

**Report of the Advisory Council 2019**

**On**

**Cluster for Science, Technology and Innovation Hub (CSTI)**

**July 29 – 31, 2019**

## Contents

1. Executive summary.....	P1-3
2. Answers from the AC, including centers, to questions from President .....	P4-10
3. Report on Sectional Committee 1.....	P11-15
• Science and Technology Hub Promotion Division	
• Industry Partnership Division	
• RIKEN Baton Zone Program	
4. Report on Sectional Committee 2 .....	P16-37
• RIKEN Drug Discovery and Medical Technology Platforms	
• Preventive Medicine & Diagnosis Innovation Program	
• Medical Sciences Innovation Hub Program	

## 1. Executive summary

The RIKEN Cluster for Science, Technology and Innovation Hub (CSTI) is tasked with creating a mechanism to urge cooperation beyond the framework of research areas, organizations, national borders and the like and also implementing measures to achieve such cooperation, while assisting the returning of research achievement at RIKEN in the form of social value. Furthermore, the 4th Mid-Term Plan states RIKEN will play an active role in taking actions to strengthen the functions of the innovation ecosystem in Japan. Here again, CSTI is responsible for their implementation.

Therefore, CSTI oversees cross-sectional operations and its activities are targeted at multi-layered areas such as:

-the promotion of problem-solving research and development: DMP, PMI and MIH

-system building: the RIKEN Engineering Network, Science, Technology and Innovation Hub, and Industrial Co-creation Program

Those activities substantially amount to constantly exploring new areas with a series of jobs involving the planning, operating and improving of a variety of programs. Carrying out those jobs requires experimental approaches, different from those to conventional research and development projects.

Starting from such recognition, the CSTI Advisory Council (AC), responsible for Sectional Committee 1 and Sectional Committee 2, intends to advise on the four following areas, based on materials submitted by the CSTI secretariat and the AC's hearings and discussion held on July 29-31, 2019.

### 1. Synergy among Drivers

Cross-sectoral programs, overseen by the CSTI, which serves as a mechanism enabling each RIKEN center to function in a cross-sectoral manner, should be considered as drivers toward the achievement of the Mid- to Long-Term Plan through the RIKEN -initiated collaboration with industry. There are a variety of drivers, largely classified into research development-oriented drivers and system-oriented drivers.

The CSTI should not just promote each individual driver, but also seek to achieve synergy effect among drivers, which the AC believes is the significance of the drivers being under the unified responsibility of CSTI. If efficiency of management is the sole objective, research and development-oriented drivers and system-oriented drivers would come under separate chains of command. But RIKEN opted to unify all of them under the CSTI, believing that there should be some justifiable reasons for that.

## 2. Data management strategy

With the expansion of research activities, the amount of important data is on the rise, encouraging nowadays the emergence of data-driven science. There have been specific examples of the accelerated creation of knowledge and opening up of new fields that have been achieved through mutual development of shared data among different organizations.

At RIKEN, rules concerning collaboration with industry and the management of intellectual properties have so far been implemented in light of contributing to innovation. In the future, moreover, data management strategies will be definitely essential as part of governance.

For the installation of functions of Science, Technology and Innovation Hub in RIKEN, principles and strategies should be clarified by the CSTI with regard to data management that is conducted not only within CSTI, but also between CSTI and other RIKEN centers or external organizations. One factor behind this advice is the fact that White Papers and presentations given by individual sections made no mention of the handling of data.

## 3. RIKEN Innovation Support Company

Following the enforcement of "Act on Revitalizing Science and Technology and Creation of Innovation," RIKEN is preparing to set up the Innovation Support Company in an attempt to contribute more directly to innovation.

Spinning off innovation-related functions into a separate entity is expected to provide the management of RIKEN with greater freedom and flexibility, while at the same time having various impacts on not only the management of intellectual properties and licensing, but also activities conducted by individual sections overseen by the CSTI.

The key to the new company's success depends on whether the following scenario can be drawn up:

Through this new channel, expertise, know-how, and networks that have so far been accumulated at CSTI will be further utilized, leading to the empowerment of the CSTI.

It is recommendable that impacts from the spinning off the innovation-related functions be reflected in the SWOT analysis conducted by the CSTI.

Although the business model of the Innovation Support Company falls outside the scope of the AC's examination, one possible opinion from the AC with regard to the fourth pillar in the concept of the company would be considering the introduction of the so-called

subscription model, rather than seeking to conclude a few alliances annually in a short-term project concept (described as "Co-creation" in the White Papers and presentations). A long-term (or infinite-term) subscription model, compensated for by access to RIKEN's firsthand information as follow gained on the assumption of anonymity is worth considering:

-such information includes knowledge from experience, challenges faced, efforts to create a mechanism including a consortium and atypical financing schemes, obtained on site through the commercialization of the latest and cutting-edge research achievements.

#### 4. Matrix type management

Cross-sectoral programs overseen by the CSTI, which have the function of connecting various RIKEN centers in a cross-sectoral manner, requires matrix type management as they have various objectives and characteristics.

Substantially, the CSTI focuses on structuring expertise by attempting, implementing and modifying new methods for each program. In implementing matrix type management, where a high-level capacity to run an organization is tested, consideration for management cost and implementation of various evaluation axes with regard to achievements, as well as the stability and durability of the CSTI's operation, is recommended.

## 2. Answers from the AC, including centers, to questions from President

### 2.1 Entire CSTI

[TOR 1]

1) Whether the center's research meets international standards and is regarded as world-leading?

The present form of RIKEN is characterized by the combination of a vertical structure of centers--which could be referred to as "Historical path" based on the idea of "Curiosity-driven"--and various schemes added later --which could be referred to as a horizontal structure seeking the maximization of research achievements, collaboration with outside organizations and financing from external funds --(S&T Hubs, Engineering network, Industrial Co-creation Program, and furthermore, Sectoral programs like DMP, PMI, MIH) . This has led to the internal creation of various supporting mechanisms. The introduction of those schemes poses challenges to RIKEN as an organization with regard to an increase in complexity and continuous adaptation.

To generate value as an organization from this horizontal structure, the environment of "under one roof" is a prerequisite but not a sufficient condition. Therefore, what is needed here is a mechanism to return to systematic synergy interaction at the individual level that happens in a bottom-up manner by introducing formal interaction (such as workshops) between programs, among others.

Furthermore, to transform complexity into something manageable and guarantee continuous adaptation and sustainability of centers, strategies should be clarified not just for programs making up the horizontal structure, but also for the entire CSTI.

Along with the clarification of the strategies for the CSTI, RIKEN's position as a leading organization in Japan's scientific research should be strengthened by thrashing out and reviewing RIKEN's internal resources (patents, research themes and availability of human resources).

2) Whether its research results have contributed to society?

To begin with, it is recommendable to clarify the definition of "society" that the entire RIKEN targets, particularly the definition of "society" that the CSTI targets. Depending on the understanding of the concept of "society," scope of achievements that the CSTI should seek would be different, ranging from items in a narrow sense, such as research

results, technology transfer, collaboration with outside organizations and RIKEN Venture, to the creation of social value, such as advancement of science and improvement of people's well-being. Furthermore, the definition also determines the balance of gravity between the factors that the CSTI can control and factors that depend on other stakeholders' actions.

The AC hopes that, in the future, the CSTI will secure human resources that have not only expertise, but also the capacity to act in an unconventional and multi-layered manner, while putting more importance to diversity, based on the idea that RIKEN seeks to achieve social contribution in a broader sense.

