RIKEN CENTER FOR SUSTAINABLE RESOURCE SCIENCE

Advisory Council Report 2019

Center for Sustainable Resource Science Advisory Council
RIKEN, Yokohama, July 8-10, 2019

The third RIKEN Center for Sustainable Resource Science (CSRS) Advisory Council meeting was held from July 8 to 10, 2019 at the RIKEN Yokohama Campus. The 2019 Advisory Council report and recommendations are based on the comprehensive report of CSRS current activities and future goals (White Paper) provided by Director Dr. Kazuo Shinozaki, on presentations of five Flagship Projects provided by the Deputy Directors, on research presentations provided by the Group Leaders, and the biographies of CSRS Principal Investigators and Group Leaders. The report summarizes the evaluation and recommendations of the CSRS Advisory Council and addresses the CSRS Directors report and future plans as well as the Terms of Reference by President Dr. Hiroshi Matsumoto and Director Dr. Kazuo Shinozaki.

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Executive Summary

Since the evaluation in 2016, the RIKEN Center for Sustainable Resource Science (CSRS) has made excellent progress in integrating plant biology, chemistry and chemical biology by strengthening the balance between these disciplines and catalyzing innovative synergistic collaborations among the research groups. Many CSRS scientists are highly visible international leaders of innovation in their fields. CSRS research is now organized around five strategic flagship projects that represent the research strength of the Center and the new strategic focus on biotechnology and metabolic engineering. Both basic and applied research projects address important United Nations Sustainable Development Goals to provide important solutions for national and global societal challenges. CSRS and RIKEN in general are critical technology hubs that drive disruptive research and development in Japan and beyond. CSRS efforts of translating basic research into innovative applications are rapidly expanding but must be met by stronger industry investments and entrepreneurial efforts to realize their full potential. With the implementation of new employment rules during the next four years, CSRS also has important opportunities of evaluating its research portfolio to expand and balance strategic directions as well as improving gender balance and international diversity among its research leaders and staff. With this, CSRS will continue its successful path of an internationally leading RIKEN research and technology center.

General Comments and Recommendations

CSRS originated from the Plant Science Center that was established in 2000. A major effort was made in 2013 to merge plant science with chemical biology, catalysis and polymers. The Biomass Research Program was integrated in 2015. This opened many opportunities but also created challenges because not only different disciplines were merged but also different cultures and research programs across three physically separated campuses (Yokohama, Wako and Tsukuba). During the last six years CSRS has become an internationally leading research center that is unique in combining plant and microbial research with chemical biology, chemical catalysis and polymer science to drive unprecedented frontier research and innovative interactions between these disciplines.

Director Kazuo Shinozaki has made tremendous and successful efforts in leading the integration of the different disciplines and facilitating interactions among the research areas, encouraging researchers from different disciplines to collaborate in a supportive atmosphere, stimulate and support the development of new leading-edge research projects, and establish the international visibility of CSRS. The performance of CSRS as a whole is outstanding and world class. There are many exciting research results that have been reported since the 2016 evaluation with many new publications in high-ranking journals. Most research projects are closely aligned with the mission of CSRS. The leadership of Dr. Shinozaki has assured the continuation of a high level of research performance and innovation. Clearly, CSRS is now the important pillar of the RIKEN mission to drive innovative research and technology development for Japan's society and also internationally. The Advisory Council affirms the values that CSRS bring to RIKEN in providing a world-class group of scientists at the interface between chemistry and biology outside the biomedical enterprise. Dr. Shinozaki must be highly commended for his inspiring leadership and achievements in building CSRS. At the same time he maintains a world-leading research program in abiotic stress tolerance that has

received many awards, acknowledgements as highly cited researcher, and the honor of being a Person of Cultural Merit in Japan.
The 2016 Advisory Council report recognized the accomplishments of CSRS and at the time recommended the development of a visionary strategic plan that focuses on flagship projects. These flagship projects should emphasize the RIKEN mission of driving research and technology innovation as well as the CSRS mission of developing new interdisciplinary research in sustainable resource development to increase the visibility of the institute.

