

Report on the 1st Meeting of the RIKEN Cluster of Life Science Platform Advisory Council (CLAC)

**Chair: Allan Bradley, Director, Wellcome Trust Sanger Institute
Tsurumi, Yokohama
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Executive Summary

The first meeting of the RIKEN Cluster of Life Science Platform Advisory Council (CLAC) took place January 26-27, 2009 at the RIKEN Yokohama Institute in Tsurumi, Yokohama. Dr. Allan Bradley chaired the meeting. CLAC members were split into two groups. Drs. Bradley, Ewan Birney, Chieko Kai, Juha Kere, Mitiko Go, Joseph Ecker, Robert Waterston, and Hiroshi Tanaka reviewed the Omics Science Centre (OSC) and the Bioinformatics and Systems Engineering division (BASE). Drs. Chris Sander, Raymond Stevens, Christopher Dobson, and Stephen Burley reviewed the Systems and Structural Biology Centre (SSBC).

The OSC is internationally recognized for past and ongoing scientific projects (especially the FANTOM projects which will have a long and laudable legacy). Its mission combines both an imperative to contribute to scientific knowledge through independent, innovative collection and analysis of data and an obligation to provide services to others through, for example, its Life Science Accelerator. The CLAC feels that the centre is handling the challenges in this mission deftly. A close-knit team of PIs, each with his own area of expertise, has made that possible. A unique management system, which they call the "matrix" system, seems appropriate given the interdependent nature of the efforts at OSC.

The CLAC advises that, given the integrated nature of the enterprise, an evaluation of conventional metrics based solely on "individual PI" performance and their impact factors significantly underestimates the scientific output of the work at OSC. For instance, innovative and high-quality bioinformatics expertise plays a crucial role in OSC research which needs to be recognized even if bioinformaticians have fewer high profile papers. The contribution of OSC to the RNA world is unparalleled anywhere. RNA structures provided through genome browsers and the physical clone sets provide a basis for experimental progress globally. OSC researchers have achieved an international presence and scientific reputation that is extremely rare for a Japanese research group. They have done it by actively participating in, and leading, large scale collaborations. Their international presence has also resulted in OSC becoming very international, OSC has one of the largest concentrations of non-Japanese scientists that we are aware of anywhere in Japan, a model for other RIKEN centres.

The OSC has a mixed mission, driven by a desire to facilitate access by Japanese researchers to its unique capabilities. While this activity, is commendable and will undoubtedly result in new scientific discoveries, there is a danger of overextending activities, especially bioinformatics, in the service of other groups' research. The CLAC advises that these arrangements need to be managed within limits to ensure that should OSC researchers can focus on their primary scientific goals.

BASE has established itself as tremendously valuable activity, particularly in delivering database and bioinformatics services, to RIKEN's Plant Science Centre (PSC). The CLAC advise that increasing emphasis over the coming year should be on providing access to the structural data from SSBC, which will require extensive interactions between the groups and leadership from SSBC in facilitating this. The expanded role envisaged for BASE, managing and distributing data from institutions throughout RIKEN is very ambitious. Full delivery will require a significant increase in resources.

The SSBC has become known internationally as a world leader in structural biology, comparable to and in part exceeding the contribution of structural genomics efforts in the USA and Europe. In particular, RIKEN's Structural Genomics Initiative (RSGI) and the national Protein 3000 project (2002-2006) made major contributions to the global structural genomics effort. The impact of the successful Protein 3000 project will be felt as a Japanese contribution with RIKEN as a major factor for years into the future, for structural biology in general, and, in particular, for drug design and development, for nanotechnology based on protein structures and for the technologically promising field of structure-based systems biology. The CLAC feels that new scientific directions of SSBC are set to move the previous outstanding contributions to large-scale structural biology and protein production technology toward detailed understanding of the functional networks in biological systems and into the era of nano-bioengineering of protein and nucleic acid complexes as key components of new technical materials of the 21st century.

