RIKEN CENTER FOR SUSTAINABLE RESOURCE SCIENCE

CSRSAC Report 2014

The RIKEN Center for Sustainable Resource Science Advisory Council
June 4-6, 2014

The first RIKEN Center for Sustainable Resource Science Advisory Council (CSRSAC) meeting was held from June 4-6, 2014 on the RIKEN Wako Campus. The 2014 CSRSAC Report is based on the comprehensive report of CSRS current activities and future goals provided by Director Dr. Kazuo Shinozaki, and on research presentations provided by the Project Directors, Group Directors, Team and Unit Leaders. The report summarizes the evaluations of the CSRSAC members present at the meeting and addresses the CSRS Directors report as well as the Terms of Reference by President Dr. Ryoji Noyori and Director Dr. Kazuo Shinozaki.

Members of the RIKEN CSRS Advisory Council present at the 2014 meeting

Dr. Wilhelm Gruissem, (Chair, Plant Science)
ETH Zurich (Swiss Federal Institute of Technology), Switzerland

Dr. Ben Shen (Vice Chair, Chemical Biology)
The Natural Products Library Initiative, Scripps Research Institute Florida, USA

Dr. Peter Kündig (Vice Chair, Chemistry)
President, Swiss Chemical Society

Dr. Dirk Inzé (BMEP Vice Chair, Plant science)
VIB Department of Plant Systems Biology, Ghent University

Dr. Akira Isogai, (Plant Science)
Professor Emeritus, Nara Institute of Science and Technology

Dr. Anne Osbourn (Plant Science)
Honorary Professor, John Innes Center

Dr. Daisuke Uemura, (Chemical Biology)
Professor, Kanagawa University

Dr. Minoru Isobe, (Chemical Biology)
Professor Emeritus, Nagoya University

Dr. Kenichiro Itami, (Chemistry)
Director, Institute of Transformative Bio-Molecules (WPI), Nagoya University

Dr. Takao Ikariya (Chemistry)
Professor Emeritus, Tokyo Institute of Technology

Executive Summary

Research at the RIKEN Center for Sustainable Resource Science (CSRS) represents a truly unique and visionary integration to advance a new era of Sustainable Science that facilitates novel connections between the excellent quality of Plant Sciences of the previous Plant Science Center (PSC) in the fields of metabolism and genomics, and Chemical Biology and Catalysis Chemistry of the Advanced Science Institute (ASI) using outstanding tools, very unique natural products library resources, chemical arrays, small molecules and catalysis research. CSRS scientists will necessarily drive cross-disciplinary research that could take international leadership. There is a huge potential for the world-leading CSRS scientist to generate innovation supported by a top level infrastructure, but this is still underutilized. The main translational research goals of the program are largely in the planning stage. They can build on the experience of the joint Biomass Engineering Program (BMEP) of the Research Cluster for Innovation (RCI) that is planned to join CSRS in 2015. The decision is strongly supported by the Advisory Council. A key challenge for the CSRS mission will be to support, integrate and build the motivation, goals and activities of the new program scientists, so that they can mature and make more investment in their future together with CSRS. Another challenge will be to reestablish worldwide awareness that CSRS comprises the excellent reputation and international leadership of the previous PSC and ASI centers and groups, via creative and innovative research that can signify this new effort. CSRS has a great opportunity and bright future, but scientists must fill its strategy and vision with content, and build a foundation that embraces entrepreneurship and creates truly disruptive and game changing research and technologies.

General Comments

CSRS represents the realization of a strong RIKEN vision and globally unique effort to integrate plant science, chemical biology and catalytic chemistry for interdisciplinary research, innovation and application towards the sustainable production of resources. With the integration of scientists from the former Plant Science Center on the Yokohama Campus and scientists from the Advanced Science Institute on the Wako campus, RIKEN has created a center that is in a strong position to tackle challenges associated with dwindling fossil fuel supplies and rapid climatic and environmental changes. Based on the existing excellence in advanced and applied research, CSRS can be expected to develop transformative and disruptive technologies that will provide sustainable solutions for societal needs. During the first year of this proposed 10 year program, CSRS made strong investments in infrastructure to implement the Green Innovation and Life Innovation strategies of RIKEN and the Government of Japan. Ultimately, outcomes from these strategies will contribute to transforming Japan into a green and sustainable society that is based on low carbon emission, smart energy management, and resource-efficient crop production for food and feed.

