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RIKEN Harima Institute
Research Promotion Division

Report on Structural Physiology Research Group Midterm Review

Laboratory Leader: Group Director, Atsuo Miyazawa (D. Sci.)
Date: Friday, February 12, 2010
Venue: RIKEN Harima Institute（SPring-8）
Reviewers:
Prof. Masayoshi Nakasako（Faculty of Science and Technology, Keio University）
Prof. Makiko Suwa（Computational Biology Research Center, National Institute of Industrial Science and Technology）
Prof. Keiichi Namba（Graduate School of Frontier Biosciences, Osaka University）
Prof. Yifan Cheng（Biochemistry Department, University of California, San Francisco）

Abstract of the reports:

REVIEWER 1

The Structural Physiology Research Group aims to study structures and functions of a number of biologically very important protein families, such as membrane channels, etc. To achieve its scientific aims, a number of novel technologies are developed, such as molecular labeling by metalloprotein-tag and GFP-pipeline for eukaryotic membrane protein expression and crystallization. Such technology developments are very impressive and will have application potential in a much broader field of structural biology. Selection of Team leaders was excellent. All team leaders have excellent track records and various backgrounds. There are coherent and synergetic activities of the Teams, which promote excellent scientific environment. There are also a large number of collaborative projects between the Teams. Overall, the Group is very well equipped and positioned to tackle difficult and important biological questions. The research group has made significant progresses in the past four years, and all teams are well positioned to continue their efforts outlined in their future research plans. Continued support to the group is necessary and important.

REVIEWER 2

1. On the consistency of the Group's mission and the RSC's mission

The RSC has missions on the scientific researches through utilizing X-rays provided from the SPring-8 and the X-ray Free Electron Laser (XFEL) facility. While the Bio-multisome research team seems to pay little attention to the RSC mission, the other research teams have missions match with the RSC's.

2. On the research objectives

The research objectives are unclear and difficult to understand probably because of the less organized research teams.

3. On the research results

The number of publications, which include significant contribution from research teams, is a few, despite a large budget has been given to the group. Among the four teams, this tendency is particular in the Bio-multisome research team. On the other hand, the Actin-research group showed the outstanding activity by the Nature paper. The group also contributes to the utilization of SPring-8 regarding the fiber diffraction method.

4. Management of the Research group

The group leader seems to abandon his important duty, the management of the four research teams in the past three years. Thus, it will be better choice for the RIKEN to recruit a new project leader who can be more responsible for the management of the research project.

Group member composition

The four research teams works independently, and the research group looks like an assembly of university laboratories. Despite the scientific achievement of the Actin-group, the number of researchers is too few.

Researchers' interaction

Young researchers and graduate students communicate well between the different research teams and discuss their research regarding the methods to prepare samples.

Facilities and equipments

Facilities and equipments of the research group are sufficient to carry out their research plans.

5. Future research plans

Except the Bio-multisome research team, the three research teams have plans to utilize effectively the SR and XFEL facilities. But, their plans are better to be reevaluated by scientists more professional in utilizing the facilities.

6. Possibility of cooperation with related fields

To improve the activity of the Bio-multisome research team, the research team may be better to collaborate with a scientist, who contributes to EM science field more significantly.

7. RIKEN's management

The Bio-multisome research team provides their equipments to an NPO organization. The equipments are given for their scientific activity not for their NPO activity. The project reader should consider this point deeply, because the budget for their research is provided from tax. Could the RIKEN stop the action? The management of the equipments would be discussed after the termination of the research project.

The budget from the RIKEN is given unevenly to the research teams. After the evaluation of the abilities and activities of the research teams, the RIKEN can supply the budget depending on their scientific activity.

REVIEWER 3

1. Research Objectives: novelty, specific significance

This group intends to elucidate a dynamic physiology from three dimensional structure analyses of proteins and complex by the total fuse of an X-ray crystallographic analysis and an electron microscopy. This group is very unique without being found elsewhere in the view point that they are performing the general development/ application in the environment where high-performance machinery is prepared. Therefore a feeling of expectation from the outside for this foothold seems very large.

2. Research Results: Originality, specific significance social impact

Four teams in this group gave us extremely superior results. 1) Bio-multisome Research Team developed the precise label method and structure analysis technology with a scanning electron microscope (SEM). 2) Three-dimensional Microscopy Research Team focused on the transporter proteins and constructed the system which settled methodology of ranging as one package from a two-dimensional crystal to structure determination. 3) Molecular Signaling Research Team founded the expression condition of the taste receptor. In addition, they developed the high-throughput screening technology using the GFP. 4) X-ray Structural Analysis Research Team determined the structure of Actin filament and analyzed the dynamics of it. Each result is superior contents which lead the world. The social ripple effect of these results seems very large, since these researches have large difficulty though they are strongly required.