3) Whether its up-to-date activities and strategies meet the aims of RIKEN's fourth mid-to long-term plan (7-year plan)?

Activities of the CSTI is in line with RIKEN's 4th Mid- to Long-Term Plan.

Based on the clear strategy of the CSTI, implementation of the 4th Mid-Term Plan is underway on site with new mechanisms, such as the Science, Technology and Innovation Hub and the RIKEN Engineering Network introduced, in addition to the existing RIKEN Baton Zone Program.

In addition, those initiatives are expected to enhance the capacity and durability to pursue "Research excellence," the *raison d'être* of RIKEN, in light of their complementary roles.

However, it is important to note here that attention should also be paid to the naming of those activities, as well as their contents. The AC highly appreciates the RIKEN Engineering Network, which attempts to softly connect researchers in RIKEN. But "engineering" used in the name is not limited to engineering in its conventional sense, but is regarded as something covering a broader sense including science. Such an interpretation, adopted only within RIKEN, is difficult for those outside RIKEN to understand. In addition to this usage of engineering in question, the naming of "Science, Technology and Innovation Hub" should also be reviewed so that RIKEN can take a global initiative in technology transfer, industry-university cooperation and innovation. It is therefore necessary to make efforts to depart from RIKEN's conventional expression and explanation.

In implementing initiatives of the CSTI, enhancement of cost-consciousness with regard to management is desirable. In addition, in introducing new schemes such as "Innovation Design," it is also important to check its consistency and complementarity with existing initiatives.

[TOR2] Center director will present a SWOT analysis on the management of the center to their AC. The AC is asked to evaluate whether the SWOT analysis and the director's management proficiency are suitable.

The significance of SWOT analysis is believed to rest with not only analysis results themselves, but also the series of processes conducting simultaneous analyses. Implementing SWOT analysis means providing those concerned within an organization with opportunities to objectively review daily operations, exchange and examine ideas and share the direction of activities. Thus, analysis results can also be interpreted as a summary of self-appraisal.

The AC believes that the CSTI's SWOT analysis should be conducted under the strategies compiled at the level of CSTI based on the strategies for RIKEN.

In addition, the latest CSTI's SWOT analysis has not conducted in-depth examination of the presence of the Innovation Support Company. As was mentioned in the " 1 . To Begin With," the Innovation Support Company will have significant impact on the operations of CSTI. It is therefore recommendable that SWOT analysis be conducted centering on the Innovation Support Company.

The following is the latest list of comments made with regard to the CSTI's SWOT analysis:

The section of [Strengths (internal/positive)] was generally appropriate. With the creation of the hub and emergence of the Innovation Support Company, new revenue sources have been secured, adding flexibility to the handling of research fund, which is advantageous for the CSTI. In addition, the presence of favorite fields and experience gained and accumulated through initiatives, such as Sponsored Laboratory, DMP and PMI, is another strength of the CSTI.

Contents mentioned in the section of [Weaknesses (internal/negative)] can be transformed into strength depending on how to interpret and how to deal with them. For example, the fact that RIKEN does not run a hospital means that it is spared the burden of operational cost, management cost, risk management and the like resulting from hospital management, while at the same time potentially serving as an incentive to strategically collaborate with existing hospitals.

Another example of weakness is the overlapping of tasks by existing RIKEN centers and through new initiatives such as Science, Technology and Innovation Hub and the RIKEN



Engineering Network. The CSTI should clarify its goals and familiarize them, which would be the first step toward overcoming this weakness. In addition, as was mentioned in "1. Executive summary" the implementation of Matrix-type management will hold the key.

The analysis in the section of [Opportunities (external/positive)] is also appropriate. At a time when the global environment changes constantly in the context of geopolitics, RIKEN is expected to attract more attention both domestically and internationally. Adjusting to environmental changes should be considered as opportunities to find new research fields and collaborative partners.

As for the section of [Threats (external/negative)], attention should be paid to conflict of interest that would arise in establishing the Innovation Support Company. When it comes to Membership-based Co-creation, the 4th project axis of the mentioned new company, consulting activities are expected to develop to joint researches. RIKEN researchers should not participate in the consulting activities in order to carry out joint researches independent of consulting.

[TOR3] Evaluate whether the center's initiatives on the items given below have resulted in improvements and recommend further measures to be implemented by the centers.

#### Collaborations/ S&T Hub

The Science, Technology and Innovation Hub is fundamentally a scheme intended to promote collaboration with other academic organizations on an organization-to-organization basis with the implementation of interdisciplinary researches as its pillar. The hub is normally based in a partner organization.

While the Science, Technology and Innovation Hub is a system designed to skillfully reconcile different interests of researches, people related to universities and others in an attempt to maximize the research achievements, attention is also required to deal with intellectual properties of participating parties.

Substantially, the hub has been established following negotiations that the CSTI has with individual academic organization to reach an accord on an organization-to-organization basis. With various possible forms of collaboration, composition of research teams and research contents, conventional forms of contract do not fit this system.

In addition, the series of processes of negotiations urge the partner organizations to get

involved in unprecedented internal collaboration and visualize a new research and development base, thereby bringing about significant ripple effects.

Given such current situations, the AC proposes the following items.

1. Along with identifying factors behind success, such as modelization of successful cases, increase in the number of collaboration opportunities based on prompt decision-making and payment and research, the know-how concerning a variety of management and collaboration obtained through the creation of the Science, Technology and Innovation Hub should be shared within RIKEN and with external organizations.
2. A hub that would serve as a unit for collaboration with other organizations should be established within RIKEN as well. Transforming loose collaboration within RIKEN, such as the RIKEN Engineering Network, into a formal form to make it serve as a stage for collaboration with external organizations and external researchers should be considered.
3. With regard to the Science, Technology and Innovation Hub, not just successful unique initiatives in term of technology transfer and acquisition of external funds, such as the RIKEN Baton Zone Program, and activities in parallel with mechanisms contributing to the enhancement of activities within RIKEN, such as the RIKEN Engineering Network, but also synergy with cross-sectoral drivers should be sought based on comprehensive strategies compiled by the CSTI.

#### Initiatives on the internationalization of the center

Partners of the Science, Technology and Innovation Hub are currently limited to domestic academic organizations and no international initiative has been achieved so far. Nevertheless, the CSTI possesses certain know-how and human network with regard to international collaboration. Some of CSTI's on-going initiatives to create hubs can anticipate the participation of overseas organizations including Kazan Federal University.

In the future, while utilizing resources within RIKEN, such as the International Affair Division, the CSTI should strategically promote activities with a view to international expansion.

[TOR4] PI's contribution to the center mission

1) Whether each of the PIs fulfill their duties in accordance with the mission of the center, taking into consideration the 7-year plan ?

By assigning PIs with various backgrounds and high expertise to the RIKEN Baton Zone Program, the Special Senior Researcher Program, DMP, PMI, and MIH, all of which are research programs of different natures, the diversity of the entire centers is guaranteed, which can be highly appreciated.

The research themes range from medical-related ones to materials and agriculture. With regard to the period of time needed to carry out researches, projects that potentially lead to product development on a 10-year basis have been adopted at a time when short-term projects tend to be prioritized today. Those initiatives are appropriate and interesting. The Special Senior Researcher Program is particularly interesting in the following respects:

- Excellent as a career path for elderly researchers and experts. (Raising the age limit age to 75 should be considered)
- Selects unique Special Senior Researchers under the mechanism
- Serves as seeds of technology transfer requiring no initial investment as research funds are obtained from enterprises
- Diverse attributions of researchers are appreciated at the laboratory, which is operated by those maintaining their positions at a start-up

In the future, the presence of women among Special Senior Researchers will be more than welcome.

