World Premier International Research Center Initiative (WPI)
FY 2018 WPI Project Progress Report

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Research Center	Institute for Chemical Reaction Design and Discovery (ICReDD)	Center Director	Satoshi Maeda

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2019) 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

At the Institute for Chemical Reaction Design and Discovery (ICReDD), the advanced integration of computational science, information science, and experimental science will make it possible to move away from reaction development through trial and error, and toward a smarter way of designing chemical reaction purposefully. In this half year, in addition to the world-class research unique to each PI, we promoted the development and integration of elemental technologies in computational science and information science and tried to identify new research themes to which these technologies would be applied successfully. As a result, several joint research projects have been started in the center.

The following three research results are particularly noteworthy in fiscal 2018, highlighting joint research opportunities.

(1) Development of a completely new material grown by a metabolic reaction (*Science*, 2019)

Gong *et al.* found a gel material that increased in strength in response to repeated stretching. The material's polymer chains break under strain and re-grow by incorporating the chains' monomers introduced into the material earlier. In order to improve the versatility of the material in the future, the control of the chemical reaction that occurs in the process in which the polymer chain takes in the monomers is key. We will conduct collaborative research to this end.

(2) Development of catalytic organic synthesis reaction in solid (*Nat. Commun.*, 2019)

Ito *et al.* found a method of inducing a cross-coupling reaction, which is usually handled in a solution requiring a costly product dissolution step, by simply mixing raw material powders. Thus, the new method may lead to a drastic reduction in manufacturing costs for devices and pharmaceuticals. In the future, the team will try to find out why the reaction could occur readily in the solid state to discover new and more efficient chemical reactions in collaboration studies.

(3) Development of catalytic asymmetric borylation of methylene C-H bonds (*J. Am. Chem. Soc.*, 2019)

Sawamura *et al.* succeeded in developing a chiral transition metal complex catalyst that enantioselectively borylates methylene C-H bonds, for which enantioselective C-H bond activation is extremely difficult but highly desirable for Suzuki cross-coupling reactions. A joint study with Maeda *et al.* was carried out for further catalyst design, and the cause of selectivity was found by Maeda *et al.*'s automated reaction path search method (AFIR method).

Several other new technologies have been developed (e.g., Maeda *et al.*, *Chem. Lett.*, 2019; Takigawa *et al.*, *J. Phys. Chem. C*, 2018; Varnek *et al.*, *Mol. Inf.*, 2019), and many unpublished new computational methods for future interdisciplinary research within ICReDD have already been made available and will be used in interdisciplinary research, such as a synthetic route enumeration system.

2. Generating Fused Disciplines

The following activities effort out as preparation for starting interdisciplinary research of

computational science, information science and experimental science.

(1) ICReDD base meetings, with each PI introducing their research (December 2018)

(2) Creation of a mixed lab environment

- Set-up of experimental MIX laboratory, communication space (ICReDD salon), and measurement equipment room.
- Installation of a high-performance computer for chemical reaction prediction, a 400 MHz nuclear magnetic resonance (NMR) measurement device, a single crystal X-ray structure analysis device, a draft chamber, etc.
- Decided to adopt 25 members (Co-PI, specially appointed associate professors, lecturers, assistant professors, postdoctoral researchers) to accelerate the system of the Mix laboratory.

(3) Efforts to create bottom-up joint research, especially through weekly and monthly exchange meetings between young and senior researchers of all fields.

(4) Establishment a research strategy unit to promote joint research among PIs

As a result, collaborative research has increased amongst members, such as in the combinations Maeda-Ito, Maeda-Sawamura, Maeda-List, Taketsugu-Ito-Hasegawa, Rubinstein-Gong-Tanaka, Takigawa-Ito, Komatsuzaki-Gong-Tanaka, etc.

3. Realizing an International Research Environment

Research organization: We recruit specially appointed faculty members and doctoral researchers internationally, and approximately 30% of all researchers (13 out of 43 researchers as of April 1, 2019) are of foreign nationality. The selection of Co-PIs (specially appointed associate professors, staff members such as specially appointed assistant professors) who carry out research locally in close collaboration with overseas PIs was also promoted, and full-scale research is expected to begin in fiscal 2019.

Hospitality System: In order to promote English as the primary working language at the center, we have established a support system jointly run by the Research Strategy Unit (international planning and public relations), the management planning unit (general affairs and accounting), and the university URA.

International exchange: We held the 1st International Symposium with attendees from home and abroad. In addition, we have so far hosted six visitors from overseas.

4. Making Organizational Reforms

Establishing an environment conducive to interdisciplinary research: We established the center in the Creative Research Institution (CRIS), which is a university-wide organization, and started the reconstruction of facilities as needed. Furthermore, we manage common resources in collaboration with the Global Facility Center (GFC) of the Creative Research Institution (CRIS). Also, in order to smoothly start the research at the center, we have established a new faculty start-up financially support system and a collaborative research start-up financially support system.

System reform: We started setting up the "MANABIYA" system that plays the role of conveying internationalization and diversification within the center and between the research fields of computational science, information science, and experimental science all over the world.

Development of a management system: In order to deliberate important matters concerning the research center, a Steering Committee has been established to make decisions on the hiring of specially appointed professors and researchers, the guidelines for implementing the start-up support, etc. In addition, for the smooth operation of the center, we have established a regular Director's meeting to support the decision making of the center director, and a young working group to gather young researchers and exchange their opinions.

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

Aiming at medium- and long-term development, we promote joint research projects beyond the framework of undergraduate and postgraduate research, such as the project titled "Exploration of photoexcited research base: Prediction of photoexcited state control and advanced utilization" (FY2019 budget: 125,784,000 yen). In addition, the university is promoting cooperation with organizations and projects within the university.

* 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 fusing fields).
  (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 2018.
* 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.

The objective of this institute is to establish the new academic field "Chemical Reaction Design and Discovery (CReDD)" through the fusion of computational, information, and experimental sciences, and to develop new useful reactions much more efficiently than ever before. To conduct world-class research through top-level collaboration, this institute has recruited topnotch researchers. As a solid strategy toward this goal, first, each PI will achieve research results at ICReDD in the respective important subject. Next, while achieving the world's best research results through merging the two research fields, we aim to achieve integration research across the three fields by fusing the third field. As this is the first half year since the institute was established, mainly studies have been led by each PI, yet collaboration has already started among the teams.

Development of computational and information science methods and improvement of computational methods and programs [Maeda Group]

Maeda et al. continued to refine a GRRM program that implements a one-of-a-kind automated reaction path search method (artificial force induced reaction method) and enhanced its functionality to broaden its application. In particular, an algorithm (kinetic navigation system) has been introduced, which, based on the chemical reaction kinetics, automatically eliminates the paths that cannot proceed under given experimental conditions (temperature and reaction time), resulting in significant improvement of calculation efficiency **(*Chem. Lett.,* 2019)**. They have also developed a technique to apply time-dependent density-functional theory in automated search of nonradiative deactivation paths of photoreactions and made it possible to discuss the photoreactions for molecules (~100 atoms) of the size that could not be handled before **(*Chem. Phys. Lett.,* 2019)**. Moreover, their verification of the artificial force induced reaction method has proved its high level of comprehensiveness **(*J. Chem. Theory Comput.,* 2019)**.

Development of innovative materials self-growing through metabolic processes [Gong Group]

Living tissues are constantly developing and optimizing their size and functions through metabolic processes, in which nutrients are taken in from outside are used to repeatedly destroy and reconstruct the structures of those tissues. Inspired by this mechanism, when a monomer (nutrition), the raw material of a double network (DN) gel, is introduced into this very strong gel itself, Gong et al. constructed the system in which the monomers are polymerized starting from a mechano-radical generated by the breakage of a polymer network chain inside the gel, and a new polymer network is reconstructed inside the gel. This resulted in **the synthesized gels that grow large in strength, size, and function responding to each deformation as if they were muscles (*Science*, 2019)**. Furthermore, in the ICReDD environment, they have started collaborative research with computational and organic synthetic chemists in an effort to improve the mechanical response performance and multifunctionality of this gel.

Development of catalytic organic synthetic reaction in solid state [Ito Group]

Most organic chemical reactions have been conducted in "solutions", where the reagents have been diluted with solvents because the reagents are expected to be diffused completely and collide freely there. Although in most cases, organic synthetic reactions are not conducted in the solid state, they can happen under the conditions that the reagents are stirred enough. From this perspective, by applying computational chemistry and information science, Ito et al. have been developing new organic synthetic reactions that work in the solid state and new organic materials that utilize structural change of solid state.

Development of solid-state cross-coupling [Ito]

Cross-coupling reactions are frequently used in organic synthesis. Ito et al. succeeded to conduct solid-state cross-coupling reactions (C-N cross-coupling) for the first time **(*Nat. Commun.*, 2019)**. The preliminary experiments taught that in the solid state under the same reaction conditions as the solution system, the cross-coupling reactions were not carried out effectively because the palladium catalyst aggregated immediately and deactivated. Then, they discovered that the addition of alkene additive suppressed the aggregation and deactivation of palladium and gave the desired cross-coupling products in high yields. They also succeeded in Suzuki-coupling and C-H borylation reaction in mechanochemical conditions. Solution-based reactions have been studied for over 100 years, whereas much of solid-state reactions are unknown. Going forward, they will tackle this emerging field by integrating computational chemistry and information science, thus leading to the efficient development of reactions.

Photoresponse prediction of manganese complex [Maeda and Daniel (University of Strasbourg)]

Maeda et al. worked with Dr. Daniel at the University of Strasbourg and her team to predict the photoresponse of $[Mn(im)(CO)_3(phen)]^+$ complex **(*J. Comput. Chem.,* 2019)**. The Mn complex has been gaining attention because of its similarity to $[Re(L)(CO)_3(bpy)]^+$ (L corresponds to a ligand such as Cl^-), which has a CO_2 photoreduction ability. Also, Mn complex is much cheaper than Re complex; thus, substituting Mn complex for Re complex has been anticipated. In this study, an automated search of potential seam of crossing structures revealed the relaxation path from the electronically excited state of this Mn complex. This result may shed light on designing Mn complex, which exhibits a CO_2 reduction ability etc.