In 2019 the Advisory Council is pleased to see that CSRS has actively and positively taken up the recommendation. In discussions with the Group Leaders in a bottom-up process CSRS established innovative and creative flagship projects. They focus on innovative plant biotechnology, metabolic genome engineering, innovative catalysts, leading edge polymers and advanced research and technology platforms that reflect the CSRS research areas as well as their integration and increasing cross-cutting activities. The Advisory Council was impressed with the ongoing integration process, the progress of CSRS research and development during the last three years, and the identification and development of the flagship projects. Their strategic focus on the United Nation 17 Sustainable Development Goals (SDGs), in particular SDGs 2, 3, 7 and 12-15, is important for Japan and internationally because they address human health, climate change mitigation as well as sustainable and safe food production. The Advisory Council agrees that flagships are important for focusing the research and communicating the science to the public. The contributions from CSRS, and RIKEN in general, to SDGs is a strongly added value to the mission of the institution.

The Advisory Council recommends that the flagship projects must better explain to the public and politicians how their excellent research results and innovations can be translated into practical applications and impact in breeding and crop production for the benefit of society.

The interdisciplinary expertise available in CSRS has great potential for collaborations to drive innovative research and development. A few laboratories are already integrating their research activities well, however, overall this potential has not been fully realized yet. The Advisory Council acknowledges the important progress that CSRS has made in strengthening chemical biology and integrating it with plant science during the last few years. But it also finds that there are still many excellent individual research projects running simultaneously, especially in plant sciences, which do not take advantage of expertise available in other laboratories. Often this prevents research from going deep enough. The Advisory Council agrees that researchers should keep their individual projects, but should increase discussions among the groups to identify overlapping interests and synergies for intensive collaborations.

In going forward, the Advisory Council also recommends increased efforts of bridging the flagship projects, for example by incentivizing new cross-cutting research projects, by expanding the interactions between plant science, polymers and catalysis, and by further integrating plant science and biotechnology. CSRS researchers agree that integrating plant biology and chemistry is a key issue. The Advisory Council understands and appreciates that the two main locations of CSRS research on the Wako and Yokohama campuses is often not conducive to close collaborations. The Advisory Council therefore recommends to increase efforts of involving the young PIs and Group Leaders in defining and planning the research in and between the flagship projects, for example in regular

scientific retreats to stimulate collaborations. The Advisory Council also recommends to further strengthen chemical biology and synthetic chemistry, especially through interactions with other RIKEN research groups in these fields, and mixing them more strongly with the plant field, both scientifically and physically. In addition to the collaborations with the Institute of transformative Biomolecules at Nagoya University and the Max-Planck Organization in Germany, CSRS should identify and reach out to other international chemical biology and synthetic chemistry groups to foster innovative collaborations with CSRS research groups. The Advisory Council is convinced that collectively these measures will facilitate CSRS in leading the world in innovation.

CSRS is very successful in training young scientists and helping them to establish their own careers in academia and industry, primarily in Japan. The Advisory Council recommends that CSRS should now also take a broader role in facilitating science education and research especially in Asian countries, but also in Europe and the U.S., by attracting young scientists to RIKEN for training and future collaborations. This will strengthen the internationalization in CSRS and further increase the visibility of the institute. Group leaders agree that Asia is becoming increasingly important in world and that building strong networks with other Asian countries will give CSRS a competitive advantage. Nationally, Japan is experiencing a rapidly aging society and among the younger generation a general lack of interest in scientific careers. This phenomenon is also observed in other countries but is exacerbated in Japan by dwindling opportunities for young people in Japan of building successful scientific careers in academia and industry. The Advisory Council recommends that CSRS, and RIKEN in general, increase efforts of reaching out to students in high schools and universities to make scientific research attractive again to the young generation. This could be done, for example, by providing short term internships that give young students the opportunity to become involved in research projects at an early age.

CSRS has already established productive collaborations with industry to facilitate translation of their research results. The White Paper lists a few concrete examples of such industry collaborations (Yokohama Rubber Company and Zeon Corporation for isoprene biosynthesis, Kaneka Corporation for developing a novel biopolyester into a new material with high biocompatibility, or Euglena Company for biofuels production). In his presentation Director Shinozaki showed interactions and collaborations with more than 40 other companies. However, the actual financial support provided by these companies to the CSRS research program currently amounts to only 10% of the CSRS annual budget. This is surprising and the Advisory Council questions if the collaboration with 40 companies involves commercial development in all cases. If they do, invoicing per company must be very low and CSRS scientists do not market their expertise appropriately. The Advisory Council recommends that efforts should be expanded to increase industry funding and visibility for societal impact. More specifically, CSRS should consider engaging in industry collaborations at an earlier stage of research and development without forgoing the publication of their research results high-visibility journals. CSRS and RIKEN should develop mechanisms and incentives for companies to increase their financial investments in pre-commercial research and development from which they ultimately profit. This would also help CSRS researchers to facilitate the translation of basic research results into promising new applications. The RIKEN Innovation Company is an important venue to explore such early interactions with industry. The Advisory Council also encourages CSRS scientists to explore how their research could be translated into own entrepreneurial opportunities. The CSRS spin-off companies Ac-Planta for commercialising acetic acid application for improved crop performance (founded in