Expertise gained through those program activities should desirably be shared in and outside RIKEN.

2) Whether their research meets international standards?

Research achievements of Special Senior Researchers have been published in science magazines with high impact factor, while producing opportunities to give lectures at academic meetings. Meeting the international standard, they deserve a high valuation. Many Special Senior Researchers have published books and given lectures for general public and are appreciated for their contribution to enhancing the understanding of research targets in terms of impact on society outside academic circles, particularly general public.

Research achievements made at some of the laboratories have been put to practical use and generated revenue from patents, which should be highly esteemed.

With regard to initiatives made for collaboration between different fields and laboratories, there has been some difference among Special Senior Researchers. Improvements should be made where sharing of data and mutual use of individual expertise have not been initiated.

3) Whether they have suitable capability on the laboratory management, including their efforts to support early-career researchers?

Special Senior Researchers can be judged to be good role models for young researchers in selecting research themes and attracting research fund from companies.

Overall, different Special Senior Researchers work on research themes that are different in terms of product development levels (ranging from early or prototype stages to licensing stages). It is also worth noting that each researcher has adopted a management style suitable for his or her research theme.

### **3. Answers to inquiries from Sectional Committee 1 (Science and Technology Hub Promotion Division, Industry Partnership Division, the RIKEN Baton Zone Program)**

#### Science and Technology Hub Promotion Division

Efforts to promote the creation of Science, Technology and Innovation Hub functions and the RIKEN Engineering Network program in an attempt to maximize research achievements should be highly esteemed. Those systems are designed to skillfully reconcile interests of researchers, university-related people and others.

Goals (set as a big picture of CSTI that serves as an enveloping concept for individual programs) and key performance indicators should be presented in a simple and clear-cut manner (ideally one-pager) that would promote better understanding of the contents.

Based on submitted materials, presentations made to the AC and exchanges of opinions, the AC has listed goals and key performance indicators below and evaluated them as answers to inquiries.

#### Goals

- Creation of new research areas through the promotion of fusion of different fields between RIKEN and universities or external research organizations
- Creation of sustainable network systems of researchers

#### Key Performance Indicators (for the benefit of RIKEN)

1. Creation of new research fields
2. Establishment of networks involving researchers, local communities, companies and the like
3. Exploration of non-covered research fields
4. Research achievements (research papers and patents)
5. Acquisition of external research fund

SWOT analysis, which has been conducted precisely, and achievements (key performance indicators) both deserve a high valuation. This trend should be maintained. The extent of activities needs to be discussed based on available assets (fund and human resources) and achievements. Increase in available fund would be a welcome move to pave the way for increase in human resources, thus creating a virtuous cycle.

The RIKEN Engineering Network is another important and interesting attempt that deserves a high valuation. It is a grass-root, effective mechanism intended to take on board ideas of researchers and their motivation. Once this mechanism is put in motion to a certain extent, efforts should be made to acquire external fund and create new

research fields, while management decision should be made on whether networks would be expanded beyond RIKEN to reach external organizations or operations would be conducted in the form of the Science, Technology and Innovation Hub. However, as was mentioned in the Executive summary of this report, the use of term "engineering" in Engineering Network is ambiguous. When the term is loosely used, as opposed to conventional definition, adequate explanation should be made.

The Science, Technology and Innovation Hub has been set up in a large number of universities and research organizations with joint research themes set strategically with the result of the creation of new integrated research areas, which can be highly appreciated. The well-crafted system also enables active participation of and cooperation among researchers, leading to the emergence of harmonious coexistence in local communities, as well as arrangements for the acquisition of external fund and exchanges of human resources. Upcoming developments appear promising.

#### Industry Partnership Division

With the maximization of research achievements set as the objective, various attempts have been made to promote open innovation and strengthen the co-creation function through the collaboration with industry on an organization-to-organization basis. Those efforts deserve a high valuation. SWOT analysis has been conducted appropriately while initiatives have been taken to respond to the previous AC. Such efforts can also be highly esteemed.

The establishment of the Innovation Support Company following another law amendment is a highly promising development that marks a fresh start. With the company's objective clarified, the company and the Industry Partnership Division should be linked organically. Needless to say, organizations should be made up of motivated human resources to implement socially meaningful and important missions.

The most important objective of the new company is to make social contributions through technologies generated by RIKEN. It is important to recognize anew that independently securing research fund available for RIKEN (generating profits) is the means to achieve this objective. It should be also emphasized that profits can be naturally generated as honest objectives are implemented.

Furthermore, with the establishment of the Innovation Support Company, it is difficult to grasp what kind of activities the Industry Partnership Division will engage in, although the White Paper mentions "linked organically." (White Paper, page 49) Private companies seeking to tie up with RIKEN for the first time may have the impression that RIKEN has become open to industry as it has become clear where to

contact. However, for companies that have had contact with RIKEN researchers since a long time ago, the three-layered structure with the Innovation Support Company, CSTI and the Administrative Division would seem even more complicated. They could have the impression that just another indirect department has been added. Thus, more efforts should also be made to streamline operations of RIKEN.

With regard to intellectual properties, patent training programs intended for researchers have been held and reforms to change their mindset have been made. Those efforts deserve a high valuation. However, at a time when papers are prioritized over anything else, awareness of intellectual properties is difficult to spread. Staff members charged with intellectual properties should do more than just to wait for researchers to contact the members. Efforts to identify intellectual properties should be even more strengthened by keeping a constant eye on researches at RIKEN. This is where brains should be used to efficiently identify intellectual properties with limited staff. Initiatives that are typical of RIKEN should be sought through the use of AI and IT, among other things.

The spin-off venture companies labelled RIKEN Venture are regarded as an important actor in the innovation process with its achievements steadily increasing. However, more efforts can be made to identify technology seeds for venture companies, optimize the process leading up to the start of ventures, carefully examine the period and content of incubation, secure human resources in charge, among other things. With regard to venture companies set up by RIKEN researchers, it is to be noted that such researchers are not allowed to become the president. In addition, when related RIKEN venture companies conduct joint researches with RIKEN, those from RIKEN are not allowed to assume other related posts. Those measures are worth a high valuation. RIKEN's good practice should be shared with other research development organizations and national universities.

Following the establishment of the Innovation Support Company, given that operations concerning university-industry cooperation and the RIKEN Venture are assumed to be transferred to the company. It is important to make a comparative study of practices at other related entities, universities and research organizations. Constantly benchmarking positions of RIKEN and the Innovation Support Company would help evaluate organizations.

In addition, as was mentioned in the sections of "TOR2" and "SWOT analysis," with regard to the company's 4th project axis (Membership-based Co-creation), RIKEN staff members should not participate in cases where they conduct joint researches with the same companies as conflict of interests arises.

### The RIKEN Baton Zone Program

Baton Zone researches are promoted for the purpose of achieving "technology transfer with a view to putting into practical use results of basic researches together with enterprises." The program, established to flexibly deal with individual situations of research themes, can be highly esteemed. SWOT analysis has been conducted precisely.