CO oxidation reaction mechanism on the surface of Pt nanoparticles [Maeda]

By applying the automated reaction path search method, Maeda et al. obtained a reaction path network when Pt(111) surface was used as a surface model for CO oxidation reaction on the surface of Pt nanoparticle, which is used to remove CO from an exhaust gas. They further applied chemical reaction kinetics to the obtained reaction path network and elucidated its reaction mechanism **(*Phys. Chem. Chem. Phys.,* 2019)**.

Mechanism analysis of the phenanthrene skeleton construction reaction [Maeda and Fukushima (Tokyo Institute of Technology)]

In cooperation with Professor Fukushima at Tokyo Institute of Technology and others, Maeda et al. have conducted theoretical analysis using the automated reaction path search method for the reaction mechanism of the phenanthrene skeleton construction method that had been experimentally discovered by Professor Fukushima and his team **(*J. Org. Chem.,* 2019)**. This reaction is very convenient because various π-conjugated molecules can be synthesized by the simple steps of mixing borafluorene and various alkynes and adding a one-electron oxidant. As a one-electron oxidant, O_2 and $FeCl_3$ were used and examined respectively, and the overall picture for the whole reaction mechanism was clarified. Although a by-product was unknown experimentally, it was uncovered that $ClBO_2$ was produced when using O_2 and $Cl_2B\text{-}FeCl_2$ was when using $FeCl_3$, respectively.

Reactivity prediction of metal cluster catalyst toward NO molecule decomposition [Maeda and Toyota Motor Corporation]

Maeda et al. collaborated with Toyota Motor Corp. to search reaction paths for NO molecule decomposition on various metal clusters **(*ChemCatChem,* 2019)**. As a result, many cases were found in which the reaction barrier was lowered and the activity increased due to large-scale deformation of the metal cluster structure. This result is expected to offer important suggestions for theoretical prediction of catalyst activity in the future.

Analysis of reaction mechanism of lactate dehydrogenase [Maeda]

Suzuki (Maeda group) et al. combined the ONIOM method with the original multistructural microiteration (MSM) method implemented in the automated reaction path search program, GRRM, and analyzed reaction mechanism of lactate dehydrogenase. Experiments have suggested that lactate dehydrogenase undergoes a large change in its surrounding structure, changing from so-called an open-loop structure to a closed-loop structure and then from the closed-loop structure to the open-loop structure as the reaction proceeds. The MSM method verified this experimental result

in which the surrounding structure changes as mentioned above along the reaction path. Further, detail analysis of the obtained reaction paths revealed that a series of changes in the surrounding structure provided a driving force for the lactate dehydrogenation reaction **(*ACS Omega*, 2019)**.

Theoretical analysis of quantum tunneling in electrocatalysts [Taketsugu Group]

Taketsugu, the leader of electrocatalyst theory group at NIMS GREEN (Global Research Center for Environment and Energy based on Nanomaterials Science), has been conducting joint research on electrocatalyst with the NIMS experimental group and reported an important work on the electrocatalyst in the Hokkaido University-NIMS joint press releases in December 2018. In this research, Taketsugu discovered that proton transfer in electrochemical reactions is dominated by quantum tunneling under specific conditions from both experimental and theoretical approaches ***(Phys. Rev. Lett., 2018)***. This is the first observation of the phenomenon of quantum-classical transition in electrochemical proton transfer, which has attracted world-wide attention. As it was shown that the tunneling effect is involved in proton transfer in the electrochemical reaction that has been discussed for a long time, in the future, basic researches are expected to be carried out more actively, which are involved in the highly efficient electrochemical energy conversion process that actively utilizes the tunneling effect. Furthermore, Taketsugu has developed a new methodology to discuss chemical reaction dynamics based on the global reaction route map obtained using the automated reaction path search method developed by Maeda and published two significant papers***(Phys. Chem. Chem. Phys., 2018; J. Chem.Theor. Comp., 2018)***. The doctoral course student working on this theme has been selected as JSPS DC1 and was awarded the Excellent Presentation Award at the Theoretical Chemistry Symposium in Japan.

Application of information science to cell diagnosis [Komatsuzaki Group]

By highly integrating reinforcement learning and measurement engineering (Raman spectroscopy), Komatsuzaki group has been working on new development of cancer early detection technology through accelerating the speed of cell diagnosis more than before. For point-scan type Raman simulation, they achieved 13 to 200 times faster (depending on the type of cell image). Accordingly, the applicable basic technology patent was submitted in Japan. In cooperation with the Tanaka group, Komatsuzaki et.al are also developing an algorithm that applies reinforcement learning to cancer drug screening. They further developed innovations around mathematical and information sciences contributing to fundamental technology of quantum computer and their practical use and released two proceedings on graph minor method necessary for annealing calculation **(*TPNC,* 2018; *ReConFig,* 2018)**.

Heterogeneous catalyst developed by utilizing machine learning and data science [Takigawa Group]

Along with the research group of Institute for Catalysis at Hokkaido University, Takigawa, the chief researcher of the information team, has been promoting the research of heterogeneous catalyst development by utilizing machine learning and data science since 2015. His paper in 2016 was published in RSC Advances and was featured as an article "Machine-learning accelerates catalytic trend spotting" in their online magazine, Chemistry World. He also gave a guest lecture at the session "CATL: Machine Learning for Catalysis Research" of the 255th American Chemical Society National Meeting, which was held at the annual meeting of the American Chemical Society in March 2018. Through the JST CREST research proposal "Experimental, theoretical, and data science research for the creation of catalytic informatics" adopted in the fiscal year 2017, he has promoted the joint research with computational science and experimental science of catalytic chemistry throughout 2018. Adsorption energies of CH_4 and related adsorbates CH_3, CH_2, CH, C and H on Cu-based metal surfaces were calculated, and the machine learning predictions were quantitatively evaluated. In addition, in the surface models of insulating oxides and semiconductor oxides, the formation energy of O vacancies was calculated by DFT, and the factors affecting the energy were analyzed **(*J. Phys. Chem. C,* 2018)**. At present, two international papers and one international review paper on the utilization of machine learning in catalyst science are being prepared. Taking advantage of the fact that the WPI headquarter is located in the same building as the Institute for Catalysis, Takigawa and his team are planning to gain new insight through the joint research with the WPI Computational Science and Experimental Science Groups.

Application of the condensed graph of reaction (CGR) [Varnek Group]

Varnek developed predictive models linking structure of molecules with their reactivity taking into account reaction conditions. Namely, this concerns the models predicting equilibrium constants of tautomeric equilibria (T. R. Gimadiev *et al*., ***J. Comput. -Aided Mol. Des.,*** **2018**), rate constants of S_N2 reactions (T. I. Madzhidov *et al.,* ***BioNanoScience*** **2018**) and regioselectivity of metabolic reactions catalyzed by CIP_1A_2 enzyme (T. R. Gimadiev *et al*., ***Mol. Inf.,*** **2018**).

Application of chemical cartography approach to the analysis and visualization of complex chemical data [Varnek]

Using his own tool developed in the laboratory implementing Generative Topographic Mapping method, Varnek critically analyzed a large set of commercially available compounds (D. Judd *et al*., ***Drug Discovery Today,*** **2018**) and the database of tautomeric reactions (M. Glavatskikh *et al*., ***Mol. Inf.,*** **2018**) and designed the database for antimalarial compounds (P. Sidorov *et al*., ***Mol. Inf.,*** **2018**).

Computer-aided development of new bromodomain inhibitors [Varnek]

By using the S4MPLE tool developed in the laboratory, Varnek conducted ligand-to-protein docking and de novo molecular design (L. Hoffer *et al*., ***J. Med. Chem.,*** **2018**). The tool was also compared with some commercial software packages (M. Zhenin *et al*., ***J. Comput. -Aided Mol. Des.,*** **2018**).

Design of chemical reactions through combining computational chemistry with experimental science [Ito]

Ito et al. showed that computational chemical optimization of the organic reaction is possible. The structures of the transition states, the key of organic reactions, were first analyzed by computational chemical method (DFT method). The "design guideline" was then established by comparing them with the experimental results. Iteration of design and implementation of new reaction based on the guideline can effectively optimize the reaction **(*Nat. Commun.,* 2018)**. Since the latter half of 2018, this method has been applied to "radical reactions," which are difficult to predict, and has achieved results.

Study of phase transition mechanism of luminescent gold(I) isocyanide complex with mechanical-stress response using MM and QM/MM calculations [Ito]

Ito et al. have found the phenomenon that when a mechanical stress is applied to a crystalline compound, a minute stimulus propagates in a domino manner to cause a phase transition of the entire crystal. For the first time, they have succeeded in explaining the polymorph stability before and after the structural changes and the luminescent properties of the polymorphs by using computational chemistry method **(*J. Comput. Chem. Jpn.,* 2018; *J. Phys. Chem. C,* 2019)**.

Development and theoretical analysis of catalytic asymmetric synthesis reaction [Sawamura Group]

Sawamura developed a reaction to convert C–H bonds into broadly transformable C–B bonds by using a uniquely designed and synthesized chiral transition metal complex catalyst to achieve enantioselective recognition and activation of inactive methylene C–H bonds in saturated hydrocarbon moieties of organic molecules. This is the world's first example of highly enantioselective realization of a C—H oxidative addition reaction in which the metal center is inserted directly into the C—H bond of a saturated hydrocarbon group that has not undergone electronic activation and cleaves it directly. Furthermore, this research is also extremely cutting-edge as it elucidated that asymmetric recognition of reaction substrates by catalysis is realized by a large number of attractive noncovalent interactions and demonstrated the importance of noncovalent interactions in asymmetric catalysis.

Reaction and function development of middle molecular weight domain (mesoscopic domain) [Inokuma Group]

Synthetic methods have been developed, in which aliphatic carbonyl compounds with a molecular weight of 500 to 10,000 corresponding to the intermediate region (mesoscopic region) of small organic molecules and polymers are unambiguously synthesized. These methods have established the foundation for the discovery of novel chemical reactions, control of molecular structures, and development of new materials. In 2018, Inokuma et al. investigated self-assembly behavior with palladium ion and analyzed higher structural control of aliphatic polyimine compounds that were

derivatized with high selectivity and yield from linear aliphatic polycarbonyl compounds. This study demonstrated that complex formation of polyimine chain and metal ion, which seems to be a very complicated process, has a certain rule, and in particular, step-wise coordination bond formation by the induced effect in the adjacent imine group plays an important role in the formation of unambiguously functional complexes. This result (***Dalton Trans.,*** **2019**) was also featured as the back-cover picture of the relevant issue.

