

Advisory Council Report
RIKEN Quantitative Biology Center (QBiC)

February 2016

Meeting Program

The Advisory Council (AC) of the RIKEN Quantitative Biology Center (QBiC) met in Osaka from February 11-13 to discuss the progress and scientific directions of this Center (established April 2011).

The meeting opened with an overview of the RIKEN and the QBiC by the Director, Dr. Yanagida. On behalf of Dr. Y. Matsumoto, RIKEN Executive Director, Dr. Yanagida summarized the history, current missions and organization of RIKEN. He drew attention to the Terms of Reference from the President H. Matsumoto to the ACs of each Center, including specific points relating to the management policy of the QBiC (see end of the report). Dr. Yanagida then described the overall mission of QBiC, which is to model whole cells so as to predict and control living systems. He outlined the organization of the Center. He presented QBiC's 10-year roadmap comprising four steps: quantitative measurement, modeling and design; the elucidation of common principles; the prediction of systems behavior; and, finally, the control of systems behavior. Further information about the overall goal of QBiC and the individual investigators was included in a White Paper, copies of which were distributed to the AC before the meeting.

In the afternoon, the AC first visited the BioSystem Building, Osaka University to tour the facilities of the Cell Design Research Core, including chemistry lab, mouse genetics lab, sleep analysis facility and the clean room. For the rest of the afternoon, the AC heard presentations from Dr. M. Ueda (Cell Dynamics Core), Dr. Taiji (Computational Biology Research Core), and Dr. H.R. Ueda (Cell Design Research Core) on progress over the last 2.5 years since the last AC in November 2013. There followed a poster session in which each of the lab leaders presented their research to the members of the AC.

On Friday February 12, there was a lab tour of QBiC Buildings A and B, followed by a poster session with junior scientists (postdocs and research associates) and lunchtime discussions. In the afternoon the three research directions for the next 5 years were presented: DECODE (Dr. Okada), Whole-body cell analysis (Dr. H.E. Ueda), Post-K (Dr. Sugita). Following this was a 10-year perspective presented by Dr. Furusawa.

Overall, the written materials, presentations and posters were of the highest quality. These two days were very busy, and the AC would have appreciated more time for discussion. A one hour closed meeting of the AC on the first day (following the introductory presentations) would have facilitated the evaluation.

On Saturday February 13, the AC drafted their report, met privately with Dr. Yanagida and then presented their report orally to Riken Executive Director Dr. Koyasu by video conference.

Summary

QBiC is a highly interdisciplinary Institute at the interface between biology, engineering, chemistry and physics. It focuses on developing new, quantitative approaches to biology—especially through single-molecule and single-cell techniques, together with systems theory. This research topic is timely and should significantly strengthen biological research in Japan. Despite being only 5 years old, QBiC has established a state-of-the art infrastructure with technological developments at the highest international standards. The institute has clear direction from strong management. There are many collaborations both within and outside of RIKEN, and internationally.

Responses to the Terms of Reference from RIKEN President Matsumoto

TOR 1. Quality of research and personnel as a world-leading research institute. Standing in its field. Strengths and weaknesses. Proposal for research directions in the next 5-10 years.

QBiC is a world-class research institute. One of its strengths is its technical leadership in microscopy, whole organism imaging, genetic engineering and computation. Another strength is that it is a leading center for collaboration between theorists and experimentalists, which is unusual in biology. The strengths are evidenced by the strong publication record, especially over the last 2 years.

While no weaknesses were found, the AC felt that there were two issues, which if addressed, would further strengthen the QBiC program. These were: a single-cell transcriptomics lab is needed for the DECODE project; and, in the long term (beyond 5 years), it was felt all the QBiC labs should be brought together at one location.

Based on the presentations on Friday, the AC suggests the following three research directions in the next 5 years

- (a) DECODE. The AC endorses the QBiC's DECODE vision, which is to combine image and single-cell omics data to develop predictive models to control complex biological systems such as neuronal development, organogenesis and others. The DECODE project builds on the existing strong collaboration between experiment and theory at the QBiC, and adds a third engineering component that will allow control of biosystems. DECODE will strengthen QBiC's role as a center for Data Science.
- (b) The AC recommends further development of whole organ and organism imaging and its application to a range of developmental and biomedical processes.
- (c) The AC endorses QBiC's leading role in life sciences applications of post-K computing.

TOR 2. (Only applicable to institutes more than 10 years old)

TOR 3. Five strategies.

(1) Pioneer a research management model for maximizing research and development results

Dr. Yanagida has provided strong management of QBiC through his vision of applying engineering approaches to biology, as well as his emphasis on technological development. QBiC has established a strong collaboration with Osaka University, especially the Graduate School of Frontier Biosciences. Through this collaboration, we expect synergy, for example between Data Science at QBiC and Information Science at Osaka University, that will maximize the efficient use of a limited budget and promote the development of QBiC.

An important aspect of the QBiC model is the appointment of many young researchers whose early independence has fostered remarkable creativity within the Center. To overcome some of the difficulties that young independent researchers face, QBiC lab leaders have been given visiting associate professor appointments at Osaka University, which provides access to PhD students and gives opportunities for teaching.

