

# NATIONAL BIORESOURCE PROJECT (NBRP) SYMPOSIUM

Sponsor: Public Relations Office of National Bioresource Project (NBRP)

Supporter: The 42<sup>nd</sup> Annual Meeting of the Molecular Biology Society of Japan

## 「Forefront of life science research supported by NBRP」

**Date : Thursday, December 5, 15:45 ~ 19:00**

**Venue : Marine Messe Fukuoka 3F Sub-Arena**

### About NBRP

The major purpose of the National BioResource Project (NBRP) is to collect, preserve, and provide bioresources (such as experimental animals and plants) that are essential experimental materials for life science research. In order to meet current scientific demands, the project also aims to increase the value of bioresources via addition of genome information and development of fundamental technologies for preservation and other necessary procedures. In addition, the information center will be upgraded in order to promote dissemination of information regarding the whereabouts and biological characteristics of bioresources.

In the NBRP from FY2002 to FY2016, systems for collection, preservation, and provision were established for bioresources such as experimental animals, plants, and microbes that are important to promote life science research. In the Fifth Science and Technology Basic Plan (FY2016 ~ FY2020), the government stipulated that intellectual infrastructures such as biological and genetic resources should be collected and utilized by public organizations both strategically and systematically. Therefore, the NBRP plans to reinforce existing intellectual infrastructures, by improving the quality of the available resources in response to diverse needs.

Under these circumstances, AMED continues to operate the fourth term of the NBRP (FY2017 ~ FY2021) to promote strategic collection and utilization of the bioresources.

# NATIONAL BIORESOURCE PROJECT (NBRP) SYMPOSIUM

## Program

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- 15:45-15:55 **Opening**  
**Opening remarks** Yuji KOHARA  
(NBRP Program Supervisor Research Organization of Information and Systems)  
**Guest greeting** Taeko ONODERA  
(Life Science Division, Research Promotion Bureau, Ministry of Education, Culture, Sports, Science and Technology-Japan)
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- Part 1 (15:55-17:25) Chairperson : Tetsuya HAYASHI (NBRP Program Officer Kyushu University)
- 15:55-16:25 **Japanese macaques**  
*Japanese monkeys as experimental animals*  
**Katsuki NAKAMURA** Kyoto University  
*Social brain research using Japanese macaques*  
**Masaki ISODA** National Institutes of Natural Sciences
- 16:25-16:55 **Xenopus tropicalis**  
*Genome sequencing and genetic variation of four inbred strains of Xenopus tropicalis*  
**Takeshi IKAWA** Hiroshima University  
*Discovering the mechanisms for endogenous organ regeneration: lessons from Xenopus tropicalis*  
**Haruki OCHI** Yamagata University
- 16:55-17:25 **Yeast**  
*One of the top international yeast resource centers: National BioResource Project -Yeast*  
**Minetaka SUGIYAMA** Osaka University  
*Reliable imaging of ATP in living budding and fission yeast*  
**Masakatsu TAKAINE** Gunma University
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- 17:25-17:35 Break
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- Part 2 (17:35-18:55) Chairperson : Satoshi TABATA  
(NBRP Program Officer Kazusa DNA Research Institute)
- 17:35-18:05 **Morning glory**  
*Bioresources of the Japanese morning glory: its development and new utilization methods*  
**Atsushi HOSHINO** National Institute for Basic Biology  
*Identification of a gene that regulates flower longevity in Japanese morning glory*  
**Kenichi SHIBUYA** National Agriculture and Food Research Organization
- 18:05-18:35 **Information center**  
*How to use bioresource information to promote research efficiently*  
**Shoko KAWAMOTO** National Institute of Genetics  
*Toward the creation of high value-added resources integrated with information*  
**Hiroshi MASUYA** RIKEN BRC
- 18:35-18:55 **ABS support**  
*When acquiring animals, plants and microorganisms from overseas, ABS Procedure is indispensable!*  
**Mutsuaki SUZUKI** National Institute of Genetics
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- 18:55-19:00 **Closing remarks** Yuichi OBATA (NBRP Program Officer RIKEN BRC)
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## Japanese monkeys as experimental animals

Katsuki NAKAMURA

Primate Research Institute, Kyoto University

Japanese monkeys are human's closest relatives among experimental animals to which we can apply invasive methods. They have well-developed brains and are docile and good with hands. Therefore, many researchers have used them in neuroscience and obtained splendid outcomes. In recent years, results of a brain study using Japanese monkeys have suggested an effective method of rehabilitation from strokes. On the other hand, medical doctors have developed a new device to use for lifesaving first aid. Unlike other macaque species, Japanese monkeys show unique responsiveness to various viruses, and this fact is attracting researchers' attention in virology. We can expect development of a new research field using Japanese monkeys with gene editing techniques.