Development of chiral Eu luminescent materials with the best circular polarization properties [Hasegawa Group]

Hasegawa et al. succeeded in synthesizing chiral Eu(III) complex attached with chiral and achiral ligands to europium ion and in achieving strong red luminescence from europium ion and high circular polarization properties (anisotropic factor g = 1.5: the world record value). Moreover, the optical measurements revealed that this excellent circularly polarized luminescence properties were affected by the achiral ligand's binding power to europium. For further improvement of these properties, Hasegawa et al. are searching for the best combination of chiral and achiral ligands of Eu(III) complexes by computational chemistry (joint research with Maeda). This result has also been filed for a patent application in Japan and will be developed as the next generation high-security light-emitting ink using circularly polarized luminescence. (to be submitted) Hasegawa confirmed that coordination and polymerization (polymerization) of chiral Eu(III) complex improves the strong luminescence and circularly polarized luminescence properties from europium **(*Chem. Commun.,* 2018)**.

Analysis and prediction of luminescent function by computational science [Hasegawa]

Thanks to quantum chemical calculations, revealing that changes in molecular orbitals due to higher-order integration of chiral Eu(III) complexes have a strong effect on light-emitting properties (joint research with Taketsugu), further academic research and functional material development have advanced. Hasegawa reported the first observation of "activation energy in photoinduced energy transfer," which has not been elucidated before, by using the spectroscopic measurement of a Tb(III) coordination polymer. Although the existence of this activation energy was predicted by theoretical quantum calculation, this result is the first to prove by spectroscopy **(*Chem. Eur. J.,* 2018, selected cover picture)**. Hasegawa also submitted the review paper summarizing the related results of this research and the research trends in the world to an international academic journal.

Medical application of high-performance hydrogels inducing cell differentiation [Tanaka Group]

In ICReDD, which aims to combine computational science information science, and experimental science, the Tanaka group's goal is to create new integration research fields and apply the results to medical fields. Specifically, Tanaka et al. will create a new academic field "material genomics" that controls cell genomes using high-performance hydrogels and apply the results to cancer diagnosis/therapy and regenerative medicine. In conventional cell biology and molecular biology, cellular behaviors have been studied on artificially prepared culture dishes. Since the culture medium contains excess nutrients and growth factors, there is considerable dissociation in the surrounding microenvironment compared with *in vivo*, and there is a critical weakness that the experimental results do not necessarily reflect the *in vivo* situation. Cells as components of each organ can differentiate and proliferate in a soft surrounding environment and acquire physiological functions *in vivo*. Pathological changes also occur in this environment. The high-performance hydrogels developed by the Gong Group are considered to mimic the surrounding environment of cells from various organs in terms of various physical properties such as water content, elastic modulus, electric charge state, etc. In fact, their joint research has revealed that hydrogels can control cell differentiation and proliferation extremely rapidly. Furthermore, gel-based alterations of cellular phenotypes are not only transient responses but may permanently control the cell phenotype by inducing epigenomic alterations. The Tanaka group aims to establish a new academic research field and uncover the regulatory mechanism of the genome by biomaterials, and apply the results to cancer medicine, regenerative medicine, and discovery of therapeutic drugs.

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."

ICReDD Core Meeting

In December 2018, almost all PIs gathered to give research presentations and lively exchange ideas to promote collaboration research.

Preparation of the MiX Laboratory

As the first stage of facility development to promote collaboration research, new space has been prepared experimental MIX laboratory, communication space (ICReDD salon), and measurement equipment room in the main building of Creative Research Institution (CRIS) of Hokkaido University. Further, the infrastructure has been set up, including a high-performance computer for chemical reaction prediction, a 400MHz nuclear magnetic resonance analyzer, a single crystal X-ray structure analyzer, a draft chamber, various office rooms, etc. Decided to adopt 25 members (Co-PI, specially appointed associate professor, lecturer, assistant professor, postdoctoral researcher) to support the MIX laboratory. the following people will be as a part of core members supporting MiX Lab: Specially Appointed Associate Professor Mita (an experimental scientist from the School of Pharmaceutical Sciences and Pharmacy), Specially Appointed Assistant Professor Higashida, Postdoctoral Fellow Reyes and Botla (Sawamura Group), Specially Appointed Assistant Professor Kubota, Specially Appointed Assistant Professor Jin, Postdoctoral Fellow Kato (Ito Group), Specially Appointed Lecturer Kitagawa (Hasegawa Group), Postdoctoral Fellow Murugavel and Sarkar (Inokuma Group). While conducting collaborative research in the same place every day, these members will realize prediction of responses using AFIR, speed-up, and visualization of data processing using information science, and verification and materialization using experimental science. Currently, research is being conducted on AFIR-led synthesis of unnatural amino acids from CO_2, the discovery of new reactions with transition metals, and development of novel organic-inorganic hybrid materials.

Bottom-Up Collaborative Research (Weekly and Monthly Seminars)

Currently, the physical space where all researchers study in the same building has not been completed yet. To promote "regular and active communication among researchers for collaborative research" for young researchers, holding weekly and monthly seminars was examined, and they will start from April 2019. At weekly seminars, hold once a week during lunch time, young researchers make presentations in English (10 minutes) and hold discussions (20 minutes). At monthly seminars, after the latest research results are presented (30 minutes) by senior or young researchers, in-depth discussions are held (60 minutes). By attending these seminars, researchers can "discover" research partners, find such a lucky "chemistry" between excellent researchers, and conduct joint research through the bottom-up approach.

Top-Down Collaborative Research

At ICReDD, the integration of world top-level researches by PIs through the top-down approach and the development of world-leading collaboration fields have started.

The details of the various collaboration are described below.

Reaction mechanism analysis of organometallic catalyst and organic catalyst by computational science [Maeda, List, Sawamura, and Ito]

a) Joint research on the reaction mechanism of organometal-catalyzed enantioselective C-H borylation

Sawamura conducted collaborative work with Maeda combining experimental and theoretical studies for elucidating the reaction mechanism of originally developed catalytic enantioselective borylation reaction of inactive methylene C–H bonds (described above). This joint team successfully applied the AFIR automated reaction path search method to analyze the catalyst structure and elucidated the mechanisms of C–H bond cleavage and C–H bond chiral recognition ***(JACS, 2019)***. Thus, this collaborative research has succeeded in a precise analysis of the structure and the chemical reaction of a metal complex catalyst with extraordinary large molecular size and complexity, demonstrating that the AFIR method can boost and speed up the research of enantioselective catalysis.

b) Creation of reaction design guidelines by iterative calculation and experiment

In the chiral catalyst design of Markovnikov asymmetric borylation of aliphatic terminal alkenes, which has rarely been done, Ito revealed that the derivation of reaction design guidelines by computational science and the iterative verification by experimental science is an effective method in computational chemistry-led reaction development ***(Nat. Commun., 2018)***. The team aims to establish clear "reaction development methods" by collecting successful examples and to realize efficient reaction design by integrating with information science. Keeping this goal in mind, Maeda and Ito are conducting joint research on the structure of active species in solid-state reactions.

c) Joint research on the reaction mechanism of the organic catalyst

Maeda and List have been working on the reaction mechanism of strongly acidic chiral organocatalyst that List newly developed. (paper in progress).

Catalysis Design and Prediction by Information Science [Takigawa, Varnek, and other researchers]

a) Materials and Catalyst Development by Materials Informatics

Takigawa, the chief researcher of the Information Team, whose specialty is machine learning, which is not necessarily related to chemistry, but information science. He has participated in the JST PRESTO Materials Informatics area from 2015 to 2018, and in parallel with his own research agenda, he has exchanged information and searched collaborative seed research within the network of researchers in computational and experimental sciences. In this fiscal year, the seed research is in progress with five groups at ICReDD —the computational science team (Maeda and Taketsugu groups), the experimental science team (Ito group), the information science team (Arimura and Komatsuzaki groups)— and the Institute for Catalysis at Hokkaido University, respectively. Further, he presented various papers both at home and abroad, including the Society of Computer Chemistry of Japan, the Catalysis Discussion Group, the Information Processing Society of Japan: SIG Mathematical Modeling and Problem Solving, the Japanese Society for Artificial Intelligence: SIG on Fundamental Problems in Artificial Intelligence, and the 21st Information-Based Induction Sciences Workshop. He has also long been involved in bioinformatics, an integrated field, and has been applying informatics to the elucidation of life phenomena by multimolecular complex systems, including cellular competition for cancer cells **(*Cell Reports*, 2018)**, the use of machine learning for peptide identification by mass spectrometry (Presentation at a Japanese study group), and the regulation of transcription termination by transcription elongation regulators (submitted).

b) Development of new functional molecule by chemoinformatics

Chemoinformatics is an interdisciplinary field at the intersection of different disciplines: chemistry, biology, physics, mathematics, and computer science. Regarding this field, Takigawa and Varnek, et al. have been actively conducting methodological researches about the development of Condensed Graphs of Reactions or Generative Topographic Mapping techniques and related software tools. The development of new bromodomain inhibitors (L. Hoffer *et al.*, ***J. Med. Chem.,*** **2018**) resulted from the group's collaboration with synthetic and medicinal chemists from the University of Marseille (France). Further, research on the database of antimalarial compounds has been conducted through close partnership with the medicinal chemists from the University of Strasbourg.

Computational scientific design of functional materials brought by excited states [Maeda, Hasegawa, and Taketsugu]

Research on the chiral emission function of lanthanide complexes

With regard to the development of chiral Eu(III) complexes exhibiting high circularly polarized luminescence properties, Hasegawa has been probing by combining ligands and europium ions through computational chemistry in cooperation with Maeda, the director of WPI-ICReDD. Furthermore, he has been collaborating with Taketsugu to clarify the quantum chemical relationship between the coordination structure and the luminescence properties of rare earth complexes. By combining theoretical chemistry with complex synthesis chemistry and photology, the team currently exploring new academic knowledge that would be difficult to achieve by studying only one field. The strong luminescent Eu(III) complex developed in this study can absorb ultraviolet light and emit red light; that is, by absorbing ultraviolet from the sun, it can irradiate light directly to chlorophyll, which is effective for plant growth. Based on the principle of light energy wavelength conversion, an agricultural film was developed by applying a rare earth complex exhibiting strong luminescence

properties to a polymer film. In a preliminary joint study with a professor of plant growth and plant anatomy (agriculture-industry collaboration), it was found that the use of this luminescent agricultural film in cultivating crops resulted in larger plants than before. The research results were highlighted by Japan Agricultural Cooperatives and HBC television in Hokkaido and were to be broadcast nationwide by television and distributed via Internet on April 13, 2019.