Background on the Cluster of Life Science Platform and the Advisory Council

Over the last two days the Cluster of Life Science Platform Advisory Council (CLAC) heard excellent presentations from the Principal Investigators (PI) associated with the RIKEN Omics Science Centre (OSC), the Bioinformatics and Systems Engineering division (BASE), and the Systems and Structural Biology Centre (SSBC) all located at the RIKEN Yokohama Institute.

These organizations are at a critical point in their development, having emerged from the dissolution of the Genomic Sciences Centre and now setting out their future directions. The CLAC has set out to evaluate each in terms of its accomplishments, its current structure and operation, and its future goals. Reference will be made to the Terms of Reference (TOR) which lay out the expectations of RIKEN President, Dr. Ryoji Noyori, and the Directors of the three organizations.

TOR 1: Are there achievements with major scientific significance or achievements with significant social impacts?

TOR 2: How does the centre compare with similar research institutions abroad?

TOR 3: Evaluate the centre's collaborations within RIKEN and with outside institutions, and evaluate the centre's efforts to promote international collaborations.

TOR 4: [For OSC only] Evaluate OSC as an infrastructure and supporting system.

TOR 5: [For OSC only] Evaluate whether each team project of OSC is organized systematically and consistently considering that OSC focuses on an integrated investigation of the molecular networks in living organisms.

TOR 6: [For OSC only] Individually evaluate the deputy director, deputy project director, and team leaders in terms of research achievement, platform activities, and contribution to OSC projects.

TOR 7: [For BASE only] Evaluate the future vision, goal, plan, function, service and performance of BASE.

TOR 8: [For SSBC only] Evaluate the future vision, goal, and plan of the SSBC.

TOR 9: [For SSBC only] Are projects of the teams organized synergistically to achieve the research goal of the SSBC?

I. OSC

Background and General Comments concerning the Omics Science Centre (OSC)

The OSC has a challenge in balancing the demands of its new mission with the commitment to carry on the core activities of its predecessor, the GSC Genome Exploration Research Group, which have given rise to a large body of innovative and internationally recognized work. The group seems to understand these challenges and seems well prepared to take them on.

During the CLAC meeting, the Director (Dr. Yoshihide Hayashizaki) and the Principal Investigators (Dr. Jun Kawai, Dr. Piero Carninci, Dr. Harukazu Suzuki, and Dr. Carsten Daub) presented past achievements and a future vision for the OSC. The quality of the preparation, both in terms of the white papers provided before the meeting and the presentation materials, has been at the highest level. The meeting materials document the extraordinary productivity and influence of this group and project an exciting set of future plans which (if appropriately funded) are likely to result in observations, discoveries and new hypothesis of similar or greater impact than those already made.

World leading scientific programme (TOR 1)

The Advisory Council judged the overall quality of science as “world leading.” The programme of work and accomplishments is unique and is clearly an activity that RIKEN should be proud of. The OSC is *dominant* in the RNA world. This group has brought a focus of activity to transcriptome analysis that is unmatched anywhere else in the world. The success of this group is based on a number of factors, but includes the development and implementation of new technology such as CAGE, the scale of data production, and the careful analysis of huge quantities of data produced by this group. Many RNA sequencing projects that were launched in parallel to this effort elsewhere have not been continued. None have had comparable impact. The primary reason for this is the position this group took in producing a quality product, achieved by technology innovation, careful experimentation and attention to detail in data analysis. This constellation of factors has enabled the group to make novel and unexpected observations about the RNA world that provide the basis for many future experiments, both by this group and by the international community.

