

Advisory Council Report
RIKEN Center for Developmental Biology

March 2008

Overview

The Advisory Council of RIKEN Center for Developmental Biology met in Kobe on March 2 to 5, 2008 for the fourth review of the Center's activities. The Director first provided a strategic and financial overview of the Center. The seven Group Directors gave presentations of research highlights and plans. They responded to questions from the Advisory Council in the context of their interim reviews. Two new Team Leaders then gave talks introducing their research activities. The Advisory council then split into groups to visit laboratories and hear reports from Team Leaders on their work. The Director had asked both Group Directors and Team Leaders to give talks about their most interesting progress, and necessarily the presentations could not cover the entire activities of any research program. Full information was accessible to the Advisory Council through the 2008 white paper that had been prepared by the CDB. Advisory Council members also had short presentations on CDB core facilities and met with postdocs and students for informal discussion. The Advisory Council then retired for closed discussion and to complete the review of the Group Directors. Following a private meeting with the Director, the Chair summarized the Advisory Council findings and recommendations to the CDB staff.

Paul Smith

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Cambridge 11 June 2008

International profile of CDB

The CDB has made rapid and impressive progress in establishing itself as a premiere research institute. The Center is now recognized as one of the best developmental biology institutes in the world and certainly the leader in Asia. The record and achievements of the Director and Group Directors, the caliber of many of the Team Leaders, the publication output, and the organization of annual high-profile international research symposia have all contributed to the impact and success of CDB.

CDB Director Masatoshi Takeichi is acknowledged worldwide as an exceptional scientist. He is President of the International Society of Developmental Biology and has launched an Asian-Pacific regional initiative to improve research and interactions among developmental biologists in this part of the world. The scientific approach of the CDB owes a great deal to his example of the pursuit of knowledge. The Advisory Council members were impressed by the outstanding leadership he delivers while maintaining excellence in his own science.

The CDB has recruited high quality mid-career researchers as Team Leaders and established a series of creative and ambitious research programs. The exceptional infrastructure and privileged funding available to CDB investigators brings expectation of high achievement in original research, which is met by publications in the major peer-reviewed journals. In this respect the Advisory Council members were generally impressed by the level of scientific productivity in CDB. The output is commendable, with 166 publications in 2007 alone, half of them in the leading international journals, including several in *Nature*, *Science* and *Cell*. The Advisory Council does consider that a small number of labs could focus more effort on in-depth research to achieve good quality publications. Overall, however, CDB research teams are performing on a par with investigators in comparable research institutes in other countries, and in several instances they are leading the field.

Maintaining CDB vitality and competitiveness

The CDB is a contemporary international research institute in which researchers do not hold tenure. Continued high level performance and productivity reviewed against international standards are the criteria for retention in CDB. The Advisory Council commends the CDB for implementing a rigorous external peer review process for evaluation and reappointment of all Team Leaders and for extending this review to the Group Directors.

The CDB has now reached steady state in numbers of research groups and staff. The Advisory Council is pleased to see there has been some positive turnover, with CDB investigators taking positions in Universities. It is vital that top research scientists are fed back from CDB into the

University system. This exchange will build a culture of partnership between CDB and the Universities. Mobility also provides openings for new investigators to benefit from the opportunities afforded by CDB. However, there are understandable concerns from CDB investigators about maintaining research momentum and competitiveness when they move into the University sector. Therefore the Universities will need to provide quality facilities if they are truly to benefit from the pool of research talent nurtured at CDB. The Advisory Council noted that a transitional award is made to departing CDB team leaders to help them establish their research in the Universities.

At this meeting, the Advisory Council undertook a mid-term review of the seven Group Directors. This was based on written submissions considered in advance by the Advisory Council and on oral presentations at the meeting. The written reports contained statements of research progress and future plans along with metrics of publications, funding and group members. Oral presentations contained some exciting science and ambitious plans. These were followed by detailed questioning by Advisory Council members. The Advisory Council evaluated each of the Group Directors positively for both past work and future plans, although some differences in level of achievement were noted. Full assessments and comments on individual Group Directors are conveyed to the Director in a separate report.

The balance of Japanese and foreign scientists provides the Advisory Council with a breadth of expertise and experience. This is sufficient for mid-term review of the Group Directors, which is essentially an advisory capacity. For the full quinquennial review, however, it is appropriate to consult external mail reviewers.

The Advisory Council also provided summary comments on the Team Leaders to the Director, to complement the external review reports. Good progress was noted in many cases, exceptional in some cases. The Advisory Council cautioned, however, against any complacency and emphasized the need to foster a culture of pursuing investigations in depth.

The Advisory Council understands that each Team Leader has a Group Director as an advisor, which allows the Group Directors to play a role in guiding and helping Team Leaders. This is an excellent arrangement that the Advisory Council suggests may be strengthened by a formal process of annual internal evaluation and appraisal. This should be beneficial for the career development of Team Leaders.

