

## **RCI Advisory Council Report**

The following are our comments and advice on the Terms of Reference which we were asked to evaluate by the RIKEN Research Cluster for Innovation (RCI).

It would have been valuable to have more in-depth discussion on these topics, but time was limited. Perhaps future AC meetings should be extended to more than 2 days. Or, it might be advisable to have one session for management issues and two parallel sessions for the Biomass Engineering Program and the Drug Discovery and Medical Technology Platforms.

Our comments and advice are presented below in three parts:

- (1) Management,
- (2) Biomass Engineering Program, and
- (3) Program for Drug Discovery and Medical Technology Platforms.

### **(1) Management**

#### **RCI's strategies, research organization, and management policies**

1. First of all, we highly respect the decision of RIKEN to establish the RIKEN Research Cluster for Innovation as the core organization for innovation at RIKEN by bringing together all of RIKEN's diverse resources to pursue innovative, problem-solving research projects.

It is of course important that all RIKEN researchers should keep in mind the RIKEN Spirit—"to pursue basic research in science and technology and apply the results to further the development of industry".

2. If the productivity of the RIKEN researcher as measured by papers vs. budget is good, it may be wise to emphasize such good productivity.
3. The purpose of technology transfer is to contribute to society. For the successful continuation of technology transfer in RIKEN, correct measures of evaluation should be taken, and one effective measure is based on the balance of royalty income vs. patent costs. A Plan-Do-Check-Action cycle for IP management is also very important.
4. Securing effective patents is important. The involvement of IP practitioners from the beginning of research instead of invention disclosure made only after completing research is highly advisable in order to have strategic and strong patent applications. The competition in most fields is so keen that patent applications should be filed as quickly as possible.

5. More education of scientists regarding the importance of intellectual property will be needed. It may be important to give personal incentives to individual researchers or to research groups that generate innovation.
6. It may be worthwhile to include in the RCI decision-making on project themes, outside persons who have actual experience in business development and commercialization of new technology in a company.

### **RIKEN's "baton zone" programs with industry**

1. The "baton zone" provided by the RIKEN Innovation Center for technology transfer and joint and collaborative research with private companies is intended to apply RIKEN "knowledge" to create "social wisdom" that will be useful to society. Under the baton zone system, RIKEN researchers having RIKEN knowledge (scientific findings) and researchers/engineers (team) of the company which is the recipient of such RIKEN knowledge collaborate in research and development directed at finding solutions for problems, thereby creating social wisdom (social value) that results in innovation, which in turn leads to the commercialization of the achievement thus obtained.

RCIAC considers the baton zone system an effective way to create innovation from RIKEN knowledge.

2. RIKEN may need to consider devising its own management system for baton zone operation which should be different from university management. The Business Development Office's participation in baton zone management is essential.
3. There are often some gaps or discrepancy between corporate management and researchers in the perception or understanding of the business aspect of the developed technology. Even if the CTO (Chief Technology Officer) of a company is willing and eager to achieve commercialization technology using such RIKEN knowledge, it does not necessarily mean that the top management of the company is equally committed. Sometimes, cooperative research and development or collaboration is not concretely understood or supported by the corporate president.

Therefore, unless the target technology is correctly understood by the president of the company and the company's top management support the collaboration taking place in the baton zone to materialize RIKEN knowledge into innovation (social value), there is always a risk that the accomplished technology will not really be commercialized.

It is our advice that RIKEN should consider, when selecting a partner company, whether the top management (president) of the company is really committed to the commercialization of the technology to be developed. It is advisable that RIKEN requires such commitment of management as a requisite in determining the partner company for baton zone operation.

4. Since the number of research themes pursued under the baton zone system is limited, it is important that all RIKEN researchers should always consider how their academic knowledge relates to social wisdom or social needs. Every researcher must eventually think of how he or she can contribute to society.
5. It is advisable that RIKEN setup a mechanism for regular presentations to all RIKEN researchers on real-time social problems, made by outside speakers who actually have experience of such social problems. By raising their awareness of real social problems, each RIKEN researcher will be able to think on their own of how his or her academic knowledge might be useful for solving a specific social problem.

## **(2) Biomass Engineering Program**

The aim of the Biomass Engineering Program is to enhance plant biomass production; to improve biomass processing and further enable the production of bioplastics. This program will contribute to provide sustainable sources of bio-energy and bio-products. The program has three strategies:

- i) The development of high-yield, easy decomposable plants, in particular trees
- ii) The efficient production of biochemical products starting from renewable raw materials
- iii) The development of novel bioplastics

### Terms of reference

1. The strategies, research organization, and management of the Biomass Engineering Program, in particular as to whether the program is composed of integration of full potential of RIKEN's research activities to create "social wisdom" in collaborations with industries and other research organizations.
2. The research plan of this program, whether it is designed to create "social wisdom" for generation of "social value" after 5 or 10 years.
3. The individual research projects, whether they are leading-edge research projects to create "social wisdom".

Although the project has only been started one year ago impressive progress has been made. The management of the project is excellent. Currently, 40

persons are directly employed on the project. A large number of national and international collaborations have been established. Below we list points of strength, weaknesses, and recommendations to address point 2 of the terms of reference (whether it is designed to create “social wisdom” for generation of “social value” after 5 or 10 years).

