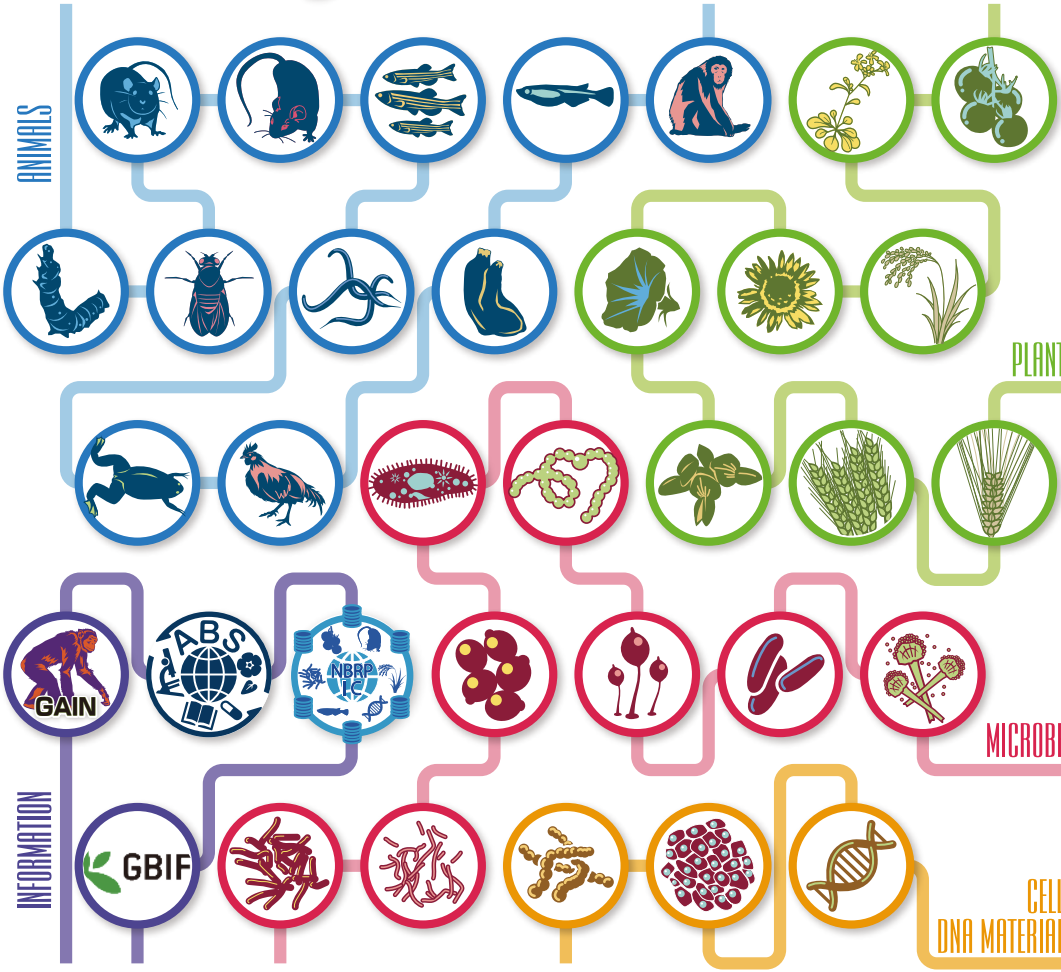
AMED NBRP

National BioResource Project



Introduction

Bio-resources (strains, populations, tissues, cells, genes of animals, plants and microorganisms as research materials) are essential infrastructures for life sciences. It is vital that researchers share various bio-resources necessary for pursuing research and development. This is because these resources, produced from years of painstaking labor, form the foundation for future research. Moreover, it is necessary for scientific communities to use a common set of bio-resources so that their research results can be effectively compared. Thus, the development of outstanding collections of bio-resources is essential to give this country an internationally competitive edge in life sciences.

Based on the Science and Technology Basic Plans of the Japanese Government, the Ministry of Education, Culture, Sports, Science and Technology (MEXT) implemented the National BioResource Project (NBRP) in FY2002 to construct the framework for systematic collection, preservation, and distribution of bio-resources, with a focus on those that required strategic development by the national government. Through the revision every 5 years, the fourth phase of NBRP has started from this year (FY2017). The current NBRP consists of the core centers for 30 categories of bio-resources and the center for information on the resources. Furthermore, the bio-resource framework has been enhanced by increasing value-added genomic resources and developing preservation technologies. Several bio-resource centers have been already recognized to meet the highest global standards.

Based on the Plan for Promotion of Medical Research and Development of the Healthcare Policy approved by the Cabinet in 2014, the operation of the NBRP has been transferred to the Japan Agency for Medical Research and Development (AMED) from FY2015. Currently the Program Supervisor (PS) and the Program Officer (PO) in consultation with the Promotion Committee are responsible for the promotion of the activities of the NBRP, taking into consideration the current trends in life sciences. Finally, I would like to emphasize that the bio-resources in the NBRP cannot be restored once they are lost, which the Great East Japan Earthquake taught us. Your cooperation and support for this project would be highly appreciated.

