Advisory Council Report
Riken Center for Developmental Biology

The CDB AC met in Kobe June 2 to 5, 2004 for its second review of the Center's activities. An overview of the Center was provided by the Director, and was followed by research presentations from the seven Group Directors and the Team Leaders who had joined the CDB since the first AC meeting in April 2002. After comprehensive closed discussions by the members, the Chair summarized the AC views to the CDB staff before the meeting was adjourned.

Overview of the CDB: Scientific Standing, Organization and Continuity

It is the unanimous view of the AC that the overall quality of scientific research carried out in the CDB is at a very high level. In its four years of existence the CDB has made an excellent start in establishing a series of creative and ambitious research programs that are solidly grounded in recent and current achievements. The Director Masatoshi Takeichi is a scientist of the very highest caliber with an international reputation for excellence and innovation in basic research. He deserves primary credit for the high standards and good morale in the Center which he fosters through his example and his management style. He is ably supported by the two Deputy Directors, Shinichi Aizawa and Shinichi Nishikawa, who bring complementary organizational and political skills in addition to the strengths of their own science. The other Group Directors also contribute significantly to the management and collegiality of the Center. These contributions by all Group Directors is most valuable, raising only the wish that care be taken not to allow managerial duties to become so large as to divert attention from research activities.

The research at CDB is broad but focused at the intersection of developmental biology with stem cell research and translational biology. Both the intellectual and physical resources available to the individual scientist at the CDB are outstanding. The Center constitutes a large community of researchers in related fields where interactions and cross-fertilization can occur to enhance the originality and productivity of research. Such interactions should continue to be fostered and encouraged. Laboratory resources at the Center are likewise exceptional. Facilities, equipment, animal resources and all types of support are as strong or stronger than in any comparable institute anywhere in the world. Thus, scientists have near-optimal conditions under which they can carry out their research.

The strength of the CDB as a Center of Excellence that is competitive with comparable institutes in the United States and Europe makes it imperative that stable financial support for the Center be assured. The historic background of the Center's creation as part of the Millennium Project cannot obscure the fact that Developmental Biology is a complex field of research that requires long-term study if significant progress is to be achieved. Any translation of insights into development to clinical practice or biotechnology application is likewise an endeavor that must be measured in decades rather than years. Further, the physical and intellectual resources assembled in the CDB during the past four years are large, and lack of assured continuity of the Center's full

operations would result in a deplorable waste of these resources. The AC therefore urges Riken leadership to provide the CDB with a charter that acknowledges the long-term nature of its research program and codifies a plan to maintain the Center's operations into the future. Assured continuity is the single most important issue facing the CDB at this stage.

Balance of Programs and Staff

The scientific programs of the CDB were considered well balanced in developmental biology and stem cell research, utilizing multiple promising model systems while maintaining coherence of approach. A particularly strong emphasis on the mouse system is certainly justified by its status as the mammalian model organism that can be manipulated most effectively in various ways. At the same time it remains clear that much can be learned from other systems that have specific advantages for certain types of study, and the CDB appropriately supports research in many areas. The AC felt that some increased emphasis on processes of organogenesis might be promising and would also buttress the stated aim of the CDB to carry out research in the area of tissue repair and regeneration. Further, studies on postnatal development might be considered, as many processes important for human development take place postnatally and might be studied in an appropriate model system. As turnover of staff takes place for any reason, the opportunities for new recruitments will provide means to strengthen some of these scientific disciplines.

A different issue of balance arises in the distribution of resources. First it needs to be stated that resources are excellent, giving every investigator the opportunity to advance his/her research. It appears that there is a fairly fixed level of resource allocation to either the Group Director or the Team Leader, modified mostly by outside funding that a particular program can attract. The AC believes that there may be some advantage in flexibility, within certain boundaries, of resource assignments to different programs. Some groups, in particular some headed by Team Leaders, are very successful in their programs and merit an increase in resources. In a vigorous and original program, such increased resources would be efficiently deployed. On the other hand, some programs may show less progress, or might be carrying out very fine research that is of a type that is less resource intensive. Such programs might be cut back for the most efficient utilization of available funds and space.

The balance of scientific staff is excellent in terms of their scientific interest and expertise, but areas of potential improvement were noted with respect to representation of foreign scientists and female scientists among Principle Investigators, that is, Group Directors and Team Leaders. Two foreign scientists are presently working as Team Leader, and one additional foreign Team Leader is scheduled to arrive later this year. While this demonstrates that the CDB leadership is making an effort in this regard it must be said that the Center is still suffering from the lack of an international environment. This fact may impede the CDB from gaining the international visibility and recognition that its scientific quality should command. The recruitment of top-quality non-Japanese scientists must be a priority. It is also noteworthy that recruitment has some features of a feedback

system where the presence of first-rate foreign scientists in the CDB would make further recruitment more feasible. Likewise, the representation of female scientists among Principle Investigators is limited to two Team Leaders who, it can be noted, appear to be progressing well. Yet this low representation makes further recruitment of female scientist more challenging, and further contributes to the difficulty in attracting international staff.

The AC recommends that efforts be continued and enhanced to recruit foreign and female Principle Investigators at the Team Leader, and if at all possible, the Group Director level. These efforts might be assisted by direct contacts to well-known laboratories world wide, by the establishment of postdoctoral and senior visiting programs that would help spread familiarity with the CDB to institutions elsewhere, and by practical assistance to foreign scientists with issues of everyday living in Japan. We shall discuss recommendations for graduate student programs below.