### Strengths

1. Strong basic research program that capitalizes on the clear strengths of the RIKEN Plant Biology groups, being used to attack problems of biomass quantity, quality, and conversion. Highly competent and internationally recognize research team.
2. The advisory committee applauds the enthusiasm by which young researchers are involved in the application of basic research towards applications.
3. Program addresses very important problems related to development of a sustainable low carbon society.
4. Excellent support from in-house infrastructure including world leading capabilities in metabolomics, eg. NMR –based methods.
5. Internationally leading and pioneering research in PHA synthesis and PHA polymer engineering.
6. Cutting edge research in enzyme improvement for bioplastic synthesis.
7. Established international collaborations in biomass production.
8. Good interactions with industrial partners.

### Weaknesses

1. A clear focus on specific traits for biomass improvement is lacking.
2. Consideration of a broad spectrum of conversion technologies is lacking. For example, biorefinery concept such as biological conversion combined with chemical catalysis is not fully explored.
3. Narrow focus on bioplastics and PHAs as bioproducts – other commodity chemicals could be considered.
4. Need to recognize and address the challenges of PHA synthesis in plants. Generating co-polymers with useful properties will be challenging to achieve.
5. No clear focus on commercial attributes of novel plant genotypes to be generated or consideration of strategies to deploy poplar or eucalyptus genotypes in the field for commercial production.
6. Lack of field trial capability in Japan.

### Recommendations: towards achieving “social wisdom” goals within 10 years

1. Clearly define specific end goals (traits) to be achieved in 10 years with respect to biomass engineering.
2. Establish quantitative phenotypes of improved biomass genotypes to be assessed: for example recalcitrance (sugar release), productivity, stress tolerance.

3. After initial 2-5 year exploration phase, move to implement generation of endproducts with specific attributes that have the potential for commercial production by 10 years.
4. Devise clear strategies for generation of transgenic plants that could be used commercially (eg constructs without antibiotic resistance genes, freedom to operate considerations).
5. Look broadly at conversion technologies and explore the biorefinery concept; expand research to include conversion of feedstock carbon into diverse products.
6. Using collaborations work towards establishing transgenic tree pipelines to increase throughput of constructs and genotypes to be transformed.
7. Consider additional personnel help to manage all the different projects, for example the appointment of a program coordinator may be appropriate to assist the current director.
8. Extra support from RCI Business Development Office would greatly strengthen the project and its ability to meet social wisdom goals.
9. For future RCIAC meetings, provide more time for technical presentations and especially time for discussion.

### **(3) Program for Drug Discovery and Medical Technology Platforms**

#### Evaluation

We commend RIKEN RCI for establishing the Drug Discovery and Medical Technology Program (DMP). The DMP has accurately identified that there is a gap between basic research and early clinical development and is looking to fulfill an important need, by bridging this gap with the 'baton zone' programs. We also recognize that Riken has world-class technologies that can make an excellent contribution to drug discovery programs. The DMP leadership has done an excellent job in identifying these technologies and associated expertise (both of which are distributed across a number of RIKEN sites) and bringing them together in the DMP matrix. Structure-based technology and *in silico* screening are excellent, and the antibody generation technology to the surface epitope and iPS-based technology are very promising. The use of the imaging technologies represents a good strategy for maximizing the program outcomes. Cell-based therapy is certainly a key mission of this program. In addition to the clinical benefit that may accrue from its current programs, RIKEN RCI can contribute further to the creation of 'social wisdom' by progressing these types of approaches in Japan and facilitating further developments by other organizations. The diverse functions have been pulled together in a flexible matrix management system, and the DMP must take credit for establishing such a system, which is very unusual outside private pharmaceutical companies. On the other hand, the current number of themes and projects do not appear to have been selected coherently: there may be too many of these programs and

should be more focused.

### Recommendations

RIKEN should cooperate with Medical Schools and Research Hospitals to pursue this Program; firstly, clinical validation of themes/projects of the Project is critical to further validate the drug targets/patient populations, and secondly the potential for clinical studies for biomarker and translational research need to be included in the project planning. RIKEN or the government should provide grants or funds for such co-operation and collaboration. Such cooperation can be initiated from the beginning possibly in collaboration with a company.

RIKEN should welcome proposals from companies for example, to progress company-identified drug targets, or co-discovery in defined disease areas. The RCI should make their best efforts to contact companies to seek such opportunities: this will help the RCI and the company to make best use of their resources and to complement each other leading to better outcomes.

Through such cooperation, the Program should seek themes more widely inside and outside RIKEN, most importantly from clinicians or people in clinical medicine.

Project leaders are currently selected as the individual proposing the theme/project: an alternative source of project leaders within DMP should be considered. The current approach has already led to themes being abandoned due to lack of enthusiasm from the PL: this should not be a reason for abandoning a good idea.

Selection criteria should be expanded to explicitly include firstly, how much RIKEN technology can contribute to each project, and secondly the likelihood of an effective exit strategy.

Each project should be more visible and each project leader should be given more autonomy. Drug discovery programs need to respond quickly to new data (and the matrix system allows for such flexibility), and so decision-making should be rapid dependent on the status of the theme/project.

The number of themes/projects being progressed needs to be assessed to ensure that they can be adequately resourced.

We support the DMP's proposal to increase medicinal chemistry capability in this Program: firstly, this is a key expertise that needs to be an integral part of the programs and secondly, in-house resource will allow follow-up of leads to be expedited.

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