April 2017

Yuji Kohara, Ph.D.
Project Supervisor, NBRP
(Director, Database Center for Life Science
Research Organization of Information and Systems
Inter-University Research Institute Corporation)

National BioResource Project

National BioResource Project

Purpose

The major purpose of the National BioResource Project (NBRP) is to collect, preserve, and provide bioresources (such as experimental animals, plants, and microbes) 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.

Background

Based on the Plan for Promotion of Medical Research and Development of the Healthcare Policy approved by the Cabinet in 2014, operation of the NBRP was transferred to the Japan Agency for Medical Research and Development (AMED) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) in FY2015.

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 phase of NBRP (FY2017 ~ FY2021) to promote strategic collection and utilization of the bioresources.

Project General Outline

The National BioResource Project implements the following four programs to facilitate the collection, preservation, and provision of bioresources and the development of related technologies; (1) core facility upgrading program, (2) genome information upgrading program, (3) fundamental technology upgrading program, and (4) information center upgrading program. These programs will accomplish the purpose of the project described above and will be coordinated to produce synergistic effects.

(1) Core facility upgrading program:

The core facilities will be established to carry out collection, preservation, and provision of bioresources. The bioresources selected for the NBRP are of fundamental importance in life sciences research and must be excellent and originally produced in Japan.

(2) Genome information upgrading program:

The aim of this program is to improve quality and increase the value of bioresources, as well as to reinforce the uniqueness and leading position of Japanese bioresources by enriching and expanding strain and characteristics information, genetic information, such as genome sequences of cDNA, and genome resources, including genome libraries of bioresources that are collected, preserved, and provided by the NBRP.

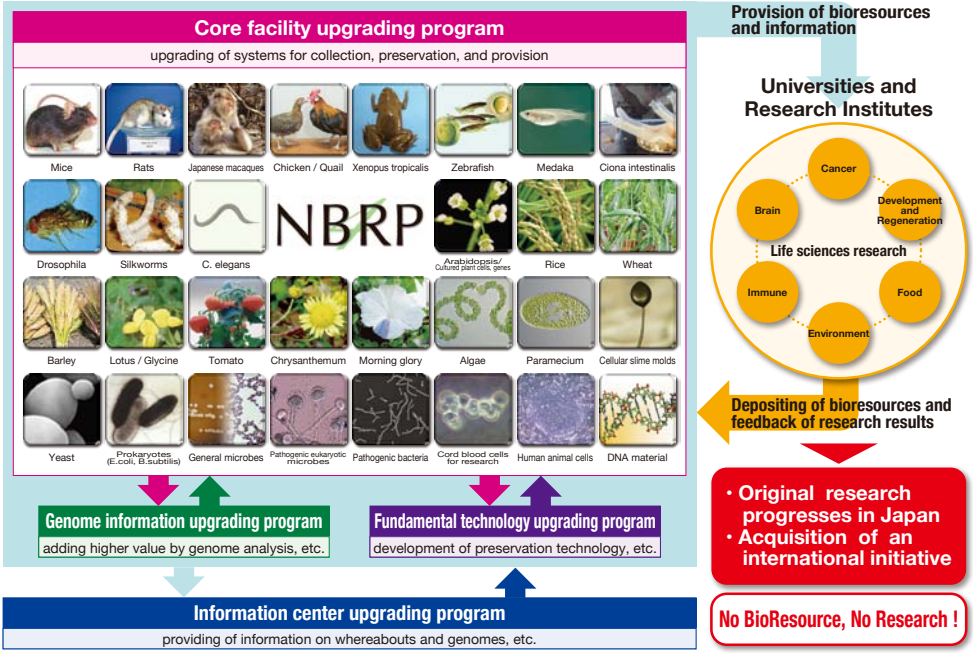
(3) Fundamental technology upgrading program:

Development of technologies relating to collection, proliferation, quality management, preservation and provision of bioresources which are the subjects of the core facilities promotion program is conducted.

(4) Information center upgrading program:

Construction of databases of whereabouts information, genetic information, and biological characteristics of bioresources that are gathered at the core facilities, and public relations of the NBRP through its home page is upgraded.

Project Aims



How to order and about handling/shipping costs

How to order:

Please go to the NBRP portal site (http://www.nbrp.jp), and click on the resource name you wish to get, which is listed on the website. Then, follow the instructions to proceed.

About handling and shipping costs:

The expenses for handling and shipping will be charged to the recipients.