The Advisory Council also recommends that attention is paid to career development of students and postdocs and to preparing the best amongst them for future independence. Several excellent examples of mentorship were noted, but questions were raised concerning the publication record of some post-docs and students. A good track record of research output is the essential currency to ensure a good foundation to their scientific career.

Collaborative activities of CDB

The Advisory Council noted several instances in which CDB groups are collaborating productively. These interactions are developing from the bottom up, driven by the individual investigators and their research questions. Such in-house collaborative projects are essential to achieve added value and demonstrate that the whole is greater than the sum of parts in CDB. The Laboratory for Animal Resources and the Functional Genomics Unit in particular are commended for facilitating a number of research projects in CDB. The CDB management are encouraged to promote further internal collaborations.

CDB investigators also have a good range of collaborations with researchers in Japanese Universities and overseas. Strong interactions are being developed with the RIKEN BioResource Center in the area of human ES/iPS cell culture. Meetings have taken place to explore potential areas of interaction in functional genomics with the RIKEN Genomic Sciences Center and in developmental neuroscience with the Brain Sciences Institute. However, productive collaborations depend on genuine complementarity in interests, expertise and resources and cannot be imposed by a top-down approach.

CDB response to previous Advisory Council

The Advisory Council commends the CDB leadership for actions and initiatives since the previous report. It is apparent that the CDB Director and staff consider the comments and suggestions of the Advisory Council very seriously.

The Advisory Council previously recommended that clear rules be established, to avoid perceptions that the renewal of a research program is the norm, rather than dependent upon outstanding performance. The Advisory Council recognises that implementation of performance based decisions regarding renewal/non-renewal or re-review of Team Leaders has been challenging. The Advisory Council endorses the actions taken in individual cases.

Research group turnover is critical to maintain the dynamism and vitality of CDB. The Advisory Council suggested that a limit of two 5-year terms should be fixed for a Team Leader research program. The Director is commended for beginning to implement this rule, which is designed to ensure that an ongoing stream of talent can be recruited to CDB.

Concern that some Group Directors may have overly large research teams has been addressed.

The Advisory Council congratulates CDB on the appointments of two promising female group leaders. It is hoped that efforts will be maintained to attract more women in future.

Proactive measures to promote internal exchange and interaction, such as CDB retreats and the lunchtime forum, are welcomed. Several Advisory Council members have taken part in the retreats and found them to be of high standard. The retreats are inclusive and evidently enjoyed by the participating CDB staff. In addition to oral presentations by post-docs, both post-docs and students present posters. It is commendable that English is the working language for these events.

The Advisory Council had the opportunity to learn more about the Center's research support facilities. The implementation of effective core support functions is impressive and their impact on and importance to the CDB was recognized by the Advisory Council members. The Advisory Council supports the initiative to open these services to scientists outside the CDB, including those in universities and other institutes. This is seen as especially important for the perception of CDB by the broader academic community in Japan. Establishment of core Proteomics and human embryonic stem cell/iPS cell Facilities are valuable and timely additions to the repertoire of CDB. The international collaborations in transgenic technology provision established by the Laboratory of Animal Resources are impressive and to the credit of CDB.

The Office for Science Communications and International Affairs continues to perform an exemplary role in promoting CDB and Japanese biomedical science in general to a wide range of public groups. The Advisory Council was particularly pleased to learn about the well-attended open days for school students.

Future challenges and directions for CDB

The strength of the CDB as a center of excellence competitive with comparable institutes in the United States and Europe makes it imperative that stable financial support for the Center be provided. The Advisory Council is concerned about the general year-on-year decline of financial support from the government. The physical and intellectual resources assembled in the CDB during the past years are precious. Lack of assured continuity in funding would present major difficulties for future recruitment, in particular at senior level. The Advisory Council therefore urges the Japanese government and the RIKEN leadership to commit support to the CDB for the long-term research programs and to guarantee the Center's operations into the future without progressive budget reductions.

Ongoing support for CDB acquires even greater importance in light of the recent discovery of induced pluripotent stem (iPS) cells by Dr Yamanaka. Due to the assembled expertise at the interface of developmental and stem cell biology, CDB is uniquely positioned to provide the

fundamental knowledge and understanding of mechanisms that are necessary to make regenerative medicine a reality. The Advisory Council considers it is imperative that CDB is empowered to maintain and expand its activities in developmental, stem cell, and regenerative biology. The Advisory Council believe that the great strengths of CDB in these areas of basic science could underpin a productive partnership with Dr Yamanaka's new institute in Kyoto to keep Japan at the international forefront in pioneering future applications in biopharmaceutical development and cell therapy. The Advisory Council was also pleased to learn that Kobe hospital will relocate to a site adjacent to CDB, which will greatly facilitate interaction with clinical researchers. Experience indicates that translation of basic research products into biotechnology applications or clinical practice is an endeavour that must be measured in decades rather than years. Fortunately for Japan, the foresight of RIKEN in establishing CDB means that, provided they enjoy continued support, a critical mass of high quality researchers is in place to take on this challenge.