#### (The System for Collaboration Center with Industry)

With the number of collaboration cases increasing for that past few years, the system is gaining ground thanks to efforts to flexibly handle operations depending on individual enterprises. However, rather than solely following the direction of each enterprise, initiatives to provide enterprises with center concepts featuring the strength of RIKEN should be promoted. Along with responding to individual situations of research themes, efforts should also be made to accumulate know-how concerning collaboration on an organization-to-organization basis.

#### (The System for Integrated Collaborative Research Program with Industry)

With regard to the system for Integrated Collaborative Research Program with Industry, efforts to review the system, increase adoption opportunities and shorten the period to achieve earlier collaboration can be highly esteemed. On the other hand, as flexible handling would also be necessary depending on individual research contents, adequate adjustments should be made with enterprises over discussion. While expansion of fund scale for enterprises is a welcome move, attention should be paid so that abilities to negotiate with them would not be undermined.

While the system effectively promotes technology transfer, research results tend to rely on conventional marketing efforts to collect as many enterprises capable of exerting initiatives as possible. The time seems to have come when the current system needs to be reviewed, considering the difficulty in securing human resources and decrease in the amount of budget that can be used within sections on a relatively free manner.

In the framework of the system, initiatives to acquire client enterprises are expected to overlap the marketing activities of the Innovation Support Company. Shift to a system that would enable organic collaboration would be welcome.

#### (The Sponsored Laboratory System)

Modifications made to the Sponsored Laboratory System deserve a high valuation. Furthermore, sponsored laboratories are steadily producing results in acquiring fund



and making social contributions, among other things.

Utilizing this system can be judged to promote collaboration with enterprises, acquisition of new fields, acquisition of external fund and cross-sectoral researches within RIKEN. However, as the system largely depends on researchers' abilities and personalities, non-stereotypical, flexible operations using various values and key performance indicators would be desirable. In addition, mechanisms to hand down their successful research styles and cases, for example, including assigning those leaving Sponsored Laboratories to the job of handing down successful models in some ways, should be created. Eying the utilization of such models in the Innovation Support Company is also recommended.

### **3. Answers to inquiries from Sectional Committee 2 ( RIKEN Drug Discovery and Medical Technology Platforms, Preventive Medicine & Diagnosis Innovation Program, Medical Sciences Innovation Hub Program)**

#### **3.1 Summary**

##### Drug Discovery and Medical Technology Platforms (DMP)

[Comments]

- CSTI-AC congratulates the success of DMP's outcome in the goals of 3rd mid-term plan that achieved six successful exits, including five licensing-out contracts, and for their large contribution to RIKEN's IP income through project alliances with companies.
- The artificial adjuvant vector cells (aAVC) project headed by Dr. Fujii is a successful model case for world-class application of cell therapy. In addition, the project is a standard model for business development division including prompt negotiation with a pharmaceutical company, and would inspire the forthcoming RIKEN Innovation Support Company.
- The stagnation in small molecule drug discovery seems to be a global trend among pharmaceutical companies. Despite Japan's strength in this field, there has also been a move by Japanese pharmaceutical companies to release their existing technologies and assets.
- DMP already established an excellent standard development model for regenerative and cell medicine, and also showed steady progress in small molecule drugs. We encourage RIKEN DMP to establish a new standard model for small molecule drug discovery combining AI, MD, phenotypic screening, protein degradation, etc.
- Integration of these technologies cannot be implemented by current pharmaceutical companies alone, so RIKEN's challenge will have a significant impact on global drug discovery.
- We expect that drug development processes will be reinforced through negotiations with PMDA and direct investments by RIKEN.
- There are also concerns about the separation of business development from DMP in view of establishment of RIKEN Innovation Support Company. It should be noted that, based on the aAVC success story, close collaboration with DMP will not be impaired in the future.

[Recommendations]

- For the future development, in view of maintaining and expanding DMP's role in medical innovation in RIKEN, CSTI-AC recommends that RIKEN should retain the matrix structure<sup>1</sup>.
- Considering the success of Dr. Goto's management, the PD successor should be a person with top management experience at a pharmaceutical company and with a deep understanding of modalities of drug discovery and cutting-edge technologies.
- Given that PMI and DMP have been jointly promoting RPE project headed by Dr. Takahashi to analyze possible genome mutation risks derived from iPSC and that MIH and DMP are also jointly promoting AI-based drug discovery technologies, further close collaboration among the three programs is recommended toward accelerating medical innovations in RIKEN.

---

<sup>1</sup> It refers to the Option A in the presentation by Dr. Goto.

## Preventive Medicine & Diagnosis Innovation Program (PMI)

### [Comments]

- PMI's activities are unique and important in that they are essential for developing RIKEN's research results into services and products that meet social needs. CSTI-AC appreciates that PMI has so far achieved excellent results, including the development of international cooperation, and that it currently has a number of projects ongoing or completed.
- PMI's mission is to fulfill medical and industrial needs by using RIKEN technical seeds. Therefore, the real value of PMI resides in the innovative use of applied sciences, facilitating translation of RIKEN technical seeds in terms of practical applications in view of implementation in society, which is unique in RIKEN, and this far beyond the creation of business itself.

### [Recommendations]

- PMI projects are entirely funded by external grants, in particular from private sector, and there are no Institutional Research Funds allocated. CSTI-AC suggests that RIKEN executive considers to offer to some projects, in their early development phase, an option to be funded by the Institutional Research Funds, based on a clearly defined criteria, in view of attracting the interest of private sector and maximizing the benefit for RIKEN.
- The governance system in place at PMI (PMI model) may inspire other programs at RIKEN as a good practice.

## Medical Sciences Innovation Hub Program (MIH)

### [Comments]

- The young MIH program is addressing important scientific and societal goals, i.e. using AI to enable personalized/precision medicine as well as using AI-driven drug discovery, and has a promising organizational form based on appropriate expertise for the above questions and associated clinical collaborators.
- The attractive setting is that MIH is organized in two complementary areas (AI for personalized medicine and AI for drug-discovery) with associated clinical groups addressing major diseases.
- Recruitment of key AI personnel is a worldwide challenge, but the program was successful in attracting investigators with interdisciplinary expertise in both areas. This is a fertile ground for future developments and the program should build on this opportunity. However, MIH has a small number of external experts to consider the ELSI issues.
- The computational infrastructure was established, which is by itself a major effort. Also, the access to a supercomputer in conjunction with the software tools for structure-based analysis is a unique opportunity and already attracted a number of pharmaceutical companies.

### [Recommendations]

- Given the challenges in the field (fierce competition by academic institutions as well as big company players like Google and Apple, fast pace of the developments in the field, ethical issues related to data protection, and technical hurdles associated with large heterogenous patient data), and the limited resources allocated to the program, CSTI-AC recommends to identify and concentrate resources on one or two specific topics in each area of “deep phenotyping<sup>2</sup>” and “drug discovery<sup>3</sup>”.

---

<sup>2</sup> Deep phenotyping: Ideally, the topic(s) should be scalable so that in the second phase the concept can be deployed on a large-scale. Given the limited time before the decision to continue MIH after FY2021, it is advisable to select a disease/cohort for which data is already available and generate only complementary data to broaden the multimodality for deep phenotyping (e.g. CT images on top of the NGS data or biochemical parameters on top of the fetal ECG) and demonstrate the proof-of-concept of the applicability of the AI-methods.