The Advisory Council was impressed with first efforts to establish interdisciplinary projects across the core CSRS scientific fields. These include, for example, using CO_2 as a resource to mitigate its contribution to climate change, improving plant functions to save water required for crop irrigation, reducing energy required for nitrogen fertilizer production, and developing new compounds to accelerate plant growth. Joint projects between plant scientists, chemical biologist and catalytic chemists also hold great promise for assembling synthetic photosynthesis complexes, developing new compounds for reducing the greenhouse gas N_2O, or for using plants to recover rare metals from the environment. To be successful, these projects must be supported by state-of-the-art research platforms that utilize the newest technologies and the most advanced instrumentation.

The Biomass Engineering Program (BMEP) that was started in 2010 is already highly successful and well underway to increase cellulose production in trees and grasses, to develop one-step synthesis technologies for novel bioprocesses, and to synthesize new bioplastics and biopolymers by utilizing microbial genes and production. BMEP is exemplary in its technology transfer and collaborations with industries in Japan, and there is great potential to expand interactions to global industries in the future. The Advisory Council applauds and strongly supports this decision as the program represents a significant added value to the mission of CSRS. Two cooperative research units (Chemical Bank and Seed Compounds) in CSRS from the Program for Drug Discovery and Medical Technology Platforms (DMP) that was also started in 2010 hold similar promise of developing new treatments for cancer and other diseases based on the excellent chemical and biological resources as well as the state-of-art technologies and facilities available at RIKEN.

The CSRS mission and planning are well articulated in the White Paper that was presented to the Advisory Council. While the comprehensive document is impressive, it could greatly benefit from a strong strategy and business plan that explains the integrated road map, milestones and deliverables of CSRS on the five- and ten-year horizon. In their presentations the Project Directors of the six core interdisciplinary projects (carbon utilization, nitrogen utilization, metallic elements utilization, research platforms, BMEP and DMP) provided outlooks and goals for 2018 and 2023, but these need to be better integrated during the next 2-3 years. The overall CSRS strategy and business plan should provide an international perspective of the Center directions, explain how CSRS future plans are aligned with RIKEN policy and strategy, explain how translational research will be facilitated, and provide convincing plans for technology transfer (national and international, including concepts for start-up companies) as well as communication and outreach efforts. The Advisory Council is

convinced that CSRS has the necessary ingredients for excellent interdisciplinary research that will spawn disruptive technologies and deliver new systems analysis approaches. To fully integrate and exploit the core research projects requires sustained long term investments and commitment to explore opportunities for innovative research beyond plants. CSRS currently spans two RIKEN campuses, but physical proximity is a key ingredient for interdisciplinary research. CSRS scientists have strong incentives to address these issues in the overall CSRS strategy and business plan.

There was extensive discussion among CSRSAC members that by dismantling the world-wide recognized RIKEN Plant Science Center CSRS may have reduced its international visibility. But the Advisory Committee is convinced that with CSRS RIKEN has created an internationally unique center with a clear vision. Thus, supported by a decisive strategy together with a strong communication plan (including hosting international CSRS conferences) and outreach efforts CSRS will quickly regain any potentially lost international visibility.