## Social brain research using Japanese macaques

Masaki ISODA

National Institute for Physiological Sciences,  
National Institutes of Natural Sciences

There is increasing attention to the study of social brain function. Owing to the refinement of neuroimaging techniques for human subjects, researchers can noninvasively identify brain structures and circuits that are dedicated to adaptive social functioning. More recently, it has been proved to be technically feasible to train macaque monkeys on behavioral tasks requiring complex “social” decision-making in the laboratory setting. The refinement of such task paradigms, combined with electrophysiological recording techniques with a fine spatiotemporal resolution, has enabled a system-level understanding of social brain function using monkeys. Here, I introduce, as an example of such a research direction, how the brain processes and integrates information about rewards to oneself and others. Using a novel behavioral procedure developed for two monkeys face-to-face, we found that neurons in the medial prefrontal cortex selectively encode the information about self-rewards or other-rewards, while neurons in the dopaminergic midbrain nuclei encode a subjective value of one’s own rewards by considering other-reward information. Simultaneous recordings in the two regions revealed that the neural information flows predominantly in a prefrontal-to-midbrain direction. These findings point to the importance of cortico-subcortical pathways in social reward monitoring and evaluation.

### Main papers:

- ◆ Noritake A, Ninomiya T, Isoda M (2018) Social reward monitoring and valuation in the macaque brain. *Nat Neurosci* 21: 1452-1462.
- ◆ Isoda M, Noritake A, Ninomiya T (2018) Development of social systems neuroscience using macaques. *Proc Jpn Acad Ser B Phys and Biol Sci* 94: 305-323.

## Genome sequencing and genetic variation of four inbred strains of *Xenopus tropicalis*

Takeshi IKAWA

Amphibian Research Center, Hiroshima University

The Western clawed frog is a model species of amphibian utilized for various kind of biological studies especially for developmental and regenerative biology. We have engaged passage breeding and succeeded to develop four vigorous inbred strains (*Nigerian A*, *Nigerian H*, *Nigerian BH*, *Ivory Coast*) in Amphibian Research Center, Hiroshima University (the NBRP resource center for *Xenopus tropicalis*). We also clarified genetic relationships of major strains used in the world. Recently genome sequence data of each strain are demanded due to rapid progress of experimental technologies such as genome editing. Therefore we conducted genome sequencing of the four inbred strains using massively parallel sequencers. The resulting data showed unique nucleotide substitutions and structural variations in each strain. The individual genome dataset of the inbred strains in the same species should be invaluable resources for the advanced model studies such as association of individuality of genomes and incidence rate. We introduce difference of genome sequences and genetic relationships inferred by the variations in the strains.

### Main papers:

- ◆ Igawa T, Watanabe A, Suzuki A, Kashiwagi A, Kashiwagi K, Noble A, Guille M, Simpson DE, Horb ME, Fujii T, and Sumida M (2015) Inbreeding ratio and genetic relationships among strains of the Western clawed frog, *Xenopus tropicalis*. *PLoS One* 10(7): e0133963.
- ◆ Kashiwagi K, Kashiwagi A, Kurabayashi A, Hanada H, Nakajima K, Okada M, Takeshi M, Yaoita Y (2010) *Xenopus tropicalis*: An Ideal Experimental Animal in Amphibia. *Exp Anim* 59(4): 395–405.

## Discovering the mechanisms for endogenous organ regeneration: lessons from *Xenopus tropicalis*

Haruki OCHI

Institute for Promotion of Medical Science Research,  
Yamagata University Faculty of Medicine

Frog can regenerate many tissues and recover normal function after injury, whereas mammals have a limited regenerative capacity. Therefore, frog is considered as an excellent model system for studying regenerative processes. On the other hand, most of the researchers who are using mouse, fish and cultured cell lines may wonder if the frog system is suitable for the cutting-edge research, and are also concerned about an establishment of the frog system in your laboratory. Nowadays, however, National BioResource Project provides us living animals, genetic experimental materials, and genomic information, and this wonderful system removes barriers to start a new research project with no experience.