3. Management of the Laboratory: Laboratory member composition, researchers interaction facilities and equipment etc.

They gather excellent talented people individually from various fields and become the very unique group. Dr. Miyazawa the leader of this group respects the individuality of each team leaders and he does not show overall directionality in "intentional". It is surely pushed forward an original study without a limitation, judging from the researcher side, and this policy produces ideal environment and has the possibility that very large result is provided.

But it is possibility and the hair's breadth that project ends after several years being spent by only finding the condition for structure determination. In addition, I am sorry that it could not see the synergy effect that all these talented people gathered in one foothold.

The equipment parts are enough with the highest devices which the purchase is difficult for universities and for the other research institutes. Therefore it is necessary to be aware that result of Structural Physiology Group is seen for a feeling of over expectation from the other groups.

4. Future research plans: possibility of cooperation with relates fields etc.

It seems that the future plan of this group is to promote more the individual themes in each team. Such directionality is too enough in the case of university because the output of individual study is splendid. However, I think that they cannot make use of the advantage enough, that they formed a group with the limited term (7 years). I hope they show the synergy effect of inter group cooperation by confirming the present progress in a road map described strategically.

5. Overall assessment

Very excellent talented people are gathered from various fields. The administration of the whole group

respects the independence of these individual researchers and does not show, definitely, the directionality as the whole group level to "intentional".

This administration succeeds for the individual team, and superior result is provided. In addition, the communication of leaders and the young researchers is planned well in the good environment. This environment is too enough if there is that of the university. But a feeling of expectation from the outside for innovative techniques is unexpectedly large for the research facility where all these latest facilities were covered all.

Therefore there will be the necessity to exhibit the result as the group whose term was limited.

I hope they show the synergy effect of inter group cooperation by confirming the present progress in a road map described strategically. For example, I think it is one of directionality that they choose the protein the structure of which is determined for the first time only when their technology is joined.

6. Other opinions: RIKEN management, RIKEN's review systems etc.

RIKEN's review system is well designed according to its Mission of RSC. As well as the presentation of the research, I thought the direct interview to researchers to be a good system.

REVIEWER 4

Since its start in April 2006, the aim of Structural Physiology Research Group is to gain physiological understanding on the mechanisms of biomolecules and their complexes, such as membrane and cytoskeletal proteins, as to how they work in the cellular activities, from the structural view points. The four team leaders recruited to start this ambitious 7-year project are those who have expertise in three-dimensional electron microscopy of biomolecules and cells, X-ray crystallography of biomolecular complexes, and X-ray fiber diffraction analysis of fibrous assembly of biomolecules. Their research themes include many important topics in biology, from cellular signal transduction, ion transport, and motility to neural signaling.

In spite of the diversity of the research topics they chose to work on, the team leaders aimed to share not only the equipments and expertise but also ideas for the development of new experimental techniques as well as for the interpretation of data to gain insights into the mechanisms as much and deep as possible, by encouraging daily communications between the members of the teams over the team boundaries. I think it is a great idea and appreciate the continued effort of the four team leaders to achieve their goals. I hope that each member of the group as well as each of the team leaders will keep his/her active communication with people around as much as possible and continue and further expand their collaborative studies.

The overall activities of the group appear to be good considering the difficult challenges that each team is facing. Although the productivity may not look so great in terms of publication at this moment after four years of the project term, it is not surprising because the goal of each team is set at an extremely high level and also requires the development of new experimental methods that are not so easy. I am sure that all the teams will achieve what they aim for within a couple of years to come. The midterm reports by the four teams actually show promising progress.

For some reason, which is probably to do with how the group started its initial activity, the financial resource is unequally distributed among the four teams. Now, since Group Director Dr. Miyazawa got an appointment as professor and the laboratory at University of Hyogo, which gives him more opportunities to seek other funding sources, it may be wise to make some changes in the arrangement of how the financial resource be distributed to allow the other three teams to have more capacities in managing their own team's research activities.

As I mentioned in my summary remarks of the review that I gave orally after the sessions of the Midterm Review held at RIKEN SPring-8 on February 12, the coordination of the efforts by the four teams may be further improved. I understand that some collaborative studies by the joint effort of multiple teams are being carried out. But when each team leader gave an oral report in the review session on the progress made so far by the team and the prospect for the remaining term, their presentations tended to sound like they are individual, independent work. Since all the research projects that are being carried out in the group are all related to the biological functions of membrane and cytoskeletal proteins involved in signal transduction, ion transport, and cell motility to neural signaling, even the present research activities of the group can be presented as an integrated approach that focuses on some of the important aspects of the cellular activity and may well be reorganized to actually integrate them into more coherent collaborative studies. More cohesive efforts by the four team leaders towards more highly integrated research projects would be appreciated.

Convergent use of X-ray diffraction and electron microscopy is one of the most powerful tools in structural biology to decipher the mechanisms of complex biological functions that are driven by large macromolecular assemblies and cellular organelles. Since this group has the intrinsic capacity and potential to make full use of this tool and develop the method further to make it even more powerful, the expectations of the research communities of structural, molecular and cellular biology are not at all trivial. I hope this group will become one of the international leaders in the field.