Members of this group have not worked in isolation. They recognized the value of their painstaking assembly of full length RNA sequences for the purposes of genome annotation under the FANTOM projects. This has greatly facilitated the annotation of the most relevant parts of several genomes including human, mouse, honeybee, and rice. The value of this contribution is not transient and cannot be overstated. It will be used for a long time to come by the global biomedical research community. **[TOR 1, 2, 3 and 4]**

In addition to providing the basis for genome annotation, the data generated by the group has led to many novel observations. For instance, they have described large numbers of non-coding RNAs and have illustrated that the genome appears to have many more promoters than previously thought. These are global observations and provide the basis for future experimental analysis. For example, researchers can now ask: What are the functions of these non-coding RNAs? Which promoters are active in different cells types? These and other types of experimental questions need to be pursued if we are to truly understand both how genes are regulated in the hundreds of different cell types in a mammalian body and how this regulation changes in response to disease and pharmaceutical intervention.

The CLAC were also treated to a fascinating real time display of a new technology termed *Smart Amp* (SMAP) which is very rapid DNA amplification assay developed to the level that it could genotype single nucleotide differences in the human genome from small samples such as a drop of blood. The scale of the development work required for this project illustrates the creativity of this group and included cloning of new polymerases and development of dyes linked to single strand DNA primers that only fluoresce once incorporated in double strand

DNA. Unlike conventional PCR, amplification was achieved at a constant temperature by using displacement polymerases held at a single temperature, making this assay very useful for applications where laboratories with thermal cyclers are not available. This assay, demonstrated using crude DNA in small drops of blood from members of the CLAC, clearly has significant potential. OSC envisage a number of potential applications, ranging from cancer diagnosis to monitoring for pathogens. Given the potential of this technology and diversity of applications [which are likely to extend significantly beyond the expertise and knowledge of the group], the CLAC encourage OSC to licence this technology rapidly and widely.

International visibility and collaboration [TOR 3]

Dr. Hayashizaki's enthusiastic and tireless leadership of the FANTOM projects has been of immense importance and has been partly responsible for the visibility of the programme internationally. This internationalization has helped bring great talent from across the globe to his laboratory, and OSC has one of the highest proportions of non-Japanese PIs and fellows in Japan. Dr. Hayashizaki's strong professional ties with researchers around the world have also ensured that research coming from the laboratory has had all of the impact that it promises. This is a record that RIKEN can be proud of—and one that other research institutes in Japan can learn from.

Matrix management and metrics of scientific output [TOR 5]

The programme itself has a unique management and responsibility structure which in the view of the CLAC is entirely appropriate for a genome centre which requires the participation PIs with very different skill sets working together as equals on a team. The result of such closely woven collaborations is obvious in terms of the measurable outputs which include many collaborative papers published in the journals with the highest impact factors.

In contrast to many single PI based programmes at RIKEN and elsewhere high impact factor papers are not the only output and the Advisory Council strongly advocated that the success of this programme should not be judged from this alone. The value that this project has brought to the annotation of mammalian genes is immeasurable. The accurate gene structures provided by layering the FANTOM data onto the human and mouse genomes provides a basis for hypothesis driven research world wide. This contribution which is used, often unknowingly, on a daily basis by thousands of laboratories globally is a permanent contribution to the community of scientists of today and of future generations. **[TOR 3, TOR 4]**

In addition to the value that has emanated from genome annotation, the physical resource, ie the individual or sets of cDNA clones which have been distributed and used as biological resources by thousands of laboratories globally, has been a tremendous contribution to global science. There are many examples of the use of these clones by other research groups, but one notable example is the analysis of the mouse brain by the Allen Brain Atlas, which would not have been possible without Dr. Hayashizaki's clones. **[TOR 4]**

Leadership [TOR 5 and 6]

The impact of science emanates to a great degree from the passion, vision and tireless leadership of Dr. Hayashizaki. This is not to diminish the role of the individuals PIs, who all contribute to the programme in unique ways since each member possesses different yet complementary skill sets. The output of the team is clearly dependent on the contributions of each member. Individuals in the team have grown in international stature and impact over the last few years, yet each member recognizes their mutual interdependence. This method of working is very valuable to the continued success of the programme and should be supported. If additional PIs are to be brought into OSC to build on the obvious scientific

opportunities, it is important that they should align their strategy with the OSC mission and adopt the interdependent working approach that has been such an important element of the success of the programme.