Recently, we screened regeneration signal-response enhancers (RSREs) at the *lhx1* locus using frog and found that the noncoding elements conserved from fish to human function as enhancers in the regenerating nephric duct. We found that *Arid3a*, a component of H3K9me3 demethylases KDM4/JMJD2 complex, binds to RSREs and reduces the H3K9me3 levels on RSREs. The conditional knockdown of *arid3a* using photo-morpholino showed that *Arid3a* is necessary for the regeneration of nephric tubule. Furthermore, we found that mouse counterpart elements of RSRE showed the enhancer activity in frog regenerating nephric tubule. In this lecture, we will discuss the regeneration mechanisms mediated by RSREs is potentially conserved in mammals and also show the contribution of NBRP of our research projects.

### Main papers:

- ◆ Suzuki N, Hirano K, Ogino H, Ochi H (2019) *Arid3a* Regulates Nephric Tubule Regeneration via Evolutionarily Conserved Regeneration Signal-Response Enhancers. *eLife* pii: e43186.
- ◆ Suzuki, S, Hirano, K, Ogino, H, Ochi H (2015) Identification of distal enhancers for *Six2* expression in pronephros. *Int J of Dev Biol* 59(4-6): 241-6.
- ◆ Ochi H, Tamai T, Nagano H, Kawaguchi A, Sudou N, Ogino H (2012) Evolution of a tissue-specific silencer underlies divergence in the expression of *Pax2* and *Pax8*. *Nat Commun* 3:848.

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## One of the top international yeast resource centers: National BioResource Project -Yeast

Minetaka SUGIYAMA

Graduate School of Engineering, Osaka University

Yeast is an important eukaryotic model organism. This is especially true of the fission yeast *Schizosaccharomyces pombe* and the budding yeast *Saccharomyces cerevisiae*, which are making significant contributions to research in a variety of areas such as life science and biotechnology. NBRP-Yeast has established a framework to collect, stock and distribute strains and DNA resources of mainly the two species. Through phases 1 to 4 of the NBRP, the NBRP-Yeast has become one of the top international yeast resource centers. NBRP-Yeast have collected approximately 50,000 yeast strains and 100,000 DNA clones, and distributes approximately 4,000 resources to more than 20 countries per year. The activity and service of NBRP-Yeast are introduced in this symposium.

Main papers:

- ♦ Nakamura T, Kitamura K, Sugiyama M (2017) National Bioresource Project Yeast. *Chemistry and Biology* 55(5): 326-332 (*in Japanese*).
- ♦ Parua PK, Booth GT, Sansó M, Benjamin B, Tanny JC, Lis JT, Fisher RP (2018) A Cdk9-PP1 switch regulates the elongation-termination transition of RNA polymerase II. *Nature* 58 (7710): 460-464.
- ♦ Memisoglu G, Eapen VV, Yang Y, Klionsky DJ, Haber JE (2019) PP2C phosphatases promote autophagy by dephosphorylation of the Atg1 complex. *PNAS* 116(5): 1613-1620.

## Reliable imaging of ATP in living budding and fission yeast

Masakatsu TAKAINE

Gunma University Initiative for Advanced Research (GIAR), Gunma University,  
Institute for Molecular and Cellular Regulation (IMCR), Gunma University

Yeasts have been exceptional model organisms for studying metabolism and bioenergetics in eukaryotic cells. Adenosine triphosphate (ATP) is a major metabolite that is essential for all living organisms. In addition to being “energy currency” for various cellular processes, ATP serves as an intracellular and extracellular signaling molecule as well as a phosphate donor for protein phosphorylation. However, little did we know about the ATP dynamics in living yeast. Using the recently developed ATP biosensor QUEEN, we established a method to visualize ATP concentrations in living budding and fission yeast cells with good spatial and temporal resolution. We also found stable maintenance of ATP concentration in wild-type yeasts regardless of growth media or cell cycle stages, suggesting that there exists a mechanism to maintain ATP at a specific concentration (ATP homeostasis). QUEEN expressing yeasts provide easy and reliable examination of ATP dynamics in various conditions, allowing us to address the mechanisms and physiological relevance of ATP homeostasis in the future.