Online integration of reinforcement learning and measurement systems, development of annealing computer [Komatsuzaki, Tanaka and Hitachi, Ltd.]

The Komatsuzaki Group consists of a joint group of researchers in information science, measurement engineering (Raman spectroscopy), and cytopathology. Traditionally, the research collaboration has been done only one-way; that is, measurement data is passed to theoretical researchers for them to analyze, and mathematical modeling and simulations are conducted by theoretical researchers and their results are passed to experimental researchers. Contrary to this conventional way, the group aims to develop the framework of a highly interactive collaboration system, where the measurement results are instantly analyzed, the analyzed data is immediately fed back to the measurement system, and the measurement is online-controlled. The same concept of reinforcement learning has been applied to cancer drug screening in cooperation with the Tanaka group. As for business-academia collaboration, working on-site style is adopted for the joint research with Hitachi to create open innovations. A certain number of Hitachi researchers are stationed at Hokkaido University and are developing basic technology for annealing computer, which is expected to be applied to quantum chemistry.

Theoretical analysis of dynamic properties of double network (DN) gel and its application to cell control [Gong, Rubenstein and Tanaka]

With regard to the aforementioned "self-growing material", the Gong and Rubinstein groups are working to elucidate how the internal polymer is stretched and destroyed when the DN gel is deformed through the combination of theory and experiment. Studies to date have shown that the internal brittle polymer chains are stretched extremely and then broken during DN gel stretching. These findings are important to understand and optimize the relationship between gel deformation and induction of chemical reactions.

The Gong and Tanaka groups are promoting "material genomics" that control cells and tissues based on their interactions with substrate materials. This is an ambitious collaboration area in which, by considering the signal transduction between a substrate gel with various chemical species and elastic modulus and cells and tissues as a chemical reaction, the differentiation, and growth of cells and tissues are controlled based on the properties of the substrate material to lead to medical applications. To date, the behavior of differentiation and dedifferentiation of certain cells has been successfully controlled only by the properties of the culture substrate gel without using additives, and this method is to be applied to medicine going forward.

Synthesis and structural analysis of "carbonyl cord" [Inokuma and outside researchers]

Inokuma initiated various collaborative research efforts to investigate what kind of conformation of the "carbonyl cord", a long-chain aliphatic carbonyl compound, takes in solution and how it changes in the presence of ions and organic compounds, leading to reactions and functions. To measure the ionic conductivity of carbonyl cord in solid or solid solutions with metal salt, joint research has started with J. Mindemark of Uppsala University in Sweden and Masahiro Fujita of Sophia University. Related to this, to elucidate theoretically and experimentally the structural change in the presence of metal ions, ion mobility mass spectrometry was also conducted in collaboration with Ichiro Ohara of Tokushima Bunri University. Currently, they are about to start collaborative research using computational science to analyze the data theoretically.

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 specially appointed faculty members and postdoctoral fellows who are newly employed at ICReDD will be selected through international open recruitment (using Nature and the newly created website etc.). As a result, there were many applicants from around the world and selected excellent researchers, and approximately 30% of all researchers will be foreign nationals (as of April 1, 2019, there are 13 foreign researchers out of total 43 researchers).

To prepare for three world-class researchers (overseas PIs) from foreign research institutes to participate in collaboration works, research plans were discussed via Skype and at the meeting in March when overseas PIs were invited on-site. There were six visitors from overseas (Appendix 5) so far, and international recognition has been raised.

Recruitment of Co-PIs (specially appointed staff such as specially appointed associate professors and assistant professors) has also been started and the research is expected to go into full swing in FY2019.

In order to perform research support and management operations in English at ICReDD, the following two research supporting units were established under the administrative director: a research strategy unit (international planning and public relations) (4 people), which sets up and provides an environment where researchers can comfortably work on research, and a management planning unit (general affairs and accounting) (9 people), which is directly linked to the university headquarter to perform day-to-day jobs. Moreover, a support system through the university URA was established. With these support members, a plan to build an international support hospitality system at ICReDD has being discussed, to support the daily lives of overseas PIs, researchers, and their families, so that they can focus on their research in peace.

The international activities of each PI are as follows.

Taketsugu received professors from China in FY2018; Prof. Yang at Beijing Normal University and Assoc. Prof. Yu at Northwest University. They stayed for several days to hold a public lecture and discuss the possibility of joint research. In FY2019, Prof. Keshavamurthy at IIT Kanpur University in India is invited as a Specially Appointed Professor through the researcher invitation system at Hokkaido University (for six months from May to October). He is planning to conduct joint research in cooperation with Maeda and Komatsuzaki regarding chemical reaction dynamics and do an intensive seminar for students. Prof. Wojcik will visit from Poland in late May to discuss tunneling in excited state proton transfer. From the beginning of 2019, Taketsugu et al. wrote a paper about the joint research on anharmonic vibrational theory with Prof. Mark Gordon, who has developed the quantum chemistry calculation program GAMESS. Also, in collaboration with Prof. Yang at National Taiwan University, Taketsugu et al. have submitted a paper about the experiments and theories on supramolecules. Taketsugu published twenty papers in 2018, five of which were internationally co-authored papers.

As the Chair of the Working Group on Soft Matter Physics of International Union of Pure and Applied Physics, Rubinstein has started to coordinate the International Soft Matter Summer School (Hokkaido in 2017, Cargese in France in 2020, USA in 2023) and International Soft Matter Conference (Europe ISMC 2019, USA ISMC 2020, Asia ISMC 2021 in Osaka). He is also the U.S. unit leader of Global Station for Soft Matter in GI-CoRE, in charge of Polymers & Soft Matter for F1000Prime, and a member of the International Advisory Board of the DoDyNet Initial Training Network. He will attend as a summer school instructor in Capri, Italy in July 2019.

Arimura had a collaborative research between Hokkaido University and University of the Pisa in Italy on substructure enumeration algorithms. Under a sparsity measure, called 'girth', they developed constant time enumeration algorithm that finds all substructures without duplicates in an input graph with bounded girth for the classes of connected subgraphs and connected induced subgraphs. This result was presented in the 29th International Conference on Combinatorial Algorithms (Kurita, Wasa, Conte, Uno, and Arimura, IWOCA 2018).

Komatsuzaki serves as an editorial board of Scientific Reports (Chemical Physics) and coedits Virtual Special Issue (VSI) of J. Phys. Chem. B (with Profs. Steve Presse at Arizona State University (visited Sapporo 2018/10/29-11/11) and Patrick Senet at University of Burgundy). In collaboration

with Assoc. Prof. Jason Green (University of Massachusetts Boston) and Prof. James P. Crutchfield (UC Davis, visited Sapporo 2019/1/13-14) through the JSPS Bilateral Program, he researches on complex chemical reaction systems. He serves as a visiting professor at ENS de Lyon (Nov 7-Dec 9). His lab is international, which is composed of members from various countries (Bangladesh 2, USA 2, France 2, Japan 5), and English is the main language in his lab. His lab members also have diverse backgrounds, such as chemical physics, biological physics, applied mathematics, information science, measurement engineering, and biology, so that young researchers, including Ph.D. students, can naturally acquire skills of an international collaboration of different disciplines.

In February 2018, Takigawa gave presentations at an international symposium held in the JST PREST area in which he participated alongside the prominent invited speakers and introduced WPI-ICReDD center as well as his research results. At a social gathering after the symposium, Takigawa exchanged opinions with guest speakers about the challenges at ICReDD. In addition, at an international symposium held at ICReDD in March, Takigawa had in-depth information exchange and discussions with Varnek, an overseas PI of the information group, and discussed holding a joint workshop in France in the future.

Varnek has conducted theoretical research on chemical reactivity using the CGR approach in collaboration with scientists at Kazan Federal University (Russia). His two Ph.D. students from Strasbourg and Kazan (Mr. T. Gimadiev and Ms. M. Glavatskikh) contributed to Publications 1-3. A project focusing on big chemical data analysis (D. Judd *et al.*, 2018) using chemical cartography was realized in collaboration with a partner at Taras Shevchenko University of Kiev (Ukraine) and a virtual screening tool with different comparative structures (Zhenin *et al.*, 2018) was conducted jointly with scientists at Bar-Ilan University (Israel).

Sawamura coordinates the collaboration of organic chemistry among eight Asian countries and regions as a coordinator of "Asian Cutting-Edge Organic Chemistry Promotion Network", commonly known as "ACP". As the chair of the steering committee of coordinators from each country at the 13th International Conference on Cutting-Edge Organic Chemistry in Asia (ICCEOCA-13), which was held in Bangkok, Thailand in November 2018, Sawamura not only promoted collaborative research and cultural exchange in Asian countries but also worked on raising the recognition of newly established ICReDD.

Inokuma attended the MIRAI seminar, jointly organized by eight Japanese and seven Swedish universities, and presented the research progress to construct a platform for international collaborative research, especially among younger researchers. As a guest speaker at an international symposium, he emphasized the strong points and world-class research results at ICReDD.

Hasegawa conducts joint research with Prof. Max, a leading complex chemistry researcher in Australia, and is also engaged in the exchange of young researchers. Recently, Hasegawa and Max successfully prepared novel lanthanide complexes with excellent luminescence properties and reported the research result (***Dalton Trans.***, **2019**).

Hasegawa is planning to organize Japan-Germany Joint Molecular Imaging Symposium held at Hokkaido University in September 2019. At this symposium, he plans to conduct research collaborations and exchanges with top Japanese and German academic researchers in molecular imaging, including JAXA members, DLR members (German Aerospace Center), and researchers at University of Hohenheim.

In collaboration with Prof. Ford (USA), Prof. Garry (Canada) and Prof. Lo (Hongkong), Hasegawa is planning to organize an international symposium on "Photofunctional Chemistry based on Metal Complexes and/or Supramolecules" for Pachifichem 2020 (Hawaii).

Gong is a core member of Global Station for Soft Matter of Global Institution for Collaborative Research and Education (Soft Matter GI-CoRE) at Hokkaido University and conducts international collaborative research in close coordination with 9 members of the France unit and 6 members of the U.S. unit in addition to 27 members of the Hokkaido University unit. Rubinstein, an overseas PI, is the unit leader of the U.S. unit and is promoting joint research at ICReDD utilizing the GI-CoRE platform of collaboration.

