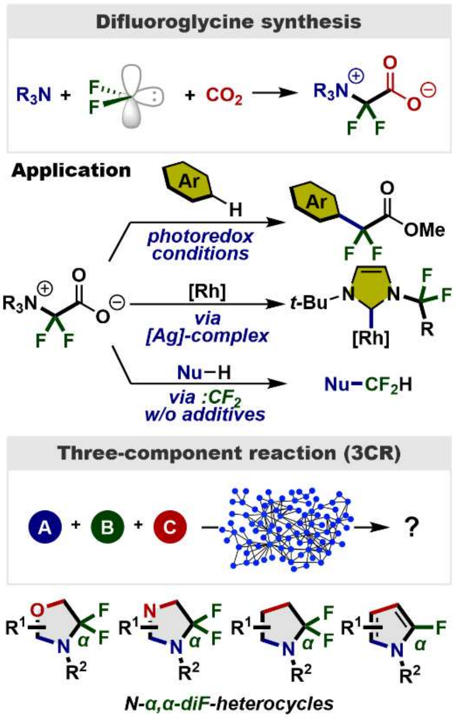
It is crucial to find the best compound, condition, etc., with the least number of trials as possible. For this purpose, **Komatsuzaki group** studied possible use of Bayesian Optimization/Gaussian Process accelerated algorithms based on Smooth Overlap of Atomic Positions (SOAP) that aim to sample chemical space in accelerated way, inventing a novel Bandits algorithm to incorporate false positive and negative rates of a given classifier (***Proceedings of PAKDD 2021***). **Komatsuzaki group** has also been discussing with **Taketsugu group**, **List group**, and Nagata (experimental scientist) of **Maeda group** about the parameters to be optimized to predict the reactivity with experimentalists, e.g., the mixture of continuous (ratio of concentration) and discrete (kinds of solvents) Bandits strategy.

(2) Design and discovery of new synthesis methods

Computational and informatics models that are constructed by a team consisting only of theoreticians and informaticians often work only poorly in the actual reaction development. This is because experimental results are affected by various factors like solubility, additive, impurity, and so on. In order to verify our models or to further construct truly useful models, we tackle the following real chemical problems: discovery of novel chemical transformations by AFIR **2-1**, development of new catalysts **2-2**, **2-3**, **2-4**, and **2-5**, precise control of chemical reactions **2-6** and **2-7**, and understanding unconventional synthetic strategy **2-8**. Here, we have utilized various tools in these systems having different complexities. Two MANABIYA results **2-9** and **2-10** are also presented.

†2-1) Small molecule activation and utilization #PJ-II#

Synthesis of useful compounds from abundant chemical species like CO_2 is one of the center's goals, which is still in progress. Although a new AFIR-assisted reaction discovery strategy, QCaRA, proposed a new synthetic route to a difluoroglycine derivative, which is a potential bioisostere of natural glycine (***Chem. Sci.*** 2020), further development for more complicated systems is the next step to synthesize the more useful chemical compounds such as pharmaceutical chemicals. In FY2020, we utilize the three-component reaction (3CR), where the three components are computationally proposed by AFIR, to explore the scope of 3CR and its synthetic application. We describe two examples of new 3CR for the synthesis of *N*-α,α-difluorinated heterocycles, which have promising drug-like structures, and a radical double functionalization of ethylene, which could lead transformation of ethylene to fine chemicals.



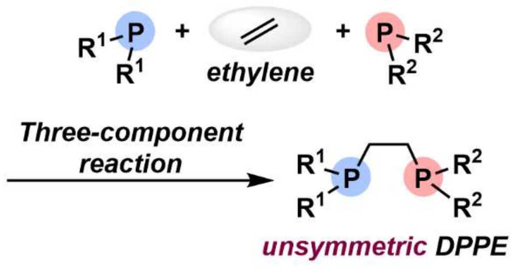
†a) Development of new 3CRs and their applications

Mita (mix-lab chief) and **Maeda group** developed a new synthetic method of difluoroglycine derivatives with the aid of QCaRA. To enhance the usefulness of the difluoroglycine synthesis toward truly useful chemicals such as pharmaceuticals, the substrate scope was significantly expanded and the synthetic application such as (i) the transfer of the difluoroalkyl group via C–N bond cleavage under photoredox conditions, (ii) the use as an *N*-heterocyclic carbene (NHC) ligand for organometallic complexes, and (iii) the use as a new difluorocarbene source, were intensively investigated (***Chem. Eur. J.*** 2021).

Next, AFIR revealed a new synthetic method of *N*-heterocycles bearing an α,α-difluoromethylene unit adjacent to a nitrogen atom: imine, difluorocarbene, and an unsaturated compound including a C=O, C=N, C=C, or C≡C bond would be perfectly assembled, affording a heterocyclic product. Based on the prediction, the synthetic protocol was established experimentally to provide *N*-α,α-difluorinated heterocycles with a broad range of electrophiles including aldehydes, ketones, imines, alkenes, and alkynes (***under review***). These results proved the general applicability of AFIR to 3RC.

†b) Double functionalization of ethylene to synthesize electronically unsymmetric 1,2-bis(diarylphosphino)ethanes

Ethylene is a fundamental molecule, and its production reaches about 170 million tons annually in the world. Although ethylene is widely used for the synthesis of polyethylene and polyvinyl chloride on an industrial scale, its synthetic application for fine chemicals (useful small molecules) has been very limited compared with other alkenes. Mita (mix-lab chief) and **Maeda group** successfully predicted new chemical transformations of ethylene by AFIR. According to the radical mechanism of 1,2-diphosphination suggested by the calculation, a further experimental demonstration led to a finding of a new double functionalization of ethylene with various P-radicals generated under the light irradiation. In this synthetic protocol, electronically different two phosphines could be incorporated on the both terminuses of ethylene, leading to unsymmetric 1,2-bis(diarylphosphino)ethanes, which are potentially utilized as novel bidentate phosphine ligands for transition-metal catalysts (***To be submitted***, ***The patent application: patent No. 2021-131481 by JST***).

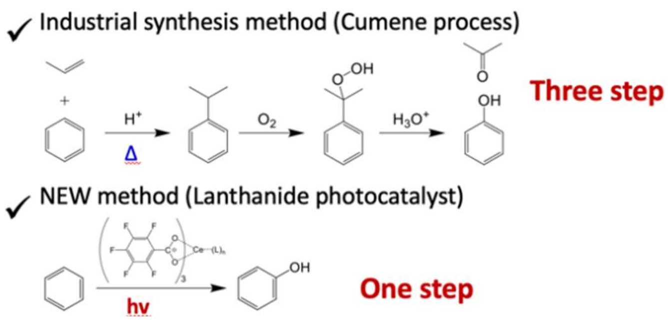


***†2-2) Asymmetric amino acid synthesis from RCHO + CO + RNH_2 #PJ-II#**

The **List group** and the **Taketsugu group** jointly work on an asymmetric reaction. The List group developed the reaction using chiral phosphoric acid and transition metal catalysts, furnishing the desired product in a moderate yield and good enantioselectivity. AFIR discovered an unexpected mechanism. Currently, a transition state modeling for its rate limiting step is in progress, which will be used to improve reactivity and enantioselectivity.

†2-3) Designing organic lanthanide-base photocatalyst with 4f orbital #PJ-II#

Development of new catalysis is also an important part of discovery of new chemical reactions, enabling unexplored chemical reactions or improving current known reactions. **Hasegawa group** and **Taketsugu group** have attempted to find new photochemical reaction using novel lanthanide complex as a photocatalyst, though the wide variety of lanthanide complex has been reported and the photo property of the complex can be manipulated by modulation of ligand. The energy level of the MLCT (metal-to-ligand charge transfer) band, which has potential of photosensitized catalytic property, was at first theoretically screened. And then, the Ce(III) complex with perfluorobenzene carboxylic acids was selected. Using selected Ce(III) complex, we successfully observed one-step phenol synthesis from benzene under UV irradiation, directly. The phenol is a key material for modern industry, where organic Cumene process requires four steps. The one step reaction is expected to open-up a new lanthanide photocatalysis. The detailed mechanism of photoredox process of Ce could be a crucial process, which have currently been being investigated experientially and theoretically.



***†2-4) Photo-induced asymmetric copper catalysis**

Another photocatalyst is a visible-light photoredox catalysis, which can realize novel molecular transformations complementary to thermal catalytic reactions. **Sawamura group** has launched an investigation for a photo-induced metal catalysis using a charge-separated species produced by MLCT photoexcitation of an organometallic catalytic intermediate which can be revealed by theoretical calculations. The group found that a copper complex with a chiral *N*-heterocyclic carbene (NHC) ligand catalytically promoted highly enantioselective umpolung allylic acylation with acylsilanes as an acyl anion precursor under visible-light irradiation. This reaction offers a straightforward access to enantioenriched α-branched β,γ-unsaturated ketones, for which the multistate mechanism is under investigation by **J. Hasegawa** (The center collaborative researcher).

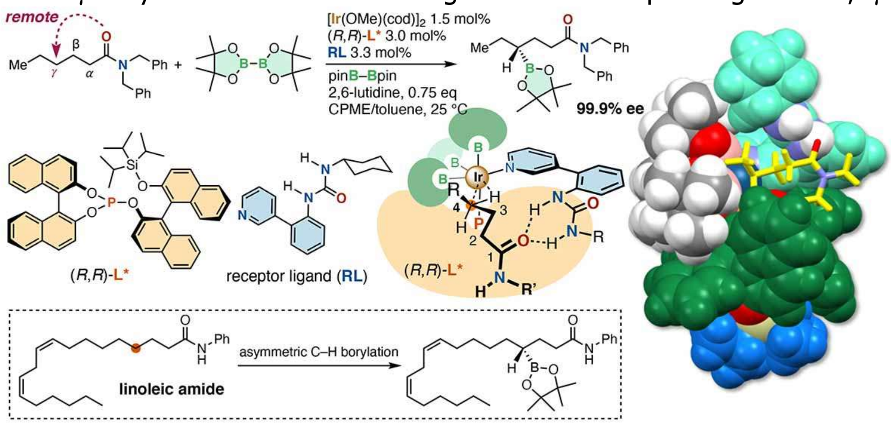
***†2-5) Rational design of asymmetric catalysis combining computation, informatics, and synthesis robot**

To develop a platform to accelerate the tedious screening process for novel catalysts with the aid of computational chemistry, chemoinformatics, and synthesis robots, young researchers from **List group**, **Varnek group**, and **Maeda group** are designing and preparing catalysts (i) for an asymmetric intramolecular hydroalkoxylation reaction using chemoinformatics approach and (ii) for an asymmetric intermolecular hydroalkoxylation reaction using a theoretical chemistry-based approach. We have built a quantitative structure-property relationship (QSPR) model using the screening data of a published transformation and succeeded in constructing model including solvent descriptors from the dataset that was not very large and consisted of mixed two reaction conditions. Based on this model, trials of prediction and experimental test were performed, resulting in similar substitution patterns. We are currently planning to apply the same strategy for the tetrahydropyran synthesis, which is preliminary and theoretically examined, to prove that the developed QSPR model-based approach can guide experimental scientists. In addition, this screening process will be performed by a synthesis robot; this whole package will deliver an efficient approach to optimize catalysts for a specific target required in biological studies or total synthesis.

†2-6) Asymmetric remote C–H borylation of amides and esters #PJ-III#

Designing reaction space like that enzymes have is one of the center's most important and challenging projects, because enzymes often have intricate active sites that can bind one portion of a molecule to orient a distant portion for the optimal reactivity. Achieving this type of orienting effect with small-molecule catalysts has proven a great challenge. This flagship project aims at establishing combined computational and informatics approaches for designing optimal reaction spaces.

A collaborative work by the **Sawamura group** and the **Maeda group** led to development of a simple ligand that can simultaneously bind to an iridium catalyst through a pyridine substituent while positioning an amide or ester reactant through a hydrogen-bonding urea (***Science*** 2020). As a result, the catalyst exclusively borylates the site three carbons away from the carbonyl group of aliphatic carboxylic amides and esters, with a second chiral ligand inducing high enantioselectivity. The asymmetric borylation tolerated a wide range of reactants including longer chain carboxylic acid derivatives. Transformations of γ-borylhexanoic acid anilide gave the corresponding alcohol, γ-arylated derivative, α-alkylglutaric acid diamide, and a γ-alkyl-γ-aminobutyric acid (GABA) derivative via oxidation, cross-coupling, isocyanate addition, and amination reactions, demonstrating the usefulness of the asymmetric remote C–H borylation in introducing molecular complexity in fatty acids that are both renewable feedstock chemicals.



Theoretical calculations, focusing on C–H bond cleavage by the catalyst, revealed a cavity formed by the catalyst components which can bind the substrate through multiple noncovalent interactions. The urea ligand binds the substrate through hydrogen-bonding so that only the γ-position C-H bond can interact with the Ir center. The interactions within this groove position the reactant bringing the targeted site in close proximity to the catalytic center making possible the desired reactivity. These features are like those of natural enzymes that have intricate active sites for substrate binding.

***†2-7) Reaction discovery by artificial enzyme design #PJ-V#**

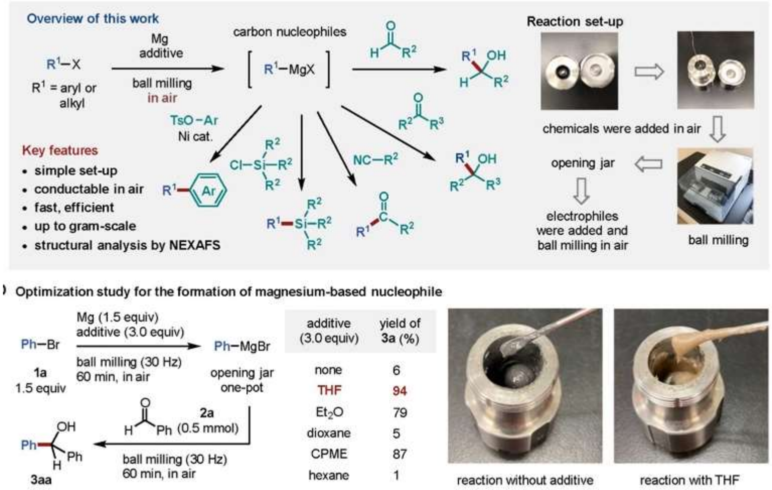
This flagship project aims at creating new chemical reactions utilizing an artificial enzyme. More specifically, we will computationally screen possible mutation patterns so that reactivity and selectivity of a desired reaction is maximized. Therefore, establishing the screening method combining computational and informatics approaches is the first step of this project.