### Main papers:

- ◆ Takaine M, Ueno M, Kitamura K, Imamura H, Yoshida S (2019) Reliable imaging of ATP in living budding and fission yeast. *J Cell Sci* 132 (8).
- ◆ Ito H, Sugawara T, Shinkai S, Mizukawa S, Kondo A, Senda H, Sawai K, Ito K, Suzuki S, Takaine M, Yoshida S, Imamura H, Kitamura K, Namba T, Tate SI, Ueno M (2019) Spindle pole body movement is affected by glucose and ammonium chloride in fission yeast. *Biochem Biophys Res Commun* 511: 820-825.



## Bioresources of the Japanese morning glory: its development and new utilization methods

Atsushi HOSHINO

National Institute for Basic Biology, National Institutes of Natural Sciences

National BioResource Project Morning Glory is the world's only repository of the Japanese morning glory (*Ipomoea nil*) bioresources, which maintains approximately 3,000 lines and 160,000 DNA clones. It also collects information on mutant lines and genome sequences, and provides a laser treatment service to enhance seed germination. *I. nil* is a traditional horticultural plant in Japan, and a number of transposon-induced mutations related to floricultural traits have been identified since the 19th century. A whole genome sequence and a high-efficiency genome editing method have been published. *I. nil* is an ideal model plant to study photoperiodic flowering, flower coloration, and rapid flower wilting, with unexplored unique traits that may help create new model systems.

### Main papers:

- ♦ Hoshino A, Jayakumar V, Nitasaka E, Toyoda A, Noguchi H, Itoh T, Shin IT, Minakuchi Y, Koda Y, Nagano AJ, Yasugi M, Honjo MN, Kudoh H, Seki M, Kamiya A, Shiraki T, Carninci P, Asamizu E, Nishide H, Tanaka S, Park K.I, Morita Y, Yokoyama K, Uchiyama I, Tanaka Y, Tabata S, Shinozaki K, Hayashizaki Y, Kohara, Suzuki Y, Sugano S, Fujiyama A, Iida S, Sakakibara Y (2016) Genome sequence and analysis of the Japanese morning glory *Ipomoea nil*. *Nat Commun* 7: 13295.
- ♦ Watanabe K, Kobayashi A, Endo M, Sage-Ono K, Toki S, Ono M (2017) CRISPR/Cas9-mediated mutagenesis of the *dihydroflavonol-4-reductase-B (DFR-B)* locus in the Japanese morning glory *Ipomoea (Pharbitis) nil*. *Sci. Rep* 7: 10028.

## Identification of a gene that regulates flower longevity in Japanese morning glory

Kenichi SHIBUYA

National Agriculture and Food Research Organization (NARO)

Flower longevity is species-specific and petals in flowering plants actively senesce and are eventually shed after pollination or a certain period after flower opening, regardless of the pollination event. Meanwhile, consumers appreciate long-lasting flowers, and flower longevity is an important trait determining the quality of commercial flowers. We searched genes that regulate petal senescence using Japanese morning glory (*Ipomoea nil*). *I. nil* has ephemeral flowers that open in the morning and generally show petal wilting within the same day. During its petal senescence, distinct programmed cell death (PCD) symptoms are observed. Since substantial bioresources have been developed in *I. nil*, this plant is a good model system to investigate petal senescence as well as other horticulturally important traits. First, we screened genes that were upregulated during petal senescence. Among these genes, suppression of *EPHEMERAL1* (*EPH1*), a NAC transcription factor gene, resulted in doubled flower longevity. In *EPH1*-suppressed plants, expression of several PCD-related gene was suppressed, and the progression of cell death was delayed. These results indicate that *EPH1* is a key regulator of petal senescence. We further produced *EPH1* knock-out mutants by CRISPER/Cas9-mediated mutagenesis. The *eph1* plants exhibited a clear delay in petal senescence, confirming that *EPH1* plays a crucial role in the regulation of petal senescence.

### Main papers:

- ◆ Shibuya K, Watanabe K, Ono M (2018) CRISPR/Cas9-mediated mutagenesis of the *EPHEMERAL1* locus that regulates petal senescence in Japanese morning glory. *Plant physiol and biochem* 131: 53-57.
- ◆ Shibuya K, Shimizu K, Niki T, Ichimura K (2014) Identification of a NAC transcription factor, *EPHEMERAL1*, that controls petal senescence in Japanese morning glory. *Plant J* 79: 1044-1051.