In the Tanaka Group, integrated research on material genomics has been conducted by one foreign postdoctoral fellow of the Gung Group two years ago, and one foreign graduate student (doctoral course) joined the research last year. In addition, the Tanaka Group added foreigners in the master's course of the second semester of the Graduate School of Life Science's Soft Matter Program in April of this year and has started interdisciplinary research under the mentorship of Assoc. Prof. Tsuda, who concurrently works at ICReDD. As such, the group has been creating an international research environment.

4. Making Organizational Reforms

* 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.

Environment setup to encourage collaboration study

In order to create a collaboration area in three fields and establish an international research and education environment, Institute for Chemical Reaction Design and Discovery (ICReDD) was established within Creative Research Institution (CRIS), a university-wide organization, and the renovation of the main building of CRIS has started. "Mix-Lab Space" and "Inter Science Cafe Space (salon)" will be available from FY2019.

Furthermore, in collaboration with the Global Facility Center (GFC) at CRIS, the plan has been discussed to maintain and manage the analytical instruments to be provided for ICReDD and an environment where researchers can focus on their research has been established.

As for the soft environment, to support a smooth start of research at ICReDD, the support systems for new faculty on-board and integration research initiation have been developed. Also, in order for Japanese researchers and relevant students to be able to collaborate with foreign researchers efficiently and to accelerate integration research, holding weekly and monthly seminars was examined, and they will start from April 2019.

System reform

The establishment of "MANABIYA (Japanese for 'school')" system has been started to discuss. The goals of this system are to promote internationalization and diversity at ICReDD by attracting young researchers and graduate students from home and abroad who conduct joint research for about three months, to create a network, and to pass the integrated research of computational, information and experimental sciences onto researchers and graduate students all over the world. In addition, since there were inquiries from several companies regarding the MANABIYA system, an outline explanation was given, and the possibility of understanding of the company's system needs and acceptance of company researchers was held in February 2019. At the center operation committee, we discussed future measures such as the use of e-learning. Centered on Maeda, he accepted off-campus researchers using the academic consulting system.

Establishment of a management system

The steering committee was set up to discuss important items about ICReDD. The committee consists of the director, the vice director, the administrative director and some PIs on-site who are designated by the director. Six meetings were held in FY2018 and decided on hiring of specially appointed faculty members and implementation guidelines of the start-up support systems, etc. Moreover, the director meeting has been held by the director, the vice director, the administrative director, the research strategy unit manager, and the management planning unit manager and supported the director's decision-making. As a place to gather young researchers and promote exchange ideas, the young working group have been held. In this way, a management system for smooth operation at ICReDD has been established.

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 the 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.

Taketsugu applied as a representative for the FY 2019 budget request project for strengthening the Hokkaido University functions and decided to work on a project continuing for 5 years with the largest budget (FY 2019 budget: 125,784,000 yen) among budget request projects. His project is called "Photo-Excitonix Research Center for Prediction and Advanced Utilization of Photoexcited State Control" and it is a large-scale project involving 24 researchers from 12 departments in Hokkaido University. Similar to ICReDD, it is based on computational science and data science with the participation of experimental researchers in a wide range of fields including chemistry, environment, pharmacy, and medicine, with the aim of creating new materials and disseminating information to society. The subjects are limited to those involving excited states, and furthermore, it is based on microscope technology, with the three pillars of environment/energy, diagnosis, and cancer treatment as exits. Joint computation-experimental research has been conducted with Mikako Ogawa, a professor of pharmacy at Hokkaido University, who is a key person in the development of near-infrared therapeutics related to optical cancer immunotherapy, which is rapidly attracting attention since its clinical trials began in 2018. The research also involves researchers at Hokkaido University Hospital and integration research area is being created while collaborating with ICReDD.

At Hokkaido University, there is the system of the International Collaborative Research and Education Bureau (GI-CoRE: Global Institute for Collaborative Research and Education), which promotes the joint research beyond the framework of graduate schools of separate departments, and six global stations have been established. The Tanaka group belongs to the Institute of Medical Research as well as Global Station for Soft Matter, which Professor Gong of the Advanced Life Science Institute started and has been conducting joint research. In particular, for the purpose of developing human resources who can understand high-performance hydrogels and can conduct research on biological systems, one foreign graduate student in a doctoral course and one post-doctoral student have been accepted, and research has been conducted by physically using equipment in both laboratories. By developing this mechanism, an environment is in place for further research in the field of material genomics. In addition, as collaboration research at ICReDD, a system will be constructed to design and discover biomaterials by using information science to predict changes in genomes based on materials.

6. Others

* Describe what was accomplished in the center's outreach activities in FY 2018 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

The 1st International Symposium was held on March 12 and 13, 2019, inviting researchers from Japan and overseas to introduce the purpose of ICReDD and the integration research conducted at ICReDD. In addition, at the WPI Science Symposium (December in Nagoya) and the 2019 AAAS Annual Meeting (February in Washington), the activities of ICReDD were introduced.

In addition, a logo, home page, and SNS (Facebook) were created, and promotional brochures, banners, pens, clear folders, neck-holders, pin badges, stickers, etc. were prepared and distributed at the above-mentioned symposiums, etc., with the aim of raising awareness of ICReDD.

Media coverage

At the time of acceptance for WPI, an interview with the director was reported at NHK Sapporo Broadcasting Station, and there were media reports on the research by Taketsugu (1 report), Komatsuzaki (1 report), Ito (10 reports), Gong (9 reports) and Hasegawa (1 report) (total 23 reports (Appendix 7)).

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 "Actions required and recommendations" in the Follow-up report, then note how the center has responded to them.
* For the center launched in FY 2018, describe the status of response to the pointed items in "Major points that need to be improved" of "The screening result for WPI centers launched in FY 2018."
* However, if you have already provided this information, indicate where in the report.

1. The project has potential to exert a significant impact, but it appears to overestimate what can be achieved. A serious risk exists if there is an incomplete strategy for selecting target molecules from a wide field of societal demands. ICRD should develop an efficient strategy for narrowing down the potential targets. It will also be necessary to articulate both short- and long-term goals.

Via the MANABIYA fostering system, the ICReDD will establish national and international collaborations with other research centers by i) developing a new area of research (CReDD), ii) restructuring the organization of Hokkaido University, and iii) establishing the new graduate school "School of Chemical Reaction Design and Discovery". The integrated research on CReDD should lead to the development of highly efficient chemical reactions that should afford high-value-added chemicals with applications in agro- and environmental chemistry, pharmaceutical and materials science, medical technology, as well as energy and resource management. The target reactions and molecules are carefully selected based on the impact to the society through discussion among broad research communities and with many companies. In the early stage of the ICReDD, we will select model reactions for proof of concept. Then, in the middle to the later stage, reactions that have a significant impact on the society will be carefully selected based on the discussion with the broad scientific community members and companies.

2. Cancer cells are stated to be one of the major targets of the research. However, it is a rather simplistic view that the proposed research will lead to rapid and complete eradication of cancer by identifying cancer stem cells with hydrogels. A more careful discussion on designing this strategy should be carried out with experts in cancer stem-cell biology and clinical cancer therapy.

Cancer cells are one of the major targets of the research. For rapid and complete eradication of cancers, mechanisms of cancer stem cells (CSCs) induced by hydrogels developed in category 2 should be clarified by the AFIR method, with respect to a regulation of monomeric hydrogels. Novel strategy of liquid biopsy targeting circulating tumor cells will be developed using the materials collaborating with researchers of National Cancer Center Research Institute (Tokyo), leading to early detection and diagnosis of cancer. As clinical cancer therapy, precision medicine should be performed at Hokkaido University Hospital, including Oncology group, using oncogene panels such as MSK-IMPACT collaborating with Dr. Marc Ladanyi (Memorial Sloan-Kettering Cancer Center, MSKCC, New York, USA), who is a developer of the panel. In addition, chemical libraries that have been developed at Hokkaido University are available for drug screening for identifying CSCs-targeted anticancer drugs. One ultimate goal is to predict and prevent human diseases through CReDD.

3. The involvement of foreign PIs (20% effort) is insufficient for carrying out meaningful research activities at the center. Effort should be made to increase the percentage of time they spend on site. Although the Co-PI system is useful, it cannot replace the actual presence of PIs.

Foreign PIs stays in ICReDD for enough period, e. g. two months, contribute the fusion research in cooperation with Co-PIs by frequently using TV-conference to increase the percentage of time they spend on site. Since foreign PIs will simultaneously serve at their home institutions and the ICReDD, we will establish research groups for foreign PIs within our center and employ Co-PIs and research staff (i.e., specially appointed associate and assistant professors as well as postdoctoral fellows) to support and manage the research groups in close collaboration with the foreign PIs.

4. ICRD should develop an international network of researchers and institutions on chemical reaction design, taking advantage of the mobility of "dry" research in computational and information sciences. This would also help ease the isolation of ICRD from the science community in Japan-isolation that stems from there being no Japanese PIs from outside Hokkaido University at the center. Although the MANABIYA system is useful for training young scientists, it is not considered effective for research collaboration done by scientists who join the center from abroad.

In 2014, as part of its mid-to-long-term strategy, Hokkaido University has established the Global Institution for Collaborative Research and Education (GI-CoRE), with a faculty organization scheme that is under the direct control of the president of the university. This institution has launched six GI-CoRE centers in research fields that are considered to be the strengths of the university and promoted organized international collaborative research with voluntary funding. Among these

centers, especially the Soft Matter GI-CoRE and the Information Science GI-CoRE are currently used as centers of collaborative research that would be connected to the ICReDD. These GI-CoRE centers will be carefully incorporated into the ICReDD as key sub-organizations. In the Soft Matter GI-CoRE, Prof. Gong will serve as a representative to promote strong collaborative research. Furthermore, we will continue to promote and support systematic collaboration with Duke University (Soft Matter GI-CoRE) and the University of Massachusetts Amherst (Information Science GI-CoRE). We will also collaborate closely with Emory University (computational chemistry), the Swiss Federal Institute of Technology in Zurich (ETH Zurich; experimental science), Peking University (experimental science), and Stockholm University (experimental science) through collaborative research and the MANABIYA system, thus generating an environment that encourages international collaboration while promoting interactions among researchers. We will try to expand the collaboration network further by actively interacting with researchers both in Japan and abroad.