In FY2020, **Maeda group** has extended AFIR to explore paths of molecular binding to enzyme. Although the developed approach is computationally more expensive than the conventional docking simulation, there are two major advantages in the new method, (1) conformational changes of the target molecule during its binding are accounted and (2) activation energy required in the binding process is computed. Using this new computational tool, we worked on Hartwig's reconstituted artificial metalloenzyme containing an iridium porphyrin and computed substrate insertion paths taking account of all ~7000 single mutation patterns of the wildtype enzyme including Hartwig's variants to confirm the applicability of the methodology. This computation provided a ranking of the substrate binding efficiency for these single mutation patters, and the experimental setup for some high-ranking mutants is now under construction in **Tanaka group**. These mutants will be used in organic synthesis by Mita (mix-lab chief) and **Maeda group**. Moreover, discussions have been made together with **Takigawa group** on how to find high-ranking double and triple mutation patterns from the 7000*7000 and 7000*7000*7000 possible mutation patterns, respectively, using machine-learning to reduce trials of virtual mutation by the methodology, because the number of patterns of multiple mutations increases exponentially.

†2-8) Solid-state reaction development using ball mill #PJ-IV#

Organic synthesis reactions are usually conducted in a solvent. But the use of solvent causes high production cost and environmental loadings, in addition, this would even limit the further possibility of organic synthesis. Mechanochemical synthesis with the ball mill technique becomes important in organic chemistry. However, despite its raising importance, little has been understood theoretically on this new method. Therefore, constructing theoretical and computational approaches for understanding its mechanism has been set as one of the center's flagship projects.

In FY2020, **Ito-group** experimentally found that this new method enables solvent-free reactions with unique selectivity and reactivity (***Angew. Chem. Int. Ed.*** 2020, ***ACS Sustain. Chem. Eng.*** 2020). We have developed Pd-catalyzed solid-state cross-coupling reactions including selective mono cross-coupling of diboromoarenes and cross-coupling of insoluble organic halides (***J. Am. Chem. Soc.*** 2020). Furthermore, we successfully conducted the Suzuki-Miyaura coupling of insoluble organic substrates, which were not used in organic synthesis (***J. Am. Chem. Soc.*** 2021). This new method can expand the possibility of chemical transformations.



For the further development of this approach, **Ito-group** and **Maeda group** focused on the solid-state preparation of Grignard reagents, which is one of the most fundamental nucleophilic reagents in organic chemistry (***Manuscript in preparation***). Although the structure of Grignard reagent in solution has been well understood, its structure in the solid state is completely unknown. Therefore, we performed an exhaustive structural exploration using AFIR and created a big structural dataset composed of thousands of stable structures. The structure of Grignard reagent in the solid state will be determined precisely by comparing the experimental near-edge X-ray absorption fine structure (NEXAFS) spectra with theoretical ones computed using the big structural dataset.

†2-9) Silane- and peroxide-free hydrogen atom transfer hydrogenation using ascorbic acid and cobalt-photoredox dual catalysis #MANABIYA#

Kojima (experimental MANABIYA researcher from Faculty of Pharmaceutical Sciences, Hokkaido University) stayed in **Maeda group** for one month using the MANABIYA system and learned AFIR. He discovered a novel reaction involving a silane- and peroxide-free HAT hydrogenation using a combined cobalt/photoredox catalysis and ascorbic acid (vitamin C) as a sole stoichiometric reactant in the lab he originally belongs to. During the stay in the center, he utilized AFIR and revealed its reaction mechanism computationally. The results were published as a joint experimental/computational paper (***Nat. Commun.*** 2021).

†2-10) Chemoselective cleavage of Si–C(sp^3) bonds in unactivated tetraalkylsilanes using iodine tris(trifluoroacetate) #MANABIYA#

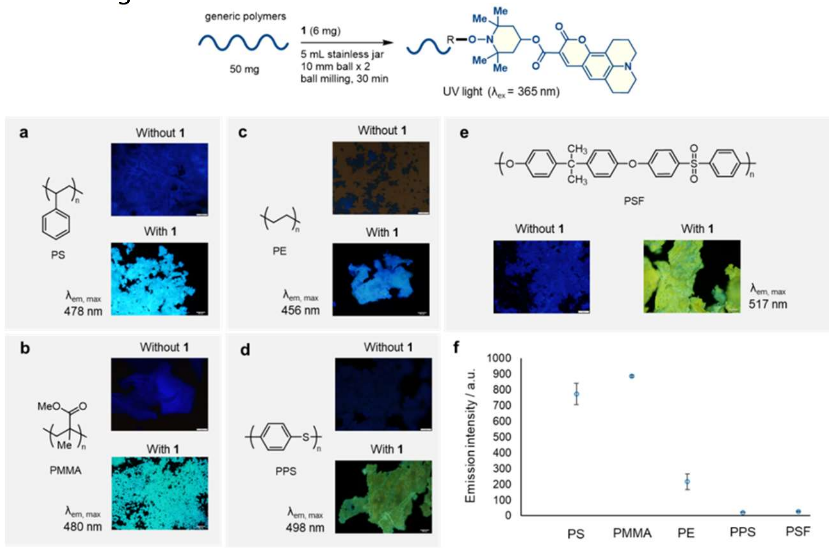
Kojima and Yoshino (experimental MANABIYA researcher from Faculty of Pharmaceutical Sciences, Hokkaido University) stayed in **Maeda group** for one month using the MANABIYA system and learned AFIR. He discovered a novel reaction involving the chemoselective cleavage of Si–C(sp^3) bonds of unactivated tetraalkylsilanes using iodine tris(trifluoroacetate) in the lab he originally belongs to. During the stay in the center, he utilized AFIR and revealed its reaction mechanism computationally. The results were published as a joint experimental/computational paper (***J. Am. Chem. Soc.*** 2021).

(3) Design and discovery of new materials

The control over chemical reactions is an essential prerequisite in the production of modern and functional materials. In other words, the center should also tackle to find out and regulate new chemical reactions to produce novel high-performance materials, which can solve environmental problems and contribute to human prosperity. Although development of functional materials usually relays on trial-and-error approaches due to difficulty of the prediction of functional properties coming from system complexity, we have been trying to develop them with guidance by computational and/or information approaches. The development of stimuli-degradable polymers is one of obvious important problems as is known for ocean pollution caused by microplastics, though we did not have clear guideline to develop such polymers. High performance luminescent materials are also one of the center's targets, because theoretical calculations can provide the detailed electronic parameters to design the exited states for luminescence. Not only solving current problems but also advancing technology such as luminescent materials, which can be applied to information technologies, is indispensable. Below, the progress of the development of the stimuli-degradable polymer material **3-1**, the development of novel functional polymers **3-2**, and the discovery of luminescent materials **3-3** are presented.

†3-1) Stimuli-degradable polymer material #PJ-VI#

As mentioned above, development of the stimuli-degradable polymer has potential to solve ocean pollution by microplastics. We first focused on visualizing mechanoradicals generated in polymers. This is because we assume that this could be the first step in the reaction design for accelerating the degradation by controlling mechanoradicals.



We are now studying mechanical stimulation to introduce a luminophore into polymers. The *in-situ* formed polymeric mechanoradicals upon ball-milling underwent a C-O radical coupling with a prefluorescent nitroxide-based reagent to incorporate a luminophore into the polymer. This method allowed the direct preparation of luminescent polymeric materials from a wide range of generic polymers such as polystyrene, polymethyl methacrylate, and polyethylene. The prefluorescent probe could also be introduced into hydrogels by mechanical stretching. These results indicate that we can distribute luminophore into polymers by mechanical stimulation and detect radical generation there. (***Angew. Chem.*** 2021). **Maeda group** is working on AFIR calculations toward detailed understanding on radical generation, **Rubinstein group** is working on polymer dynamics and modeling toward revealing the kinetics of polymer cleavages, and **Takigawa group** is working on machine-learning prediction toward prediction on polymer properties from monomer information.

***†3-2) Copolymerization mechanism of monomer pairs having cation-π interactions**

The Center's theoretical approaches would also pave the way for designing new polymers showing unique properties. **Gong group** and **Maeda group** worked on the copolymerization mechanism of cationic/aromatic monomer pairs, which can regulate the sequence of monomers in polymers toward highly structurally regulated functional polymers. Although the control of the sequence is generally difficult, theoretical calculation can guide and design monomers to achieve the control. **Gong group** experimentally found that cationic and aromatic monomer pair with equimolar ratio can form copolymers with adjacent sequences by the simple free-radical polymerization. Experimental results suggest that the readjustment of the monomer reaction rate in pairs caused by forming cation-π association is the key factor for the synchronized reaction rates. Based on the experimental speculation, **Maeda group** theoretically calculated the interaction strength and conformation between cationic and aromatic monomers, and the reaction barrier energy of monomer reactions during polymerization. The calculation results are consistent with experimental findings and clarify underlying mechanistic features of the copolymerization reaction. The results give guidance to synthesize hydrogels with controlled monomer sequence which is one of the ultimate goals in gel material science.

†3-3) Luminescent lanthanide molecular glass with large dissymmetry factor for CPL

Design and development of useful material for advanced technology is one of the center's missions. **Hasegawa group** successfully synthesized luminescent lanthanide molecular glass with large dissymmetry factor for circularly polarized luminescence (CPL), which can be utilized for advanced photonic security device applications (***Commun. Chem.*** 2020). The transparent amorphous glass shows CPL with extra-large dissymmetry factor of gCPL = 1.2. The brightness of the lumino-glass is one thousand times larger than that of Eu(III) luminophores embedded in polymer films of the same thickness at an Eu(III) concentration of 1 mM. The application of such a chiral lanthanide lumino-glass in an advanced security paint is demonstrated.

Maeda group conducted computational exploration of possible stable structures using AFIR and provided rational understandings on the formation of amorphas structure, the existence of multiple lifetime components, and the number of ligands that actually coordinated to the Eu center.

(4) Creation of innovative measurement and diagnosis methods

In advanced researches aiming at the development of new chemical reactions, analyzing a reaction mixture is an essential but time-consuming task. Also, in the clinical diagnosis, for instance drug screening, huge amount of data must be analyzed. To overcome these time consuming and costly processes, the center is also challenging innovation in chemical measurements and clinical diagnosis through fusion researches between experimental and information scientists. Below, progresses in the development of an image analysis method for reaction mixtures **4-1**, the development of a cancer diagnosis method utilizing the hydrogel activated reprogramming phenomenon **4-2**, and the development of a cancer diagnosis method using luminescent materials **4-3** are presented.

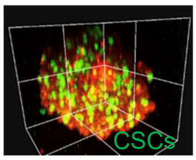
*†4-1) Image diagnosis for quantitative analysis of chemical reactions

To analyze reaction mixtures in chemical reactions, chemists usually use nuclear magnetic resonances (NMR) or high-performance liquid chromatography (HPLC). On the other hand, experienced researchers can estimate the progress of reaction, namely, rough reaction yield, with a glance at the reaction flask. This project qualifies such a 'educated guess' by experienced researchers using information science.

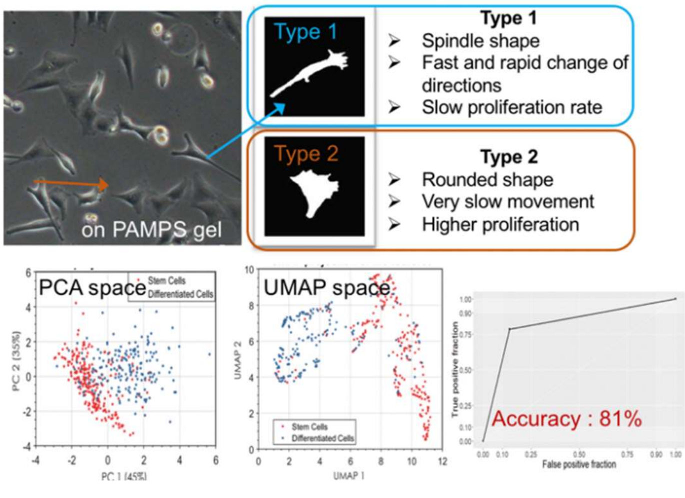
Young researchers from **Inokuma group** and **Takigawa group** have developed an image diagnosis system that can determine the molar ratio of two components in their mixture from a picture of the mixture using machine learning (ML). We have established a picture format suitable for reproducible ML. As a proof-of-concept example, we took pictures of hundred sets of solid mixtures of sugar and dietary salt at various component ratio using high-resolution microscope camera. These pictures were used as supervising data for ML. Then, testing analysis showed that ML can predict the component ratio within error bar of less than 10%. This system was also applied for determination of reaction yields in solid-state thermal decarboxylation of 4-amino-2-hydroxybenzoic acid. This research will be able to largely contribute to shortening the time to for the chemical reaction development that is the center's most important research mission by providing quick reaction analysis method.

†4-2) Cancer diagnosis using the rapid reprogramming of tumor cells into cancer stem cells on double-network hydrogels toward quick diagnosis and drug screening #PJ-VII#

The center's informatics approaches also accelerate clinical diagnosis requiring the analysis of the huge amount of data. Cancer recurrence can arise owing to rare circulating cancer stem cells (CSCs) that are resistant to chemotherapies and radiotherapies, thus CSCs should be a therapeutic target for eradicating cancer. We have shown that a double-network hydrogels composed of poly-2-acrylamideo-2-methylpropane sulfonic acids (PAMPS) and poly-*N*,*N*-dimethylacrylamide (PDMAm) can rapidly reprogram differentiated cancer cells into CSCs. Six human cancer cells placed onto the DN hydrogel showed sphere structures, elevation of stemness markers within 24 hours, and tumorigenicity *in vivo* (***Nat. Biomed. Eng.*** 2021). This rapid detection system of CSCs could be useful for the prediction of therapeutic reagents for complete eradication of CSCs in cancer patients, leading to the development of an innovative method for diagnosis of CSCs using hydrogel.