Recommendations

CDB Research Mission and Competitiveness

The mission of CDB is to bring new insights and understanding in developmental biology and regenerative medicine. This will be achieved by addressing key questions through rigorous and comprehensive investigation. Following the discovery of iPS cells, the CDB management is urged to prepare a strategic plan for a 10 year program of basic research in stem cell biology, directed differentiation and reprogramming that will maximise participation and contribution of CDB to the national and international effort. In this context, special consideration should be given to retention of key individuals in CDB who are recognized leaders in the stem cell field, and to replacement of those who will retire or leave with individuals of comparable expertise. Consideration should also be given to recruitment in related areas such as limb regeneration and tissue stem cells. CDB is also encouraged to seek out and pursue realistic opportunities for translational research that should increase with the relocation of Kobe hospital.

CDB is intended to be different from a University and to provide a hot-house environment, constantly stimulating and challenging the researcher. Turnover amongst group leaders is essential in this context to provide fresh input and dynamism. It is also appropriate for CDB to return high quality researchers to the Japanese University system. The Advisory Council supports a transparent formal policy of no renewal of Team Leaders beyond 10 years (with appropriate extension allowance for ill health and parental leave).

The Advisory Council reiterates the opinion that Group Directors vacancies must be widely advertised and appointments made in open competition. Major efforts should be made to attract foreigners and/or women to such positions. The Advisory Council is willing to provide suggestions for possible recruits. The Advisory Council recommends that a truly exceptional Team Leader may be considered for a Group Director position, but only via open competition, not by internal promotion.

The leadership of CDB is encouraged to redouble efforts to promote both originality and quality in basic research. The Advisory Council has some concern that in a small number of cases Group Directors and Team Leaders are allowing their research effort to become too diffuse rather than concentrating on depth of analysis. This can also be related to the generous resources provided at CDB. It is recommended that funding levels of Group Directors and Team Leaders should be performance-related and adjusted based on interim and term reviews. It would be reasonable if budgets could be adjusted up or down by up to 25% depending on how performance is judged against international standards. The remit for reviews should explicitly include recommendations on future funding levels, although final decisions should remain with the Director.

The Advisory Council noted that a few Team Leaders appeared not to be managing the resources provided to them to maximum benefit. The circumstances will differ between individuals but it is recommended that new Team Leaders with no previous experience in managing a research group should start off with a modest group (3 or 4 persons) and expand only after demonstrating management capability and research productivity as judged by interim and 5 year reviews.

Metrics and examples of collaborative interactions should be provided in future reports.

Internationalism

The Advisory Council recognise the efforts made by CDB to promote use of English throughout the Center. The impression is that an English speaking environment may be increasingly attractive to ambitious young Japanese scientists. The time may be ripe to encourage use of English as the working language in all CDB laboratories. To be recognised as truly multi-national it would be invaluable to recruit a foreigner as new Group Director or even future Director. The Advisory Council could provide some suggestions for potential recruits.

Consideration could also be given to an annual post-doctoral “prize” fellowship scheme for foreigners to come to CDB and join a laboratory of their choosing. This could be advertised in *Nature*, *Science* etc for high visibility, with visits/interviews linked to CDB Symposia.

Financial issues

The Advisory Council is strongly of the opinion that the impact of enforced budget reductions should be borne primarily by Administration and Group Directors rather than Team Leaders. It is vital to maintain the overall number of Team Leaders, even at the expense of individual resource allocations.

Measures should be implemented to maximise accountability and return for expenditure of the available budget. Economic charging should be applied for use of animals and other in-house services. A transparent process should be developed to recover full costs from external users of services. The cost-effectiveness of in-house DNA sequencing versus use of commercial services for routine short sequence determination should be evaluated and resources redeployed if appropriate. Consideration may be given to rationalising activities of the Functional Genomics Unit and the Genomic Resources Unit to keep in pace with technological advances such as the likely substitution of much current microarray hybridisation by next generation sequencing technologies.

Career development

Group Director/Team Leaders have an important responsibility in managing and mentoring their post-docs and research staff. The Advisory Council had some concern over post-doc publications/productivity/career progression. Some post-docs and students commented that they had little opportunity to discuss with their Group Director/Team Leader who was deemed “too busy”. RIKEN/CDB should provide workshops or course(s) in staff and project management for new Team Leaders. Possibly the Office for Science Communications and International Affairs could provide a career advice function for PhD students and post-docs.

Mentoring arrangements for Team Leaders may also need strengthening. The Advisory Council recommends a formal annual appraisal process, distinct from scientific review.

The Advisory Council has some concern that leading CDB investigators do not become overburdened or distracted from primary research by obligations to provide human ES/iPS cell technology as a core support function within CDB and externally. It will be important to ensure an appropriate balance in these activities.

The Advisory Council approves transition packages for departing investigators and recommends continued support and access to CDB facilities to ensure research momentum is maintained as investigators move into the University sector.