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Atsuo Ogura, Chief Scientist
RIKEN BioResource Center, Bioresource Engineering Division research
evaluation report

A review committee member composed of two external experts and five RIKEN internal experts gathered at RIKEN campus on October 30, 2015 for Dr. Atsuo Ogura research evaluation. Dr. Ogura presentation started with his missions at the RIKEN BioResource Center and then followed by his research activities and achievements from period of 2008 to 2015. The evaluation report comprises of Scientific and management part which is summarized in the following paragraph.

General evaluation (Published on the RIKEN website)

General Evaluation

1) Science. The mission of the Bioresource Engineering Division at the RIKEN Bio-Resource Center (BRC) is to develop new techniques and to keep the existing routine technologies at highest standards to strongly promote the BRC mission and its essential high quality services. As head of the division since

2002, and as Chief Scientist since 2013, Dr. Ogura has worked in four areas to enhance reproductive engineering technologies. These 4 technologies are a part of his core mission at BRC: (1) Cryopreservation of wild-derived mouse strains, (2) Microinsemination, (3) Nuclear transfer, and (4) Stem cell technologies. He is maintaining a high level in these 4 technologies, a unique achievement for any single laboratory. These achievements have tremendous benefits for the foundation of the BRC infrastructure and will considerably impact future developments in the field. In addition, as a Chief Scientist working on curiosity-driven research, he has addressed (5) developmental epigenetics, to solve basic problems in developmental biology and provide deep insight into the molecular basis of development and reproductive biology. In particular, his interest is focused around the “embryo-soma epigenetic barrier” that exists in the embryonic stage between pre- and post- implantation. Altogether, this places him in a very unique position in the field of developmental biology and epigenetics/epigenomics.

In more detail: Capitalizing on the above-mentioned strengths, Dr. Ogura has made outstanding achievements in basic research on X-chromosome inactivation in somatic nuclear transfer cloning, genomic plasticity (chromatin modification) and DNA demethylation during early embryogenesis. In particular, his finding that the *Xist* expression in all the existing alleles in female, as well as in male SCNT embryos, is responsible for the global downregulation of X-linked genes in the embryos is spectacular in the context of epigenetics in development.

It is highly probable that this global gene repression in the X chromosomes is responsible, at least in part, for the embryo-soma epigenetic barrier that reduces the success rate of mouse cloning. Based on this finding, he has succeeded in developing a critical method for increasing the birth rate of cloned mice and has revealed the importance of oocyte imprint in repressing the *Xist* expression during embryogenesis.

Most of these studies are driven by his motivation to address outstanding technology problems such as increasing the success rate of SCNT, speed of creation of congenic mice lines, and supply of primordial germ cells. These very focused objectives, both in technology development, which is very well suited to the mission of the division, and in broad applications of technology that address basic problems in developmental biology and life sciences, are very

complementary to the missions of the BRC. The findings of these studies have high academic value and many have been published in high impact journals and are frequently cited.

2) Management. The laboratory has been well managed in terms of both human resources and research funding. Judging by the productivity of the laboratory both in terms of support of the Center and scientific productivity as Chief Scientist, it is clear that Dr. Ogura has been doing excellent work, identifying the synergies between technology development for the BRC and the curiosity-driven research that is the mandate of the Chief Scientist. He has made the most of his lab members who all have top-level training. Four permanent staff members have their own major responsibilities for important reproductive engineering techniques. Since 2008, 9 staff scientists have been working for the laboratory as contract employees, and all of them have been successfully promoted to positions outside at universities, companies, and research institutes. Both Dr. Ogura and his lab members have won awards and he deserves credit for this. External research funding has exceeded internal funding, and external funding has been stable since 2008. Dr. Ogura has been actively collaborating with other universities and institutions.

Due to the importance of the technologies he has developed, this committee recommends that Dr. Ogura's laboratory should be even more generously funded by RIKEN. We do encourage Dr. Ogura to attract more foreign scientists to his laboratory so that his great contributions will be much more visible to the international research community.

Although Dr. Ogura was reviewed for his research achievements as a Chief Scientist, most of his activities are strongly correlated with his mission as a division head at BRC to both develop bioresource-related techniques and to maintain and distribute bioresources of very high quality. The technology development is very complementary to outstanding applications and is harmoniously managed with excellent synergistic effects. He has achieved dynamic balance between research development and public service, in which the development of new methodology and technology can drive new science and a higher level of service, making significant contributions to both the basic research and the foundation of the BRC infrastructure. For example, the generation of the congenic mouse was much accelerated by assisted

reproduction technology using immature sperm. It is prodigious that he has successfully achieved academic research and development of techniques, as well as stable management of bioresources, given the small number of laboratory members. It could not have been easy to clearly distinguish the core mission of BRC from the research being conducted as a chief scientist laboratory, but it is understandable that there would be partially overlapping and complementary activities related to both the Center's mission and the mission of the chief scientist laboratory. In addition, his work reveals that the activities of the infrastructure centers requires high-quality research by top scientists, and the needed scientific services cannot be provided without high quality science.

Overall, Dr. Ogura deserves words of highest praise for his outstanding achievements and sound management of a comprehensive research group. Although this is his final review, there will still be many more things to be investigated, developed, and distributed over the coming years by his laboratory and by BRC.