For further development, **Tanaka group**, **Gong group**, and **Komatsuzaki group** are closely collaborating and focusing on quick analysis of CSCs to incorporate the study of morphological and chemical changes of the cancer cells on hydrogels using information science techniques to learn implicitly how cancer cells are responding differently to induce stemness. It was found that mouse myoblasts that mimic Ewing sarcoma changed the morphology significantly on PAMPS gel, and stemness markers increased by about 114-fold. Approximately 90 percent of the cells induced SOX2 expression after 48 hours cultured on PAMPS gel. The cells are well separated in a 2D nonlinear projection based on the differences between their intensity profiles from phase-contrast images in different cell type implying that they may exhibit different features depending on different culture duration. In addition to the analysis of the morphological changes, **Komatsuzaki group** attempted to accelerate to discover anti-cancer drugs that selectively eradicate CSCs by contextual Bandits algorithm with referencing effective molecular descriptors. The group formulated a new Bandits algorithm termed as bad arm existence checking (BAEC) problem which can be applied to fast detection of cancer/noncancer Raman images (***Machine Learning 2020***, ***Proceedings of PAKDD 2021***) and enables us to accelerate drug screening to eradicate solely CSC by performing as fewer number of experiments as possible. **Tanaka group** and **Gong group** applied this algorithm to 284 drugs and showed 20-30 times

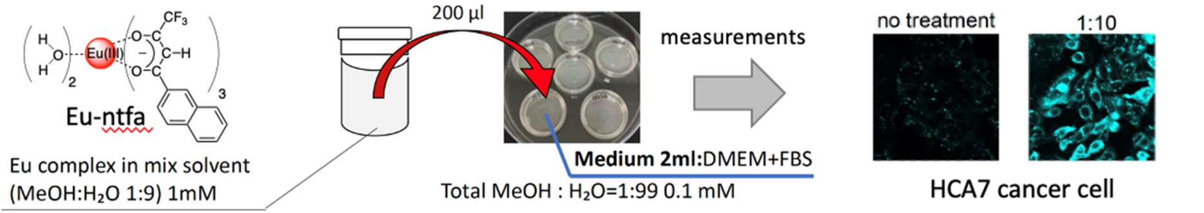


acceleration from a naïve screening in finding the desired drugs. We also developed a prototype of novel Raman microscope combined with BAEC Bandits algorithm expected to apply faster detection of CSCs than the conventional microscope (***Manuscript in preparation***). These results will accelerate cancer diagnosis and drug screening, which can be realized by cancer cell on hydrogel approached by information science.

†4-3) Development of cancer GPS using light-emitting materials #PJ-VII#

The center's another approach of novel diagnosis of cancer cell is visualization by luminescent molecules, which can be theoretically designed toward cancer specific luminescence. Photophysical and informatic analysis for cancer growth process and mechanism (reaction) also opens new medical science and engineering. The strategy to develop novel "cancer GPS system" is the following three points: 1) Visualization of cancer cells by **Tanaka group** using water-soluble luminescent Ln(III) complexes developed by **Hasegawa group** supports future medical check for understanding the growth mechanism of cancer. 2) Photophysical information and data mining of Luminescent Ln(III) micelles on cancer by **Takigawa group** is useful for finding new aspects of cancer growth. 3) After theoretical design of luminescent properties, cancer cells will be detected on patient's tissue specimen and finally in cancer patients *in vivo*.

In order to understand the cancer-cell growth, **Hasegawa group** together with **Tanaka group** attempted to prepare the cancer growth positioning system using luminescent lanthanide complex. Using water-solved Eu-ntfa complex, luminescent images of cancer cells (Hela: Colon cancer, Lung cancer, Brain cancer etc.) are successfully observed. **Tanaka group** also real-time monitored the endocytosis process in living cancer cells using luminescent images. In order to analyze the photophysical properties of Eu-ntfa with cancer cells, **Hasegawa group** also prepared new laser-induced optical system (digital optical analysis) for lifetime measurements of Eu-ntfa in cancer cells. Now, we have attempted to informatic-analyze the luminescent images by **Takigawa group** for the endocytosis process in living cancer cells, because we will collect various lanthanide complex and cancer cell, which generate too much data to analyze and interpret manually and rapidly. The use of machine learning methods for images for pattern detection, prediction, and quantification is under investigation.



DMEM (Dulbecco's Modified Eagle Medium)- Amino acids, glucose etc.)
FBS (Fatal Bovine serum)

2. Generating Fused Disciplines

* Describe the content of measures taken by the center to advance research by fusing disciplines. For example, measures that facilitate doing joint research by researchers in differing fields. If any, describe the interdisciplinary research/fused discipline that have resulted from your efforts to generate fused disciplines. You may refer to the research results described concretely in "1. Advancing Research of the Highest Global Level."

In FY2020, despite the difficulties due to COVID-19, we took measures to improve research environment for the center's scientific mission, promoting the revolution in chemical reaction design and discovery by integration of computational science, information science, and experimental science. For the increasing number of the center members (increased to 66 in FY2020), we secured more space to be more readily able to start interdisciplinary researches, to efficiently carry out and to accelerate them by sharing time together. Furthermore, we established systems to find seeds of new interdisciplinary researches, to support newly started researches and to integrate them into further advanced interdisciplinary researches by sharing their achievements. Those measures are summarized in **(1) Expand incubation space**, **(2) Improve ICReDD seminar**, **(3) Assign interdisciplinary research start-up support**, **(4) Organize various type of meetings, (5) build a system to lead research/researcher**.

(1) Expand incubation space: New three mix-labs, analytical instrument rooms, data analysis room, and PI office

We launched new two synthesis laboratories next to the mix-office, one bio experimental laboratory and one data analysis room on the same floor, in addition to the mix-labs and mix-office launched in the last fiscal year. The data analysis room was designed for theoretical and information scientists to work closely together. The developed data base and theories are now being applied to the theory-experimental and/or information-experimental collaborations. The new synthetic laboratories are mainly used by material scientists to develop new materials, while the other two laboratories have been mainly used to develop new chemical reactions. The bio experimental lab can be used for biosystems with materials or chemicals developed in the center together with the theory/information scientists. We completed to set up a full research environment where we can explore interdisciplinary research with a full scale from a few atomic systems to huge complex systems, as needed. Indeed, the environment produced not only scientific results but also a system which enables informatics scientists to collect experimental data efficiently: a data management system of chemical regent stocks for the utilization of experimental data through informatics, which enables us to create a database of which reagents are used in which experiments.

We also introduced a system to share the information on the presence of PIs in the PI rooms adjacent to the mix-office. This system made it easier for PIs and researchers to have casual discussion even though they are from different groups. The new prepared PI rooms in front of the mix-office, where PIs can usually stay to enrich frequent and casual discussion. Because the rooms started to work effectively, new collaborations by PI groups, for example Profs. Taketsugu and Yoshioka, which we have not seen before, were started collaborative work.

To realize further fused environment, we also started to design the new building that can secure the dynamic mix room which enables all field members to work in one room.

(2) Improve ICReDD seminar: Stirring, Seeds/Needs, Tutorial, Skill-up, Special seminars

These various types of seminars are important to come up with new ideas, to find suitable collaborators, to solve problem, and to overcome difficulty for interdisciplinary researches.

Stirring seminar: This seminar, which were held from FY2020 to the earlier of FY2021, is led by a pair of researchers from two different fields, in which one researcher prepares a presentation on his/her research and the other presents it to the audience. This was shifted to the seeds/needs seminar, because we shifted from learning phase to actual execution phase.

Seeds/Needs seminar (via Zoom): This is not a typical seminar to present excellent achievements or published results. This aimed to present ongoing research projects, in which the presenter must introduce potentially helpful techniques or ideas for interdisciplinary research or stuck points to discuss with the center members. Indeed, some interdisciplinary researches were started. e.g. Relationship between dynamics of molecules and experimental NMR spectra by Mikhail Tsitsvero (information scientist) and Jenny Pirillo (computational scientist)

Tutorial seminar: This is the tutorial type seminar to share an overview of one approach, one topic, one technique, etc. with a broader perspective. This is an irregular type seminar, and the AFIR tutorial seminar, "GRRM tutorial 2020: AFIR in GRRM17", was held in FY2020 by the Director, because the knowledge about AFIR must be shared with informatics scientists to develop new approaches for discovery of new chemical reactions and experimental scientists to apply it for new experimental reactions.

Skill-up seminar (via Zoom): Presentation techniques were explained in "How to create an easy-to-read-presentation file", with the aim of improving skills of preparation for presentation materials.

Special seminar (via Zoom): Prof. Iwata, who are welcome to the center in FY2020, presented "Submodular Optimization and Chemoinformatics" to share his research and background knowledge with the center members

(3) Assign interdisciplinary research start-up support

The Director and the RSU assigned 13.15 million JPY in total to seven research projects in FY2020 after reviewing proposed research projects, to support their challenge of bottom-up interdisciplinary research ideas from daily spontaneous discussion. We also expect that this support leads to obtain external funding. The representative researchers of each project are three information scientists, one computational scientist, three experimental scientists. Indeed, the support led initiation of various interdisciplinary projects and significantly contribute to the progress of which are described in 1-1-c, 1-1-d, 1-1-h, 2-7, 4-2 in the section 1. Two papers have already been published. The effect of this support is evident. Therefore, in the next fiscal year, we will more flexibly support more researchers for more challenging interdisciplinary projects.

(4) Organize various type of meetings

In the last fiscal year, the Director set challenging and long-term flagship projects that could revolutionize current scientific concepts. To realize these projects, we not only organized monthly meetings (listed below) attended by the Director and RSU manager, but also encouraged closer and frequent discussions prior to the monthly meetings. The Director or/and RSU Manager also participated the prior meetings.

List of monthly meeting:

- Meeting of dream reaction (List, Taketsugu groups)
- Meeting of cancer GPS (Tanaka, Hasegawa, Takigawa groups)
- Meeting of degradable polymer (Gong, Maeda, Ito, Rubinstein, Takigawa groups)
- Meeting of cavity design for CH activation (Sawamura, Taketsugu, Komatsuzaki, Varnek groups)
- Meeting of lanthanide catalyst (Hasegawa, Taketsugu, groups)
- Meeting of artificial enzyme (Tanaka, Maeda, Takigawa groups)

These project-based meetings were effective not only to advance research but also share the center's mission. The university research administrator also started to attend the monthly meeting supportively. In addition to the monthly project-based meetings, research progress in each group has been reported in the monthly PI meeting. The sharing research progress in each group by PIs will be effective in challenging and strongly promoting new interdisciplinary research among groups.

(5) Build a system to lead research/researcher

RSU manager and RM interviewed PIs to understand the status of each group and their progresses on research, and the summary of these interviews are reported to the Director. The Director comprehends the center's research and its progresses in each group based on the research reports in the PI meetings, participation in monthly meetings, and the report above mentioned to organize the center's research and initiate new interdisciplinary research from the top down. Under the Director's vision, RSU manager and RM also proposed suitable collaborators in the center and external research funds to each project, as needed. Furthermore, the Director decided to introduce the pre-checking system for the grant application of young researchers, such as Grants-in-Aid for Scientific Research for interdisciplinary research, to improve the application adoption rate and the total amount of obtained budgets.

3. Realizing an International Research Environment

* Describe what's been accomplished in the efforts to raise the center's recognition as a genuine globally visible research institute, along with innovative efforts proactively being taken in accordance with the development stage of the center, including the following points, for example:
- Efforts being developed based on the analysis of number and state of world-leading, frontline researchers (in Appendix 2); exchanges with overseas entities (in Appendix 4); number and state of visiting researchers (in Appendix 5)
- Proactive efforts to raise the level of the center's international recognition
- Efforts to make the center into one that attracts excellent young researchers from around the world (such as efforts fostering young researchers and contributing to advancing their career paths)

The center has continuously advanced the formation of an international research environment in FY2020. To raise the center's recognition as a highly visible research institute of genuinely global rank, the center continued its efforts on **Human resources internationalization**, **organizational internationalization**, **internationalization of young researchers**, and **international public relations**.

Human resources and organizational internationalization

(1) Strategy of recruiting international researchers

As a result of refining our recruitment process, in the last stage of the interview process all final candidates are interviewed by the Director directly to ensure that they share the center's mission. We received a large number of domestic and international applications (143) for 14 positions, 10 of which were filled with foreign nationals. As of March 31, 2021, 24 among the total of 66 researchers (36%) are foreign nationals, and 7 researchers (11%) are female. After recruitment, the center provided start-up support (7 researchers in total 22.05 million JPY), and gave guidance in applying for external funding (see 5. (4)-a), to help the newly hired researchers achieve outstanding results during their tenure, and to become prime candidates for faculty and postdoctoral positions at other international research institutions. In FY2020, one center researcher was promoted to an associate professor in Faculty of Engineering.

(2) Establishment of relationships with domestic and international sites

The center concluded inter-departmental academic exchange agreements (MOU) with Chubu University, the University of Tokyo, and the University of Strasbourg. We continued our joint researches with Chubu University and the University of Tokyo under the JST-ERATO project, and held the 3rd International Symposium with the University of Strasbourg. Collaborations with the University of Oslo and with Stockholm University focusing on computational and information science are continuously ongoing. But joint symposia with these universities planned for in FY2020 were postponed due to COVID-19.

In order to accelerate fusion researches based on the information science and to construct an effective database of chemical reaction networks by using information science, Professor Satoru Iwata from Graduate School of Information Science and Technology at the University of Tokyo, joined as a PI in FY2020 and MOU was concluded. Professor Iwata developed an informatics tool to extract useful information for chemical reaction design and discovery from the AFIR reaction path map database used at the center (see 1. III-(1-1-c)).

(3) Rhythm of international symposia (Internationalization of young researchers)

In COVID-19 situation, a series of symposia was postponed in FY2020, including at the university of Oslo, Stockholm University, TACC2020, Pacifichem, and the University of Strasbourg planed in FY2020. The 3rd International Symposium was held from February 22 to 24, 2021, jointly with the University of Strasbourg. The symposium was originally scheduled to be held in France, but, due to COVID-19, it was held online. 13 world-class researchers from Japan and abroad, including two Nobel laureates, gave lectures, and a web poster session (39 poster presentations) was held. A total of 279 participants from Japan and abroad (118 of whom were foreign nationals) attended the conference. It was a great success, with more participants than expected, and the all lectures were recorded for use in the center's internal research activities. The poster presentations were also a good opportunity for young researchers.

(4) Establishment of Akira Suzuki Award and ICReDD Award

Although the award winners have already been selected, the award ceremony (September 2020) was postponed due to COVID-19. The award ceremony and award lectures will be held at a future international symposium if possible.

(5) Development of the MANABIYA system (Internationalization of young researchers)

In the COVID-19 situations, 7 (1 postponed) (in 22 applications) researchers were accepted to participate in MANABIYA (ACADEMIC). 7 companies (around 20 corporate researchers) were recruited as part of the MANABIYA (INDUSTRY) trial through joint research contracts and academic consultancy agreements, etc. The MANABIYA curriculum provided by each PI has been completed and was prepared as Inter Graduate School Classes Course for credit in our graduate school system. "GRRM20" program including the latest version of AFIR was completed and is commercially available from HPC SYSTEMS Inc under the center's patent. In FY2021, MANABIYA (Industry) will start the joint research and consulting contracts with companies that use the GRRM20 program.

