

Recommendations
from the
1st Cluster for Pioneering Research
Advisory Council
to President Hiroshi Matsumoto

11 April 2019

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EXECUTIVE SUMMARY

Over the span of two days, this Advisory Committee was provided with an overview of RIKEN's *Cluster for Pioneering Research* (CPR). The provided summary of world-class research at RIKEN and its future vision for CPR comprised an impressive series of oral presentations; a large set of written reports that clearly showed the power of bottom-up fundamental research organization and individual excellence; and meetings with the scientific management team, The chief Scientists and Hakubi Team Leaders, research staff, postdocs and graduate students. We preface this report by stating that our CPR Advisory Council compliments RIKEN for their strong support of these fundamental research programs, and we express our sincere hope that this support will continue in force.

TERMS OF REFERENCE

TOR 1: Evaluate the accomplishments of the startup of CPR's research plans of the fourth mid- to long-term plan (7-year plan) to date, whether CPR's research outperforms the international standard and is regarded as a world class leader, and whether its research results have contributed to society.

[Research]

CPR provides an excellent new opportunity for interdisciplinary projects. We have seen, in fact, excellent examples of such interdisciplinary projects connecting bottom-up research from the four areas of physics, biology, chemistry and engineering. The scope of the projects is particularly visible within the All-RIKEN Projects but also reflected in the Pioneering Projects. The overall quality of the research is at the highest level, and is comparable with other world-leading research institutions. Below we summarize examples from the four fields that highlight the strong creative and interdisciplinary character of research in the CPR.

In **Chemistry**, many projects were rated outstanding. All PIs are internationally highly-recognized scientists performing world-class research. This is documented by their impressive publication records and the recognition they have attained through their international distinctions and awards. Their research covers a broad variety of disciplines, ranging from synthesis, materials development, spectroscopy and materials characterization to computational chemistry and in vivo therapeutic chemistry. Particular highlights include spectacular work on synthesis of self-healing polymers being pursued by the Organometallic Chemistry Laboratory of Zhaomin Hou. This group applies highly innovative organometallic synthesis developing new catalysts, new reactions and new materials that are superior to those existing. Another highlight is the work of the Surface and Interface Science Laboratory of Yousoo Kim, which aims to develop novel experimental techniques to perform unprecedented studies of the excitation dynamics of single molecules in both extreme time (ps) and space (sub nm) domains. Furthermore, their collaborations with the Star and Planet Formation Laboratory of Nami Sakai (see below) beautifully demonstrate the collaborative research character of the CPR.

The research performed by the Chief Scientists in the field of **Physics** is at a very high standard, competitive with that of their high-profile international colleagues. World-class results have been obtained in tests of fundamental symmetries, atomic clocks, rare ion beams, astrophysics and quantum physics, with outstanding and highly-cited publications. We highlight just two specific efforts here. Dr. Nami Sakai of the Star and Planet Formation Laboratory provided an survey of impressive science being carried out on an international collaborative scale, which addresses fundamental questions about how stars are formed. Previous work had found ~ 200 molecular species ranging from 2 atoms to more than 12 atoms, mainly by radioastronomy. About 15 years ago complex organic molecules (COMs) were discovered that differed amongst stellar objects. The question arose regarding the reason for the diversity of molecules in dark interstellar clouds, which take millions of years to form. Using recent data from the telescope ALMA in Chile, which now provides remarkable *intra*-stellar resolution, Sakai came up with a novel model invoking

non-equilibrium chemistry for the formation of these interstellar molecules. Her group had also developed a novel THz spectrometer of highly excited species to help elucidate the origin of ALMA data acquired. Stefan Ulmer and his team in the Fundamental Symmetries Laboratory have developed unique techniques for particle cooling, trapping and precision measurement. Dr. Ulmer's group has been a worldwide leader of the stringent tests of CPT symmetry using antiprotons. They have recently attained remarkably precise measurements of the magnetic moment and the charge-to-mass ratio of the antiproton, which have great impact in fundamental science. This excellent previous work from the laboratories, along with efforts within Dr. Hidetoshi Katori's laboratory (Engineering) have recently engendered a newly-funded 5-year Center (see below). This demonstrates the international visibility and interdisciplinary of the research emerging from strong collaboration.