5. A strategy to attract international scientists and postdocs to ICRD and to Hokkaido University is not given sharp focus in the current plan. ICRD and Hokkaido University need to take a more active role in developing an infrastructure and environment to support the foreign researchers who will be involved in the project. It is important that international postdocs believe that they can launch and develop their careers at ICRD and in Hokkaido University.

Described in the realizing an international research environment (Page 10-13).

In addition, the international hospitality support system by utilizing the resources of the already established GI-CoRE and the Institute for International Collaboration at Hokkaido University, will provide assistance for the foreign PIs and their families regarding non-research-oriented issues such as visas and housing to ease the transition. As a result, the foreign PIs will be disengaged from the affairs of daily life and it will promote the efficiency of their research activities. The outstanding researchers at the ICReDD will be appointed following a competitive selection process and offered tenured faculty positions in order to ensure the continuation of internationally leading education and research at Hokkaido University.

6. It is not clear how ICRD will create a constructive relationship with industry. A concrete strategy for transferring knowledge and research outcomes between the center and the industrial sector is missing.

CReDD and MANABIYA will be firmly rooted in the university’s organizational structure via the establishment of the "Graduate School of Chemical Reaction Design and Discovery”. The necessary reorganization and integration of existing graduate school(s) will begin after the sixth year of the program. We also will create a permanent organization for the acquisition of private funding by e.g. hosting researchers from industry and establishing research consortia with industrial partners. Concretely, managers at Institute for the Promotion of Business-Regional Collaboration, Hokkaido University, will mediate between researchers at ICReDD and corporation members of the research consortia to promote research collaboration.

Appendix 1 FY 2018 List of Center's Research Results and Main Awards

1. Refereed Papers

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

(1) Divide the papers into two categories, A and B.

A. WPI papers

List papers whose author(s) can be identified as affiliated with the WPI program (e.g., that state "WPI" and the name of the WPI center (WPI-center name)). (Not including papers in which the names of persons affiliated with the WPI program are contained only in acknowledgements.)

1. Original Article

(1) Kazuhiro Yachi, Masumi Tsuda, Shinji Kohsaka, Lei Wang, Yoshitaka Oda, Satoshi Tanikawa, Yusuke Ohba, and Shinya Tanaka, "miR-23a promotes invasion of glioblastoma via HOXD10-regulated glial-mesenchymal transition", *Signal Transduct. Target. Ther.*, **2018**, *3*, 33. (DOI: 10.1038/s41392-018-0033-6)

(2) Ken-ichi Hoshino, Tasuku Nakajima, Takahiro Matsuda, Takamasa Sakai, and Jian Ping, Gong, "Network elasticity of a model hydrogel as a function of swelling ratio: from shrinking to extreme swelling states", *Soft Matter*, **2018**, *14*, 96930-9701. (DOI: 10.1039/c8sm01854e)

(3) Ken Sakaushi, Andrey Lyalin, Tetsuya Taketsugu, and Kohei Uosaki, "Quantum-to-Classical Transition of Proton Transfer in Potential-Induced Dioxygen Reduction", *Phys. Rev. Lett.*, **2018**, *121*, 236001. (DOI: 10.1103/PhysRevLett.121.236001)

(4) Ran Shi, Tao Lin Sun, Feng Luo, Tasuku Nakajima, Takayuki Kurokawa, Yue Zhen Bin, Michael Rubinstein, and Jian Ping Gong, "Elastic-Plastic Transformation of Polyelectrolyte Complex Hydrogels from Chitosan and Sodium Hyaluronate", *Macromolecules*, **2018**, *51*, 8887-8898. (DOI: 10.1021/acs.macromol.8b01658)

(5) Kunpeng Cui, Tao Lin Sun, Xiaobin Liang, Ken Nakajima, Ya Nan Ye, Liang Chen, Takayuki Kurokawa, and Jian Ping Gong, "Multiscale Energy Dissipation Mechanism in Tough and Self-Healing Hydrogels", *Phys. Rev. Lett.*, **2018**, *121*, 185501. (DOI: 10.1103/PhysRevLett.121.185501)

2. Review article

(No publication)

3. Proceedings

(No publication)

4. Other English article

(No publication)

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.)

1. Original article

(No publication)

2. Review article

(No publication)

3. Proceedings

(No publication)

4. Other English article

(No publication)

Newly selected centers in FY2018 are to list papers under category C below (in addition to categories A and B above).

C. Previously published important WPI-related papers
List previously published papers that provided the basis for the center's research project plan. (Around 30 papers as a yardstick.)

1. Original article

(6) Bae Han Yong, Hoefler Denis, Kaib Philip S. J., Kasaplar Pinar, De Chandra Kanta, Doehring Arno, Lee Sunggi, Kaupmees Karl, Leito Ivo, and List Benjamin, "Approaching sub-ppm-level asymmetric organocatalysis of a highly challenging and scalable carbon-carbon bond forming reaction", *Nat. Chem.*, **2018**, *10*, 888-894. (DOI: 10.1038/s41557-018-0065-0)

(7) Button Brian, Goodell Henry P., Atieh Eyad, Chen Yu-Cheng, Williams Robert, Shenoy Siddharth, Lackey Elijah, Shenkute Nathan T., Cai Li-Heng, Dennis Robert G., Boucher Richard C., and Rubinstein Michael, "Roles of mucus adhesion and cohesion in cough clearance", *Proc. Natl. Acad. Sci. U. S. A.*, **2018**, *115*, 12501-12506. (DOI: 10.1073/pnas.1811787115)

(8) Dalafu Haydee A., Rosa Nicholas, James Derak, Asuigui Dane Romar C., McNamara Michael, Kawashima Akira, Omagari Shun, Nakanish Takayuki, and Hasegawa Yasuchika, Stoll Sarah L., "Solid-State and Nanoparticle Synthesis of EuS_xSe_{1-x} Solid Solutions", *Chem. Mat.*, **2018**, *30*, 2954-2964. (DOI: 10.1021/acs.chemmater.8b00393)

(9) Gatzenmeier Tim, Kaib Philip S. J., Lingnau Julia B., Goddard Richard, List Benjamin, "The Catalytic Asymmetric Mukaiyama-Michael Reaction of Silyl Ketene Acetals with α,β-Unsaturated Methyl Esters", *Angew. Chem. Int. Ed.*, **2018**, *57*, 2464-2468. (DOI: 10.1002/anie.201712088)

(10) Gatzenmeier Tim, Turberg Mathias, Yepes Diana, Xie Youwei, Neese Frank, Bistoni Giovanni, and List Benjamin, "Scalable and Highly Diastereo- and Enantioselective Catalytic Diels-Alder Reaction of α,β-Unsaturated Methyl Esters", *J. Am. Chem. Soc.*, **2018**, *140*, 12671-12676. (DOI: 10.1021/jacs.8b07092)

(11) Harada Tomoya, Ueda Yusuke, Iwai Tomohiro, and Sawamura Masaya, "Nickel-catalyzed amination of aryl fluorides with primary amines", *Chem. Commun.*, **2018**, *54*, 1718-1721. (DOI: 10.1039/c7cc08181b)

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3. Proceedings
（No publication）

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

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

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

  C. Previously published important WPI-related papers

(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.

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

- List up to 10 main presentations during FY 2018 in order from most recent.
- For each, write the lecturer/presenter's name, presentation title, conference name and date(s)

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
2019.3.4 -2019.3.8	Michael Rubinstein	Structure and Dynamics of Coacervates formed by Oppositely Charged Polyelectrolytes	March Meeting of the American Physical Society
2019.2.18	Alexandre Varnek	Chemography Concept in Chemical Space Analysis	Invited lecture; Institute of Supramolecular Science and Engineering
2019.1.24	Hajime Ito	Gold(I) Isocyanide Complexes with Mechanical Response Properties	The 4th International Conference on Aggregation Induced Emission
2018.12.16 -2018.12.20	Tetsuya Taketsugu	On-the-fly molecular dynamics approach to photoisomerization of stilbene derivatives	10th Asian Photochemistry Conference (APC2018), Taipei, Taiwan
2018.12.16 -2018.12.20	Yasuchika Hasegawa	Luminescent Eu(III) coordination polymers for organic EL devices	10th Asian Photochemistry Conference (APC2018), Taipei, Taiwan
2018.12.10 -2018.12.11	Jian Ping Gong	Multi-scale Design of Hydrogels with Reversible Sacrificial Bonds -From Toughness to Adhesion to Composites –	Soft Matter Physics: from the perspective of the essential heterogeneity
2018.12.4 -2018.12.7	Yasuchika Hasegawa	Lanthanide coordination polymers with strong luminescent and photo-functional properties	The 12th SPSJ International Polymer Conference (IPC2018)

2018.11.1	Satoshi Maeda	Reaction Path Network and its Analysis	The 18th Japan-Korea Joint Symposium on Organometallic and Coordination Chemistry
2018.11.1	Hajime Ito	Mechanical Response of Gold(I) Isocyanide Complexes via Crystal Structure Change	The 18th Japan-Korea Joint Symposium on Organometallic and Coordination Chemistry
2018.10.29 -2018.10.31	Masaya Sawamura	Catalytic Enantioselective Borylation of Unactivated Methylene C–H Bonds	The Junior International Conference on Cutting-Edge Organic Chemistry in Asia, Singapore

3. Major Awards

- List up to 10 main awards received during FY 2018 in order from the most recent.
- For each, write the recipient's name, the name of award, and the date issued.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
2019.3.17	Tetsuya Taketsugu	The CSJ Award for Creative Work, "Ab Initio Elucidation of Electronically-Excited Reaction Processes and Dynamics"
2018.2.14	Masaya Sawamura	Synthetic Organic Chemistry Award
2019.1.17	Tasuku Nakajima	10^{th} RSC Meeting RSC Soft Matter Presentation Award
2018.12.25	Satoshi Maeda	World Association of Theoretical and Computational Chemists The Dirac Medal 2019
2018.10	Michael Rubinstein	Bingham Medal, Society of Rheology

Appendix 2 FY 2018 List of Principal Investigators

NOTE:

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

*In the case of researcher(s) not listed in the latest report or in the proposal for newly selected centers in FY2018, attach a "Biographical Sketch of a New Principal Investigator"(Appendix 2a).