2018) and the Japan Moss Factory for production of moss culture and phytoremediation (founded in 2019) are good examples of translating basic research results into promising commercial applications.

The CSRS budget has been essentially flat for the last 5 years while internal budget allocations have shifted and competitive external funding generated by the scientists has probably reached a ceiling. CSRS researchers must be strongly commended for their efforts in attracting competitive funding for their research projects. But this targeted external research funding and the shrinking direct CSRS funding from RIKEN make it difficult for the Director and the leadership to develop new research areas and incentivize cross-cutting activities. The Advisory Council understands that in times of shrinking government research funding this is difficult to change. Therefore the Advisory Council recommends that CSRS considers and explores novel funding sources. While the culture of private philanthropy is not yet strongly developed in Japan compared to the U.S., the CSRS flagship projects to address SDGs are a strong basis to approach national and international foundations as well as affluent private individuals who share the vision of CSRS to make a difference through innovative research.

Comments and Recommendations on Flagship Projects

Innovative Plant Biotechnology

The Innovative Plant Biotechnology Flagship focuses on the development of plants with high yield and resistance to environmental stresses to secure sustainable food and biomass production for society. This flagship is led by Dr. Minami Matsui and has 3 research groups, 4 research teams and 3 research units. Most of them use the model plant Arabidopsis for their research but increasingly also translate their results to important crop plants such as cassava and rice. The individual research projects of the Innovative Plant Biotechnology Flagship are all excellent and exciting, as is convincingly demonstrated by the evaluations of the individual group leaders. Scientists are continuing to make ground-breaking discoveries, mostly in the model plant Arabidopsis, and continue to publish their work in top journals. Excellent examples include the discoveries of small molecules such as the CLE25 peptide, acetic acid and ethanol that mediate drought tolerance and have interesting potential for applications for crops in the field. Similarly, the enzyme galactinol synthase, which was first reported in Arabidopsis in 2002 to catalyse the production of the raffinose family of oligosaccharides, was recently shown to increase yield in drought conditions when overexpressed in upland rice. The newly established RIKEN integrated plant phenotyping system will facilitate precise growth measurements and discoveries of control mechanisms.

While the individual projects of the Innovative Plant Biotechnology Flagship continue to produce important discoveries, the Advisory Council recommends that their scientists also focus more strongly on cross-cutting aspects of their research projects to accelerate translation and biotechnology development. Several of the groups work on drought tolerance, but they do not appear to collaborate in order to facilitate the contextual understanding of their results. For example, if CLE25-type peptides that were discovered in Arabidopsis roots are also found in crop plants to control stomatal closure and water-deficit control, then it will be important to understand how this mechanism relates to the functions of acetic acid and the potential new hormone karrikin in the modulation of drought responses. Some of the groups have initiated collaborations with chemical

biologists to probe biochemical pathways and mechanisms with small molecules. The Advisory Council recommends intensifying these interactions and taking advantage of the available unique RIKEN chemical library resources to facilitate our understanding of biological processes. The Advisory Council also recommends to better integrate the analysis of large-scale data by including machine learning and automated phenotyping to identify, probe and modify gene regulatory networks rather than focusing on individual genes. While understanding the function of individual genes in plant stress remains important, it is now increasingly clear that different abiotic stress responses, which in the field often occur together (such as drought and heat) are mediated by complex integrated regulatory networks. This is also the case for biotic stress responses. The Advisory Council recommends that researchers of the Innovative Plant Biotechnology Flagship organize regular meetings to discuss their project results and find common ground for collaborations. They should also take advantage of synthetic biology approaches such as the construction of regulatory gene switches to drive disruptive innovation in plant and microbial research with links to catalysis and polymer science. The Advisory Council is convinced that this will facilitate the implementation of translational work to improve crop performance and biomass production.