(6) International public relations and outreach activities

In addition to enhancing the website and SNS, we published "Monthly News Postcard" to convey monthly research highlights (Since Jun. 2020, ten cards have been mailed to researchers around the world), "Quarterly News Poster" to convey research content in an easy-to-understand manner for high school and undergraduate students (Since Aug. 2020, three versions have been mailed to high schools and Universities in domestic), and "Annual Report" to disseminate information widely both domestically and internationally. The center's website was continuously revised to make frequently posted news updates more visible, and we use a variety of channels to target different audiences (international vs. domestic audiences, established vs. young researchers, academic vs. non-academic audiences, etc.).

4. Making Organizational Reforms

* Describe the system reforms made to the center's research operation and administrative organization, along with their background and results.
* If innovated system reforms generated by the center have had a ripple effect on other departments of the host institutions or on other research institutions, clearly describe in what ways.
* Describe the center's operation and the host institution's commitment to the system reforms.

We implemented measures to ensure that the center's vision and mission is shared among all members of the center and so that the Director has the final decision in all matters related to the center's operation and management. The measures are as follows: (1) Improvement of the management structure, (2) revision of the organizational structure.

(1) Improvement of the management structure

To ensure that the center's research policy is directly communicated from the Director to the researchers, the Director had interviews with all researchers immediately after newly hired and before the employment contract renewal. Under the direction of the Director, ED also evaluated faculty members' achievements and have face-to-face conversations to share the center's vision and mission, to increase the researcher's motivation and to encourage the discovery of new research seeds. RM participated in various committees to share information on research strategies of the entire university. Monthly meeting with the President was held to secure the sustainable development of the center.

(2) Revision of organizational structure

In FY2020, three working groups (WGs), Future Planning WG, New Building Preparation WG, and Equipment Installation and Management WG were newly established to strengthen the center's operations. **Future Planning WG** discussed the organizational structure during and after the subsidy period, future financial plans and the budget requests as the flagship research institute of the university. This WG has also started discussion on the graduate school concept with Graduate School of Chemical Sciences and Engineering along with the University Headquarters. **New Building Preparation WG** considered innovative research space in the new building. **Equipment Installation and Management WG** discussed the strategic introduction and use of shared equipment. The following committees and meetings have been established to ensure the efficient operation and to share the vision and mission among all members.

Steering Committee: The Director, Vice Director (VD), Administrative Director (AD), ED and three principal investigators appointed by the Director, one from each of the three fields, met 11 times in FY2020 to discuss matters related to the center.

Executive Committee: 30 Meetings were held between the Director, VD, AD, ED, Advisor, RSU Manager, RM, Mix-lab Chief and Management Planning Unit Manager to assist the Director in his decision-making.

PI Meeting: The meeting was held every month as a place for all PIs including three oversea PIs to exchange opinions among each other and for sharing the center's vision, mission and research & management strategy. Every other month, this meeting was adjusted the meeting times to the

US or Europe time.

Advisory Board: In order to realize the center's concept and create a world-class research center, the Advisory Board was established to contribute to the center's future management by obtaining advice, recommendations, and evaluations from experts on future prospects, strategies, and efforts to solve problems. Eight prominent researchers from Japan and abroad (three from Japan and five from overseas, including one female) were appointed as members of the Advisory Board. The advisory board members reviewed the progress and follow-up reports from an international perspective twice in FY2020, made recommendations on the center's future direction, and provided advice on how to promote research. In particular, we received advice for the FY2019 follow-up comments on diversifying the personnel structure, appointing outstanding young researchers from world-leading research institutions, promoting fusion research with information science, reforming the RSU for strengthen the leadership of the Director, strengthening the support such as the development, outreach, marketing, and communications from the University, and holding international symposia at top research institutes such as Harvard, MIT, Cambridge, Oxford, etc. These advices led to improved management such as hiring three Junior PIs for appointing outstanding young researchers. collaborating with the Research Development Section, the Institute for the Promotion of Business-Regional Collaboration, the Institute for International Collaboration, and the University Public Relations for strengthening the RSU, signing an MOU with the University of Strasbourg and holding a joint symposium for internationalization of the center.

5. Efforts to Secure the Center's Future Development over the Mid- to Long-term

* Address the following items, which are essential to mid- to long-term center development:
- Future prospects with regard to the research plan, research organization and PI composition; prospects for fostering and securing of next-generation researchers
- Prospects for securing resources such as permanent positions and revenues; plan and/or implementation for defining the center's role and/or positioning the center within the host institution's institutional structure
- Measures to sustain the center as a world premier international research center after program funding ends
- Host institution's organizational reforms carried out for the center's autonomous administration simultaneously with the creation of the center.

In the following, medium- and long-term organizational developments are discussed in highlighting the initiatives taken by Executive Committee, New Building WG, Future Planning WG, and Institute for the Promotion of Business-Regional Collaboration, Hokkaido University.

(1) Researcher composition and the final personnel composition

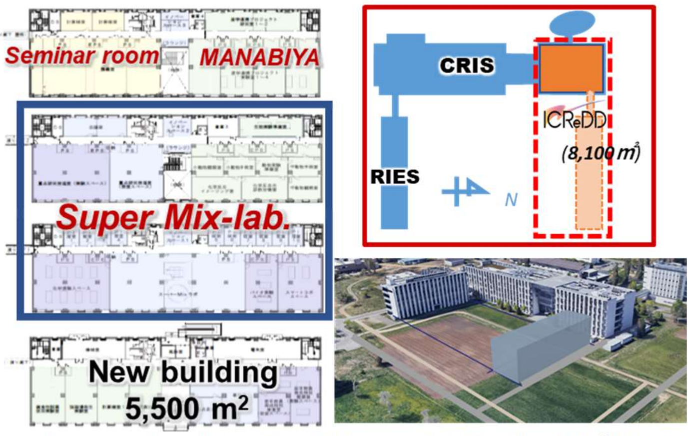
Researcher composition to carry out the research plans:

In FY2020, the number of foreign researchers and female researchers did not increase as planned due to COVID-19. We will review the personnel composition plan for FY2023 and strengthen recruitment of foreign nationals and female in the future. Currently, 47% of the center researchers are from computational/informatics, and 53% are experimental scientists, for FY2023, we aim for a researcher composition of 50% from computational/informatics, and 50% experimental scientists.
- At the end of March 2021, 24 among a total of 66 researchers (36%) are foreign nationals, and 7 researchers (11%) are female (PIs: 15 [3 computational, 5 information and 7 experimental scientists], faculty members: 27, researchers: 14, research collaborators: 10).
- At the end of March 2023, 35 among a total of 75 researchers (45%) to be foreign nationals, and 12 researchers (16%) to be female (PIs: 15 [3 computational, 5 information and 7 experimental scientists], faculty members: 28, researchers: 21, research collaborators: 11).

(2) Buildings and Facilities

Improvement of the environment for promoting integrated research and the future of the mix office and labs:

The currently developed research space (about 1,400 m^2) in the University's CRIS building comprises an analytical instrument room, a large computer server room, a dry Mix-office for computational and information sciences and a wet Mix-lab for experimental science. An additional 1,200 m^2 of research space in the CRIS building was secured with top-down financial support from the university. In order to promote fusion researches in the three fields, we renovated the CRIS building where the center is installed, and built a total of about 1,200 m^2 of laboratories (two organic synthesis laboratories and one bio laboratory), an analytical instrument room, a data analysis room, a server room, and a PI's office in the building, and installed basic



The conceptional drawing of the new building (5,500m^2) that will be connected to the CRIS building.

experimental equipment such as gas chromatographs and flow cytometers. Furthermore, in order to realize an international research environment, we requested a new building, the "New building for the center" (4 floors above ground, 5,500 m^2, Completion in FY2022), in the FY2021 budget request for the construction of facilities for national universities. In making the request for the new building, the University decided to provide support of up to 1.22 billion yen, and the design work was started in October 2020.The new building will prominently feature a "Super Mix-lab." where 75 researchers from all three fields can mingle on an every-day basis, further accelerating fusion researches.

(3) Form of organization
New institute organization:

The Future Planning WG discussed the future organizational structure and finance with the University Headquarters. We discussed re-organization of the institute for the establishment of our new graduate school toward establishment in FY2028, the space management for the new building and facilities in the CRIS building, financial plans, the system of cooperation with other research institutes in the university, etc. The center is a special organization under the direct control of the President, operated under a fast-track decision-making system with regular monthly meetings, and will contribute to the organizational reform of the university.

(4) Finance (external funds and joint research funds with companies)

We prepared a future financial plan and started regular meetings with the University Headquarter regarding the center's future organization after the subsidy period. The composition of the operating expenses for FY 2020 is as follows.

･**454 million JPY Top-down Financial Support from the host institution**: The relocation and renovation costs for newly installed labs in the CRIS building, operational expenses including laboratory costs for PIs and research space and costs for reducing the educational duties of PIs, etc.

･**934 million JPY in external funding**: To expand the acquisition of external funds, we also considered (a) measures to promote the acquisition of external funds, and (b) the development of a financial plan for the end of the grant period.

a) Measures to increase fund acquisition

Start-up supports for fusion researches: 7 research projects in total 13.15 million JPY were supported to challenge bottom-up fusion projects. These projects led to the acquisition of Grant-in-Aid for Scientific Research.

Pre-checking system for the grant application: We introduced a pre-checking system to review and revise the application for Grant-in-Aid for Scientific Research, etc. before the submission. More than 40% of the applications for Grants-in-Aid for Scientific Research were granted for FY2021. The numbers of applications and granted funds of the center researchers have been increased, compared to that of the previous year (see below).

FY2021 Newly adopted Grants-in-Aid for Scientific Research

	Scientific Research A	Scientific Research B	Scientific Research C	Scientific Research on Innovative Areas	Early-Career Scientists	Total	Average of adoptions for the center	Average of adoptions for HU
FY2021 number of adoptions/applications	0/1	2/6	3/5	1/1	6/14	12/27	44.4%	38.0%
FY2020 number of adoptions/applications	0/1	1/3	0/1	1/3	3/7	5/15	33.3%	37.1%

The number is the number of applications from overseas PIs, specially appointed faculty members, and postdoctoral researchers affiliated with the center, excluding domestic PIs.

b) The development of a financial plan for the end of the grant period.

We drew up a finance plan to obtain 700 million JPY (100 million JPY in indirect cost) from external funding to operate the center after the support period in addition of support from the university.
･Grants-in-Aid for Scientific Research, etc.: 600 million JPY (90 million JPY in indirect cost)
･Joint research funds with companies: 100 million JPY (15 million JPY in indirect cost)

(5) Human resource development
MANABIYA and the promotion of the recruitment of specially appointed faculty:

Through MANABIYA, the center fosters the next generation of international researchers in the three fields of computational science, information science, and experimental science. Due to the COVID-19 situations, only 7 researchers were accepted to participate in MANABIYA (ACADEMIC), although we received 22 applications including young researchers from abroad.

As a part of the curriculum of MANABIYA, the "Advanced Computational Chemistry" course was held from August 24 to 26, 2020, at the Hokkaido Summer Institute, where 5 PIs and faculty members gave cutting-edge lectures (53 students took the course).

Hokkaido University has established the "Smart Materials Science (SMatS) Doctoral Program" in

April 2021, with the aim of fostering researchers who can accelerate materials science research and bring about innovation by breaking away from the conventional trial-and-error approach to research, by integrating materials science in a broad sense with mathematical science, computational science, and data science, based on the center. MANABIYA (ACADEMIC) was set as a part of the SMatS curriculum. Many graduate students in SMatS are expected to participate in MANABIYA.

(6) Graduate School

In FY2020, we discussed the establishment of a new graduate school (15-20 students per year in a doctoral course) with the Graduate School of Chemical Sciences and Engineering (the establishment in FY2028). The new building will have two IT-equipped 30-person lecture rooms to prepare a state-of-the-art educational environment that integrates computational, information, and experimental science for graduate education. MANABIYA, in conjunction with the SMatS Program, will actively contribute to the graduate education of the University and become the foundation for the establishment of the center's own graduate school.

6. Others

* Describe what was accomplished in the center's outreach activities last year and how the activities have contributed to enhancing the center's "globally visibility." In Appendix 6, describe concretely the contents of these outreach activities. In Appendix 7, describe media reports or coverage, if any, of the activities.
* In addition to the above 1-5 viewpoints, if there is anything else that deserves mention regarding the center project's progress, note it.

Outreach activities headed by research strategy unit (RSU)

The main goal of the center's public relations strategy is to increase the institute's international visibility among the academic, scientific and industrial communities. In conjunction with the university's international public relations team and Institute for International Collaboration, we implemented a strategic public relations strategy with a clear target community and annual goals. In FY2020, the RSU put special efforts into advertising the institute as an attractive career development opportunity for talented young researchers.

Press release and Outreach activities:

For academic and industrial communities, we issued 10 research press releases as well as hosted 1 press conference. We participated in 4 events, gave one general public lecture, one lectures for elementary, junior high and high school students, and two inter-departmental joint symposia at Hokkaido University. These Inter-departmental symposia are planned to continue in FY2021, and symposia with the Faculty of Engineering & Information Science and Technology, and the Faculty of Medicine were planned. In addition to enhancing the website and SNS, we published ten Monthly News Postcards to convey monthly research highlights for international visibility, three Quaternary News Posters to convey research content in an easy-to-understand manner for high school and undergraduate students, and Annual Reports to widely disseminate information both domestically and internationally.

7. Center's Response to Results of Last Year's Follow-up

* Transcribe the item from the "Actions required and recommendations" section in the site visit report and the Follow-up report, then note how the center has responded to them.
* If you have already provided this information, indicate where in the report.

1) The Center needs to improve its diversity at all levels of its researchers and committees by recruiting more foreign and female researchers.

   We shared among our members to recruit more foreign and female researchers, and efforted to improve diversity at all levels of researchers and committees, and in the 13 new hired researchers from December 2020 to March 2021, 12 (92%) researchers were foreign nationals and 3 (23%) researchers were female. We are also planning to offer positions only for female researchers. According to the suggestion of the member of the program committee, one female researcher has been newly added to the Advisory Board. In addition, the junior PIs to be hired in FY2021 will be foreign nationals and, at least, one of them will be a female.

2) It is recommended that the Center recruit new PI(s) at an appropriate opportunity, preferably young researcher(s) from abroad who can carry out research in Sapporo.

   The university allowed us to hire three tenure-track independent researchers of associate professor level (Junior PIs) from abroad, and their personnel expenses will be fully supported by the university. The candidate will mainly promote the researches on new chemical reaction design that integrates computational, information and experimental sciences independently based on the center's research policy. We expect that young researchers in the 30s from international top institutions, computational chemists or information scientists with an understanding of organic chemistry or organic chemists who can make full use of computational chemistry or information science, will join the center. A job performance will be evaluated before

FY2025, and a successful candidate will be offered a full-time tenured Professor. We support for start-up budget (5-10 million yen per year for the first three years). and for labor costs for one postdoctoral researcher. We have already started the selection process of candidates through PI's connections.