<Results at the end of FY2018> **Principal Investigators Total: 14**

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	39	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	54	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	
Michael RUBINSTEIN	62	Professor, Duke University	Ph.D., polymer physics	20	October 2018	- Primarily stays at Partner institution attends meeting (by Skype)	- Facilitate interdisciplinary research - Recruitment of researcher
Hiroki ARIMURA	53	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Graduate School of Information Science and Technology, Hokkaido University	Ph.D., data mining	80	October 2018	Usually stays at the center	
Alexandre VARNEK	63	Professor, University of Strasbourg	Ph.D. chemoinformatics	20	October 2018	- Primarily stays at Partner institution - participates in person with the ICReDD International Symposium - attends meeting (by Skype)	- Facilitate interdisciplinary research - Recruitment of researcher
Ichigaku TAKIGAWA	42	Associate Professor, Institute for Chemical Reaction Design and Discovery / Graduate School of Information Science and Technology, Hokkaido University	Ph.D., machine learning	80	October 2018	Usually stays at the center	
Tamiki KOMATSUZAKI	54	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	

Hajime ITO	51	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	57	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	51	Professor and Director, Max Planck Institute for Coal Research	Ph.D., Reaction design	20	October 2018	- Primarily stays at Partner institution - participates in person with the ICReDD International Symposium - attends meeting (by Skype)	- Facilitate interdisciplinary research - Recruitment of researcher
Yasuchika HASEGAWA	50	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	37	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	57	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	54	Professor, Institute for Chemical Reaction Design and Discovery / Global Institution for Collaborative Research and Education / Faculty of Medicine, Hokkaido University	Ph.D., tumor pathology	80	October 2018	Usually stays at the center	

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

Appendix 3-1 FY 2018 Records of Center Activities

1. Researchers and center staffs, 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, 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		

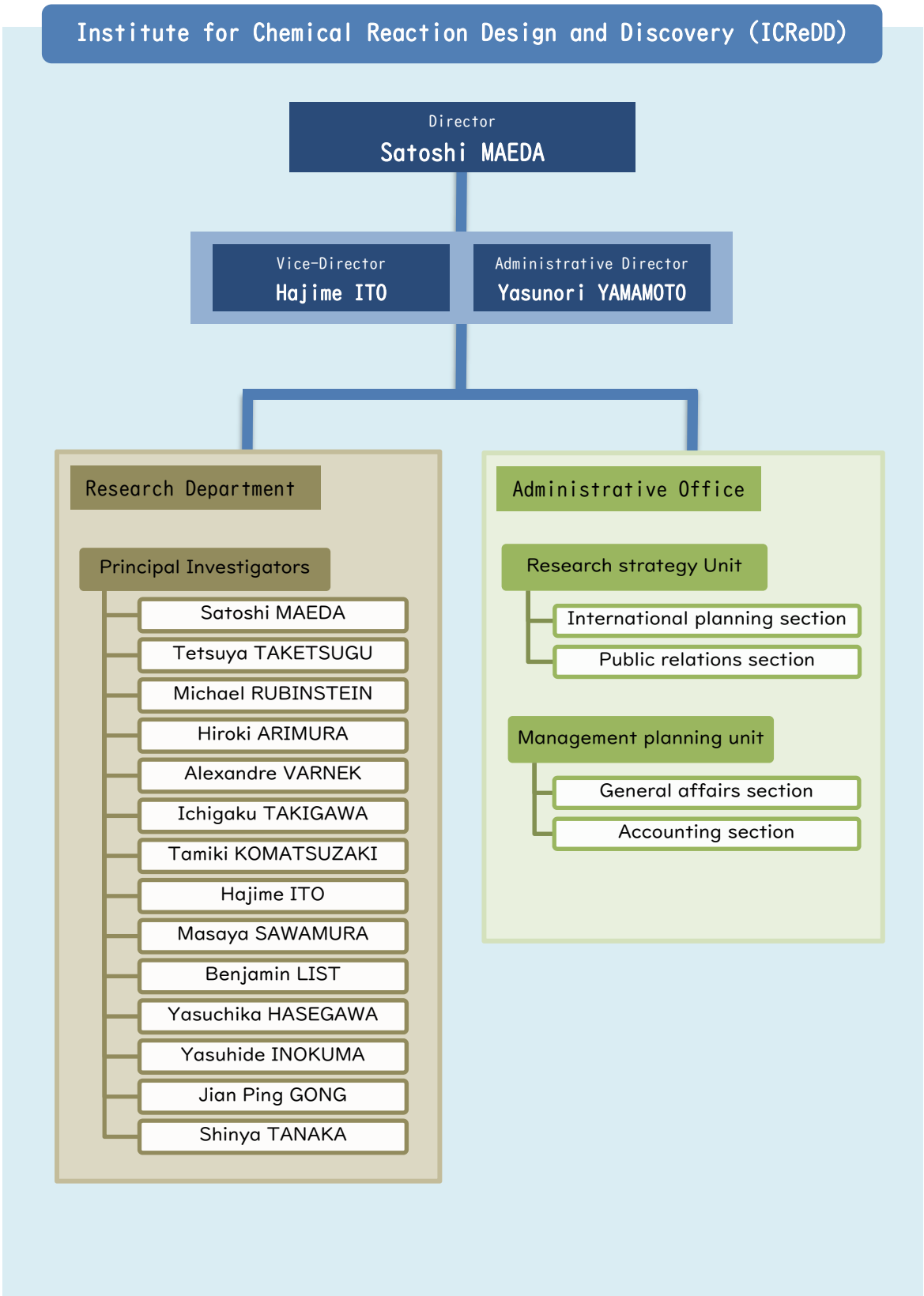
2. Holding international research meetings

- Indicate the number of international research conferences or symposiums held in FY2018 and give up to three examples of the most representative ones using the table below.

FY 2018: 1 meeting	
Major examples (meeting titles and places held)	Number of participants
1st ICReDD International Symposium FMI Hall, Hokkaido University (Sapporo) March 12-13, 2019	From domestic institutions: 202 From overseas institutions: 3

3. Diagram of management system

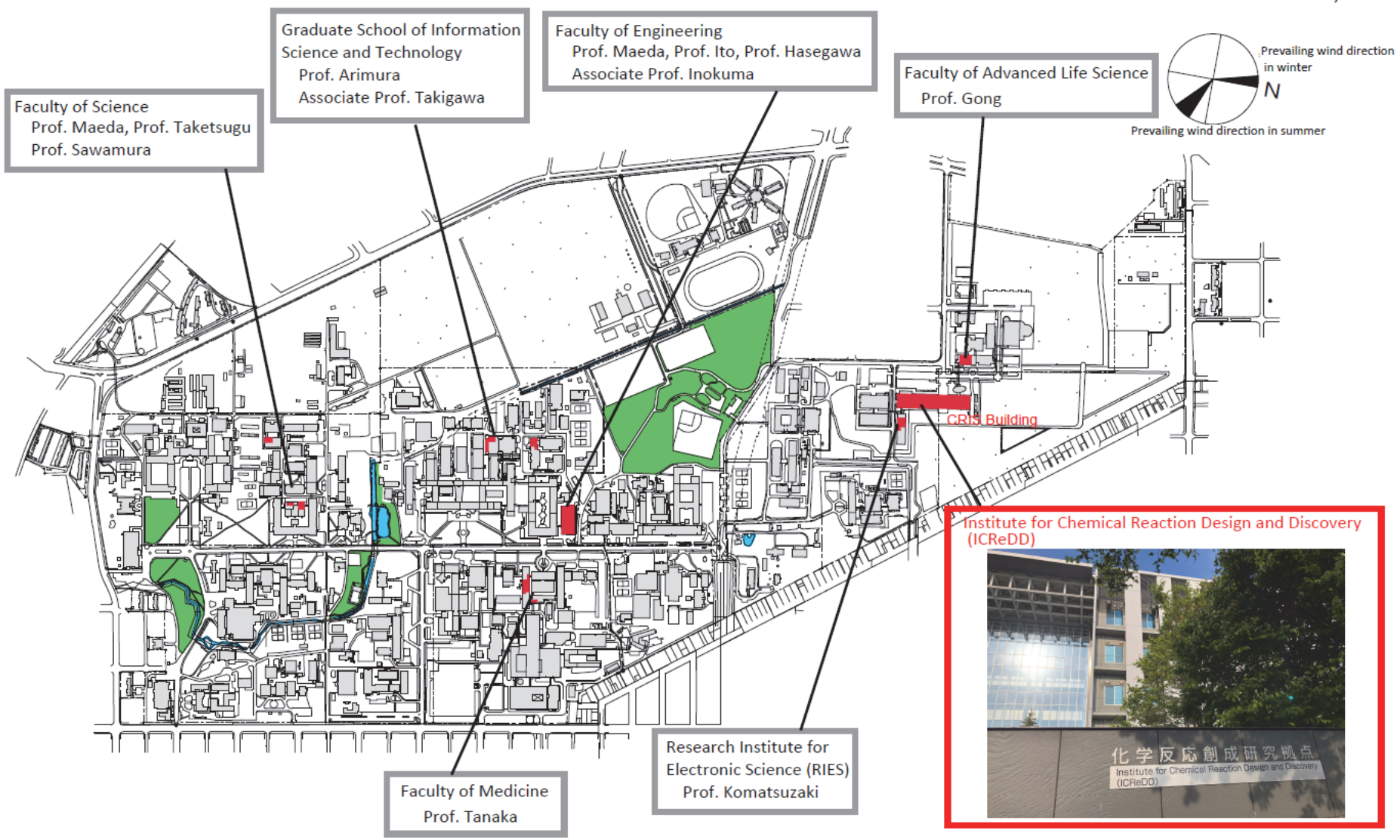
- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any new changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such 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, 2019



5. Securing external research funding*

External research funding secured in FY2018

Total: 141,169,161 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," and for "joint research projects" as listed under "Research projects" in Appendix 3-2, Project Expenditures.