Education programmes [TOR 1, TOR 3]

The uniqueness and importance of the genomics and bioinformatics training opportunity afforded by this centre to society cannot be overstated. Training students, postdoctoral and clinical fellows in genomics and bioinformatics is important for the progress of biomedical research in Japan and globally. The Advisory Council met privately with the graduate students and postdoctoral fellows in the programme to get some feedback from this group. Like the PIs, these individuals came from many different countries, reflecting the international visibility of the programme. This clearly is a strength. The international students advised the Advisory Council of the tremendous support provided by RIKEN in moving to Japan, obtaining housing etc. However, there remain some frustrations about funding and becoming registered as a graduate student in Japan.

The Advisory Council feels that it is important for RIKEN formally recognize the importance to Japanese society of a well structured, properly funded and organized international training programme for students, postdoctoral and clinical fellows, in partnership with a local leading university. While we recognize that “training programmes” per se may not fall under the remit of RIKEN, we also suggest if Japanese society is to fully benefit from the progress being made in genomics at RIKEN, it will be necessary to reconsider this restriction. We also recognize that this is likely to result in paying fees for these students to register at a Japanese university.

A structured programme including an open competition for a limited number of places on an annual basis would have huge benefits. It would likely lead to large numbers of international applicants and the increased exposure of Japanese graduate and postdoctoral students to other scientific cultures. It would also be a step towards what has been an elusive goal—making Japan a place where foreigners can establish a lifelong career in science. The Advisory Council suggests numerical limits on the number of students so that they obtain adequate supervision from the available PIs. Although the remit of Advisory Council has been limited to OSC and BASE, we further recommend that a graduate programme that crosses some of the centre boundaries in Yokohama would be very beneficial to the overall research programme and would enable other centres to benefit from the international visibility of the OSC.

The Advisory Council advises RIKEN that many international research institutes have had to reconsider their remits with respect to funding graduate students. The science and training opportunities at research institutes is different to that being conducted in universities and it is no longer an appropriate or viable model for research institutes to depend on universities for training the next generation of scientists. Two Advisory Council members advised that the training models in their institutes [EMBL & Sanger] could be adopted by RIKEN.

Outreach [TOR 1]

The OSC has embraced its broader societal role to a much greater extent than many research Institutions both in Japan and globally. There is an established visitors programme, both for accomplished members of society as well as children. The OSC have developed educational materials for this purpose. Although there was not adequate time to review this activity, the CLAC enjoyed a short animation of RNA polymerase over lunch. The CLAC recommend that this activity continues to be supported and would further suggest that the impact of these activities could be further enhanced with engagement and exchange of materials with groups

who share the same remit at Cold Spring Harbor NY and at the Wellcome Trust Sanger Institute.

Collaborations and external relationships [TOR 4]

OSC PIs clearly recognize that their science is unique in Japan, both in terms of the technology platform and the commitment to understanding the RNA world. The Advisory Council understands the well-intentioned desire to engage more with other research groups in Japan in the PI300 programme and other outreach programmes. This is a huge consultative effort that the Advisory Council greatly admires. While such engagement is important and is likely to lead to many new collaborations, it is also potentially a distraction for the OSC since one of the strengths of this group has been the strong focus they have brought to specific scientific questions. Engagement will undoubtedly enhance the output of the external groups external but consideration should be given to unintended impact and the potential distortion of the scientific mission. The Advisory Council does not wish to discourage collaboration, but rather recommends that the groups should engage in a small number of strategic collaborations, which may like FANTOM, be predominantly international.