# NATIONAL BIORESOURCE PROJECT (NBRP) SYMPOSIUM

## How to use bioresource information to promote research efficiently

Shoko KAWAKOTO

Genetic Resource Center, National Institute of Genetics

In order to facilitate life science research, the National BioResource Project (NBRP) began in 2002 and has been continued for 17 years in Japan. Currently, 30 categories of bio-resource core centers are active in all over the nation with the support of Japanese government and have been grown the fundamental infrastructure in Japan. The NBRP information center supports IT infrastructure for each resource centers through provision of information regarding the locations of bioresource collections, scientific knowledge related to resources, genomic data, and other essential information. From our portal site, the resource user can be accessed to 6.5 million bioresources and the reference database of 28,000 papers related to NBRP resources through the integrated cross-referenced search (<http://www.nbrp.jp>). NBRP possesses a wide variety of resources from wild type, inbred lines to genetically modified strains like transgenic lines, knockout strains, RNAi strains, and so on. We explain how to find the resources for the research using the NBRP database. And furthermore, the latest information related to genome and literature will be introduced.

NBRP Information center URLs:

- ◆ NBRP portal site : <http://www.nbrp.jp>
- ◆ Integrated cross-resource search : <http://resourcedb.nbrp.jp>
- ◆ Resource reference database : <https://rrc.nbrp.jp>

## Toward the creation of high value-added resources integrated with information

Hiroshi MASUYA

BioResource Research Center, RIKEN

The RIKEN BioResource Research Center has launched the Integrated Bioresource Information Division in 2018 aiming the development of information infrastructure for dissemination and international sharing of bioresource information in important research areas such as health, food, environment and resources.

The Division has three main programs: 1) R & D for metadata integration, international standardization, cross-searching, etc., 2) Enhancement of website contents, 3) Development of large-scale data analysis and data visualization technology. In the metadata integration of 1), we aim to integrate the data in the important areas of life science and bioresource information, which is the key to the reproducibility of research, and provide a life science research foundation continuously. We will actively participate in the international standardization and technology development. In addition, we will work on the development of the interlinking of information and bioresources that are useful for medical science and agriculture. In the 2) homepage release, content for “viewing, reading, and searching by people” will be created as a key to transmitting resource information. In 3) large-scale data analysis, we will analyze various big data related to bioresources, aiming development and proposal of new methods of use for research.

We link these three programs. Furthermore, by collaborating with related businesses in Japan such as the NBRP Information Center, we aim to contribute to the creation of high value-added resources integrated with information. As expressed as “no value of resources without information”, information plays an extremely important role in the use of bioresources, and that role is expected to grow in the future. In this presentation, I will outline the businesses and research and development that the Division is working on.

### Main papers:

- ◆ Kobayashi N, Kume S, Lenz K, Masuya H (2018) RIKEN MetaDatabase: A Database Platform for Health Care and Life Sciences as a Microcosm of Linked Open Data Cloud. *Int J Semantic Web Inf Syst* 14(1): 140-164.
- ◆ Tanaka N, Masuya H (2018) Mouse phenome as biological resource. *Impact* 12: 93-95(3).
- ◆ Suzuki K, Nakaoka S, Fukuda S, Masuya H (2019) Energy landscape analysis of ecological communities elucidates the phase space of community assembly dynamics. *bioRxiv* DOI : <https://doi.org/10.1101/709956>

## When acquiring animals, plants and microorganisms from overseas, ABS Procedure is indispensable!

Mutsuaki SUZUKI

ABS Support Team for Academia, National Institute of Genetics

Regarding the handling of overseas genetic resources in the Convention on Biological Diversity, the access to genetic resources from overseas and the benefit arising from their use (Access and Benefit-Sharing: ABS) have become essential to do research. We are working on the NBRP information program the ABS-Project for the purpose of smooth and lawful acquisition of genetic resources and the establishment of a compliance system in academic institutions in Japan.

Specifically, in support of the acquisition of genetic resources, together with the Sub Organizations (Kyushu University, Tokyo Metropolitan University Tokyo, University of Tsukuba), we provide information on the providing country, support for obtaining permission from the government, and advice on contract terms, etc. In the university system construction support, each university supports the establishment and operation of a window for the construction of an ABS support system.

In addition, individual consultations were conducted on NBRP resource organizations, which contributed to strengthening the response to ABS issues when operating resource organizations. As for international response, we participate in the COP of the Conference of the Parties to the Convention on Biological Diversity and provide support for Digital Sequence Information. We convince that our activity contributes to the prevention of ABS-related troubles and the smooth acquisition of genetic resources in the academic field and continue to implement them.

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