3) The three academic PI's from outside of Japan need to be encouraged and aided by all the PI's in Sapporo to further integrate their projects across the Center.

Communication with PIs from outside of Japan has increased using online tools, e.g., Zoom. And they frequently participate in flagship project meetings and seminars. Sufficient research space and resources for research activities of three oversea PI's group were secured (500m^2 as a laboratory and rooms for analytical instruments, data analysis and server, three Co-PIs and four researchers) in FY2020 and their Co-PIs are also active in the center labs. As mentioned in section 2(4), to effectively realize each research project, three PIs from outside of Japan not only organized monthly project meetings attended by the Director, RSU Manager and RM, but also met closer and frequent discussions by the weekly group meetings. Moreover, the research progress in each PI group has been reported in the monthly PI meeting. All these meetings, held online, were not only effective in advancing the research project but also in sharing the center's mission with all members.

4) The Center needs to make every effort to establish itself on the international scene as a place that international postdocs from international top institutions want to be.

We strengthened the follow-up system for foreign researchers, including support for their daily lives and offering posts in other departments, and the pre-checking system for application of external funding such as Grant-in-Aid for Scientific Research, establishment of a research environment with state-of-the-art equipment. The support environment for foreign nationals have been established through the shift to English for administrative work. In addition, we focused on public relations activities such as introduction of the center researchers on SNS, frequent research results through monthly news postcards, and videos of our young researchers introducing the center.

5) Information science should make a stronger contribution to ICReDD's research. In order to take advantage of the rapid progress being made in quantum computation technologies, ICReDD may wish to increase its external exchanges with major new projects such as the Japanese National Project on Quantum Information Sciences and the European Commission's "Quantum Flagship" project.

As mentioned in section 1-III-1), one of the top information scientists, Prof. Satoru Iwata in Graduate School of Information Science and Technology at the University of Tokyo, joined the center as a PI. Collaborative researches in information and computational sciences in the center are accelerating. Various informatics tools for accelerating chemical reaction discovery such as AI of reaction generation (with Varnek), a database and navigation system for large data generated in quantum chemical calculations (with Varnek), molecular graph autocompletion by graph neural networks (with Takigawa), a systematic method to select diverse molecules using supervised learning and submodular optimization (with Iwata), were developed through close collaborations with computational/experimental scientists. Regarding the quantum inspired computing, we have already industry-university collaborative projects and JST-PRESTO external exchanges, and we will increase external exchanges with new projects in the future.

6) To establish and strengthen the leadership of the Center Director, continuous efforts should be made to assemble a strong administrative/scientific team.

RM and the Manager of Institute for the Promotion of Business-Regional Collaboration (PBC) were added to the management team, which supports the strong governance of the Director. ED had continuously interview with all researchers including PIs to share the center's mission, to increase them motivations and to evaluate them. RM participated in various committees to share information on research strategies of the entire university. With the manager of PBC, the management system has been established to commercially release GRRM 20 and other research achievements to society.

7) The advisory board should be activated, and a system established through which the Center Director and ICReDD obtain useful advice at regular intervals from the board.

In FY2020, we received advice twice from an advisory board of domestic and international experts on progress reports and follow-up to further strengthen the management system. In particular, we received advice on diversifying its personnel structure and recruiting talented young researchers from world-leading research institutions by using PI's international connections and international symposia and lecture-series, and promoting fusion research with information science by investing one of the new tenure-track positions (Junior PIs) towards the hiring of and expert in the application of information science to chemistry.

8) Regarding the MANABIYA system, it is urgently required to clarify how it is to be managed and how to link it to the graduate school systems of Hokkaido University.

The process from application to screening and adoption was formulated. MANABIYA researchers were selected based on evaluation of their application documents by the Steering Committee. We received 22 applications, but, due to the COVID-19 situations, only 7 (1 postponed) researchers were accepted to participate in MANABIYA (ACADEMIC). 7 companies (around 20 corporate researchers) were recruited as part of the MANABIYA (INDUSTRY) trial through joint research contracts and academic consultancy agreements, etc. The MANABIYA curriculum provided by each PI has been completed and was prepared as Inter Graduate School Classes Course for credit in our graduate school system. Such On-the-Job Training (OJT) type curriculum will be one of the advanced courses for human resource development in cutting-edge research institution like the center. We also plan to institutionalize the MANABIYA Industry to include corporate researchers by making it mandatory for them to purchase GRRM20 and participate in the MANABIYA Industry. The Future Planning WG had frequent discussions on the re-organization of the institute for the establishment of our new graduate school, the space management for the new building and facilities in the CRIS building, financial plans, the system of cooperation with other research institutes in the university, and developed a roadmap to FY2032.

9) Securing more lab space is an urgent matter; the construction of a new building is highly desirable.

The University decided to provide support of up to 1.22 billion yen and the design work was started in October 2020. The new building will be completed in FY2022. The new building will provide "Super Mix-lab" in which researchers of three fields (75 researchers) can interact daily to accelerate fusion research further.

10) Strong support from Hokkaido University is essential for securing the sustainable development of ICReDD. Close communication with the new University President should be established as soon as possible and be regularly maintained.

The center was operated a special organization under the direct control of the President with regular monthly meetings since October 2020 and was directly connected to the organizational reform of the university. The results led to the hiring of Junior PIs and greatly advanced discussion on making the center permanent and establishing a graduate school.

Appendix 1　FY 2020 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2020. (Note: The list should be for the calendar year, not the fiscal year.)

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

Note: On 14 December 2011, the Basic Research Promotion Division in MEXT's Research Promotion Bureau circulated an instruction requiring paper authors to include the name or abbreviation of their WPI center among their institutional affiliations. From 2012, the authors' affiliations must be clearly noted.

(2) Method of listing paper
- List only refereed papers. Divide them into categories (e.g., original articles, reviews, proceedings).
- For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is consistent. (The names of the center researchers do not need to be underlined.)
- If a paper has many authors (say, more than 10), all of their names do not need to be listed.
- Assign a serial number to each paper to be used to identify it throughout the report.
- If the papers are written in languages other than English, underline their serial numbers.
- Order of Listing
A. WPI papers
1. Original articles
2. Review articles
3. Proceedings
4. Other English articles

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

(3) Submission of electronic data
- In addition to the above, provide a .csv file output from the Web of Science (e.g.) or other database giving the paper's raw data including Document ID. (Note: the Document ID is assigned by paper database.)
- These files do not need to be divided into paper categories.

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

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

A. WPI papers

1. Original articles

1. A Bad Arm Existence Checking Problem: How to Utilize Asymmetric Problem Structure? K. Tabata, A. Nakamura, J. Honda, T. Komatsuzaki, *Mach. Learn.*, **2020**, 109, 327-372

2. A Glove-box- and Schlenk-line-free Protocol for Solid-state C-N Cross-coupling Reactions Using Mechanochemistry. K. Kubota, R. Takahashi, M. Uesugi, H. Ito, *ACS Sustai. Chem. Eng.* **2020**, 8, 16577–16582.

3. A Quantum Chemical Study of Substituent Effects on CN Bonds in Aryl Isocyanide Molecules Adsorbed on the Pt Surface. B. Wang, M. Gao, K. Uosaki, T. Taketsugu, *Phys. Chem. Chem. Phys.*, **2020**, 22, 12200-12208

4. A Theoretical Study on the Alkali Metal Carboxylate-Promoted L-Lactide polymerization. C. Ozen, T. Satoh, S. Maeda, *J. Comput. Chem.*, **2020**, 41, 2197-2202

5. AFIR Explorations of Transition States of Extended Unsaturated Systems: Automatic Location of Ambimodal Transition States T. Ito, Y. Harabuchi, S. Maeda, *Phys. Chem. Chem. Phys.*, **2020**, 22,

13942-13950

6. Aggregation-Induced Emission of a Eu(III) Complex via Ligand-to-Metal Charge Transfer. Y. Kitagawa, M. Kumagai, K. Fushimi, Y. Hasegawa, *Chem. Phys. Lett.*, **2020**, 749, 4

7. Air- and Moisture-Stable Xantphos-Ligated Palladium Dialkyl Complex as a Precatalyst for Cross-Coupling Reactions. R. Takahashi, K. Kubota, H. Ito, *Chem. Commun.*, **2020**, 56, 407-410

8. All-Electron Relativistic Spin-Orbit Multireference Computation to Elucidate the Ground State of CeH. Y. Kondo, Y. Goto, M. Kobayashi, T. Akama, T. Noro, T. Taketsugu, *Phys. Chem. Chem. Phys*., **2020**, 22, 27157-27162

9. Ammonia Combustion Properties of Copper Oxides-Based Honeycomb and Granular Catalysts. S. Hinokuma, T. Iwasa, K. Araki, Y. Kawabata, S. Matsuki, T. Sato, Y. Kon, T. Taketsugu, K. Sato, M. Machida, *J. Japan Pet. Inst.*, **2020**, 63, 274-281

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11. Anisotropic Double-Network Hydrogels via Controlled Orientation of a Physical Sacrificial Network. D. R. King, R. Takahashi, T. Ikai, K. Fukao, T. Kurokawa, J. P. Gong, *ACS Appl. Polym. Mater.*, **2020**, 2, 2350-2358

12. Application of Singularity Theory to Bifurcation of Band Structures in Crystals. H. Teramoto, A. Tsuchida, K. Kondo, S. Izumiya, M. Toda, T. Komatsuzaki, *J. Singul.*, **2020**, 21, 289-302

13. Application of the Mol2vec Technology to Large-Size Data Visualization and Analysis. S. Shibayama, G. Marcou, D. Horvath, I. Baskin, K. Funatsu, A. Varnek, *Mol. Inform.*, **2020**, 39, 10

14. Asymmetric Remote C-H Borylation of Aliphatic Amides and Esters with a Modular Iridium Catalyst. R. L. Reyes, M. Sato, T. Iwai, K. Suzuki, S. Maeda, M. Sawamura, *Science*, **2020**, 369, 970-+

15. Asymmetric Synthesis of α-Aminoboronates via Rhodium-Catalyzed Enantioselective C(sp^3)-H Borylation. RL. Reyes, M. Sato, T. Iwai, M. Sawamura, *J. Am. Chem. Soc.*, **2020**, 142, 589-597

16. Aurophilicity-Mediated Construction of Emissive Porous Molecular Crystals as Versatile Hosts for Liquid and Solid Guests. T. Seki, K. Ida, H. Sato, S. Aono, S. Sakaki, H. Ito, *Chem. Eur. J.*, **2020**, 26, 735-744

17. Bactericidal Effect of Cationic Hydrogels Prepared from Hydrophilic Polymers. Y. Shibata, T. Kurokawa, T. Aizawa, J. P. Gong, *J. Appl. Polym. Sci.*, **2020**, 137, 10

18. Catalytic Intramolecular Coupling of Ketoalkenes by Allylic C(sp3)-H Bond Cleavage: Synthesis of Five-and Six-Membered Carbocyclic Compounds. T. Mita, M. Uchiyama, Y. Sato, *Adv. Synth. Catal.*, **2020**, 362, 1275-1280

19. Characteristic Evaluation of Chameleon Luminophore Dispersed in Polymer. M. Kasai, Y. Sugioka, M. Yamamoto, T. Nagata, T. Nonomura, K. Asai, Y. Hasegawa, *Sensors*, **2020**, 20, 15

20. Chiral Lanthanide Lumino-Glass for a Circularly Polarized Light Security Device. Y. Kitagawa, S. Wada, M. D. J. Islam, K. Saita, M. Gon, K. Fushimi, K. Tanaka, S. Maeda, Y. Hasegawa, *Commun. Chem.*, **2020**, 3, 119

21. Chiral Macrocycles HavingC(3)Symmetry Resulting from Orientation of Thiophene Rings. T. Miura, T. Nakamuro, Y. Ishihara, Y. Nagata, M. Murakami, *Angew. Chem., Int. Ed.*, **2020**, 59, 20475-20479

22. Chiral Monolayers with Achiral Tetrapod Molecules on Highly Oriented Pyrolytic Graphite. H. Asakawa, S. Matsui, Q. T. Trinh, H. Hirao, Y. Inokuma, T. Ogoshi, S. Tanaka, K. Komatsu, A. Ohta, T. Asakawa, T. Fukuma, *J. Phys. Chem. C*, **2020**, 124, 7760-7767

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Kurokawa, JP. Gong, *Biomacromolecules*, **2020**, 21, 4220-4230

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129. QSAR Without Borders. E. N. Muratov, J. Bajorath, R. P. Sheridan, I. V. Tetko, D. Filimonov, V. Poroikov, T. I. Oprea, I. Baskin, A. Varnek, A. Roitberg, O. Isayev, S. Curtarolo, D. Fourches, Y. Cohen, A. Aspuru-Guzik, D. A. Winkler, D. Agrafiotis, A. Cherkasov, A. Tropsha, *Chem. Soc. Rev.*, **2020**, 49, 3525-3564

130. Rate Constant Matrix Contraction Method for Systematic Analysis of Reaction Path Networks. Y. Sumiya, S. Maeda, *Chem. Lett.*, **2020**, 49, 553-564

131. Steric and Electronic Control of Chiral Eu(III) Complexes for Effective Circularly Polarized Luminescence. Y. Kitagawa, M. Tsurui, Y. Hasegawa, *ACS Omega*, **2020**, 5, 3786-3791

132. The Scope of 3-Acetyl-4-Hydroxy-6-Methyl-2H-Pyran-2-One (DHA). E. A. Ghaith, H. H. Zoorob, M. E. Ibrahim, M. Sawamura, W. S. Hamama, *Curr. Org. Synth.*, **2020**, 24, 1459-1490

133. Tough and Self-Healing Hydrogels from Polyampholytes. T.L. Sun, K.P. Cui, SELF-HEALING AND SELF-RECOVERING HYDROGELS in *Adv. Polym. Sci.*, **2020**, 285, 295-317.