(2) Lead the world in achieving new research and development results through scientific excellence

Over the past five years since its establishment, QBiC has delivered high quality, internationally respected science, which integrates the physical, engineering and biological sciences. The results are evident in numerous high-quality papers and outstanding research achievements. Of particular note are:

- (i) technical developments, including ultrafast super-resolution microscopy, selective plane illumination microscopy, a new generation of luminescent probes, automated in-cell single molecule imaging system (AISIS), the Hi-CO method for assessing chromatin organization with high resolution, CUBIC organ clearing protocols, TALEN based knockout system, single-molecule lipidomics, simulation of molecular crowding, and the successful modeling of bacterial evolution and amoeboid motility.
- (ii) biological discoveries including the synthetic reconstitution of notch-delta symmetry breaking in cultured cells, the discovery of genes involved in aging in *C. elegans* through the DECODE approach, development of cortical factor feedback model for the cell membrane dynamics, the discovery of a new sleep gene, and further evidence for chromatin disorder.
- (iii) development and applications of glass-based micro(fluidic)-devices fostering novel advances in single-cell analysis.
- (iv) design of synthetic symmetry-breaking, lateral inhibition and developmental pattern formation to understand the most basic programs controlling the development of multicellular organisms.

(3) Become a hub for science and technology innovation

- (i) The cooperation with Osaka University, especially in data and information science, promises to further develop QBiC into a national and international research hub.
- (ii) Several lab leaders have or will have appointments at Tokyo University, thereby expanding cooperation and bringing students to QBiC.

- (iii) A number of labs have collaborations with industry, especially with microscope development (Olympus) and single-cell omics (Pharma).
- (iv) There is a strong collaboration with the CDB in Kobe, with four QBiC lab leaders located at CDB. There are existing and planned collaborations with the RIKEN institutes in Yokohama.
- (v) There are strong experimental and theoretical collaborations with the National Institute of Genetics (Mishima) on chromatin structure.
- (vi) QBiC is playing a major role in biological applications of the K-computer and post-K computing.

(4) Serve as a focal point for global brain circulation

- (i) QBiC invites prominent researchers from around the world for scientific exchange including international symposia such as the High-Dimensional Data for the Design of the Life Sciences (2015) and through visiting international seminar speakers.
- (ii) The AC met with several foreign junior scientists hired through the International Senior Researcher Program and the International Program Associate (IPA) systems of RIKEN.
- (iii) QBiC has a large number of formal and informal collaborations with International Universities and research institutes

(5) Foster the development of world-class leaders in scientific research

QBiC has continued to recruit and develop young PIs and researchers. Because a wide variety of techniques and training are required, researchers need to become independent early in their careers to fully realize their potential. The recent appointment of Lab leaders to University of Tokyo is proof of the success of the QBiC in developing the talent of its lab leaders.

The members of the AC were pleased to participate in a poster session and lunch with junior scientists (postdocs and research associates) and were very impressed by the high quality of the science and discussion.

The AC was very pleased with the appointment of a female unit leader (Ebisuya). It notes however, that QBiC still has only two female lab leaders. While the number of female researchers is high, about 1/3, more work needs to be done to appoint female recruitments at the senior level. More detailed statistics should be provided in the annual report on the breakdown of female researchers in various categories: technicians, PhD students, postdocs, research scientists and lab leaders.

TOR 4. Evaluate how appropriate and effective the Center's activities are towards maximizing RIKEN's achievements as a whole, including collaboration between centers.

QBiC benefits RIKEN as a whole by serving as a national center for microscope and imaging development, together with biological modeling and computing. QBiC has active collaborations with CDB, IMS with NMR in Yokohama and is taking a leading role in the K-computer and post-K computing in the biological sciences.

QBiC response to previous recommendations (11/2013)

1. The AC recommends that additional space be made available adjacent to the new building at Osaka University.

Most of the QBiC labs have moved to Buildings A and B in Osaka, adjacent to the Osaka University campus.

2. The AC recommends that QBiC recruit three additional team leaders to bring in biological expertise to the projects.

Three labs from RIKEN CDB have joined QBiC. One is a biologist, one a physicist and the other a mathematician.

3. Now that the QBiC has successfully established itself, the AC recommends that emphasis now be given to the publication of high-quality papers and the dissemination of the results at international meetings.

QBiC has a very strong publication record over the last 3 years.

4. The AC recommends the establishment of a mentoring program for unit and team leaders.

A mentoring program has not yet been established. It is felt that such a mentoring program would benefit the junior lab leaders by providing scientific and career advice. **The AC recommends establishing this program in the near future.**

5. The AC recommends that more female scientists be recruited at all levels.

One female lab leader (Ebisuya) has been hired. **The AC recommends hiring more female lab leaders.**

6. The AC recommends that QBiC establishes an International PhD program

Six PhD students have been hired under the RIKEN International Program Associate (IPA) system. This is an increase from a total of four at the time of the previous report.

7. The AC recommends the establishment a Postdoctoral Fellows program.

QBiC has nine RIKEN Special Postdoctoral Researchers (SPR) and two RIKEN Foreign Postdoctoral Researchers (FPR). This is an increase from a total of three at the time of the previous report.

8. The AC recommends that in future it meet with representatives of the graduate students, postdoctoral fellows and research scientists.

There was a poster session and lunch meeting with postdoctoral fellows and research scientists. **The AC recommends meeting with PhD students during the AC.**

Summary of new recommendations (2/2016)

1. Build up a new lab in single-cell transcriptomics
2. Ensure the long-term continuation of the single-cell metabolomics technology
3. Provide additional microscope and computational support, especially within the DECODE program, for the laboratory for Reconstitutive Developmental Biology
4. Strengthen Data Science in QBiC.
5. Provide continuity of access to supercomputing during the transition to post-K
6. Recruit more female lab leaders.
7. Establish a mentoring program for junior lab leaders.
8. Meeting with PhD students during the AC.



Jonathon Howard,
Chair of the Advisory Council
Saturday 13 February 2016

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