The Advisory Council recognizes that the RIKEN Administration strives to position CSRS as a national and world-leading institute to address challenges that society is facing already, such as mitigating the effects of climate change, improving human health, reducing the ecological footprint of agriculture, ensuring food security, or production of biomass and novel compounds as industry feedstocks. In this context CSRS is a hub to promote sustainable resource science based on the visionary integration of plant science, chemical biology and catalyst chemistry. Plans for collaboration with the Nagoya University WPI Institute of Transformative Bio-Molecule focusing on chemistry and biology, or other future collaboration with similar international research centers, will further strengthen the CSRS research portfolio and facilitate basic and solution-driven research.

In summary, CSRSAC members are extremely enthusiastic in supporting RIKEN and CSRS for their unique and groundbreaking cross-disciplinary approach to take existing basic and applied plant research beyond more narrow goals of food supply to strive for promising new synergies with chemical biology and catalyst chemistry. There is no doubt that CSRS will strengthen the Japanese research contribution to international science and global challenges that must also be crucial priorities for RIKEN and the government of Japan.

Recommendations on Terms of Reference

The CSRSAC reviewed the performance of the CSRS with respect to the terms of reference provided by RIKEN President Dr. Ryoji Noyori and CSRS Director Dr. Kazuo Shinozaki. Overall, CSRS current operations and planning are exemplary and contribute to the center's success today under the leadership of Director Kazuo Shinozaki, Deputy Directors and Group Directors Hiroyuki Osada, Kazuki Saito and Zhaomin Hou, and Group Directors Hitoshi Sakakibara, Mikiko Sodeoka, Ken Shirasu and Minoru Yoshida.

CSRS research output and personnel are of high international standard

Overall, CSRS research is excellent and of highest international standard and reputation. CSRS plant science has a long-standing history of important discoveries that have greatly advanced our knowledge of plant function. The Green Innovation strategy and especially BMEP represent important and critical components of the CSRS basic and applied plant research program. They provide the basis for the development of new technologies and discoveries needed for Green Innovation and biomass engineering. Research themes are carefully selected and built on strong expertise, which positions CSRS plant scientists favorably for involvement in new research strategies of national and international importance. CSRS plant scientists remain at the forefront of research in plant metabolism, hormonal regulation of plant functions, as well as stress tolerance and yield stability. They are developing leading-edge functional genomics technologies for gene discovery and understanding metabolic networks. At the same time CSRS scientists are making remarkable advances in the field of catalysis that have high potential for bringing the Center to the forefront of sustainable resource science. This is clearly a very strong sector of CSRS that must be continued with high priority. The mild conversion of N_2 into ammonia and amines, incorporation of CO_2 into useful organics, catalytic trifluoromethylation for advancing medicinal chemistry or novel flow systems and heterogenation of catalysts to enhance efficiency are just some examples of leading CSRS research in this field. Chemical biology has increasingly critical roles in linking plant sciences to chemistry and in facilitating communications and synergistic interactions between CSRS biologists and chemists to use small molecules in discovery research and applications. For example, the innovative natural product discovery platform and the unique natural product library are important CSRS resources that will drive the discovery of small molecule probes and utilization of small molecules to interrogate and regulate biological processes. Each of the CSRS groups is well recognized nationally and internationally as leaders in their respective areas of research. They complement each other, work synergistically, and are well positioned to apply their strength, expertise, and unique resources to promote cross-disciplinary research within CSRS. Excellence in these research areas promises to bring international recognition to CSRS.

CSRS has world-leading potential in its field

CSRS represents a unique and unprecedented opportunity of interdisciplinary research to address societal challenges, and the Advisory Council applauds Director Shinozaki on implementing his unique vision. There are now many centers around the world that focus their research on food security and mitigating climate change. Although CSRS research also impacts on these issues implicitly, the vision and the scope of CSRS is much broader and represents the direction of sustainable resource science that industry and academia should follow going forward. The Advisory Council encourages the promotion of a bottom up approach to facilitate interactions between biologists and chemists and to drive cross-disciplinary research. Most CSRS research groups have a very strong international presence in their respective disciplinary fields. However, integrating the three different RIKEN disciplines represented by plant science, chemical biology and catalytic

chemistry into a new Center also represents a challenge because scientists must maintain their international presence in the respective disciplines while engaging in new and innovative cross-disciplinary research programs. The Advisory Council is convinced that within 2- 3 years CSRS will have the same or even higher reputation because of the uniqueness of combining different scientific fields in a way that has not been done before. But as discussed above, this will require a convincing strategy and business plan supported by strong communication and outreach efforts.