The Advisory Council recognizes that some of these collaborations can perhaps be served by their plans to establish a more open service style operation. While the technical side of delivering projects can perhaps be scaled and delivered, the Advisory Council believes that servicing the bioinformatics needs of hundreds of small projects will require substantial new resources.

Future plans

Transcriptome analysis applied to define the molecular phenotype of cells is a very exciting project. Such a project will be informative about stable phenotypes, about changes that occur during the cell cycle, and also about normal transitions between states (differentiation). It will also provide gene lists to achieve experimental transitions (reprogramming) between one cellular differentiation state and another. There are many exciting discoveries which will emerge from such a project. The CLAC was presented with one preliminary example.

The magnitude of a project to define the transcriptome of each cell type is several orders greater than what has been achieved to date. Advances in sequencing technology will facilitate this. The CLAC would advocate that a fundamental component of such a project is an accurate description of the cell types or cell states to which the transcriptome data is connected. This will require close collaborations with experts to obtain the relevant biological samples. While there is merit in progressing experimental programmes using mice in parallel with human tissues, there is an urgent need to decide where to focus effort in the short term to achieve maximum impact. The accessibility of mouse tissues [and the quality and reproducibility of material derived from this source] compared with human tissue derived from warm autopsies present compelling arguments in favour using mouse tissues in the first instance.

Recommendations concerning OSC

- Continue support at the highest possible level is recommended towards the ambitious objectives outlined in the future plans.
- Continue efforts to internationalize the programme, perhaps including a structured international graduate programme in partnership with one university and other RIKEN centres in Yokohama.
- Separate the management of the technical service so that this pipeline can support some external collaborations and deliver internal projects without interference with one another. However, as this plan moves forward and is implemented, there will need to be an

appropriately scaled bioinformatics component to support the service enterprise. Securing the resources needed to support this is essential.

- Add more value to deciphering the ncRNA discovered in the FANTOM project by engaging more with technology providers. It is recommended, for instance, for the OSC to work closely with Affymetrix and Illumina on making a non-coding RNA chip.
- Make FANTOM clones *even more* available to the scientific community by providing links to distributors from genome browsers and other means.
- Continue to add value to the CAGE data sets by extending them to describe the transcriptome by linking the CAP sites to the rest of the transcript. Next-generation sequencing (Pacific Biosciences or Nanopore) may facilitate this, but in the meantime it will be useful to progress by using read-pairs.

II. BASE

General Comments and Recommendations on BASE

The BASE platform is an extremely important part of RIKEN's efforts to strengthen bioinformatics, database publication, cooperation and international visibility of its scientific outcomes in terms of large scale data production. Its bioinformatics capabilities will play an increasingly important role within RIKEN. The CLAC applauds RIKEN for establishing a special database division to serve all the life-science centres of RIKEN.

BASE director, Dr. Tetsuro Toyoda, has an ambitious plan to integrate many database functions into an "ideal life science information infrastructure" called "Life Science Networking System" (Life SciNeS). Dr. Toyoda has proven himself extraordinarily capable at tackling difficult problems, especially in his work with RIKEN's Plant Science Centre. Considering RIKEN's central position in the Japanese research community and considering that Dr. Toyoda hopes to serve RIKEN, Japanese universities, and the international community, a platform of the scale planned by Dr. Toyoda is appropriate.

Still there is cause for concern. Although BASE's cost-performance is at the world's highest rank, the CLAC worries that there will continue to be a mismatch between demands on bioinformatics capacity and resources in the form of computer power, disc power, and manpower. One CLAC member estimated that it would take 80 people to make good on Dr. Toyoda's remit. RIKEN must consider how to support BASE. For BASE to be able to support RIKEN as hoped, it might need to be expanded to a regular size database division

The CLAC would also like to emphasize that a conventional evaluation based on citation-based impact factors of publications would not well reflect the worldwide scientific community's dependence on BASE and similar programmes. BASE's major contributions are delivered to the global scientific community through its original internet-based infrastructure rather than journal papers. BASE is playing an increasingly central role in many bioinformatics and database collaborations inside and outside RIKEN. The high-impact publications of other centres cannot be achieved without the assistance of the bioinformatics specialists and infrastructure of BASE. Interactions with the PSC, OSC and RCAI (RIKEN's Research Centre for Allergy and Immunology), in particular, have been very good, and the CLAC would encourage BASE to increase these interactions.