Metabolic Genome Engineering

The Metabolic Genome Engineering Flagship focuses on maximizing the capabilities of plants and microorganisms ('smart organisms') in expanding the production and use of bioproducts to replace fossil fuel-based chemical production processes with sustainable production systems. This is based on a strong vision how to reach impact in metabolite engineering and production by also integrating metabolic modelling, which already has high international visibility. The flagship project is led by Dr. Kazuki Saito and includes five research groups with expertise in plant, microorganism and environmental research. The large potential of this project has already been demonstrated by engineering pathways for triterpenoid/steroid biosynthesis (e.g., the natural sweetener glycyrrhizin), neolignane biosynthesis, butadiene or maleate bioproduction. The engineering of the isoprene biosynthesis for natural rubber production using an artificial metabolic pathway is another example of the capabilities that are being developed in this flagship. More recently, researchers are also using genome editing technologies (CRISPR-Cas, TALEN) to engineer metabolic pathways and produce new metabolites. This is clearly an exciting development with significant potential. The flagship project has identified bioinformatics and mathematical modelling as an important basis for the research program and therefore developed a web-based platform (PASMet, Prediction, Analysis and Simulation of Metabolic networks) to support these activities. But the Advisory Councils finds that the available expertise in bioinformatics and modelling is still sub-critical in this flagship, and CSRS as a whole, and therefore recommends to strengthen these important areas.

Innovative Catalysts

The Innovative Catalysts Flagship project is led by Dr. Zhaomin Hou and has two research groups and three research teams. This flagship project focuses on the development of more efficient and selective catalysts for synthesis of fine chemicals and functional materials to reduce the consumption of fossil fuels and increase the use of natural renewable resources. This flagship already has strong impact, high international visibility and outstanding accomplishments. The achievement of efficient catalytic ammonia formation in the reaction of N_2 and H_2 under mild conditions is an excellent

example of an alternative to the energy-intensive Haber-Bosch process. The iron-catalyzed selective direct C–H/C–H cross-coupling reaction of two substrates in a stoichiometric amount is an important world-class demonstration of using earth-abundant metal catalysts for organic synthesis. Similarly, the development of reusable catalysts is another example of innovation driven by the researchers in this flagship who are internationally recognized for their achievements. For example, Dr. Mikiko Sodeoka is the first female scientist in Japan to receive Cope Scholar Award of the American Chemical Society, which reflects her international leadership.

Considering the small size of the Innovative Catalysts Flagship, the Advisory Council discussed at length how the current exciting achievements of this flagship can benefit renewable biomass resources. The Advisory Council recognizes that person-power in this flagship remains limited and recommends that researchers forge closer interactions with the Innovative Plant Biotechnology Flagship for additional opportunities of using novel catalysts and biomass for product development. The Advisory Council also recommends looking for additional resources to expand the number of researchers in inorganic chemistry and solid catalysis for developing new frontiers, for example in collaboration with industry.

Leading-Edge Polymers

The Leading-Edge Polymers Flagship Project is led by Dr. Hideki Abe and focuses on the development of new functional polymer materials with strengthened specific or interesting novel functions. It is the smallest of the CSRS flagship projects and consists of the Advanced Catalysis Research Group (Dr. Hou) and the Bioplastic Research Team (Dr. Abe) and the Biomacromolecules Research Team (Dr. Numata). The flagship project is already producing interesting novel polymers, such as self-healing ethylene-anisylpropylene copolymers or polymers with excellent shape-memory properties. The chemo-enzymatic synthesis of peptides is another example of the rapid progress in this flagship that has the potential for further development into a novel chemical protein synthesis platform. The current use of the plant substrates vanillin or gallic acid for building novel polymers such as GDA polyesters, however, is not novel. These and similar plant-derived substrates are also used by research groups in other countries and therefore they are not very original for RIKEN as a leading institution. The Advisory Council recommends to broaden the scope in utilizing biomass substrates to develop innovate and environmentally-friendly polymers (for example, those that under seawater conditions degrade within three months). The Advisory Council also recommends to explore and evaluate opportunities from close collaborations with the Metabolic Genome Engineering Flagship to take advantage of engineering metabolic pathways for novel metabolites that can become the basis of innovative polymers.