Name	Provider	Project	Period	Total (in units of 1,000 yens)
Satoshi Maeda	Japan Science and Technology Agency	Strategic Basic Research Programs (CREST)	2014 - 2019	245,180
Hajime Ito	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research on Innovative Areas	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
Jian Ping Gong	Japan Science and Technology Agency	Impulsing Paradigm Change through disruptive Technologies Program (ImPACT)	2014 - 2019	170,000
Tamiki Komatsuzaki	Japan Society for the Promotion of Science	Grant-in-Aid for Scientific Research on Innovative Areas	2018 - 2022	98,280
Tamiki Komatsuzaki	Japan Science and Technology Agency	Strategic Basic Research Programs (CREST)	2016 - 2020	123,370

Appendix 3-1a FY 2018 Records of Center Activities

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

1-1. Number of researchers and other center staffs

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

a) Principal Investigators

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

(number of persons)

	At the beginning of project	At the end of FY 2018	Final goal (Date: March, 2023)
Researchers from within the host institution	11	11	11
Researchers invited from abroad	3	3	3
Researchers invited from other Japanese institutions	0	0	0
Total principal investigators	14	14	14

b) Total members

	At the beginning of project		At the end of FY2018		Final goal (Date: March, 2023)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	14		18		53	
Overseas researchers	3	21.4	4	22.2	16	30.2
Female researchers	1	7.1	3	16.7	6	11.3
Principal investigators	14		14		14	
Overseas PIs	3	21.4	3	21.4	3	21.4
Female PIs	1	7.1	1	7.1	1	7.1
Other researchers	0		4		39	
Overseas researchers	0	0	1	25.0	13	33.3
Female researchers	0	0	2	50.0	5	12.8
Research support staffs	0		0		28	
Administrative staffs	6		9		10	
Total number of people who form the "core" of the research center	20		27		91	

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" culumn may be changed to coincide with the project's actual content.

(Million yens)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center Director and Administrative Director	9	0
	Principal investigators (no. of persons):10	58	0
	Other researchers (no. of persons):3	5	1
	Administrative staff (no. of persons):10	30	3
	Allowance for principal investigators	5	5
	Subtotal	107	9
Project activities	International symposiums (no. of symposiums):1	2	2
	Public relations	2	1
	Consumables	17	15
	Desing and repair of facilities	7	6
	Relocations	5	5
	Facility Rentals	12	0
	Others	29	0
	Subtotal	74	29
Travel	Domestic travels (Host/Invited scientists)	1	1
	Overseas travels	2	2
	Travel cost for scientists on transfer (no. of domestic scientists):1	1	1
	Subtotal	4	4
Equipment	Costs of establishing and maintaining facilities	92	92
	Costs of equipment procured	233	216
	Depreciation of buildings	0	0
	Depreciation of equipment	0	0
	Subtotal	325	308
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	13	0
	KAKENHI	78	0
	Commissioned research projects, etc.	47	0
	Joint research projects	16	0
	Ohers (donations, etc.)	49	0
	Subtotal	203	0
Total		713	350

Costs (Million yens)

WPI grant in FY 2018	350
Costs of establishing and maintaining facilities	92
Facility repairs for Creative Research Institution	92
(Number of facilities:1 , 408 m²)	
Costs of equipment procured	216
High Performance Computer System	81
(Number of units:1)	
Nuclear Magnetic Resonance System	28
(Number of units:1)	
X-Ray Structural Analysis System for Single Crystals	56
(Number of units:1)	
Others	51

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

Appendix 5 FY 2018 Visit Records of Researchers from Abroad

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

Total: 6

	Name	Age	Affiliation (Position title, department, organization)	Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
1	Le Yu	34	Associate Professor, College of Chemistry & Materials Science, Northwest University	Reaction dynamics, Doctor of Science (Physical Chemistry)	Staying at the lab of Prof Masahiko Takahashi, Tohoku Univ, as JSPS Postdoctoral Fellowships for Research in Japan during 2017-2019.	2018.10.21. - 2018.10.25. (5 days)	Giving a lecture at the 87th Hokkaido Univ Theoretical Chemistry Seminar on 22 Oct. "Trajectory based on-the-fly nonadiabatic ab initio molecular dynamics with Zhu-Nakamura surface hopping algorithms." Visit Maeda lab and Taketsugu lab for collaborated work.
2	Steve Presse	37	Professor, Dept. of Physics and School of Molecular Sciences, Arizona State University	Chemical Physics/Biological Physics, Data Science. PhD Chemical Physics	Chem. Rev., 117, 7276 (2017); Proc. Natl. Acad. Sc. (2015), Nature (2015) Phys. Rev. Lett. (2013) Rev. Mod. Phys. (2013) Proc. Natl. Acad. Sc. (2010)	2018.10.31. (1 day)	Co-edition of J. Phys. Chem. B Virtual Special Issue (VSI)
3	James P. Crutchfield	63	Professor, Physics Department, University of California, Davis	Complex System Sciences, PhD Physics	Directors, Complexity Sciences Center, University of California, Davis; Network Dynamics Program, Santa Fe Institute; Computation, Dynamics, and Inference Program, Santa Fe Institute. Member, Committee on Information Technology and Creativity, Computer Science and Technology Board, National Research Council. Bernard Osher Foundation Fellow, San Francisco Exploratorium. Distinguished Visiting Research Professor, Beckman Institute, University of Illinois, Urbana Champaign.	2019.1.13. - 2019.1.14. (2 days)	short-term stay for joint research
4	John D. Tovar	-	Professor, Department of Chemistry, Materials Science and Engineering, Johns Hopkins University	Materials-oriented synthetic organic chemistry, pi-conjugated molecules and polymers, supramolecular chemistry, organic	Invitational Fellowship, Japan Society for the Promotion of Science (2019) Journal of Physical Organic Chemistry "Early Excellence" profilee (2012) Thieme Chemistry Journal Award (2010) NSF CAREER Award (2007) Princeton Applied Research New Young Investigator Award (2004) Baxter-IBNAM Early Career Development Award, Northwestern (2003) Wyeth-Ayerst Scholar, MIT (2001)	2019.2.3. - 2019.2.5. (3 days)	participation in symposium
5	Alexandre Varnek	63	Professor, Laboratory of Chemoinformatics, University of Strasbourg	Chemoinformatics	Member of Advisory Board and Guest Editor in "Molecular Informatics" Director of French national network in chemoinformatics (2011-2014)	2019. 3. 9. - 2019. 3. 15. (7 days)	participation as principal investigator talk on the ICREDD congress
6	Benjamin List	51	Professor and Director, the Max-Planck-Institut für Kohlenforschung	Organic chemistry, Organocatalysis	Gottfried Wilhelm Leibniz-Prize, German Research Foundation (2016), Thomson Reuters Highly Cited Researcher (2014, 2016) Arthur C. Cope Scholar Award, ACS (2014)	2019. 3. 11. - 2019. 3. 14. (4 days)	participation as principal investigator talk on the ICREDD congress

Appendix 6 FY2018 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2018 by each activity.
* Describe the outreach activities in the “6. Others” of Progress Report, including those stated below that warrant special mention.

Activities	FY2018 (number of activities, times held)
PR brochure, pamphlet	5
Lectures, seminars for general public	1
Participating, exhibiting in events	3
Press releases	4
Others（IYPT event)	1
Others（ICReDD goods)	7
Others（HP, SNS)	2

*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.

Appendix 7 FY 2018 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2018 resulting from press releases and getting reported.

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2018.10.28	NHK Sapporo	PI (Maeda): Mornig News (domestic) "Interview to Director of WPI-ICReDD"
2	2019.1.10	Nature Research BEHIND THE PAPER	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
3	2019.1.11	Nikkei Sangyo Shimbun	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
4	2019.1.11	National Institute for Environmental Studies web	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
5	2019.1.12	NHK	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
6	2019.1.15	Nikkan Kogyo Shimbun	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
7	2019.1.15	Selected as Nature Communications Editor's Highlights	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
8	2019.1.24	Highlighted in Chem Station	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
9	2019.1.31	New Scientist	PI (Gong) : Self-growing material could make muscles that become stronger with use" https://www.newscientist.com/article/2192376-self-growing-material-could-make-muscles-that-become-stronger-with-use/
10	2019.1.31	Chemical&Engineering News	PI (Gong) : "Stretchy hydrogel heals like muscle Material made from intertwined polymers gets stronger when stressed" https://cen.acs.org/materials/Stretchy-hydrogel-heals-like-muscle/97/i5
11	2019.2.1	Science World Report	PI (Taketsugu): "Current generation via quantum proton transfer" https://www.scienceworldreport.com/articles/60521/20190201/current-generation-via-quantum-proton-transfer.htm
12	2019.2.1	NHK Sapporo	PI (Gong): Research introduction regarding the paper, "Mechanoresponsive Self-growing Hydrogels Inspired by Muscle Training"
13	2019.2.1	Asahi Shimbun Digital	PI (Gong): Research introduction regarding the paper, "Mechanoresponsive Self-growing Hydrogels Inspired by Muscle Training"
14	2019.2.1	Wissenschaft aktuell (Germany)	PI (Gong) : "Fitnesstraining für Künstliche Fasern" https://www.wissenschaft-aktuell.de/artikel/Fitnesstraining_fuer_kuenstliche_Fasern1771015590666.html
15	2019.2.1	Chemistry World	PI (Gong) : "Self-growing polymers repair themselves when fractured" https://www.chemistryworld.com/news/self-growing-polymers-repair-themselves-when-fractured/3010066.article
16	2019.2.3	Physics World	PI (Gong) : "Hydrogel material flexes its muscles" https://physicsworld.com/a/hydrogel-material-flexes-its-muscles/
17	2019.2.4	The Nikkei	PI (Gong): Article regarding the paper, "Mechanoresponsive Self-growing Hydrogels Inspired by Muscle Training"
18	2019.2.5	Der Chemische Reporter (Germany)	PI (Gong): "Hydrogel wächst mit seinen Aufgaben" https://chemreporter.de/2019/02/05/hydrogel-waechst-mit-seinen-aufgaben/
19	2019.2.8	Highlighted in Technology News	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
20	2019.2.11	Highlighted in Converter News	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
21	2019.2.11	Highlighted in Technology Networks	PI (Ito): Cross-Coupling in Solid Using Mechanochemistry
22	2019.3.28	Hitachi Website	PI (Komatsuzaki): Reports on a new type of industries-universities collaboration between Hitachi on annealing computing. (https://social-innovation.hitachi/ja-jp/case_studies/hitachi_hokudai_labo)
23	2019.3.30	HBC	PI (Hasegawa): Hasegawa prepared red-luminescent transparency film including Eu(III) complex for agriculture. Under collaboration between coordination chemistry, photochemistry, plant cultivation and cell-biology, effective promotion of luminescent film for plant growth was observed.