Recommendations for BASE

- The remit of the project is hugely ambitious compared to resources provided. If the goals are to be met, the CLAC would strongly advocate developing a long term plan with

adequate articulation of the resource needs (space, computer, personnel) for the future including appropriate risk maps.

- The result from engaging with the plant centre is an exemplar of the results that Dr. Toyoda can expect from other activities. However, as more groups engage and realize what bioinformatics can bring it is likely that the analytical resources will become limiting. It is likely that significant additional support teams will be needed.
- CLAC would recommend increasing rather than decreasing interactions with the OSC, especially as OSC is likely to be one of the largest data producers in Japan for the foreseeable future. An analogous situation in Europe is the interaction between Sanger and EBI.
- BASE is in an excellent position to push for more data release. Perhaps BASE should require data release on publication as THE default position.
- We recommend that RIKEN stipulates that each centre expected to transfer data to BASE designate a person responsible to execute the data transfer through the system that BASE provides. A clear chain of responsibility might head off some of the problems and confusion present now.
- Evaluation of individual centres by RIKEN executive directors should take into consideration how much of each centre's data is released through BASE. This would help in the evaluation both of the centres and of BASE. It would also motivate the centres to take advantage of BASE resources.

III. SSBC

General Comments and Recommendations on SSBC

Evaluating the work at RIKEN over the past decade, the SSBC has become known internationally as a world leader in structural biology, comparable to and in part exceeding the contribution of structural genomics efforts in the USA and Europe. In particular, RIKEN's Structural Genomics Initiative (RSGI) and the national Protein 3000 project (2002-2006), under the leadership of Shigeyuki Yokoyama, made major contributions to the global structural genomics effort, as coordinated by the International Structural Genomics Organization (<http://www.isgo.org>), in several respects: (1) by meeting the goal of solving a large number of high-quality, scientifically valuable protein structures, many of which are the first solved representative of an entire protein domain family, with a strong component of pharmaceutically relevant human protein structures; (2) by depositing these structures in public databases, such as the international Protein Data Bank; (3) by facilitating the construction of hundreds of homology models for each of these structures; (4) by pioneering, as international leaders, methods for cell-free protein synthesis that have been essential for solving the structures of many difficult proteins and using this technology to build a uniquely efficient pipeline for protein production broadly useful for protein biology and engineering; (5) by developing advanced software of NMR spectral analysis and automated protein structure determination. The impact of the successful Protein 3000 project will be felt as a Japanese contribution with RIKEN as a major factor for years into the future, for structural biology in general, and, in particular, for drug design and development, for nanotechnology based on protein structures and for the technologically promising field of structure-based systems biology.

The current work of SSBC is of the highest scientific calibre. The team of leading scientists, under the leadership of Shigeyuki Yokoyama, is clearly world-class and overall the quality of the group leaders is excellent. In particular, the structural elucidation of RNA-protein interactions, including the central components of the RNA-protein production system, the ribosome and RNA polymerase complexes, and the re-engineering of aminoacyl-tRNA

synthase catalysts, which are key molecular adaptors in the production of all proteins in living systems, represent unique scientific-technical contributions. Innovative development of therapeutic compounds has recently become a strong focus of SSBC and synergizes with the Japanese pharmaceutical industry, especially in the areas of infectious diseases and cancer. In a major advance, the development of technology to incorporate non-natural amino-acids in a cell-based production systems has potentially far-reaching implications for a new generation of biological nano-technology, in which versatile biological materials can be engineered and selected for use in this century's smart, ubiquitous and energy-efficient materials. A second major emerging contribution is invention of a novel nucleic acid base pair that opens the doors to development of extended molecular living machinery, with potentially major technological impact.