The Advisory Council also considered what could be done in CSRS that would result in quantum leaps to gain a world leading status. It is difficult to make concrete proposals, but the integration of BMEP into core CSRS activities will be a significant step towards this goal. From a chemistry perspective, focusing chemical biology and catalytic chemistry on the development of sustainable resources represents a drastic change that creates new opportunities. For example, combining expertise in plant science and abiotic stress with small molecule chemistry and chemical biology and tapping into RIKEN's Natural Compound Libraries can accelerate the development of resilient crop plants. Similarly, CSRS can further strengthen its international position by facilitating and supporting synergies between plant metabolism and small molecules chemistry and by developing synthetic biotechnology approaches to recreate biosynthesis pathways in plants and organisms for the sustainable production of value-added metabolites. Quantum leaps can be expected not only from novel interdisciplinary approaches, however, but also from understanding biological processes at the molecular level for problem-solving translational research that creates new job opportunities.

Evaluation of the CSRS management policy

- **Appropriateness of the research roadmap.**

CSRS has presented an excellent vision and research plan in the White Paper. But as discussed above, CSRS now also needs to develop a forward looking strategy and business plan that explains (i) how plant science, chemical biology and catalytic chemistry will be integrated to create a truly new scientific field, (ii) how goals, deliverables and milestones of interdisciplinary efforts will be reached, (iii) how one or two flagship projects can create needed visibility of the Center, and (iv) how research directions or projects that are not well aligned with the CSRS mission will be phased out. Because CSRS is more than the sum of its individual units, such strategy and business plan presents an important opportunity to embrace the innovative Center configuration and explain how CSRS will take advantage of this unique structure and how the roadmap will drive new initiatives. All CSRS PIs should take ownership of the strategy and business plan and the decision-making process. While there is currently good coherence at the senior level, most senior PIs also have other responsibilities that may prevent them from fully engaging in CSRS activities.

The Advisory Council encourages the CSRS management to include the early career scientists in the decision-making process and encourage them to be proactive and vest themselves in the mission and goals of the center. The future of the CSRS will rely on them. In this context, the multilayer hierarchy of research groups may be problematic. The many different types of appointments create pressure on the way CSRS scientists conduct their research. Scientists in tenured positions are much more prepared to take risks and project their research programs into 5-10 years plans. Scientists working on short-term contracts typically feel pressured to publish as many papers as possible in order to advance their careers. Small research units often cannot afford to become vested in the CSRS mission and goals because they are too busy surviving. Tenured scientists should therefore embrace their non-tenured colleague and integrate them into their more risky long-term thinking and planning. Mentoring and coaching are important, and CSRS has the responsibility of training early career scientists to look beyond their own research project and become more interactive. To

avoid fragmentation in the longer term, CSRS management should reconsider the hierarchy of Unit, Team, Group, Project Head, Chief Scientist, and Director. The Advisory Council recommends keeping the hierarchy as flat as possible, ideally using a structure of groups and projects only.

- **Measures for attracting top international researchers.**

The Advisory Council acknowledges that CSRS has mechanisms in place to attract and employ international researchers, but CSRS management must continue to evaluate why these are not working well. CSRS will be attractive based on its science, unique resources and facilities. CSRS management might want to consider establishing a "CSRS Senior and Postdoctoral Fellow Program" to attract high level researchers at senior and junior levels, similar to the RIKEN Fellow Program. This will further promote the visibility of CSRS.