Technology platforms

The Advanced Research and Technology Platforms Flagship is excellent and of national and international strategic importance. The flagship is led by Dr. Hiroyuki Osada and Dr. Kazuki Saito and involves four groups on the Yokohama campus and seven groups on the Wako campus. The Advisory Council discussed if technology platforms should be considered a flagship project. It acknowledges the unique mission of RIKEN of building world-class and cutting-edge technology platforms that would be difficult to realize in universities. Therefore it is warranted to give technology platforms a

flagship status, especially since they are accessible for all researches in Japan and internationally. Research in the flagship projects is strongly driven by small molecules and metabolites as well as genome-centred and bioinformatics approaches utilizing large molecular and genome databases in combination with machine learning applications. The Advisory Council agrees that the Advanced Research and Technology Platforms have an important service function and therefore recommends that the scientists should make strong efforts of bridging the other flagship projects. The Advisory Council also recommends that in addition to the technology support role, the Advanced Research and Technology Platforms should be facilitating cutting-edge, disruptive technology development to strengthen RIKEN's national and international position as a technology leader.

The strengths of the Advanced Research and Technology Platforms are the available expertise and instrumentation for metabolomics, proteomics and high-resolution microscopy (including cryo-EM), leading edge technologies, and chemical library resources. It is planned to integrate and expand bioinformatics for building a comprehensive information infrastructure to support the other flagship projects. However, there is also genuine concern that the shrinking CSRS budget will no longer be sufficient to maintain the internationally leading edge of this flagship. The Advisory Council shares this concern and recommends that RIKEN therefore continues and ideally increases the necessary instruments and infrastructure investments to keep the excellence high. The CSRS platform resources are highly attractive at the international level. The Advisory Council recommends that RIKEN should make strong efforts of maintaining and expanding this international treasure to attract the most promising young scientists in Japan who can drive leading-edge method and technology development. As a rapidly moving field, technology development is difficult to predict. The Advisory Council therefore recommends to carefully monitor the technologies that need to be developed and implemented for CSRS to keep its international competitive edge.

The international strength and leadership of RIKEN in chemical biology is based on a very small number of research groups, most prominently represented by Dr. Hiroyuki Osada. These groups have developed cross cutting activities with plant sciences to probe biochemical pathways with small molecules. The Advisory Council recommends that CSRS and RIKEN should continue to search for excellent early career scientists to continue strengthening chemical biology. The Advisory Council further recommends that CSRS should develop a plan for stewardship for the natural product library that Dr. Osada has developed over many decades. For example, the natural product library could be an important opportunity and starting point for a new entrepreneurial venture supported by the RIKEN company to rejuvenate natural product discovery in the 21st century.

CSRS-associated collaborative research activities and co-operations

The Drug Discovery Platforms Corporation Division, the RIKEN-Max Planck Joint Research Division for Chemical Systems Biology and the RIKEN-KRIBB Joint Research Unit are administered by CSRS but have separate budget lines. The **Drug Discovery Platform**, which was established as a 10-year program during the Presidency of Dr. Ryoji Noyori and is led by Dr. Minoru Yoshida, is focused on the discovery of interesting new compounds for medical applications, such as the molecular tryptolinamide that inhibits phosphofructokinase 1 for the treatment of patients with mitochondrial dysfunctions. Increasingly the research is shifting from small molecules to the discovery of other molecules with therapeutic potential. While the Drug Discovery Platform continues to make

important contributions, its future is uncertain. Discussions are underway to extend the program until 2024. The Advisory Council recommends that RIKEN should evaluate its role in high-throughput screening and drug discovery for medical diseases. A commitment to continued leadership in this field will give the Drug Discovery Platform more planning security and longer-term stability. This also requires financial investments to assure that RIKEN remains competitive at the national and international levels.

The **RIKEN-Max Planck Joint Research Division for Chemical Systems Biology** includes three scientists from RIKEN and two scientists from the Max Planck Institutes of Molecular Physiology and Colloids & Interfaces. At RIKEN this research division is led by Dr. Hiroyuki Osada. In addition to joint screening for bioactive compounds and identification of their targets, the participating laboratories also actively exchange young researchers and chemical compounds. The recently established **RIKEN-KRIBB Joint Research Unit** exploits the complementary strengths of three chemical biology scientists each from CSRS and the Korea Research Institute of Bioscience and Biotechnology. At RIKEN the joint research unit is led by Dr. Hiroyuki Osada. The joint research unit focuses on the screening and isolation of novel bioactive compounds from bacteria and fungi as well as the identification of their targets. A primary goal is the exchange of scientists and development of know-how.