134. ゲノム医療におけるエキスパートパネル 分子病理専門医. 田中伸哉, *病理と臨床*, **2020**, 38, 489-494

135. 肉腫-基礎・臨床の最新知見-肉腫の発生メカニズムと基礎研究　染色体転座を有する肉腫. 小田義崇, 津田真寿美, 田中伸哉, *日本臨床*, **2020**, 78, 58-68

136. 病理学会オフィシャルジャーナル Pathology International. 田中伸哉, *病理と臨床*, **2020**, 38, 761-763

137. 実践的な診断・治療方針決定のために(第3部)腫瘍の鑑別に用いられる抗体(各臓器別)　脳. 田中伸哉, *病理と臨床*, **2020**, 38, 263-278

3. Proceedings

138. Compiling Higher Order Binary Optimization Problems into Annealing Processors. Sugie Y, Mertig N, Iwata Y, Teramoto H, Nakamura A, Takigawa I, Minato S, Komatsuzaki T, Takemoto T, *The 25th International Symposium on Artificial Life and Robotics (AROB 25th 2020)*, Beppu, Japan, January 22-24, **2020**

139. Efficiently Enumerating Substrings with Statistically Significant Frequencies of Locally Optimal Occurrences in Gigantic String. Nakamura A, Takigawa I, Mamitsuka H, *The 34th AAAI Conference on Artificial Intelligence (AAAI-20)*, New York, USA, February 7-12

140. Minimizing customer waiting time with a new delivery-tour planning algorithm based on tour division and dynamic route optimization. H. Uchigaito, T. Shirai, Y. Iwata, N. Mertig, Y. Sugie, T. Oizumi, H. Teramoto, A. Nakamura, S. Minato, T. Komatsuzaki, T. Takemoto, *International Symposium on Nonlinear Theory and Its Applications (NOLTA2020)* **2020** November 16-19, 2020, 4pages

141. Word-Level Chemical Named Entity Recognition Based on Subword Sequence Analysis. K. Machi & M. Yoshioka, In Proceedings of Fourth International Workshop on SCIentific DOCument Analysis (SCIDOCA2020) associated with JSAI International Symposia on AI 2020 (IsAI-2020), pp. 288-297, *The Japanese Society of Artificial Intelligence*, **2020**. Paper12.

4. Other English articles

142. Acute Anterior Myocardial Infarction Complicated by Takotsubo Syndrome: the Value of Multimodality Imaging. T. Konishi, N. Funayama, T. Yamamoto, D. Hotta, S. Tanaka, T. Anzai, *Kardiol. Po.l*, **2020**, 78, 1055-1056

143. Biophysical Research in Hokkaido University, Japan. T. Aizawa, M. Demura, K. Gohara, H. Haga, K.

Ishimori, M. Kinjo, T. Komatsuzaki, K. Maenaka, M. Yao, *Biophys. Rev*. *(IUPUB)* **2020**.

144. Cerebral Embolization from Left Atrial Myxoma Causing Takotsubo Cardiomyopathy Complicated with Congestive Heart Failure. T. Konishi, N. Funayama, T. Yamamoto, D. Hotta, S. Tanaka, *Cardiol. J.*, **2020**, 27, 439-440

145. Dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin, 4-[[(1R)-2'-[(triisopropylsilyl)oxy][1,1'-binaphthalen]-2-yl]oxy]-, (11bR)-(9CI). R. L. Reyes, M. Sawamura, *Electronic Encyclopedia of Reagents for Organic Synthesis*, Rovis T., Ed.; Wiley; http://onlinelibrary.wiley.com/doi/10.1002/047084289X.rn02326

146. Editorial for the Special Issue of Biophysical Reviews Focused on the Biophysical Society of Japan with Select Scientific Content from the 57th BSJ Annual Meeting, Miyazaki, Japan. T. Komatsuzaki, H. Nakamura, J. Tame, S. Yanaka, T. Nagai, K. Nagayama, *Biophys. Rev. (IUPUB)* **2020** 12, 183-185

147. Histopathologically Confirmed Very Late Stent Thrombosis Associated with Stent Fracture after Implantation of First-Generation Drug Eluting Stent. T. Konishi, N. Funayama, T. Yamamoto, D. Hotta, Y. Kobayashi, H. Komoriyama, Y. Kato, K. Omote, T. Sato, L. Kamiya, T. Nagai, S. Tanaka, T. Anzai, *Cardio. J*, **2020**, 27, 204-205

148. Paths of Chemical Reactions and Their Networks: From Geometry Optimization to Automated Search and Systematic Analysis. Y. Sumiya, S. Maeda, in *"Chemical Modelling: Volume 15 (RSC Specialist Periodical Reports)"* ed. by M. Springborg and J.-O. Joswig, Royal Society of Chemistry, **2020**, 28-69

B. WPI-related papers

1. Original articles

149. Catalytic enantiocontrol over a non-classical carbocation. R. Properzi, P. S. J. Kaib, M. Leutzsch, G. Pupo, R. Mitra, C. K. De, L. Song, P. R. Schreiner, B. List, *Nature Chem.* **2020**, 12, 1174–1179.

150. Chiral Brønsted Acids Catalyze Asymmetric Additions to Substrates that Are Already Protonated: Highly Enantioselective Disulfonimide-Catalyzed Hantzsch Ester Reductions of NH–Imine Hydrochloride Salts. V. N. Wackchaure, C. Obradors, B. List, *Synlett*, **2020**, 31, 1707–1712

151. Detection of VHL Deletion by Fluorescence in situ Hybridization in Extraneuraxial Hemangioblastoma of Soft Tissue. K. Segawa, S. Sugita, T. Aoyama, S. Minami, K. Nagashima, M. Tsuda, S. Tanaka, T. Hasegawa, *Pathol. Int.*, **2020**, 70, 473-475

152. Dual Graph Convolutional Neural Network for Predicting Chemical Networks. S. Harada, H. Akita, M. Tsubaki, Y. Baba, I. Takigawa, Y. Yamanishi, H. Kashima, *BMC Bioinform.,* **2020**; 21(Suppl 3):94.

153. Homologation of the Fischer Indolization: A Quinoline Synthesis via Homo-Diaza-Cope Rearrangement. G. G. Gerosa, S. A. Schwengers, R. Maji, C. K. De, B. List, *Angew. Chem. Int. Ed.* **2020**, 59, 20485–20488.

154. Kinetic Study of Disulfonimide-Catalyzed Cyanosilylation of Aldehydes by Using a Method of Progress Rates. Z. Zhang, M. Klussmann, B. List, *Synlett*, **2020**, 31, 1593–1597.

155. MM2 Cortical Form of Sporadic Creutzfeldt-Jakob Disease without Progressive Dementia and Akinetic Mutism: A Case Deviating from Current Diagnostic Criteria. I. Takahashi-Iwata, I. Yabe, A. Kudo, K. Eguchi, M. Wakita, S. Shirai, M. Matsushima, T. Toyoshima, S. Chiba, S. Tanikawa, S. Tanaka, K. Satoh, T. Kitamoto, H. Sasaki, *J. Neurol. Sci.*, **2020**, 412, 116759

156. Polyketones as Host Materials for Solid Polymer Electrolytes. T. Eriksson, A. Mace, Y. Manabe, M. Yoshizawa-Fujita, Y. Inokuma, D. Brandell, J. Mindemark, *J. Electrochem. Soc*. **2020**, 167, 070537

157. Polyzwitterions as a Versatile Building Block of Tough Hydrogels: From Polyelectrolyte Complex Gels to Double-Network Gels. H. Yin, D. R. King, T. L. Sun, Y. Saruwatari, T. Nakajima, T. Kurokawa, J. P. Gong, *ACS Appl. Mater. Interfaces,* **2020**, 12, 50068-50076

158. Prognostic Role of H3K27M Mutation, Histone H3K27 Methylation Status, and EZH2 Expression in

Diffuse Spinal Cord Gliomas. Y. Ishi, S. Takamiya, T. Seki, K. Yamazaki, K. Hida, K.C. Hatanaka, Y. Ishida, Y. Oda, S. Tanaka, S. Yamaguchi, *Brain Tumor. Pathol.*, **2020**, 37,81-88

159. Strong and Confined Acids Control Five Stereogenic Centers in Catalytic Asymmetric Diels–Alder Reactions of Cyclohexadienones with Cyclopentadiene. S. Ghosh, S. Das, C. K. De, D. Yepes, F. Neese, G. Bistoni, M. Leutzsch, B. List, *Angew. Chem. Int. Ed.* **2020**, 59, 12347–12351.

160. The Role of Mediator and Little Elongation Complex in Transcription Termination. H. Takahashi, A. Ranjan, S. Chen, H. Suzuki, M. Shibata, T. Hirose, H. Hirose, K. Sasaki, R. Abe, K. Chen, Y. He, Y. Zhang, I. Takigawa, T. Tsukiyama, M. Watanabe, S. Fujii, M. Iida, J. Yamamoto, Y. Yamaguchi, Y. Suzuki, M. Matsumoto, KI Nakayama, M.P. Washburn, A. Saraf, L. Florens, S. Sato, C. Tomomori-Sato, R.C. Conaway, J.W. Conaway, S. Hatakeyama. *Nat. Commun.,* **2020**; 11(1):1063.

161. The Silicon–Hydrogen Exchange Reaction: A Catalytic σ-Bond Metathesis Approach to the Enantioselective Synthesis of Enol Silanes. H. Zhou, H. Y. Bae, M. Leutzsch, J. L. Kennemur, D. Becart, B. List, *J. Am. Chem. Soc.* **2020**, 142, 13695–13700.

162. Unveiling the Delicate Balance of Steric and Dispersion Interactions in Organocatalysis Using High-Level Computational Methods. D. Yepes, F. Neese, B. List, G. Bistoni, *J. Am. Chem. Soc.* **2020**, 142, 3613–3625

2. Review articles

163. Confinement as a Unifying Element in Selective Catalysis. B. Mitschke, M. Turberg, B. List, *Chem* **2020**, 6, 2515–2532.

3. Proceedings

NA

4. Other English articles

164. Walter Thiel (1949–2019). A. Fürstner, B. List, T. Ritter, F. Schüth, F Neese, *Angew. Chem. Int. Ed.* **2020**, 59, 1382-1383

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

- List up to 10 main presentations during FY 2020 in order from most recent.
- For each, write the date(s), lecturer/presenter's name, presentation title, and conference name.

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
2021/03/19	Benjamin LIST	Very Strong and Confined Chiral Acids: Universal Catalysts for Asymmetric Synthesis?	Chemical Record Lecture 2021
2020/12/16	Yasuhide INOKUMA	Development of novel structural organic chemistry using carbonyl ropes	Symposium at Laboratory for materials and structures, Tokyo Institute of Technology
2020/12/14	Masaya SAWAMURA	Never-ending Story of Ligand Design	Kanazawa University Sakigake Project Seminar
2020/12/8	Hajime ITO	Rise of Mechanochemical Organic Synthesis	MRMforum2020 (Keynote Lecture)
2020/11/23 -26	Tetsuya TAKETSUGU	Visualization of reaction path, global reaction route map, and on-the-fly trajectories	New Horizons in Scientific Software: from Legacy Codes to Modular Environments (NHISS 2020)
2020/09/22	Benjamin LIST	Opening lecture: organocatalysis and its concepts	Young Chemists Summit, Innsbruck, Austria
2020/9/17-23	Tetsuya TAKETSUGU	On-the-fly molecular dynamics approach to excited-state branching reaction	The 6th Quantum Science (QS) symposium – The Main Symposium of ICCMSE 2020 – Computational Chemistry and Computational Physics
2020/7/1	Michael RUBINSTEIN	Polymer physics	Invited Lecture at Garcia Program of Stony Brook University
2020/5/31	Hajime ITO	Mechanical Response of Gold(I) Complexes	The 6.5th Crystal Engineering and Emerging Materials Workshop of Ontario and Quebec
2020/5/4	Tamiki KOMATSUZAKI	Geometrical aspect of chemical reaction dynamics in thermally fluctuating environments and Future Directions	International Conference on Chaos Indicators, Phase Space and Chemical Reaction Dynamics, organized by Prof. Steve Wiggins, Department of Mathematics, University of Bristol (ONLINE)

3. Major Awards

- List up to 10 main awards received during FY 2020 in order from the most recent.
- For each, write the date issued, the recipient's name, and the name of award.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
2021/2/24	Tsuyoshi MITA	Hokkaido Science and Technology Incentive Award
2021/2/19	Tasuku NAKAJIMA	President Teaching Award of Hokkaido University
2021/2/19	Tetsuya TAKETSUGU	The Hokkaido University President's Award for Excellence in Research and Education for AY2020
2021/1/7	Yu HARABUCHI	CSJ Award for Young Chemists (The Chemical Society of Japan)
2020/12/14	Yuuya NAGATA	Thieme Chemistry Journals Award
2021/12/9	Hiroki HAYASHI	Central Glass Company Award in the Society of Synthetic Organic Chemistry, Japan
2020/6/3	Tsuyoshi MITA	Ube Industries Foundation Prize
2020/5/15	Yu HARABUCHI	The 1st prize for Outstanding Young Researcher, Japan Society of Theoretical Chemistry
2020/4/7	Yuuya NAGATA	MEXT Young Scientist's Prize
2020/4/7	Tomohiro SEKI	MEXT Young Scientist's Prize

Appendix 2 FY 2020 List of Principal Investigators

NOTE:
*Underline names of principal investigators who belong to an overseas research institution.
*In the case of researcher(s) not listed in the latest report, attach a "Biographical Sketch of a New Principal Investigator"(Appendix 2a).
*Enter the host institution name and the center name in the footer.