In the field of **Engineering**, many projects were also rated as outstanding, highlighted by two researchers showing distinction. Hidetoshi Katori's Quantum Metrology Laboratory is carrying out exciting and forefront research in several areas that are connected through the theme of using extreme precision measurements to explore new fundamental physics, such as the time variation of the fine structure constant, anchored by shared technological bases. The three ongoing efforts within the Pioneering Project entitled "*Extreme precision to explore fundamental physics with exotic particles*" by Katori, Ulmer and Uesaka are world class. This encompasses: ultraprecise clocks based on both optical lattices and excited nuclei; precision physical measurements and quantum logic with antiprotons; and, precise mass and lifetime measurements of rare ions to understand nucleosynthesis. The fruit of this nearly-complete Pioneering Project is the creation of the newly-launched international "*Center for Time, Constants, and Fundamental Symmetries*". This is a prominent and excellent outcome of one of the first major investments in a cross-disciplinary pioneering research program by the CPR. At the junior level, Hirofumi Shintaku's Microfluidics Laboratory focuses on development of combined microfluidic and electro-kinetic methods for advanced single cell RNA sequencing (scRNA-seq). The team has developed a pioneering advance; analysis of separated nuclear and cytoplasmic components of cells by scRNA-seq. They call this single cell integrated nuclear and cytoplasmic RNA sequencing (SINC-seq). His target metrics for a 7-year plan were clearly defined, improving the throughput of SINC-seq, and the plan will have a strong positive impact on biological research.

In the field of **Biology**, our overall assessment of the efforts was very high, demonstrating international excellence in this group, in which a significant number of projects were perceived to be excellent. A substantial range of subject fields is represented within RIKEN, and in many projects highly original research is being pursued. Two particular highlights noted were the work of Tatsuya Hirano in the Chromosome Dynamics Laboratory, who is unique in the world in having developed methods to reconstitute DNA not only into chromatin but also into higher-order structures that possess key features of mitotic chromosomes. His work is a remarkable testament to the ability of an individual laboratory with limited resources to tackle major problems and overcome large obstacles in pursuit of understanding fundamental scientific questions. At the other end of the seniority spectrum, we were very impressed by

the rapid progress of Iwasaki's RNA Systems Biology Laboratory, who are studying the process of translating mRNAs into protein using genome-wide methods. Among their interesting results is the demonstration that the anti-cancer drug, RocaglamideA (RocA) acts to inhibit the movement of the small ribosomal subunit initiation complex (43S) to the translation initiation site by binding to eIF4A (a 43S component) and, acting together with part of the protein, forming a sequence-specific RNA binding complex. Once bound to a specific site on the targeted mRNA, this complex inhibits protein production. This has clear implications for the mode of action of RocA in killing cancer cells. Impressive also was the range of internal (CPR) and external interdisciplinary collaborations already used by Iwasaki to progress his project.

[Contributions to society]

By nature, and underlying focus of RIKEN research is upon societal impact. Spanning activities from solar fabrics, ultraprecise machining processes, biomaterials, photonics, to DNA engineering – RIKEN is already having substantial impact. The most unique and important value of CPR is its bottom-up policy in research, which allows for challenging research in basic science fields and the development of new fields of research. Such research has a high intrinsic value *per se*, and is the source from which tomorrow's innovation will spring. World-leading achievements in basic science fields produced by CPR also attract public interest to science in general and encourage young people to learn science and to enter STEM careers. Breakthrough research in engineering helps address a broad range of needs, from healthcare to heavy industry. As one prominent example of societal contributions we wish to highlight is the excellent work of the Materials Fabrication Laboratory (Dr. Ohmori). Their continually-evolving ultraprecise surface engineering and fabrication activity has engendered a cohort of collaborators worldwide who are making use of this technology for applications ranging from large-scale, precision optical elements for astronomy and earth monitoring to biomedical applications including simplifying the production of medical needles.