<sup>3</sup> Drug discovery: The newly developed tools such as graph convolution network, three-dimensional convolution network, multi-task learning, fragment molecular orbital method,

- To take advantage of running two these complementary areas, the collaboration within the program needs to be strengthened and the PIs should define common goals and join forces to reach these goals. Specifically, the AI-concepts for deep phenotyping can be tested using available clinical data in the program. Similarly, the reverse translational efforts (network analysis) in the drug discovery area can be adopted in order to provide novel biological insights using the clinical data and/or interpret mouse results in a human context.
- Related to the personal, beside the recruitment of investigators, MIH should make effort to attract additional students. Also, CSTI-AC recommends to hire specialists in ELSI. Alternatively, it is a good idea to collaborate with other consortiums and institutions such as LINC and National Hospital Organization to form a team of experts jointly.
- Regarding the exploitation of computational infrastructure, for both areas “deep phenotyping” and “drug discovery”, the projects should have a perspective on the data size, that is not clearly stated. Broad Institutes produces 26TB data every day, including image data though K and FUGAKU are referred. BGI produces 20TB genome sequence data every day. From the top international standing, the MIH should clarify this point and put it in the future scope. Also, an advice of a structural bioinformatician should be sought.
- Collaboration of the three programs (MIH, PMI, and DMP) should be enhanced. There is certain thematic overlap between the three programs and it is recommended to actively promote close collaboration between the three programs and exploit potential synergies. The AI-driven drug discovery platform built by the Okuno group has begun to be applied to RIKEN DMP's actual drug discovery targets,

---

and three-dimensional reference interaction site model are original and very useful in order to provide a versatile AI drug discovery platform for pharmaceutical companies. Okuno group has already organized a consortium (LINC) consisting of 110 pharmaceutical and IT companies and the AI platform is being enhanced collaborating with the consortium members. Amalgamation of publicly and proprietary data is to be appreciated, and Okuno group has started to establish a new data sharing project with more than 15 pharmaceutical companies. Though the project goals and AI technology developments have rationality, AI is a fusion of algorithms and data. The weakness of MIH is that it lacks a strong team for ELSI research for data science (as is indicated above as “ethical issues related to data protection”). US NIH has been promoting ELSI research for genomic data, but currently the biggest issue is all data which are related to human.

and such activities should be promoted in the future, demonstrating the usefulness of AI technology.

## 3.2 Detailed Report

### Drug Discovery and Medical Technology Platforms (DMP)

【General comments】

#### **(1) Creation of an ideal healthcare system for future society through the collaboration of the three programs (MIH, PMI and DMP)**

- PMI and DMP have been jointly promoting RPE project headed by Dr. Takahashi to analyze possible genome mutation risks derived from iPSC. MIH and DMP are also jointly promoting AI-based drug discovery technologies.
- Further close collaboration among the three programs is recommended toward accelerating medical innovations in RIKEN.

#### **(2) Notable achievements**

- DMP is to be congratulated on making significant advances that achieved five exits including four licensing out since the last AC meeting.
- During the 3<sup>rd</sup> mid-term, six exits including those mentioned above, were recorded and the achievement exceeded the 3<sup>rd</sup> mid-term goals.
- The artificial adjuvant vector cells (aAVC) project headed by Dr. Fujii is a successful model case for world-class application of cell therapy. In addition, the project is a standard model for business development division including prompt negotiation with a pharmaceutical company. The new Innovation Support Company should learn from this case and maintain the speed of project development.

#### **(3) Challenge for the stagnation in small molecule drug discovery**

- The stagnation in small molecule drug discovery seems to be a global trend among pharmaceutical companies. Despite Japan's strength in this field, there has also been a move by Japanese pharmaceutical companies to release their existing technologies and assets.
- DMP already established an excellent standard development model for regenerative and cell medicine, and also showed steady progress in small molecule drugs. We encourage RIKEN DMP to establish a new standard model for small molecule drug discovery combining AI, MD, phenotypic screening, protein degradation, etc.
- Integration of these technologies cannot be implemented by current pharmaceutical companies alone, so RIKEN's challenge will have a significant impact on global drug discovery.



#### **(4) Relationship with RIKEN new Innovation Support Company**

- We expect that drug development processes will be reinforced through negotiations with PMDA and direct investments by RIKEN.
- There are also concerns about the separation of business development from DMP. It should be noted that, based on the aAVC success story, close collaboration with DMP will not be impaired in the future.

#### **(5) Post DMP organization**

- We congratulate the success of DMP's outcome in the 3<sup>rd</sup> mid-term plan goals, especially for their large contribution to RIKEN's IP income through project alliances with companies.
- To maintain and expand DMP's role in medical innovation in RIKEN, we recommend RIKEN should take Option A (where the matrix structure is retained).  
Considering this success of Dr. Goto's management, the PD successor should be a person with top management experienced at a pharmaceutical company and one who understands many of the modalities of drug discovery and cutting-edge technologies.

**【TOR 1】** Evaluate (1) whether the center's research meets international standards and is regarded as world-leading, (2) whether its research results have contributed to society, (3) and whether its up-to-date activities and strategies meet the aims of RIKEN's fourth mid- to long-term plan (7-year plan).

Note:

DMP is regarded as a center in RIKEN's organizational structure. Regarding the research activities indicated by the Program Director, please evaluate research achievement, contribution to society, conformity with the fourth mid- to long-term plan, etc. RIKEN have to make a decision that whether DMP should be continued after 2021(2022). We would like to hear proposals regarding the direction and organization of DMP for the later part of RIKEN's fourth mid- to long-term plans.

#### **[Research]**

- The artificial adjuvant vector cells (aAVC) project headed by Dr. Fujii is an excellent example of world-class application of cell therapy. In addition, the project is a standard model for business development division including prompt negotiations with the pharmaceutical company. The new Innovation Support Company should

learn from this case and maintain the speed of project development.

- The ALK2 project is a good example for small molecule development, showing world-standard application of different technologies (including X-ray crystallography, computational chemistry and medicinal chemistry) and subsequent animal model evaluation is promising.
- The iPSC & NKT technologies are further examples of unique expertise that has been nurtured within DMP.
- The molecular dynamics and artificial intelligence approaches are at or near the world level, and practical applications to small molecule projects are expected.
- iPSC screening demonstrated iPSC-based phenotypic screening using natural products. Since phenotypic screening need not be limited to iPSCs, other types of phenotypic screening should also be considered.
- Protein degradation approach can be a new modality of drugs. To establish RIKEN original methods, collaborations with in silico design and X-ray analysis are desirable.

#### **[Contributions to society]**

- DMP aggressively adopted all Japan drug discovery targets including rare, intractable, neglected disease targets collaborated with AMED drug discovery network.
- DMP successfully transferred quit a few preclinical and clinical projects to pharmaceutical companies and medical institutions. We hope these projects will contribute medical innovations in RIKEN especially for the patient's wellness who suffered from intractable diseases.

#### **[Consistency with 7-year plan]**

- DMP is to be congratulated on making significant advances that achieved five exits including four licensing out since the last AC meeting.
- During the 3rd mid-term, six exits including those mentioned above, were recorded and the achievement exceeded the 3rd mid-term goals.
- DMP's 7-year plan goals to transfer 4 projects to pharmaceutical companies and medical institutions presented by Dr. Goto are consistence well with RIKEN 7-year plan in terms of medical innovations.

**[TOR2]** Center director will present a SWOT analysis on the management of the center

to their AC. The AC is asked to evaluate whether the SWOT analysis and the director's management proficiency are suitable.