The Advisory Council finds these to be valuable activities and recommends to evaluate other opportunities for synergistic activities with leading institutions overseas because this will further expand and strengthen the internationalization of CSRS. While the number of CSRS researchers from India other Asian countries is increasing, CSRS continues to find it difficult to attract young scientists from the U.S. and Europe. Although CSRS lists 26 international collaborations, mostly with universities, the Advisory Council found it difficult to evaluate their effectiveness in strengthening the internationalization of CSRS by promoting the exchange of scientists and attracting young researchers from other countries to RIKEN.

At the national level CSRS has established a partnership and cooperation with Nagoya University and the WPI Institute of Transformative Biomolecules for joint research and utilization of infrastructure and resources. Other co-operations were established with Yokohama City University and Saitama University for access to the graduate programs, which allows CSRS scientists to supervise PhD students. The Advisory Council recommends to strengthen and expand such co-operations, also with the goal of building more joint graduate program for the benefit of university PhD students who are being trained at RIKEN.

The recently established **Integrated Symbiology Project (iSYM)** is a cross-cutting RIKEN program led by Dr. Ken Shirasu with an independent budget that involves researchers from several RIKEN research departments. The goal is the utilization of symbiotic systems in humans, animals, agriculture and the environment to transform the bioindustry. The research efforts, which are supported by cutting-edge technologies and instruments, have already generated interesting results in a short time. The Advisory Council applauds the RIKEN initiative to bring its scientists from different fields and with different expertise together to open new research directions. This clearly reflects the strength and competitive advantage of RIKEN and could help to increase its visibility at the national level by exploring the Japanese gut microbiome. But it was not clear to the Advisory Council why the iSYM project focuses only on symbiotic interactions but excludes disease caused by

microbes, especially when those disrupt beneficial symbiotic interactions for the human, animal and plant hosts.

CSRS personnel and administrative management

The Advisory Council appreciates that the CSRS Directors are now engaging the group leaders in planning processes and discussions of research directions. The development of the flagship projects is a good example for this bottom-up process because it allows researchers to support and identify with their mission. The Advisory Council recommends that this engagement can be further strengthened by clearly communicating how decisions in CSRS are made, by including the group leaders in discussions on the future of CSRS and longer-term planning beyond the current flagship projects or defining new flagship projects. In addition to the monthly CSRS group leader meetings, the Advisory Council recommends to hold regular annual CSRS retreats to build community spirit and facilitate collaborations among the researchers. Despite significant progress, group leaders see the integration of plant biology and chemistry and interactions between the Wako and Yokohama campuses still as challenges that need to be overcome. The Advisory Council also recommends to establish an effective career path development program in CSRS to evaluate the potential of young scientists and help them chart their future.

The new government employment laws impact current and future employment at RIKEN and will affect many staff members with fixed-term contracts and research areas, also in CSRS. This is particularly relevant for the historically-grown but currently imbalanced employment contracts between the Wako campus where most group leaders have tenured positions and the Yokohama campus where most group leaders have fixed-term contracts. However, the Advisory Council is convinced that the employment transition in RIKEN is also a timely and important opportunity for increasing internationalization, diversity and gender balance, as well as building new research areas in CSRS. The Advisory Council strongly supports Dr. Saito, who will lead CSRS beginning in April 2020, and his plans for continued integration of CSRS's existing pillars of scientific strength as well as his human resource plans necessitated by changes mandated by the Japanese government. The Advisory Council recommends that all balanced employment and hiring decisions in CSRS must be the result of transparent processes and based on clear policies and evaluation mechanisms for recruitment and promotion to indefinite term appointments.

The recruitment and promotion of female scientists in CSRS remains ineffective. Although CSRS has a well-balanced gender distribution at the postdoc, PhD and technical research levels, this does not translate to the group leader level where the number of female scientists is still below 20% and remains unchanged since the last evaluation in 2016. Although CSRS has made efforts to recruit female group leaders, the Advisory Council recommends that these efforts should be strengthened. For example, future tenured positions should be used as an opportunity to recruit excellent female scientists to research leadership positions. The Advisory Council recommends to aggressively promote excellent female scientists to leadership positions also outside of CSRS. For example, in recognition of her outstanding achievements Dr. Sodeoka should also assume a leading role in RIKEN

in addition to her CSRS Group Leader position. Additional efforts to recruit non-Japanese female and male researchers also need strengthening.