[Consistency with 7-year plan]

CPR's overarching vision for the next seven years was briefly summarized for us by the CPR Director; our perspective combines this information with individual visions for the future various Chief Scientists within CPR that they conveyed to us. From the CPR Director's presentation, and through researchers' discussions with this Advisory Committee, we glean that creation of new fields (via the Chief Scientists' laboratories and All-RIKEN research projects) and the creation and management of shared research infrastructures are paramount in the future vision for CPR. By its nature, this high-risk / high-reward research strategy will never provide 100% success, but if just a few of the pursuits come to fruition, the outcome should be judged as eminently worthy. Generally, we found the individual 7-year plans for Chief Scientists within CPR to be excellent. The general consensus among CPR PIs is that the primary mission of CPR should be to seed transformational and cross-disciplinary research that could ultimately culminate in entirely new Research Centers at RIKEN. Such an example has already been demonstrated in the case of the "MPG-RIKEN-PTB

Center for Time, Constants and Fundamental Symmetries” which evolved from an original Pioneering Research effort. Of course, generation of ideas for promising emerging fields will be dependent on the individual members’ creativity and interests. We note that research subjects currently pursued within RIKEN in its totality are so diverse that it can be difficult to identify optimal starting points for cross-disciplinary collaboration. Despite its central importance, this should not be forced from top downward. We believe that engendering new opportunities for frequent interactions amongst personnel at all levels – from Chief Scientists to postdocs and students – should be emphasized. While the proposed idea of a “common room” to promote interdisciplinary interactions has significant merit, spatially-disparate (delocalized) researchers are not likely to make use of this unless specific events are convened to promote cross-disciplinary discussion. Possible examples might be a cross-disciplinary seminar series or social gatherings, which we understand are already occurring biannually. Finally, we note that there was some variability in some of the most senior Chief Scientists’ 7-year plans; we attributed to these PIs individual proximity to retirement.

TOR 2: CPR director will present *Strength-Weaknesses-Opportunities-Threats* (SWOT) analyses of the management of Cluster for Pioneering Research to their Advisory Committee. Accordingly, the AC will evaluate if the SWOT analyses are appropriate.

[Strengths]

The CPR's main strength is that it provides an environment for curiosity-driven research, allowing PIs the freedom to explore what interests them. There are no barriers between fields leading to interdisciplinary science, as evidenced by Pioneering Project grant mechanism. The attempt of the CPR to promote collaboration and interdisciplinarity is essential. Access to RIKEN's extensive infrastructure and support facilities is a key driver to the Institution's success.

[Weaknesses]

Our perception is that PI budgets within CPR are too small; we feel this deficit will not engender efforts that are competitive with expectations or with long-term personnel involvement. Only a small number of CPR PIs can participate in the few Pioneering Research projects that are funded. Beyond that specific funding mechanism, CPR PIs must rely on additional funding from outside the Cluster – and indeed outside RIKEN, to support a viable research program. Without enhanced support, long-term research themes will be difficult to develop and sustain; this will impair CPR's ability to spawn new fields of research. Outside of CPR and RIKEN, the widespread conservatism of funding agencies makes it difficult to launch truly original and, therefore, uncertain projects. It seems clear to us that continued budget cuts will likely further compromise collaborative research efforts. We are concerned that continued cost-cutting will lead to a significant drop in RIKEN's international reputation.

Regarding personnel, low postdoc and staff scientist turnover can stifle development of fresh ideas and perspectives. Further, there seems to be only a small number of graduate students participating in CPR projects. Left unchanged, this combination will likely lead to aging laboratories. Furthermore, if only a small fraction of researchers are junior PIs, the number of faculty overall will decline. We perceive that junior PIs are presently not allocated staff positions in their laboratories, and we feel this could inhibit their development. Accordingly, we strongly recommend the CPR leadership and assembly of Chief Scientists to address this counterproductive policy.

Cross-fertilization with international thought-leaders seems to be rather limited. We stress that this is essential for maintaining a world-class institution. We suggest that frequent international exchanges between scientists at all levels is of utmost importance for the future success of CPR's mission.