Note:

Please evaluate the suitability of SWOT analysis for operation of the program specified by the Program Director.

Following SWOT analysis are suitable and DMP director's matrix management in RIKEN worked very well.

**[Strengths (internal/positive)]**

- Portfolio management and matrix management by experienced managers from pharmaceutical companies.
- DMP aggressively applies new technologies including MD and AI as well as iPSC screening, protein degradation, and genome editing.
- DMP has a pioneering role in trailblazing cell-based therapies (for example, with respect to the evolving regulatory environment etc.). This was flagged as an important role at last AC, and it is good to see that the progress and momentum has been maintained (including adaptation to new legislation).
- Strong interaction with pharma.

**[Weaknesses (internal/negative)]**

- Incentives for RIKEN researchers not employed by DMP to devote time and resource to DMP activities, are still unresolved. For experienced researchers in charge of drug discovery activities, longer term or permanent employment should be considered.
- When option or licensing income is generated by DMP activities, a proportion needs to be returned to DMP.
- Although it is not necessary to make a profit, it is desirable for drug discovery to be able to create an ecosystem that circulates funds and maintains a constant level of research and development.

**[Opportunities (external/positive)]**

- Regular interactions with RIKEN centers are encouraged. The recent Collaboration Centers Program is an example of the benefits of such interactions.
- DMP, PMI, and MIH started to be involved in common projects. The cases of cell

therapy by DMP and PMI and difficult small molecule targets by DMP and MIH Okuno group are good examples. In the future, new target identification by PMI and MIH Sakurada group is expected.

- Establishment of RIKEN Innovation Support Company.

**[Threats (external/negative)]**

- The proportion of new modalities such as cell therapy and antibodies has increased, and relatively small molecule stagnation (time-consuming, requiring collaboration in many research fields, etc.) is noticeable.
- Decrease in easily handled drug targets
- Increase in similar program outside RIKEN

**[TOR3]** Evaluate whether the center's initiatives on the items given below have resulted in improvements and recommend further measures to be implemented by the centers.

- RIKEN is conducting a program to enhance its function as the core organization for research partnerships, which we refer to as the "Science and Technology Hub." The AC is asked to evaluate the center's achievements in collaborative activities, including those belonging to the Science and Technology Hub.
- Initiatives on the internationalization of the center

Note:

Please evaluate collaboration in the DMP (Science and Technology Hub, other cooperation efforts), and internationalization initiatives.

**[Collaborations/S&T Hub etc.]**

- DMP as a cross-sectional organization at RIKEN collaborates quite well with various Japanese organizations, including academia and AMED, as well as each of the centers at RIKEN.
- Since the last AC, DMP adopted 2 projects and 18 themes including outside RIKEN.
- Collaborated with AMED, outside targets should be adopted more aggressively.
- The business development office conducted 40 to 80 meetings per year with 121 pharmaceutical and related companies.
- DMP has concluded 16 collaboration agreements with pharmaceutical and biotech companies since 2016.

**[Internationalization]**

- DMP collaborates with overseas companies (3 collaborations) and academia (1 collaboration) to promote themes/projects as well as domestic collaboration.
- A new biotech company was established in 2015 for exit of projects (Flash Therapeutics, LLC, for the “Leukemia treating drug targeting stem cell” project and the non-clinical development is underway in the US.
- In addition to these themes/project promotion, platform units conduct a variety of overseas collaborations based on science and technology. As part of our collaboration with American national research institutes, the National Center for Advancing Translational Sciences and DMP conducted mutual visits and information exchange.

**【TOR4】**Evaluate (1) whether each of the PIs fulfill their duties in accordance with the mission of the center, taking into consideration the 7-year plan; (2) whether their research meets international standards; (3) and whether they have suitable capability on the laboratory management, including their efforts to support early-career researchers.

Note:

DMP has no “PI” position. Instead, please evaluate the organization and operation of the Program Director regarding this matter.

**[Program Directors’ contribution to the program mission]**

- (1) Dr. Goto properly settled vision, mission, and goals aligned with the 7-year plan for DMP. His strategies consisting of RIKEN drug discovery seeds, RIKEN technology platforms, experienced managements from pharmaceutical companies are working well.
- (2) The output of DMP at least matches if not exceeds international standards for comparable drug discovery organizations.
- (3) Dr. Goto educated young managers (Honma, Hashizume, and Yamauchi) to promote drug discovery with world standard. In addition, he has fostered young researchers to make career both in RIKEN and pharmaceutical companies.

**[Program management]**

- Portfolio management and matrix management are working very well
- The recruitment of 1) Dr. Uemura to Clinical Development Support Office, and 2) experienced medicinal chemists, has significantly improved the capability and capacity of DMP

## Preventive Medicine & Diagnosis Innovation Program (PMI)

### **【General comments】**

- (1) PMI's activities are unique and important in that they are essential for developing RIKEN's research results into services and products that meet social needs. CSTI-AC appreciates that PMI has so far achieved excellent results, including the development of international cooperation, and that it currently has a number of projects ongoing or completed.
  
- (2) PMI's mission is to fulfill medical and industrial needs by using RIKEN technical seeds. However, the real value of PMI's activities is not the creation of business itself but the innovative use of applied science to develop RIKEN technical seeds into practical applications for implementation in society. This is a unique activity within RIKEN.

### **【Recommendations for PMI】**

- The role of PMI is to promote social implementation of RIKEN technical seeds. As indicators for the evaluation of PMI, CSTI-AC proposes using the research resources acquired by PMI, which include external funding, and the number of research outcomes transferred to outside organizations for social implementation.
- PMI should define more clearly the criteria used for selecting and rejecting projects. PMI should also understand and then evaluate the development phase of each project and explain these activities to the RIKEN management.

### **【Recommendations for the RIKEN management team】**

- For each PMI project, the RIKEN management team should evaluate the development phase as well as the degree of difficulty and market size for the promotion of the development results. The RIKEN management team should also determine the timing and conditions for investment of the institutional research fund and of starting external collaborations. The RIKEN management team should have the ability to flexibly make these decisions.
- The RIKEN management team should understand that "PMI has already completed comprehensive needs and seeds survey in the early stages of project development, and that this is an asset for RIKEN. However, there is a shortage, in both quantity and quality, of human resources to advance the results of these needs and seeds surveys into the development phase."

## **Response to TOR**

**【TOR 1】** Evaluate (1) whether the center’s research meets international standards and is regarded as world-leading, (2) whether its research results have contributed to society, (3) and whether its up-to-date activities and strategies meet the aims of RIKEN’s fourth mid- to long-term plan (7-year plan).

Note:

Regarding (1) and (2), PMI is not a standard research center in that it was established to plan, promote, and manage internal and external collaboration projects. Please evaluate whether PMI’s overall activities, not its research achievements, meet international standards and contribute to society. Item (3) is the main item for evaluation, so please evaluate whether PMI’s strategy (see 3. Program Overview; 8. Future Plans) conforms with RIKEN’s fourth mid-to long-term plan (7-year plan).

### **[Research]**

- TOR1(1) should be eliminated from the PMI evaluation items, because PMI is not a research center. The item concerning evaluation of research activities and research achievements should therefore be eliminated from the PMI evaluation items.

### **[Contributions to society]**

- TOR 1(2) should be eliminated from the PMI evaluation items. Because PMI is not a research center, the evaluation item asking whether the research results have contributed to society should be eliminated from the PMI evaluation items.