- **Budget allocation system** (balance between research and human resource costs)

In general, CSRS has established a balanced policy of budget allocations. Going forward, CSRS management should ensure that early career scientists have access to resources and be treated fairly in competitive proposals. Short and long term resources should be allocated to support the mission and short- as well as long-term goals of the Center, and especially interdisciplinary collaborations between scientists. The Advisory Committee recommends that CSRS Group Directors should not have to write a new project proposal every year to justify RIKEN funding of their research. This creates an unnecessary burden. Time could be used more effectively to secure third-party funding from other funding agencies or industry in Japan.

- **System for personnel turnover**

In general, CSRS personnel management and turnover should be guided by a strategy and business plan to ensure that they are flexible and aligned with the Center's mission and goals, and not based on preserving the status quo. Appointments at the senior level should involve a recruitment committee with one or two committee members from outside CSRS and preferably outside RIKEN. The Advisory Council does not question the CSRS Group Leader's ability of making good appointment decisions, but such recruitment committees are international standard at top universities and provide the necessary level of transparency. Similarly, CSRS management should make appointments to five-year or tenure-track positions a transparent process that is guided by external letters of support and internal appraisals.

To make positions more attractive to early career and active scientists, CSRS management should demonstrate how they can benefit from RIKEN appointments and find job opportunities after their CSRS contracts end. This could be done using well-documented statistics, agreements with industry or universities to promote the hiring of excellent early career scientists, and by aggressively developing core Center strategies that will translate into job opportunities. The appointment of women scientists who are world-class or who are recognized as having the potential to become world-class into senior positions should be facilitated by central funds in the RIKEN President's office. The emphasis must be firmly on the caliber of the applicants to avoid positive discrimination. Also, RIKEN and CSRS management must communicate clearly and transparently that they will strive to provide job security but that this does not equal job permanency.

- **Collaboration**

The Advisory Council acknowledges that CSRS scientists are already actively engaging in collaborations within RIKEN as well as with academia and industry. Considering the broad portfolio of collaborations, it is important now that CSRS scientists prioritize those that are productive and

contribute to the Center mission and goals. Collaborations could be expanded to include other institutions around the world to address problems that are of global concern, such as increasing carbon utilization and improving nitrogen utilization. Group Directors should have a pivotal role in assessing and coordinating research collaborations to optimize the potential for successful outcomes.

- **Requests from the RIKEN CSRS Director, Dr. Kazuo Shinozaki:**

Dr. Shinozaki had requested specific advice from CSRSAC members on the quality of core research activities, synergies between CSRS key projects, contributions to the scientific community and general society, and on the future vision.

The Advisory Council finds that research in each individual laboratory remains at very high standards, with mostly excellent output. CSRS research has absolutely raised the bar in terms of impact in the fields of plant science, chemical biology and catalytic chemistry, and the new interdisciplinary science direction has similar potential impact as well. Many scientists expressed strong interest in future collaborations, but there is still considerable room for increasing motivation and curiosity among individual CSRS research groups to learn about and engage with other groups and projects. This is especially important considering that CSRS research spans two different RIKEN campuses.

Each four key projects (Carbon, Nitrogen, Metallic elements and Research platforms) has interesting lines of research, but the Advisory Council recommends to increase efforts of better integrating these projects. This can be formulated in the strategy and business plan discussed above. For example, CSRS should consider building an infrastructure to effectively integrate knowledge from the key projects and develop disruptive technologies based on this knowledge. Importantly, chemistry and chemical synthesis in CSRS needs to be strengthened as these areas are rapidly becoming focal points of innovative research projects. The Advisory Council is concerned that currently there are not enough staff to accelerate research in these areas, even if strengthened by collaborations with plant scientists.

The future of CSRS would greatly benefit from uniting the research groups and disciplines to facilitate interactions and collaborative projects. The Advisory Council acknowledges the constraints RIKEN has for constructing a new building on one of the two campuses. Currently most of plant science is located on the Yokohama campus while most of chemistry is located on the Wako campus. CSRS should consider breaking up this disciplinary structure and mix research groups between the campuses, making sure that infrastructure needs are secured. The Advisory Council understands that this may be temporarily disruptive but is convinced that there will be long-term benefits.