We also perceive that promotion mechanisms within CPR (and perhaps with RIKEN at large) are not well defined and transparent to non-permanent / non-“indefinite” and in particular for distinguished younger “Hakubi” researchers a more transparent and concrete path to the level of Chief Scientist must be developed such that those who succeed can be retained.

The lack of possibilities to recruit students from Japanese universities and the rigidity of governmental administration are major drawbacks for the labs at RIKEN.

[Opportunities]

There appear to be major opportunities for future improvements within CPR by strongly enhancing international activities. Of special note is the exchange of PhD students and postdocs to and from international locations, but most especially to sponsor travel from Japan elsewhere.

At RIKEN itself, making special efforts to remove barriers and nurture close interactions between individual CPR members, in particular at the non-PI level and from disparate fields, could greatly intensify cross-disciplinary collaborations. We also strongly encourage the exploitation of the geographical location of the WAKO campus in connection with the universities to further enhance such collaborations.

The panel perceives that the distribution of so-called “indefinite-term staff” is unbalanced at the present time. The intrinsic structure of CPR provides the opportunity to distribute the researcher cohort according to the needs of the individual laboratories. Further, future retirements of faculty will allow additional reshaping of research directions.

We encourage CPR to consider sponsoring short-term (e.g., 2-week) visitation mechanism that would bring in external international experts for research exchange, and mini-workshops. To develop advanced instrumentation and materials to drive the pioneering research envisaged within CPR requires a true multidisciplinary approach. It is precisely in this “space” that CPR can singularly excel, perhaps even serving as a paradigm for future Japanese scientific efforts.

RIKEN should undertake every possible mechanism to motivate and finance international short and medium-term exchange at all levels. Here, RIKEN should especially stress development of options to make such exchange attractive for incoming researchers at both the student/postdoc and senior scientist levels. We feel certain that engaging with a regular cohort of visitors will prove invaluable to research exchange and thought-fertilization.

We perceive that RIKEN could greatly benefit by increasing the diversity of the scientists, post-docs, and graduate students. This includes both increasing the representation of women and international participants. We recommend broadening the pool of applicants by advertising and aggressively recruitment efforts. Also, using modern methods of interviewing – such as making sure all persons interviewed for a specific position is asked the same questions, and creating a rubric for consistent evaluation – will facilitate selection of the best candidates.

We view the **RIKEN Innovation, Inc.** as being key to RIKEN’s future ability to provide long-term funding for CPR cross-disciplinary efforts. Given CPR’s charter for blue-sky research and development of entirely new fields of research, CPR is definitely the most auspicious home for this new enterprise within RIKEN. It is also of central importance to the long-term vision of CPR. It would be a major achievement to restore

RIKEN's former prominence as a major driver of innovation and commercialization within Japan. Further, this entity has the potential to significantly augment financially RIKEN's fundamental research thrusts – providing a singular avenue for obtaining difficult-to-obtain funds for blue-sky, high-risk/high-reward research efforts. While we realize that plans for this entity are still being formulated, we were provided with an overarching picture of this new strategic effort from presentations by Director Koyasu (on Monday evening) and Mr. Furuya (on Tuesday morning). A brief and intensely-informative meeting was also held between several of our AC with Advisor Higuchi and Deputy Executive Director Aburatani (on Wednesday afternoon). We view it as a well-conceived effort to engage Advisor Higuchi – who has immense experience as a corporate director in the pharmaceutical sector – to survey and solicit input from major R&D centers worldwide. His team's formulation of the plan for RIKEN Innovation, Inc. based on this worldwide input, and the subsequent recruitment Deputy Executive Director Aburatani to lead this effort are excellent first steps. We especially noted advisor Higuchi's highest praise and immense confidence in the choice of Mr. Aburatani to lead this new effort.