### **[Consistency with 7-year plan]**

- PMI PD presented RIKEN’s mid-to long-term goals and plans and explained that PMI is sharing them and promoting its activities. CSTI-AC acknowledges that PMI’s activities and strategies are consistent with RIKEN’s mid-to long-term plans.
  - In other words, PMI is promoting joint research into preventive medicine and diagnostic techniques that can be used at medical sites by matching the results of basic research at RIKEN with the needs of medical institutions and companies. “The POCT for infectious diseases” project and the “Diagnostic marker for cancer” project are good examples. PMI is helping to create innovations aimed at meeting RIKEN’s goals through activities that effectively and promptly turn these innovative research seeds into social value.
- To maximize its research results and solve social issues, with a focus on the medical field, PMI promotes open innovation by performing needs surveys and creating plans for the development of new technologies for social implementation.

- Specifically, PMI conducted RIKEN's technology seeds survey (192 interviews), medical needs survey (857 interviews), and company needs survey (743 interviews). From the results of these interviews, PMI created 160 trans-disciplinary projects. "Studies of adipocyte differentiation" is a typical example of a company's open innovation.
- Remarkably, PMI conducts each project with the policy of "exclusive collaboration with its partner company."
- PMI itself is a social experiment to seek for the new RIKEN center management to diversify RIKEN research revenue. PMI has shown there is an optimal size for the ratio of external contracted funding to institutional research funds. In their experience, the maximum ratio should be 2.8 to 1.

**【TOR2】** Center director will present a SWOT analysis on the management of the center to their AC. The AC is asked to evaluate whether the SWOT analysis and the director's management proficiency are suitable.

Note:

Please evaluate the appropriateness and relevance of a SWOT analysis of PMI's activities as overseen by PD and the capability of the PD.

- PD accurately performed SWOT analysis and explained clearly in CSTI-AC
- The three main activities set by PMI and the development of PMI model is one of the styles of center management and can be a concrete strategy of the mid-to long-term plan.

**【TOR3】**Evaluate whether the center's initiatives on the items given below have resulted in improvements and recommend further measures to be implemented by the centers.

- RIKEN is conducting a program to enhance its function as the core organization for research partnerships, which we refer to as the "Science and Technology Hub." The AC is asked to evaluate the center's achievements in collaborative activities, including those belonging to the Science and Technology Hub.
- Initiatives on the internationalization of the center

Note:

This is the main item for evaluation. Please evaluate PMI's efforts regarding internal, external, and international collaboration, taking into account PMI's specific budgetary system in which PMI does not receive an Institutional Research Fund for the direct research cost from RIKEN-HQ and therefore depends entirely on external funds secured through its own efforts to cover all direct research costs for RIKEN internal projects.



**[Collaborations/S&T Hub etc.]**

- PMI has made significant progress in strengthening the Science & Technology hub functions that RIKEN is promoting.
- PMI has set up 31 joint research projects with multiple partners; RIKEN has fulfilled a hub function in those projects.

**[Internationalization]**

- PMI has actively developed international collaborations (with Russia, Qatar, Sweden and the Philippines) to meet medical needs.
- PMI established the “KFU–RIKEN collaboration lab” at Kazan Federal University (KFU) and the “RIKEN–KFU collaboration unit” at RIKEN in collaboration with KFU in Russia (2016). PMI used the same strategy to establish the “RIKEN–HMC collaboration unit” at RIKEN in collaboration with Hamad Medical Corporation in Qatar.
  - PMI has developed partnerships with KFU and has built a network-type of international collaboration with RIKEN as a Science & technology hub; more than a dozen domestic and international research institutions are participating.

**[TOR4]**Evaluate (1) whether each of the PIs fulfill their duties in accordance with the mission of the center, taking into consideration the 7-year plan; (2) whether their research meets international standards; (3) and whether they have suitable capability on the laboratory management, including their efforts to support early-career researchers.

Note:

PMI has no PI position as a subordinate of PD. Instead, please evaluate the capability of the PD. The evaluation of the PD overlaps with (TOR2), so please write your comment in (TOR2).

- PMI has only one PI (PMI PD); evaluation of PD and the activities promoted by PD are described in other TORs.

**[Program Director’s contribution to the program mission]**

- Program Director's contribution is reflected in the program level assessment TOR 1(3).

**[Program management]**

- Program Director's management is reflected in the program SWOT analysis TOR2..

## Medical Sciences Innovation Hub Program (MIH)

### 【General comments】

#### (1) MIH goals and international standing

a) The young MIH program is addressing important scientific and societal goals, i.e. using AI to enable personalized/precision medicine as well as using AI-driven drug discovery, and has a promising organizational form based on appropriate expertise for the above questions and associated clinical collaborators. However, given the challenges in the field (fierce competition by academic institutions as well as big company players like Google and Apple, fast pace of the developments in the field, ethical issues related to data protection, and technical hurdles associated with large heterogenous patient data), and the limited resources allocated to the program, it is recommendable to identify 1-2 specific topics in each area and focus resources towards these topics:

- Deep phenotyping. Ideally, the topic(s) should be scalable so that in the second phase the concept can be deployed on a large-scale. Given the limited time before the decision to continue MIH after FY2021, it is advisable to select a disease/cohort for which data is already available and generate only complementary data to broaden the multimodality for deep phenotyping (e.g. CT images on top of the NGS data or biochemical parameters on top of the fetal ECG) and demonstrate the proof-of-concept of the applicability of the AI-methods.
- Drug discovery. The newly developed tools such as graph convolution network, three-dimensional convolution network, multi-task learning, fragment molecular orbital method, and three-dimensional reference interaction site model are original and very useful in order to provide a versatile AI drug discovery platform for pharmaceutical companies. Okuno group has already organized a consortium (LINC) consisting of 110 pharmaceutical and IT companies and the AI platform is being enhanced collaborating with the consortium members. Amalgamation of publicly and proprietary data is to be appreciated, and Okuno group has started to establish a new data sharing project with more than 15 pharmaceutical companies. Though the project goals and AI technology developments have rationality, AI is a fusion of algorithms and data. The weakness of MIH is that it lacks a strong team for ELSI research for data science (as is indicated above as “ethical issues related to data protection”). US NIH has been promoting ELSI research for genomic data, but currently the biggest issue is all data which are related to human.

MIH has a small number of external experts to consider the ELSI issues, but it

should hire specialists inside and concentrate on it. Alternatively, it is a good idea to collaborate with other consortiums and institutions such as LINC and National Hospital Organization to form a team of experts jointly.

b) Recruitment of key AI personnel is a worldwide challenge but the program was successful in attracting investigators with interdisciplinary expertise in both areas. This is a fertile ground for future developments and the program should build on this opportunity and devote resources to attract additional students.

c) The computational infrastructure was established which is by itself a major effort. Also the access to a supercomputer in conjunction with the software tools for structure-based analysis is a unique opportunity and already attracted a number of pharmaceutical companies. To enhance the exploitation of these opportunity, an advice of a structural bioinformatician should be sought.

For both “deep phenotyping” and “drug discovery”, the projects should have a perspective on the data size that is not clearly stated. Broad Institutes produces 26TB data every day including image data though K and FUGAKU are referred. BGI produces 20TB genome sequence data every day. From the top international standing, the MIH should clarify this point and put it in the future scope.