Recommendations from the CSRS Advisory Council to President Dr. Hiroshi Matsumoto

The Advisory Council reviewed the current CSRS research achievements and its 7-year plan with respect to the terms of reference provided by RIKEN President Dr. Hiroshi Matsumoto and CSRS Director Dr. Kazuo Shinozaki. Since the 2016 review, CSRS research progress and achievements continue to be excellent and contribute to the RIKEN mission and societal progress. The SWOT analysis is comprehensive and appropriately identifies the strengths and weaknesses of CSRS as well as the opportunities for further development. These have been discussed in detail above and recommendations on the SWOT analysis are summarized below.

TOR 1: CSRS research achievements, contributions to society and consistency with 7-year plan

CSRS research is recognized nationally and internationally with an impressive output of outstanding quality research papers, also as a result of excellent technology platform support. CSRS continues to synergize plant science, catalytic chemistry and chemical biology and has bundled research in these different disciplines into five strategic flagship projects, including biotechnology and metabolic engineering. Based on this CSRS will create novel scientific approaches, also through increasing and strengthening synergistic interactions with other chemistry and chemical biology research groups in RIKEN to maintain international competitive leadership. The five CSRS flagship projects address important United Nations sustainable development goals and therefore make important contributions to society. They are consistent with the CSRS 7-year plan and RIKEN mission of driving innovative research and technology development for the benefit of society.

TOR 2: CSRS SWOT analysis

Strengths in management: CSRS brings together scientists from plant biology, chemical biology and chemistry into a unique and highly successful research institute with excellent output. The comprehensive and balanced SWOT analysis critically analyzes the progress and achievements of CSRS since the 2016 review. Director Dr. Shinozaki has excellently managed the integration of different disciplines in CSRS. He led the development of flagship projects, has made new appointments of promising young group leaders to strengthen chemical biology and chemistry, implemented important national and international collaborations, and continued efforts to increase diversity. These accomplishments provide an important foundation for the future direction of CSRS with the visionary leadership of the new Director Dr. Saito, whose plans are strongly supported by the Advisory Council.

Weaknesses: The location of CSRS scientists on the Wako, Yokohama and Tsukuba campuses remains an obstacle for building strong synergies and close research collaborations as well as frequent personal interactions among the group leaders and researchers from the different

disciplines. The new CSRS building on the Wako campus has relieved the situation somewhat. The decreasing CSRS operating budget and internally shifting budget allocations present a challenge for the Director and researchers to maintain excellence and the international leadership of CSRS. RIKEN has been generally successful in promoting their fixed-term contract researchers to good positions in academia and industry. But the declining number of PhD students in Japan and scarce number of academic positions to build long-term careers is making the hiring of talented young researchers and promotion to independent positions outside of RIKEN increasingly difficult.

Opportunities: The focus of the newly developed CSRS Flagship Projects on sustainable development goals defined by the United Nations allows CSRS to strengthen interactions with the society in Japan. They can raise awareness for the importance of research and acceptability of new breeding tools such as genome editing to address challenges for sustainable agriculture, food security and reducing the societal footprint of greenhouse gases. They are also opportunities to translate basic research into applied research for the benefit of industry, not only in Japan but globally.

Threats: The transition to the new government employment policies and increased number of tenured positions by 2023 are perceived as a threat. But if managed well and communicated transparently, hiring and tenure decisions in CSRS over the next four years will become an opportunity to focus research programs, build new research directions, and achieve an optimal strategic balance between the five flagship projects. The stagnant budget, increasing labor costs and ceilings to competitive public funding are of concern for future developments in CSRS. But this could be mitigated by exploring philanthropic funding sources and by expanding collaborations with industry, also in promising basic research and technology development.

TOR 3: Collaborations, including those in Science and Technology Hub program

CSRS has already established important and close collaborations with Nagoya University and the Institute of Transformative Biomolecules. Collaborations with Yokohama City University and Saitama University provides access to their graduate programs and PhD students. International research collaborations and co-operations involve, for example, the Max-Planck Society in Germany, Michigan State University in the U.S., the Korea Research Institute of Bioscience and Biotechnology, and the Agricultural Genetics Institute in Vietnam. The effectiveness of collaborations with other international universities and research institutions that are part of the RIKEN International Program Associates are more difficult to evaluate. The CSRS Advanced Research and Technology Platforms Flagship Project has high international visibility and is of central importance for RIKEN's efforts of becoming a science and technology hub. The internationalization of the CSRS research staff is progressing but needs to be accelerated and further strengthened.