The Advisory Council also recommends that CSRS should have state of the art plant phenotyping facilities at RIKEN that can serve as “a field in the lab” to support innovative and interdisciplinary research projects. Current plant growth facilities (CER, glasshouse, field) are inadequate to accommodate future high impact research on drought tolerance and biomass engineering from genotype to the phenotype levels. Funding should be made available to provide such facilities as a matter of urgency. This will be crucial in order to enable Prof. Shinozaki and other CSRS group leaders to take their research to even higher levels by integrating mechanistic studies with phenomics and imaging, so gaining real insights into plant stress responses under a variety of rigorously controlled (and ideally also field) conditions. This could enable CSRS researchers to establish *the* world-leading plant phenomics platform, which along with the advanced imaging platform would provide powerful enabling facilities for other CSRS programs. Considering the integration of BMEP, an experimental Biorefinery is also much needed.

The Advisory Council is pleased to see the increasing interest of industry in CSRS research projects. As CSRS is moving basic research output into translational research and applications, technologies developed in collaboration with the Research Cluster for Innovation (RCI) will become increasingly attractive to industry as well. At present most of the interactions are with companies in Japan. The Advisory Council encourages CSRS to nurture national business collaborations, but since much of CSRS research also addresses global problems, CSRS should remove barriers that stifle interactions with global industries. Ideally, interactions with industry should be mutually beneficial and not be contract research only. To promote interactions with industry, CSRS should consider holding one or two day meetings with research directions from international and national companies, perhaps by taking advantage of RIKEN offices located internationally.

The Advisory Council is aware of the political issues around carrying out research with CSRS that is overtly crop-related. However the Advisory Council firmly recommends that the CSRS endeavors to ensure that fundamental work with implications for crop improvement realizes its full potential by translation through appropriate channels.

In this context, CSRS management should be more proactive in the communication with the public. The Advisory Council applauds the institution of new CSRS positions for international and public relations and outreach. Now is the opportune timing for this.

Summary Recommendations

1. CSRS was created recently and is advancing a new scientific field. It has a strong vision and clear mission. Therefore it is now timely to develop a convincing strategy and business plan that fills the mission with scientific directions and research content, and that explains where CSRS is and where it wants to be in five and ten years.

2. CSRS scientists must take ownership of the strategy and business plan, and subscribe to the mission and goals of the Center. CSRS management is encouraged to engage early career scientists in decision-making processes, and CSRS early career scientists are encouraged to proactively vest themselves in the Center goals. The future of CSRS will rely on them.

3. CSRS combines world-class research in plant science, chemical biology and catalytic chemistry that will have to re-establish high international visibility as a new research institution. One or two innovative flagship projects anchored in CSRS research can facilitate this process.

4. CSRS scientists are actively engaged in collaborations with academia and the industrial sector. They should prioritize the most effective and productive collaborations that are best aligned with the CSRS mission and goals.

5. CSRS scientists have an excellent understanding of various networks including abiotic stress. They should now connect functional networks to phenotypic output, taking full advantage of chemical biology, small molecules, and even catalysts. CSRS scientists are in a worldwide unique position to explore small molecules and their chemical space for applications to societal problems.

6. CSRS should find a way to better integrate the four key projects and their interesting lines of research and synergies such that this integration spawns new disruptive technologies. It should also ensure that all CSRS projects are aligned with the Center's mission and goals.

7. CSRS resources or new resources should be dedicated to strengthening and enhancing chemistry and especially chemical synthesis. Currently these areas are understaffed to accelerate collaborative research with plant groups and other sciences.

8. Researchers from different groups and disciplines across the two campuses should be encouraged to work together, and even be relocated, for the future benefit of CSRS.

9. CSRS needs to increase greenhouse facilities and create state of the art phenotyping facilities here in Japan including field facilities. An experimental biorefinery is also much needed.