<Results at the end of FY2020> **Principal Investigators Total: 15**

Name	Age	Affiliation (Position title, department, organization)	Academic degree, specialty	Effort (%)*	Starting date of project participation	Status of project participation (Describe in concrete terms)	Contributions by PIs from overseas research institutions
Center Director Satoshi MAEDA	41	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Ph.D., Computational Chemistry	80	October 2018	Usually stays at the center	
Tetsuya TAKETSUGU	56	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Ph.D., Quantum Chemistry	80	October 2018	Usually stays at the center	
<u>Michael RUBINSTEIN</u>	64	Professor, Duke University	Ph.D., Polymer Physics	20	October 2018	- Primarily stays at Partner institution - attends meeting (by online)	- Conducting interdisciplinary research - Recruitment of young researchers
Masaharu YOSHIOKA	52	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Graduate School of Information Science and Technology, Hokkaido University	Doctor of Engineering, Knowledge Engineering	20	January 2020	Usually stays at the center	
<u>Alexandre VARNEK</u>	65	Professor, University of Strasbourg	Ph.D., Chemoinformatics	20	October 2018	- Primarily stays at Partner institution - attends meeting (by online)	- Conducting interdisciplinary research - Recruitment of young researchers
Ichigaku TAKIGAWA	44	Specially Appointed Associate Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Researcher, Center for Advanced Intelligence Project, RIKEN	Ph.D., Machine Learning	30	October 2018	- Generally stays at the center once a month (In FY 2020, due to COVID-19, participates in mainly by online) - attends meeting (by online)	

Tamiki KOMATSUZAKI	56	Professor, Institute for Chemical Reaction Design and Discovery / Research Center of Mathematics for Social Creativity, Research Institute for Electronic Science, Hokkaido University	Ph.D., Mathematical Science	80	October 2018	Usually stays at the center	
Satoru IWATA	52	Specially Appointed Professor, Institute for Chemical Reaction Design and Discovery, Hokkaido University Professor, Graduate School of Information Science and Technology, The University of Tokyo	Doctor of Science, Mathematical Engineering	20	November 2020	- Generally stays at the center once a month (In FY 2020, due to COVID-19, participates in mainly by online) - attends meeting (by online)	
Hajime ITO	53	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Doctor of Engineering, Synthetic Chemistry	80	October 2018	Usually stays at the center	
Masaya SAWAMURA	59	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Science, Hokkaido University	Doctor of Engineering, Catalysis	80	October 2018	Usually stays at the center	
Benjamin LIST	53	Professor and Director, Max Planck Institute for Coal Research	Ph.D., Reaction Design	20	October 2018	- Primarily stays at Partner institution - attends meeting (by online)	- Conducting interdisciplinary research - Recruitment of young researchers
Yasuchika HASEGAWA	52	Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Ph.D., Optical Materials Science	80	October 2018	Usually stays at the center	
Yasuhide INOKUMA	39	Associate Professor, Institute for Chemical Reaction Design and Discovery / Faculty of Engineering, Hokkaido University	Ph.D., Structural Chemistry	80	October 2018	Usually stays at the center	
Jian Ping GONG	59	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Advanced Life Science, Hokkaido University	Doctor of Science, Doctor of Engineering, Polymer Chemistry	80	October 2018	Usually stays at the center	
Shinya TANAKA	56	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Medicine, Hokkaido University	M.D., Ph.D., Tumor Pathology	80	October 2018	Usually stays at the center	

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

Principal investigators unable to participate in project in FY 2020

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

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) **Satoru IWATA (52)**

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

Professor

Graduate School of Information Science and Technology, The University of Tokyo, Japan

Specially Appointed Professor

Institute for Chemical Reaction Design and Discovery, Hokkaido University, Japan

Academic degree and specialty

Academic degree: Doctor (Science), Kyoto University

Specialty: Mathematical Engineering, Mathematical Optimization, Discrete Mathematics

Effort **20 %**

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

Research and education history

1991.3 Bachelor of Engineering, The University of Tokyo, March 1991.

1993.3 Master of Engineering, The University of Tokyo, March 1993.

1996.3 Doctor (Science), Kyoto University, March 1996.

1994.4 – 1997.3 Research Associate, Research Institute for Mathematical Sciences, Kyoto University.

1997.4 – 1999.6 Lecturer, Graduate School of Engineering Science, Osaka University.

1999.7 – 2000.3 Associate Professor, Graduate School of Engineering Science, Osaka University.

2000.4 – 2001.3 Associate Professor, Department of Mathematical Engineering and Information Physics, The University of Tokyo.

2001.4 – 2006.3 Associate Professor, Department of Mathematical Informatics, The University of Tokyo.

2006.4 – 2008.3 Associate Professor, Research Institute for Mathematical Sciences, Kyoto University.

2008.4 – 2013.1 Professor, Research Institute for Mathematical Sciences, Kyoto University.

2013.2 – Professor of Mathematical Informatics, The University of Tokyo.

2020.11 – Specially Appointed Professor, Principal Investigator, Institute for Chemical Reaction Design and Discovery, Hokkaido University.

Achievements and highlights of past research activities

- In a joint work with Lisa Fleischer and Satoru Fujishige, he developed the first combinatorial strongly polynomial algorithm for minimizing general submodular functions. This work resolved a major long-standing open problem in combinatorial optimization. The paper appeared in Journal of the ACM and shared the Delbert Ray Fulkerson Prize from AMS and MPS in 2003.
- He devised index reduction methods for differential-algebraic equations using discrete optimization and combinatorial relaxation techniques. This research was conducted in collaboration with Mizuyo Takamatsu, Caren Tischendorf and Taihei Oki.
- In a series of papers that appeared in SIAM Journal on Optimization, he provided efficient methods for solving certain types of nonconvex optimization problems via generalized eigenvalue computation. This research was conducted in collaboration with Akiko Takeda, Yuji Nakatsukasa, Satoru Adachi, and Shinsaku Sakaue.
- In a joint paper with Yusuke Kobayashi, he devised the first polynomial algorithm for solving the weighted linear matroid parity problem. This work resolves another long-standing open problem in combinatorial optimization. The paper obtained the Best Paper Awards in STOC 2017.

Achievements

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

a) Recipient of international awards
Delbert Ray Fulkerson Prize, 2003.
Best Paper Award at the 49th Annual ACM Symposium on Theory of Computing (STOC), June 2017.

b) Member of a scholarly academy in a major country
N/A

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field
Semi-plenary speaker: International Symposium on Mathematical Programming, Rio de Janeiro, 2006.
Invited speaker: International Congress of Mathematicians (ICM), Hyderabad, 2010.

d) Editor of an international academic journal
Associate Editor, SIAM Journal on Discrete Mathematics (since 2008).
Associate Editor, Mathematical Programming, Series A (since 2008).
Associate Editor, Mathematics of Operations Research (since 2014).

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

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

Grant-in-Aid for Scientific Research (B), JSPS, 17H01699, 2017.4—2022.3.
CREST, JST, JPMJCR14D2, 2014.10—2020.3.

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

1) S. Iwata, L. Fleischer, and S. Fujishige: A combinatorial strongly polynomial algorithm for minimizing submodular functions, Journal of the ACM, 48 (2001), pp. 761-777. [700]
2) S. Iwata: A faster scaling algorithm for minimizing submodular functions, SIAM Journal on Computing, 32 (2003), pp. 833-840. [127]
3) S. Iwata: Submodular function minimization, Mathematical Programming, 112 (2008), 45-64. [144]
4) S. Iwata and J. B. Orlin: A simple combinatorial algorithm for submodular function minimization, Proc. 20th Annual ACM-SIAM Symposium on Discrete Algorithms (2009), pp. 1230-1237. [158]
5) M. X. Goemans, N. Harvey, S. Iwata, and V. Mirrokni: Approximating submodular functions everywhere, Proc. 20th Annual ACM-SIAM Symposium on Discrete Algorithms (2009), pp. 535-544. [173]
6) S. Iwata, K. Nagano: Submodular function minimization under covering constraints, Proc. 50th Annual IEEE Symposium on Foundations of Computer Science, 671-680. [141]
7) M. X. Goemans, S. Iwata, and R. Zenklusen: An algorithmic framework for wireless information flow, Proc. 47th Allerton Conference on Communication, Control, and Computing (2009), pp. 294-300. [57]
8) S. Iwata and M. Takamatsu: Index minimization of differential-algebraic equations in hybrid analysis for circuit simulation, Mathematical Programming, 121 (2010), pp. 105-121. [17]
9) M. Takamatsu and S. Iwata: Index characterization of differential-algebraic equations in hybrid analysis for circuit simulation, International Journal of Circuit Theory and Applications, 38 (2010), pp. 419-440. [40]
10) S. Iwata, M. Takamatsu, and C. Tischendorf: Tractability index of hybrid equations for circuit simulation, Mathematics of Computation, 81 (2012), pp. 923-939.
11) S. Iwata, Y. Nakatsukasa, A. Takeda: Computing the signed distance between overlapping ellipsoids, SIAM Journal on Optimization, 25 (2015), 2359-2384. [10]
12) S. Sakaue, Y. Nakatsukasa, A. Takeda, S. Iwata: Solving generalized CDT problems via two-parameter eigenvalues. SIAM Journal on Optimization, 26 (2016), 1669-1694.
13) S. Adachi, S. Iwata, Y. Nakatsukasa, A. Takeda: Solving the trust-region subproblem by a generalized eigenvalue problem, SIAM Journal on Optimization, 27 (2017), 269-291. [61]
14) S. Iwata, T. Oki, M. Takamatsu: Index reduction for differential-algebraic equations with mixed matrices, Journal of the ACM, 66 (2019), 35:1-35:34. [3]
15) S. Iwata, Y. Kobayashi: A weighted linear matroid parity algorithm, SIAM Journal on Computing, STOC 17 (2021), 238-280. [20]

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

NA

Appendix 3-1 FY 2020 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions

1-1. Number of researchers in the "core" established within the host institution

- Regarding the number of researchers at the Center, fill in the table in Appendix 3-1a.

Special mention

- Enter matters warranting special mention, such as concrete plans for achieving the Center's goals, established schedules for employing main researchers, particularly principal investigators.
- As background to how the Center is working on the global circulation of world's best brains, give good examples, if any, of how career paths are being established for the Center's researchers; that is, from which top-world research institutions do researchers come to the Center and to which research institutions do the Center's researchers go, and how long are their stays at those institutions.

1-2. Satellites and partner institutions

- List the satellite and partner institutions in the table below.
- Indicate newly added and deleted institutions in the "Notes" column.
- If satellite institutions have been established overseas, describe by satellite the Center's achievements in coauthored papers and researcher exchanges in Appendix 4.

<Satellite institutions>

Institution name	Principal Investigator(s), if any	Notes

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
University of Strasbourg	Alexandre Varnek	
Max Planck Institute for Coal Research	Benjamin List	
Duke University	Michael Rubinstein	
ESPCI		
Swiss Federal Institute of Technology in Zurich		
Peking University		
Kyoto University, Graduate School of Informatics		
Chubu University, Molecular Catalyst Research Center		
The University of Tokyo, Graduate School of Information Science and Technology	Satoru Iwata	
Stockholm University		
University of Oslo		

2. Holding international research meetings

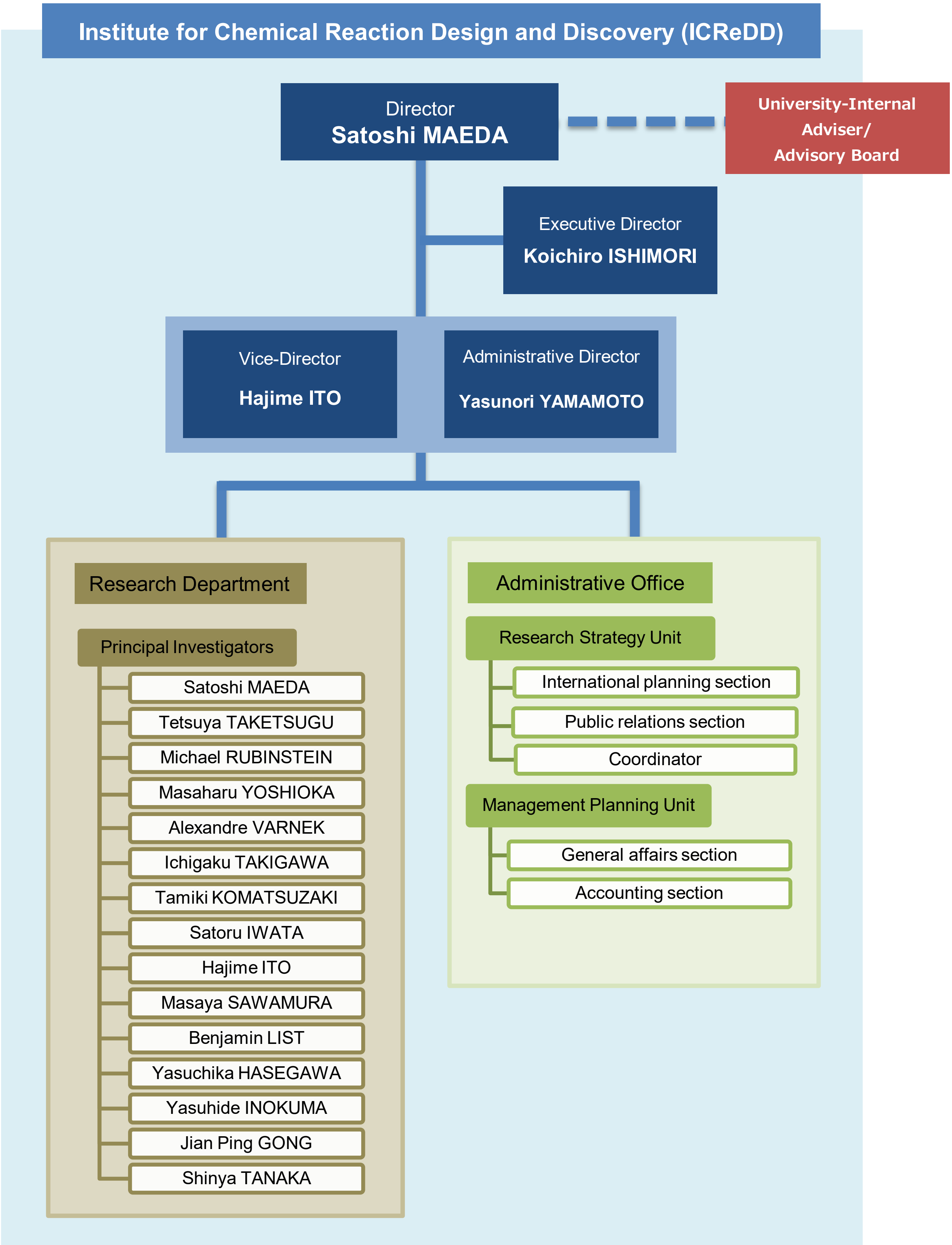
- Indicate the number of international research conferences or symposiums held in FY2020 and give up to three examples of the most representative ones using the table below.