Although we find the plans to be very well thought through in large part, we do have several suggestions to enhance these efforts:

1. We suggest that a culture of entrepreneurship be engendered from top to bottom within CPR. Specifically, the researchers themselves must be encouraged and rewarded for development of the new IP within RIKEN's portfolio. This will take some time given the current landscape within Japan, so special forethought and strategic efforts will be required to achieve this culture change. Achieving success here will also require the cultivation of trust between the RIKEN Innovation Corp. and RIKEN researchers *at all levels*.
2. The encouragement for individual researchers to directly engage themselves in launching start-ups should be carefully considered. The prospect for benefitting in their creation – both financially and through personal satisfaction – will strongly incentivize researchers.
3. Perhaps contrary to one's initial assumptions, it is not the case that researchers should be left to pursue fundamental research while others take researcher's ideas and the IP to create start-ups. It has been repeatedly demonstrated that the individuals with the most passion to drive new ventures and make them successful are the inventors themselves. Both fundamental and applied researchers should be allowed, moreover, *encouraged* to participate in the spin-outs their work engenders, if they have such inclination.
4. In contrast to IP common to the pharmaceutical sector, RIKEN's patent portfolio will often (but not exclusively) encompass "hard" technologies. The formulation of sufficiently strong claims within patent applications absolutely requires participation and insights from the inventors themselves. Success cannot be achieved if this is left to patent lawyers alone, in the absence of interactive input with the researchers.

[Threats]

We perceive attempts to make the system more efficient by continuous shrinking of research budgets poses a very serious threat to the future vitality of CPR. Cross-disciplinary efforts cannot likely be nurtured and sustained without such resources. Further, a lack of commitment these resources by RIKEN would risk creating the perception amongst its staff that management places minimal value toward such efforts. Further, the ever-increasing emphasis of top-down compared to bottom-up research in Japan is dangerous for the country's future prosperity.

Overall, CPR researchers appear to have insufficient access to graduate student researchers. We feel strengthening their numbers within the research labs would be immensely beneficial. Additionally, it appears to us that the salary and promotion system may not be competitive at present, compared to other countries. There seems to be rather limited support systems for international researchers and their families—e.g. international schools that are affordable.

We are concerned that, unaddressed, the aging researcher population within RIKEN – without vigorous efforts to nurture more young scientists domestically, or to recruit top international young scientists – is an additional and serious threat.

Finally, we stress that decreasing governmental funding, especially for 'blue sky' projects, also poses a danger to RIKEN's attempts to engender a cross-disciplinary culture.

TOR 3: Evaluate whether CPR's initiatives on the specific items below have accomplished improvements and recommend further measures to be implemented by the cluster.

- RIKEN is conducting a program to enhance its function as the core of research partnerships, namely, the Science and Technology Hub. The AC is asked to evaluate CPR's accomplishments in collaborations including Science and Technology Hub.
- Initiatives on the internationalization of the cluster.

[Collaborations/S&T Hub]

CPR's structure provides a mechanism for cross-disciplinary collaborations in the context of existing and ongoing research support. In that context each scientist must, at present, acquire most of their own separate support. The exception to this rule appears to be the Pioneering Project program, however these are currently highly competitive and appear to have greater emphasis on collaboration. We feel that the PI's must have greater financial support within CPR to pursue these collaborations effectively. When asked about collaborations, PIs indicated rather universally stated that interdisciplinary interactions within Japanese universities and research institutes are quite uncommon, and they stressed to us that RIKEN is one of the few places where this is possible. In this light, the PIs find the advent of CPR a very positive development. However, given that RIKEN's existing research centers still have boundaries between disciplines, overcoming such obstacles will require incentives.

We also witnessed an increasing number of collaborations that connect science and technology. In future, we expect more will arise through the work of RIKEN Innovation, Inc. If this initiative is executed optimally it will enhance collaborations with industry significantly.

