国立研究開発法人理化学研究所 眞貝細胞記憶研究室 眞貝 洋一 主任研究員 殿

国立研究開発法人理化学研究所 理事 松本 洋一郎

平成29年度実施主任研究員の研究業績レビュー(中間)の結果について

研究開発等評価実施規程(平成15年10月1日規程第74号)及び主任研究員及び上席研究員研究業績評価実施細則(平成27年10月23日細則第84号)を踏まえ、レビューアーから送られた評価結果は以下のとおりです。なお、評価委員の総意のもと、意見を取りまとめた報告書として提出いただいたこと、申し添えます。

1. 評価対象: 眞貝細胞記憶研究室 眞貝 洋一主任研究員

1) 評価体制

実施日:平成30年1月29日(月曜日)

4名の所外有識者を評価委員とするヒアリングレビューを実施。

評価者:

Tetsuji KAKUTANI, Professor The University of Tokyo, Japan

Haruhiko SIOMI, Professor Keio University, Japan

Toshikazu USHIJIMA, Chief National Cancer Center Research Institute, Japan

Yi ZHANG, Professor Harvard Medical School and Boston Children's Hospital, U.S.A

2) 評価結果の概要等

General comments:

Objectives: Dr. Yoichi Shinkai has been addressing important questions in epigenetics, including mechanisms of endogenous retrovirus silencing, disease models of Kleefstra syndrome, and identification of methylated non-histone proteins. Focusing on these three areas appears to be appropriate as he has managed to make progress, in addition to the fact that all of the three areas are important and competitive fields. Most of the projects were started in RIKEN, and take advantage of his previous strength in G9a/Glp studies. To increase understanding of how Glp mutations cause Kleefstra syndrome, he attempted phenotype rescue experiments and achieved partial rescue when rescued at 3 weeks. Determination of the precise timing and cell type for a complete rescue will be important in understanding the cause of the disease and developing novel strategies for therapy.

<u>Results:</u> The results obtained so far have wide-reaching implications. For example, the involvement of the H3K9me3 methyltransferase ESET in endogenous retrovirus silencing revealed a novel modification independent of DNA methylation for retrovirus silencing. The partial phenotypical rescue of the Glp disease model raised hope for

finding a potential treatment for Kleefstra syndrome. Thus, Dr. Shinkai's work has important implications both in basic biology and disease. In addition, Dr. Shinkai has also performed a biochemical screen for additional protein substrates for G9a and identified several potentially interesting non-histone protein substrates.

<u>Management:</u> Based on his productivity and the fact that the two associates we interviewed are generally happy to work with him, we do not have concerns about his general management skills. He also appears to have many international collaborations, which is important for his continued success. We feel that it would be even better if more attention could be paid to the training of the junior faculty so that they can gradually become more independent.

<u>Future plans</u>: In general, his future plans are excellent and would be very fruitful in the coming years. Considering that the epigenetics field is highly active and competitive, it might be better if he could set up some priorities for fields in which he has unique materials and experimental systems, such as the disease model and substrate of G9a/GLP.

Others: Based on the information we gathered, we would like to make four suggestions to the general management of the RIKEN Institute that include: 1) Extending the retirement age to 65 or 70, depending upon an investigator's performance; 2) The timing of the review should be more than 1 or 2 year(s) in advance so that the Investigator may have more time to prepare for future plan should the review process not be successful; 3) Establishing an independent graduate program of the RIKEN Institute is important, although it might be difficult; 4) Including some specialists in the field in the internal reviewer panels might be helpful.

以上