TOR 4: Principal investigators

The principal investigators embrace the CSRS flagship projects and 7-year plan. Their research programs are aligned with the mission of the Center and they increasingly engage in synergistic and productive collaborations with colleagues from different disciplines inside CSRS, nationally and internationally. The performance of the CSRS PIs is uniformly excellent and meets highest international standards. They are highly successful in attracting competitive research funding, which

now represents more than 30% of the annual CSRS budget. All PIs publish in leading journals, many are international leaders in their field, and several are highly cited researchers during the last five years, exemplifying the international impact of CSRS research. The PIs manage their laboratories and research programs well. They actively and effectively engage in the training and mentoring of early-career scientists, helping them to develop successful research projects and finding positions and careers outside of RIKEN. They also have a role in translational research and attracting industry interest and funding. This aspect will be further strengthened by the flagship projects and expanded interdisciplinary collaborations.

Comments on the requests from the CSRS Director, Dr. Kazuo Shinozaki

The comments and advice of the CSRS Advisory Council on the newly started five flagship projects in CSRS are provided in the above report. The individual PI evaluations are attached to the CSRS Advisory Council report.

Recommendations from CSRS AC to President Hiroshi Matsumoto

TOR 1	CSRS research is recognized nationally and internationally with an impressive output of outstanding quality research papers, also as a result of excellent technology platform support. CSRS continues to synergize plant science, catalytic chemistry and chemical biology and has bundled research in these different disciplines into five strategic flagship projects, including biotechnology and metabolic engineering. Based on this CSRS will create novel scientific approaches, also through increasing and strengthening synergistic interactions with other chemistry and chemical biology research groups in RIKEN to maintain international competitive leadership. The five CSRS flagship projects address important United Nations sustainable development goals and therefore make important contributions to society. They are consistent with the CSRS 7-year plan and RIKEN mission of driving innovative research and technology development for the benefit of society.	
TOR2	Director Dr. Shinozaki has excellently managed the integration of different disciplines, developed flagship projects, and made new appointments in chemical biology and chemistry. The new Director Dr. Saito has a strong vision for the future of CSRS.	The problem of CSRS scientists located on three RIKEN campuses and the decrease in operating funds have been clearly identified. The declining number of PhD students in Japan and scarce number of academic positions becomes increasingly problematic for PI's.
	The focus of the Flagship Projects on sustainable development goals allows CSRS to strengthen interactions with society and raise awareness for the importance of research to address challenges for sustainable agriculture, food security and reducing the societal footprint of greenhouse gases.	The transition to the new government employment policies is perceived as a threat but also provides opportunities to achieve an optimal strategic balance between the five flagship projects. The declining CSRS operating budget and ceilings to competitive funding are of concern for new developments in CSRS.
TOR3	CSRS has established important and close collaborations with Nagoya University and the Institute of Transformative Biomolecules. Co-operations with Yokohama City University and Saitama University provide access to graduate programs and PhD students. International research collaborations and co-operations are well established, for example with the Max-Planck Society in Germany. The CSRS Advanced Research and Technology Platforms Flagship Project has high international visibility and is of central importance for RIKEN's efforts of becoming a science and technology hub. The internationalization of the CSRS research staff needs to be accelerated and further strengthened.	

Results of PI Evaluations—Overview

TOR 4	The principal investigators embrace the CSRS flagship projects and 7-year plan. Their research programs are aligned with the mission of the Center and they increasingly engage in synergistic and productive collaborations with colleagues from different disciplines inside CSRS and RIKEN, as well as nationally and internationally.
	The performance of the CSRS PI's is uniformly excellent and meets highest international standards. They are highly successful in attracting competitive research funding, which now represents more than 30% of the annual CSRS budget. All PI's publish in top journals, many are international leaders in their field, and several are highly cited researchers during the last five years, exemplifying the international impact of CSRS research.
	The PI's manage their laboratories and research programs well. They actively and effectively engage in the training and mentoring of early-career scientists, helping them to develop successful research projects and finding positions and careers outside of RIKEN. They also have a role in translational research and attracting industry interest and funding. This aspect will be further strengthened by the flagship projects and expanded interdisciplinary collaborations.