FY 2020: 1 meeting

Major examples (meeting titles and places held)	Number of participants
The 3rd ICReDD International Symposium (Online) February 22-24, 2021	279 (Online*) *From domestic :161 From overseas :118

3. Diagram of management system

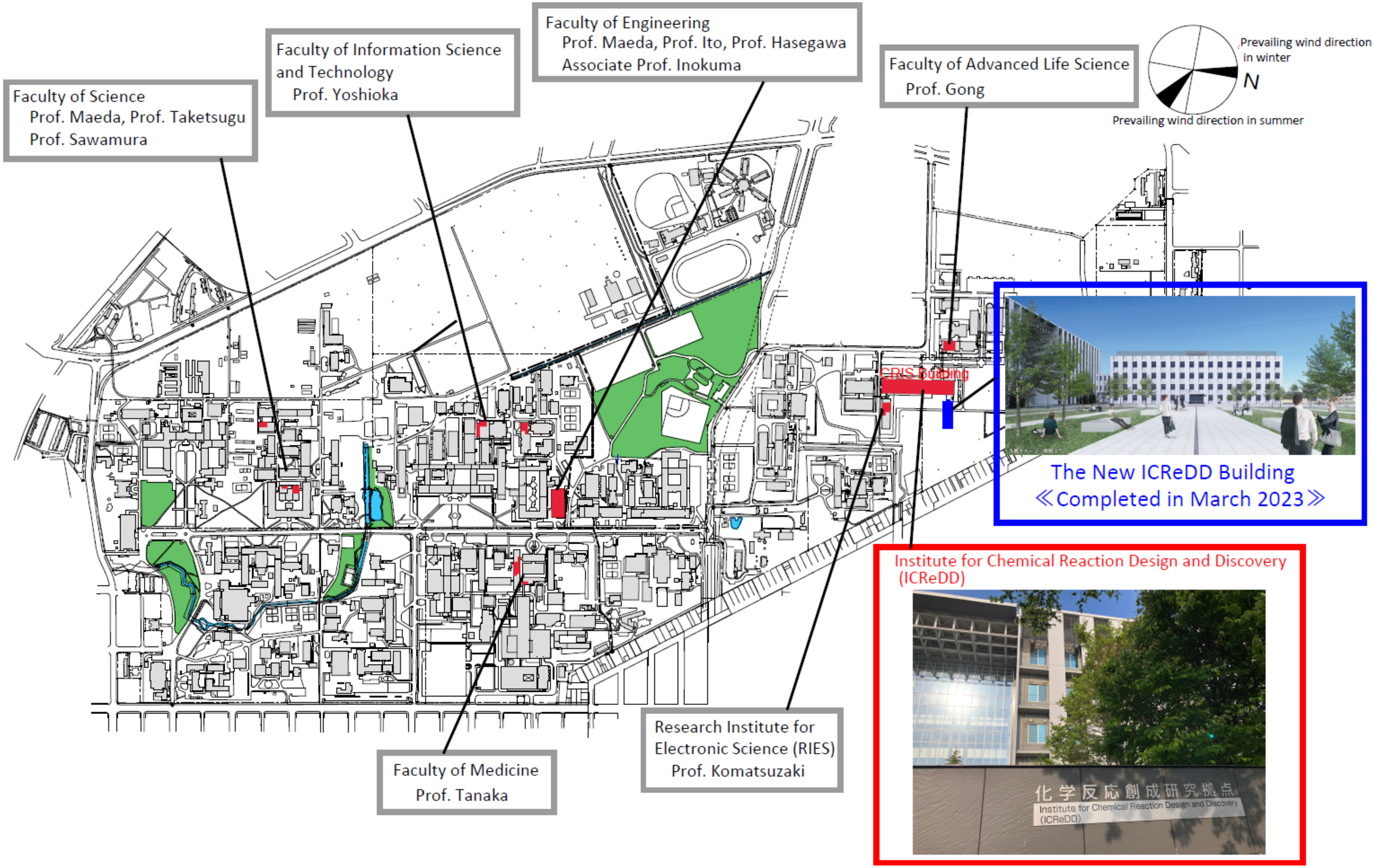
- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any new changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such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



4. Campus Map

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

As of March 31, 2021



5. Securing external research funding*

External research funding secured in FY2020

Total: 539,651,481 yen

- Describe external funding warranting special mention. Include the name and total amount of each grant.

* External research funding includes "KAKENHI," funding for "commissioned research projects," "joint research projects," and for others (donations, etc.) as listed under "Research projects" in Appendix 3-2, Project Expenditures.

Name	Provider	Project	Period	Total amount during the research period (Unit: 1,000 yen)
Satoshi Maeda	Japan Science and Technology Agency	Strategic Basic Research Programs（ERATO）	2019 - 2024	1,200,000
Hajime Ito	Japan Science and Technology Agency	Strategic Basic Research Programs（CREST）	2019 - 2024	150,000
Hajime Ito	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research on Innovative Areas（Research in a Proposed Research Area）	2017 - 2021	84,110
Hajime Ito	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（A）	2018 - 2021	44,200
Masaya Sawamura	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（A）	2018 - 2021	43,810
Jian Ping Gong	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（S）	2017 - 2021	204,100
Tamiki Komatsuzaki	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research on Innovative Areas（Research in a Proposed Research Area）	2018 - 2022	98,280
Tamiki Komatsuzaki	Japan Science and Technology Agency	Strategic Basic Research Programs（CREST）	2016 - 2021	130,163
Tamiki Komatsuzaki	Hitachi, Ltd.	Joint Research Funding	2016 – 2021	37,802
Shinya Tanaka	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research（A）	2019 - 2022	45,110

Appendix 3-1a FY 2020 Records of Center Activities

Researchers and other center staff

Number of researchers and other center staff

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

a) Principal Investigators

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

(number of persons)

	At the beginning of project	At the end of FY 2020	Final goal (Date: March, 2023)
Researchers from within the host institution	11	12	12
Researchers invited from overseas	3	3	3
Researchers invited from other Japanese institutions	0	0	0
Total principal investigators	14	15	15

b) Total members

	At the beginning of project		At the end of FY 2020		Final goal (Date: March, 2023)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	14		66		75	
Overseas researchers	3	21	24	36	34	45
Female researchers	1	7	7	11	12	16
Principal investigators	14		15		15	
Overseas PIs	3	21	3	20	3	20
Female PIs	1	7	1	7	1	7
Other researchers	0		37		39	
Overseas researchers	0	0	11	30	13	33
Female researchers	0	0	3	8	5	13
Postdocs	0		14		21	
Overseas postdocs	0	0	10	71	18	86
Female postdocs	0	0	3	21	6	29
Research support staffs	0		2		5	
Administrative staffs	0		14		19	
Total number of people who form the "core" of the research center	14		82		99	

Appendix 3-2 Project Expenditures

1) Overall project funding

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

(Million yen)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center Director, Executive Director, Administrative Director	33	11
	Principal investigators (no. of persons): 11	108	6
	Part-time faculty members (no. of persons): 11	99	0
	Specially appointed faculty members (no. of persons): 28	189	189
	Postdoctoral fellows (no. of persons): 15	56	56
	Other researchers (no. of persons): 2	8	8
	Research support staff (no. of persons): 1	2	2
	Administrative staff (no. of persons): 15	67	30
	Center allowance	19	19
	Subtotal	581	321
Project activities	Startup research project costs	23	23
	Outreach-related costs	2	2
	Symposium costs	1	1
	Center operating costs	6	6
	Environmental improvement costs	71	45
	Center improvement costs	51	0
	Facility rental fees	19	0
	Utility costs	17	0
	Others	69	0
	Subtotal	259	77
Travel	Domestic travel costs	0	0
	Overseas travel costs	0	0
	Travel costs for scientists on transfer (no. of domestic scientists/overseas scientists): 1/0	1	1
	Subtotal	1	1
Equipment	Facility improvement costs	189	184
	Facility/equipment procurement costs	124	117
	Subtotal	313	301
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	394	0
	KAKENHI	111	0
	Commissioned research projects, etc.	357	0
	Joint research projects	20	0
	Others (donations, etc.)	52	0
	Subtotal	934	0
Total		2,088	700

Costs (Million yen)

WPI grant in FY 2020	700
Costs of establishing and maintaining facilities	189
- Renovation of CRIS Building	189
(Renovated floor area: 1,005 m²)	
Costs of equipment procured	124
- Fume hood (Number of units: 8)	14
- Flow cytometer	15
- Others	95

*1. Management Expenses Grants (including Management Enhancements Promotion Expenses (機能強化経費)), subsidies including National university reform reinforcement promotion subsidy (国立大学改革強化推進補助金) etc., indirect funding, and allocations from the university's own resources.
*2 When personnel, travel, equipment (etc.) expenses are covered by KAKENHI or under commissioned research projects or joint research projects, the amounts should be entered in the

*1 運営費交付金（機能強化経費を含む）、国立大学改革強化推進補助金等の補助金、間接経費、その他大学独自の取組による学内リソースの配分等による財源
*2 科研費、受託研究費、共同研究費等によって人件費、旅費、設備備品等費を支出している場合も、その額は「研究プロジェクト費」として計上すること

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):OO		
	Other researchers (no. of persons):OO		
	Research support staff (no. of persons):OO		
	Administrative staff (no. of persons):OO		
	Subtotal	0	0
Project activities	Subtotal		
Travel	Subtotal		
Equipment	Subtotal		
Research projects	Subtotal		
Total		0	0

Appendix 4 FY 2020 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2020 that were coauthored between the center's researcher(s) in domestic institution(s) (include satellite institutions) and overseas satellite institution(s). List them by overseas satellite institution in the below blocks.
- Transcribe data in same format as in Appendix 1. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2021 and not described in Appendix 1.

Overseas Satellite 1 Name (Total: OO papers)

1)
2)
3)
4)

Overseas Satellite 2 Name (Total: OO papers)

1)
2)
3)
4)

Not applicable.

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2019. Enter by institution and length of exchange.
- Write the number of principal investigator visits in the top of each space and the number of other researchers in the bottom.

Overseas Satellite 1:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2020					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2020					

Overseas Satellite 2:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2020					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2020					

Appendix 5 FY 2020 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.
* Enter the host institution name and the center name in the footer.

Total: OO Not applicable.

	Name	Age	Affiliation		Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
			Position title, department, organization	Country				
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								

Appendix 6 FY2020 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2020 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2020 (number of activities, times held)
PR brochure, pamphlet	7: ICReDD pamphlet J/E, recruitment brochure J/E, Monthly post card J/E, Quarterly news poster J/E, Annual report J/E, HU Magazine "LITTERAE POPULI" J / MANA NEWS LETTER "CONVERGENCE" J/E
Lectures, seminars for general public	10: EML Webinar (Gong), 1st Chem-station virtual symposium (ito), Periodic table of the elements club (Ito), 3rd Chem-station virtual symposium (Tsuji), Symposium for reaction path search 2020 (Taketsugu), RCC supercomputer workshop 2021 (Kobayashi), Seminar in artificial intelligence advanced research center (Kobayashi), PCoMS symposium & annual meeting of supercomputing consortium for computational materials science 2020 (Lyalin), 10th CSJ Chemistry festa (Takigawa), Citizen lecture (Tanaka)
Teaching, experiments, training for elementary, secondary and high school students	3: Lecture at Ishikawa Kanazawa Fushimi HS (Ito), WPI Online Symposium 2020 for High School Students (Tsuji), MINT ring lecture at broich high school (List)
Participating, exhibiting in events	1: WPI Science Symposium
Press releases	11: 10 press releases, 1 press conference
Publications of the popular science books	3: Material stage (Kobayashi), Chemistry and Industry (Taketsugu), データサイエンスのためのデータベース (Yoshioka)
Others（Original goods）	7: Pen, Notepad, Sticker, Pin, Name holder, Word Reactor, Periodic Pen Stand
Others（Social media）	3: Twitter, Facebook, YouTube

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

Outreach Activities and Their Results

List up to three of the Center's outreach activities carried out in FY 2020 that have contributed to enhancing the brand or recognition of your Center and/or the brand of the overall WPI program, and describe its concrete contents and effect in narrative style. (Where possible, indicate the results in concrete numbers.)

Examples:
- As a result of using a new OO press-release method, a OO% increase in media coverage was obtained over the previous year.
- By holding seminars for the public that include people from industry, requests for joint research were received from companies.
- We changed our public relations media. As a resulting of using OO to disseminate information, a OO% increase in inquiries from researchers was obtained over the previous year.
- As a result of vigorously carrying out OO outreach activity, ¥OO in external funding was acquired.

The English press release was sent out to the media through online platforms such as EurekAlert! and Asia Research News. "Reach", which is the number of potential visitors of the news site per month, provided by a media monitoring company, and "Altmetric score", which is a measure of the impact of an individual paper on social media and news sites on the web (https://www.altmetric.com/) were used as evaluation indicators. The representative results were as follows.

Press release article	Reach and Altimetric Score
Nature Biomedical Engineering, March **2021** (DOI: 10.1038/s41551-021-00692-2)	Reach: 309 million and Altimetric score: 117 (Top 5%).
Science, **2020**, 369, 970-974 (DOI: 10.1126/science.abc8320)	Reach: 13 million and Altimetric score: 103.
Proceedings of the National Academy of Sciences of the United States of America (PNAS), **2020**, 117, 18962-18968 (DOI: 10.1073/pnas.2006842117)	Reach: 16 million and Altimetric score: 92.
ACS Applied Materials & Interfaces, **2020**, 12, 9448-9456 (DOI: 10.1021/acsami.9b21261)	Reach: 13 million and Altimetric score: 53.

Appendix 7 FY 2020 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2020.

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

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2020/8/27	online news	Article on ICReDD research press release (2020/8/26) about luminescent lanthanide molecular in OPTRONICS online
2	2020/8/27	online news	Article on ICReDD research press release (2020/8/26) about luminescent lanthanide molecular in CHEMNET TOKYO online
3	2020/6/5	television	ARD alpha Campus Talks: "Catalysis for the World" ("Katalyse für die Welt")
4	2020/8/20	online news	Article on ICReDD research press release (2020/8/20) about functionalization for remote C–H bonds in EurekAlert
5	2020/8/21	television	Article on ICReDD research press release (2020/8/20) about functionalization for remote C–H bonds on NHK news Ohayo Hokkaido
6	2020/8/24	magazine	Article on ICReDD research press release (2020/8/20) about functionalization for remote C–H bonds in C&E News
7	2020/12/16	journal	Article on ICReDD research press release (2020/8/20) about functionalization for remote C–H bonds in synform
8	2020/8/21	newspaper	Article on ICReDD research press release (2020/8/20) about functionalization for remote C–H bonds in Japan Chemical Daily
9	2020/6/23	online news	Article on ICReDD research press release (2020/6/23) about photochemical reaction process using near-IR in ChemViews Magazine
10	2021/1/20	newspaper	Article on ICReDD research press release (2020/6/23) about the mechanism of photochemical smog-causing PM2.5 in Nikkan Kogyo Shimbun
11	2020/7/29	newspaper	「重複がん　高齢で増加」in Hokkaido Shimbun
12	2021/3/31	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in NHK news web
13	2021/3/30	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in Nihon Keizai shimbun

14	2021/3/30	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in Hokkaido shimbun
15	2021/3/30	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in Yahoo news
16	2021/3/30	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in Nikkan Kogyo Shimbun
17	2021/3/30	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in jiji.com
18	2021/3/30	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in 47news
19	2021/3/30	online news	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in Hokkoku Shimbun
20	2021/3/31	newspaper	Article on ICReDD research press release (2021/3/30) about reversion of cancer cell to the cancer stem cell by hydrogel in Nihon Keizai shimbun