[Internationalization]

RIKEN is one of the most internationalized institutions in Asia – in terms of foreign faculty, postdocs, and international recognition. However, we feel that RIKEN has not yet achieved the highest international standards in this regard. Accordingly, our suggestion is that RIKEN should promote internationalization by increasing the number of non-Japanese PIs. For this, the conditions, for personal and family support, and the salaries offered must be adapted to realistic, present living conditions in Japan. The total population of PhD students at RIKEN is low at present but, within the current cohort, there is a reasonable (if variable by discipline) proportion of international fellows. The total number of graduate students in this category could be increased by broadly advertising the existence of PhD positions within CPR and by evaluating the applicants via PI committees. In addition, establishing mechanisms to make international participants more welcome, and providing them with assistance to deal with the challenges of life in a new country and culture, would greatly help in recruitment of international scientists. Optimal advertising is a key to successful recruitment.

TOR 4: Evaluate

- (1) whether all Principle Investigators (PIs) fulfill their duties in accordance with the mission of CPR in the view of the 7-year plan,
- (2) whether their research outperforms international standards from the perspective of contributing to CPR,
- (3) and whether they have proper laboratory management, including efforts to develop early career researchers.

[PIs' contribution to the center mission]

We noticed that knowledge of the mission of CPR is not widespread – even on the PI level in some disciplines, but especially on the junior researcher level throughout CPR. We feel this should be addressed by management and PIs communicating the mission more broadly. In some disciplines we witnessed low uptake of the idea of CPR. The sustainability of the projects is not trusted, in part because of the overly frequent re-organization and rebranding activities of RIKEN. This does not diminish the quality of the bottom-up research produced by the CPR groups but reduces enthusiasm for engaging with “another new initiative”.

[PIs' Performance]

【Research output and impact】

As mentioned above, the research output of CPR PIs is at similar level with other world-class institutions. Their research output is, in total, outstanding. Citations and bibliometric analysis reflect their high-level performance.

【Extramural activities/Accomplishments other than R&Ds】

RIKEN makes an effort to communicate with the public by organizing an “Open Day” which is hugely popular, but more could be done to engage the interested public through other types of outreach events. This could include engaging with local schools, having more visits by school and University students, etc. We encourage PIs to do more to polish their presentation skills and to engage with the public, both to explain their research and to engage in a dialogue about the value of supporting research in general and basic research in particular.

[Laboratory management]

Most junior co-workers are in general quite happy with the management of their laboratory by their PI. The results of a survey of PI leadership performance were presented to us, and this was very positive. This satisfaction was also reflected by junior staff members during our lunch meeting with them.

[Support for early-career researchers]

We felt that support for (PhD and postdoc) fellows could be greatly expanded. At present, there seems to be no career development program; this is a glaring deficiency in the 21st century for a leading research institute such as RIKEN. There also seems to be no mechanism for postdocs to obtain teaching experience beyond an infrequent interactions with Universities. The fellows indeed seem very isolated, and communicated this to this AC. They do not present their research to people outside their groups and there are few if any PhD or postdoc social activities with their peers and superiors. Accordingly, we suggest that networking events should become much more frequent (and given minor financial support), and that PhD and postdoc talks should be regularly convened for all CPR-participating groups. The Spring Training Camp by Kato's Pioneering Project is an excellent example of this kind of career support, but the approach must to be implemented across the CPR to have significant impact.

Finally, to enable more objective future assessment of mentoring, future Advisory Committees should be provided with information describing the number and career of (PhD and postdoc) fellows who have "graduated" from each lab and knowledge their subsequent career trajectory should be available. Also important in this regard is documenting the number of fellows who leave Riken without publishing, and the percentage of those who do publish but leave without a first-author publication.

We suggest that support for young PIs and new hires, to permit build up staff in their lab, must be improved. We hoped that the new measures that have been enacted regarding the employment and the evaluation system within RIKEN, as installed by its President, will help to improve the career chances for some of the outstanding young researchers who have presented their research at the review, as well as their peers. Focusing upon this carefully, will also secure the bottom-up strategy within CPR.

POSTSCRIPT

This CPRAC offers the many, hopefully constructive, points mentioned in this report in the spirit of helping RIKEN in general, and the CPR in particular, to achieve an even higher level of achievement. **Our overarching assessment is that we are deeply impressed by the achievements of the CPR and of the scientists involved.**