## **(2) MIH organization**

The attractive setting is that MIH is organized in two complementary areas (AI for personalized medicine and AI for drug-discovery) with an associated clinical groups addressing major diseases. However, the collaboration within the program needs to be strengthened and the PIs should define common goals and join forces to reach these goals. Specifically, the AI-concepts for deep phenotyping can be tested using available clinical data in the program. Similarly, the reverse translational efforts (network analysis) in the drug discovery area can be adopted in order to provide novel biological insights using the clinical data and/or interpret mouse results in a human context.

## **(3) Collaboration of the three programs (MIH, PMI, and DMP)**

There is certain thematic overlap between the three programs and it is recommended to actively promote close collaboration between the three programs and exploit potential synergies. The AI drug discovery platform built by the Okuno group has begun to be applied to RIKEN DMP's actual drug discovery targets, and such activities should be promoted in the future, demonstrating the usefulness of AI

technology.

**【TOR 1】** Evaluate (1) whether the center’s research meets international standards and is regarded as world-leading, (2) whether its research results have contributed to society, (3) and whether its up-to-date activities and strategies meet the aims of RIKEN’s fourth mid- to long-term plan(7-year plan).

Note: MIH is entering the third year since beginning its initiative to build a data platform that will bring about an unprecedented level of personalized healthcare. Please base your evaluation on criteria of whether MIH is defining the right problems, adopting the best strategies to solve these problems, whether the outcomes so far are world-class, and how promising they are with respect to the future benefit of society. In addition, RIKEN is to decide whether MIH should be continued after FY2021; therefore, we would like to hear proposals regarding the organization and direction of MIH for the latter part of the fourth mid-to long-term plan.

The MIH program is organized in 2 areas: 1) AI-driven drug discovery, and 2) Precision medicine by deep phenotyping. Additionally, there are 3 clinical groups working on specific questions (dermatology, cancer immunology, and developmental disorders). Given the fact that the program started recently (started 1.5 years ago), it cannot be expected that the center’s research already meets international standards and is regarded as world-leading. At this AC timing, it is too early to expect social contribution. The program is heading in the right direction and if the program adheres to the general suggestions/recommendations, the likelihood is high that the researcher will make an important contribution to the field until the next AC.

As mentioned above, the organization and budget are not sufficient to lead this research field on world-leading scale. On the other hand, RIKEN has many centers and programs related to MIH research. For example, RIKEN AIP has talented researchers in terms of basic research of artificial intelligence. RIKEN BDR and IMS collected and analyzed wet biological data such as omics experiments for patient cells. RIKEN DMP is responsible for actual drug discovery research and promotes dozens of drug discovery projects. The key to success of both MIH research areas, Deep Phenotyping and Drug Discovery AI, to collaborate closely with the research centers listed above for new technology development as well as applications of the technologies to drug discovery and medical care.

**[Research]**

The research activities span a wide range from conceptual theoretical work to addressing important biological questions to supporting pharmaceutical companies for drug development. The two subprograms are at different developmental stages. The AI-driven drug discovery is more mature and the group already established a number of collaborations with pharmaceutical companies. The presented AI approaches including the 3-dimensional general convolutional network are promising and the PIs are encouraged to publish their results so a broader audience can be attracted. An attractive component is the molecular modeling in conjunction with the access to the supercomputers such as FUGAKU. The Precision medicine by deep phenotyping group is very young and has already developed some interesting approaches like the information geometry to predict ovarian cancer or the Generative Adversarial Network as well as useful resources like the Gene Expression Commons. The major challenge now is to identify a well-annotated data set to test the methods/approaches developed by the group.

It is very important to build a framework so that data can be used for research and development which requires a strong support by ESLI for data science (that is missing in this project).

**[Contributions to society]**

Without doubt, if the research activities are successful, the contribution to the society will be enormous. The program could contribute considerably to the faster development of new drugs and to the establishment of personalized/precision medicine.

**[Consistency with 7-year plan]**

Based on the initial results I can say that the research activities are consistent with the 7-year plan.

**[TOR2]** Center director will present a SWOT analysis on the management of the center to their AC. The AC is asked to evaluate whether the SWOT analysis and the director's management proficiency are suitable.

Note: With respect to the management of the MIH program director, please also include the vital contributions of the two deputy program directors in your evaluation.

**[Strengths (internal/positive)]**

The management proficiency of the MIH program director are suitable and the two deputy program directors are making vital contributions. The SWOT analysis can be improved by including measurable/realistic goals that can be achieved during the course of the program. While the overall goals are clear, the program director and the deputies are encouraged to define specific goals for each area or sub-areas which could be evaluated by the end of the 7-year plan. Moreover, specific goals could be very helpful for making decision if the program will be continued.

**[Weaknesses (internal/negative)]**

There is a general impression that the program is heterogeneous and mainly driven by the individual PIs. An overall umbrella of the activities is missing (except for using AI/machine learning for addressing different questions).

**[Opportunities (external/positive)]**

An opportunity to make a major impact could arise if the individual groups collaborate strongly with each other. For example, the developer can strive to set up a common AI platform (e.g. using docker containers) with the tools/methods they develop which could be then used also in other areas within the program and within RIKEN. Similarly, strong collaboration based on joint projects with the clinical groups as well as RIKEN DMP/PMI represent an opportunity to demonstrate the applicability and usefulness of the developed AI methods.

Another opportunity is more general, not easily measurable but very important: building expertise due to the recruitment of key interdisciplinary personnel who can move between the two worlds, AI/machine learning and drug discovery/precision medicine. The recruited PIs could be a kernel for developing larger research groups that can tackle challenging problems.

In the SWOT analysis, opportunities are correctly evaluated and the relations between PIs and participating organizations are well understood.

**[Threats (external/negative)]**

Major threats are research activities from big competitors who have access to large resources for developing and deploying tools as well as access to huge datasets that can be used for training. In this light, it will be important to focus on topics that are rather specific for the Japanese society and not universal, so the contribution can be done only with knowledge of the local/national circumstances. This could be the analysis of a specific cohort, unique dataset such as FMO database developed by Okuno group, access

to rare resources or the like.

**[TOR3]** Evaluate whether the center's initiatives on the items given below have resulted in improvements and recommend further measures to be implemented by the centers.

- RIKEN is conducting a program to enhance its function as the core organization for research partnerships, which we refer to as the "Science and Technology Hub." The AC is asked to evaluate the center's achievements in collaborative activities, including those belonging to the Science and Technology Hub.
- Initiatives on the internationalization of the center

Note: Since collaboration with outside institutions is an essential component of MIH activities, please evaluate the effectiveness and efficiency of current collaborations.

**[Collaborations/S&T Hub]**

The collaborative activities within individual programs as well as across individual programs need to be strengthened and consolidated. Albeit acting as individual PIs for research partnerships with outside partners is successful, exploiting existing synergies of overlapping themes could make the Science and Technology Hub much stronger and more visible. As a first step towards this goal, a joint meeting to identify possible synergies is definitely recommendable. The program directors could consider a concept of "one-stop-shop" for outside institutions where a specific question can be addressed by first developing a concept, then developing own or adopt available tools to solve the problem, and the applying the tools.

**[Internationalization]**

The developed databases such as Dr. Seita's Gene Expression Commons and Dr. Honma's FMO database are publicly released for world-wide and the PIs interact with foreign researchers.

The degree of internationalization could be further increased by developing joint research projects with other international institutions. Networking and exchanging resources is helpful to establish a connection, but efficient collaboration requires joint research project with common goals where each partner contributes with the own expertise.