An important issue of scientific infrastructure is the re-factoring of the park of NMR (nuclear magnetic resonance) machines for structural biology, a key factor in the internationally successful structural genomics project. An excellent model for the reduction and technical re-factoring of this facility combines an access program for external users, the export of some of the equipment to universities with specialized needs and the upgrading of a core set of machines to the next generation technology for the purpose of structural systems biology at RIKEN. The new scientific directions of SSBC are set to move the previous outstanding contributions to large-scale structural biology and protein production technology toward detailed understanding of the functional networks in biological systems and into the era of nano-bioengineering of protein and nucleic acid complexes as key components of new technical materials of the 21st century.

The review committee evaluated the scientific performance of the leading scientists at the Centre and wishes to highlight outstanding achievements.

Shigeyuki Yokoyama - Systems and Structural Biology Research Team and Overall Leader

Yokoyama is a world-class scientist and indispensable leader of SSBC. His scientific contributions are outstanding, especially his work on RNA-protein interactions, RNA unwinding, cell-free protein synthesis and modified nucleosomes, as well as his herculean contribution, with the RIKEN team, to structural genomics, including regular submission of high-quality data to the international databases, such as the Protein Data Bank. After SSBC's internationally recognized leadership in RIKEN's and Japan's structural genomics efforts, he has expertly re-positioned the department as focussing on structure-based systems biology and strengthened the key areas as outlined in the comments on individual group leaders. RIKEN can expect further major contributions from him both in terms of science as well as from a management perspective.

Kensaku Sakamoto - Expanded Genetic Code System Research Team

Sakamoto has made major achievements in structure determination, method development and engineering. The large number of aaRS structures and complexes solved is a remarkable achievement. His efforts to develop novel orthogonal pairs of AA-tRNA-synthase and tRNA are proceeding very well, and if completely successful, would rewrite the genetic code linking codons and amino-acids and represent a breakthrough bioengineering achievement with major impact on the biotechnology industry, in Japan and internationally. In the face of strong international interest and competition in this area, Sakamoto is uniquely positioned to produce these achievements.

Ichiro Hirao - Nucleic acid Synthetic Biology Research Team

Hirao is a pioneer, of international rank, in the invention of non-natural base pairs that extend the genetic code. He has already achieved good selectivity in enzymatic replication of modified nucleic acids using new base pairs. The foundation of a venture-backed company, TagCyx, reflects the potential technological importance of his inventions for the production of novel biomaterials. As with the work of Sakamoto, Hiroa's work, twenty years from today, may come to represent one of the most noted achievements of Japanese science.

Hideaki Maeda - NMR Technology Research Team

Maeda is simply one of the world's foremost experts involved in the development of the next generation of high-field NMR machines. He is on track to achieve the engineering goals for these powerful machines as a major technological contribution to biology and chemistry worldwide.

This concludes the report of the review committee and we thank our scientific hosts for their hard work and institutional leaders for their trust and hospitality.

Summary of recommendations for SSBC

- Focus increasingly on the core strengths of SBCC, including RNA-protein interactions, macromolecular complexes, development of next-generation NMR instruments, cell-free protein production systems, engineering of non-natural amino-acid expression systems rewriting part of the genetic code and engineering of non-natural base-pairs extending the genetic code.
- Reconfigure, share, reduce and modernize the NMR Park facility. Avoid a situation where the costs for the modernized NMR Park depend on leasing to commercial users. Instead, develop a sharing model between RIKEN and publically funded research institutions for this valuable and unique national resource.
- Pursue engineering and biotechnology applications of the core scientific strengths as a major opportunity of a new class of bio-nanotechnology industrial development.