Maintaining High Scientific Standards

The CDB is a Center of Excellence with a remarkable level of quality throughout its programs. As already noted, this is a major achievement and a credit to the Director and the entire senior leadership of the Center. Every effort should be made to maintain and enhance this level of quality. It is important that the Principle Investigators of the Center keep in mind the exceptional resources put at their disposal and the obligation that comes with it to carry out research at the highest possible level of originality, significance and quality. CDB investigators should aim high and not be satisfied with any research but the most original and significant.

Maintenance of excellence requires continuous effort. The CDB has in place a rigorous review system that evaluates the progress and promise for the future of its scientists at regular intervals. This review process is well conceived, and the Center will be well-served by its application. The AC strongly supports this process and believes that only the rigorous application of peer review-based quality control procedures can assure the long-term excellence and vitality of this or any institution. At the same time it is necessary to consider the available opportunities and the career development of any staff member whose contract may not be renewed as a result of the review process. The Center, and Riken as a whole, should be encouraged to assist its staff by mentoring and through practical means to continue their careers in the most appropriate environment possible.

The Desirability for a Sustainable System to Attract Graduate Students

As the senior members of the CDB were previously professors at different universities they brought with them a number of graduate students when moving to the Center. With the passage of time the association of CDB scientists with universities is changing, which in itself is a natural and positive development. It is clear that university associations are desirable, but it is also clear that the first responsibility of CDB staff must be to the Center. In practice this means that, as current graduate students finish their doctoral work, the number of students at the CDB is expected to decline. While we do not intend to

recommend a specific number of graduate students that should receive training at the CDB, it is clear that the presence of students is highly desirable. Thus the AC strongly recommends that arrangements be considered to bring students to the CDB on a regular basis.

Some ways of recruiting graduate students will remain the consequence of personal connection of CDB investigators, usually Group Directors, with individual universities that will allow them to accept graduate students into their laboratories. This is certainly a valid approach, but it may not be sufficient. The AC discussed this issue carefully and suggests that steps be taken, preferably by Riken as a whole but if need be by CDB itself, to enter into agreements with Japanese and international universities that would bring graduate students to Riken laboratories and centers. Before discussing specific models for such an arrangement it should be noted that some AC members felt that the suggestion detailed below would not be acceptable to universities and therefore would not be feasible. While such arrangements currently function in other institutions they may not be applicable here, but we offer these ideas as a basis for further consideration. Under any model, separate funds would be required that would have to be requested from Riken central organization and government bodies. The specific model of such a program is modeled after ongoing and largely successful efforts by the Max-Planck Society (MPG) and the NIH. In both cases the institutions are not degree granting, just as Riken is not degree granting. These institutions arrange with universities to create and advertise specific programs under which students accepted into them will receive formal education such as lectures at the university for a specified time, say two years, and then move to an affiliated research institute to carry out their thesis research. During that time, the research institute provides additional education not only in the lab but also through lecture series, practical courses, etc. The program is funded separately from the standard university programs through cooperative ways between the institutions and their respective funding agencies. These proved to be “win-win” programs, as the research institution gains access to graduate students and, importantly, the university has a separate and separately-funded means to increase the number of students accepted in a given year beyond its usual rate. Thus the university does not feel that the research institution is “stealing” its students but rather helping it to gain more students.

As mentioned, programs of this nature have been successfully initiated elsewhere and have attracted many very well-qualified applicants. Obviously, the specifics mentioned above are examples only, but the principle is clear – cooperative agreements between Riken and universities in Japan or elsewhere could be highly beneficial, provided that a solution can be found that will be satisfactory to all participants.

Community Outreach Programs

The CDB conducts various outreach programs in its community by lectures suited for a lay audience, interactions with schools, a yearly open house that attracts a large number of visitors, and other activities. The CDB is to be commended for these efforts, which appear to be highly effective. The AC felt that the level of effort expanded in this area by CDB members is appropriate. Any broader programs of public outreach may have to be

initiated and conducted by the Riken Central Office. There is little doubt that the CDB could assist with such programs in their area of expertise.

Translational Research

Research at the CDB has the potential to lead to significant application to regenerative medicine and in biotechnology. It is a long-term aim of CDB research to contribute to such applications. The concentration of expertise in mouse ES cell biology in the CDB is possibly unmatched anywhere else in the world. With the favorable legislative climate in Japan, the CDB is ideally positioned to drive the basic science of human ES cell biology and pave the way for future clinical applications. It should be kept in mind, though, that developments of this nature are necessarily long-term, giving additional urgency to the issue of continuity and stability of the CDB, as discussed above. Given the nature of CDB research it can be expected that translational applications to medicine may ultimately have greater significance than industrial applications. The support of translational research is an important and complex issue that should be addressed by Riken in its entirety in addition to being a concern for the CDB. Through its proximity to the IBRI and Translational Research Informatics Center, the CDB has the opportunity for contacts that will be helpful in this area. At the same time it must be remembered that translational research is complex, slow, associated with substantial risks in financial and public relations terms, is not assured of success at the outset, and must be done in close collaboration with appropriate medical institutions. These considerations should not be a deterrent to moving forward but should provide a framework of realistic expectations for this effort.

Conclusions

The Riken CDB has rapidly established itself as a center of excellence in the area of developmental biology. The major issue the Center faces in the future is to receive assurance of its continued full operations. Given such assurance, and with several comparatively minor adjustments suggested herein, the CDB will strengthen its standing in the scientific community and contribute greatly to advances in its field.

Igor B. Dawid, Chair, Advisory Council
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