NBRP portal site

Homepages of individual NBRP Bioresource Databases

List of NBRP Implementing Organizations

Core Facility Upgrading Program

Organism, etc	✳	Principal Investigator	Implementing Organization	Page
Mice	○	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource Research Center	1
Rats	○	Masahide Asano	Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University	2
		Tomoji Mashimo	The Institute of Experimental Animal Sciences, Graduate School of Medicine, Osaka University	
	B	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource Research Center	
Japanese macaques	○	Katsuki Nakamura	Primate Research Institute, Kyoto University	3
		Atsushi Nambu	National Institute for Physiological Sciences, National Institutes of Natural Sciences	
Chicken/Quail	○	Yoichi Matsuda	Avian Bioscience Research Center, Nagoya University	4
Xenopus tropicalis	○	Hajime Ogino	Amphibian Research Center, Hiroshima University	5
Zebrafish	○	Hitoshi Okamoto	RIKEN Center for Brain Science	6
		Koichi Kawakami	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	
		Shinichi Higashijima	Exploratory Research Center on Life and Living Systems, National Institutes of Natural Sciences	
	B	Kiyoshi Naruse	National Institute for Basic Biology, National Institutes of Natural Sciences	
Medaka	○	Kiyoshi Naruse	National Institute for Basic Biology, National Institutes of Natural Sciences	7
		Masaru Matsuda	Center for Bioscience Research and Education, Utsunomiya University	
	B	Hitoshi Okamoto	RIKEN Center for Brain Science	
	B	Ryo Akashi	Faculty of Agriculture, University of Miyazaki	
Ciona intestinalis	○	Yasunori Sasakura	Shimoda Marine Research Center, University of Tsukuba	8
		Yutaka Satou	Graduate School of Science, Kyoto University	
		Manabu Yoshida	Misaki Marine Biological Station, Graduate School of Science, The University of Tokyo	
Drosophila	○	Kuniaki Saito	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	9
		Toshiyuki Takano	KYOTO Stock Center, DGRC, Kyoto Institute of Technology	
		Takeshi Awasaki	Kyorin University, School of Medicine	
Silkworms	○	Yutaka Banno	Institute of Genetic Resources, Faculty of Agriculture, Kyushu University	10
		Toru Shimada	Faculty of Science, Gakushuin University	
		Zenta Kajiura	Faculty of Textile Science and Technology, Shinshu University	
C. elegans	○	Shohei Mitani	Tokyo Women's Medical University School of Medicine	11
Arabidopsis/Cultured plant cells, genes	○	Masatomo Kobayashi	Experimental Plant Division, RIKEN BioResource Research Center	12
Rice	○	Yutaka Sato	Department of Genomics and Evolutionary Biology, National Institute of Genetics, Research Organization of Information and Systems	13
		Toshihiro Kumamaru	Institute of Genetic Resource, Faculty of Agriculture, Kyushu University	
Wheat	○	Shuhei Nasuda	Graduate School of Agriculture, Kyoto University	14
Barley	○	Kazuhiro Sato	Institute of Plant Science and Resources, Okayama University	15
Lotus/Glycine	○	Ryo Akashi	Faculty of Agriculture, University of Miyazaki	16
		Shusei Sato	Graduate School of Life Sciences, Tohoku University	
Tomato	○	Hiroshi Ezura	Tsukuba-Plant Innovation Research Center University of Tsukuba	17
		Koh Aoki	Graduate School of Life and Environmental Sciences, Osaka Prefecture University	
		Kentaro Yano	School of Agriculture, Meiji University	
Chrysanthemum	○	Makoto Kusaba	Laboratory of Plant Chromosome and Gene stock, Graduate School of Integrated Sciences for Life, Hiroshima University	18
Morning glory	○	Eiji Nitasaka	Faculty of Sciences, Kyushu University	19
		Atsushi Hoshino	National Institute for Basic Biology, National Institutes of Natural Sciences	

Core Facility Upgrading Program

Organism, etc	✳	Principal Investigator	Implementing Organization	Page
Algae	○	Masanobu Kawachi	National Institute for Environmental Studies (NIES)	20
		Hiroshi Kawai	Kobe University Research Center for Inland Seas	
	B	Kazuhiro Kogame	Faculty of Science, Hokkaido University	
Paramecium	○	Masahiro Fujishima	Graduate School of Science and Technology for Innovation, Yamaguchi University	21
Cellular slime molds	○	Yoichiro Kamimura	RIKEN Center for Biosystems Dynamics Research	22
		Hidekazu Kuwayama	Faculty of Life and Environmental Sciences, University of Tsukuba	
Yeast	○	Taro Nakamura	Graduate School of Science, Osaka City University	23
		Minetaka Sugiyama	Graduate School of Engineering, Osaka University	
	B	Kenji Kitamura	Natural Science Center for Basic Research and Development, Hiroshima University	
Prokaryotes (E.coli, B.subtilis)	○	Hironori Niki	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	24
	B	Tsutomu Katayama	Faculty of Pharmaceutical Sciences, Kyushu University	
General microbes	○	Moriya Ohkuma	Microbe Division/Japan Collection of Microorganisms (JCM), RIKEN BioResource Research Center	25
Pathogenic eukaryotic microbes	○	Takashi Yaguchi	Medical Mycology Research Center, Chiba University	26
		Kenji Hirayama	Institute of Tropical Medicine (NEKKEN), Nagasaki University	
Pathogenic bacteria	○	Kaori Tanaka	Center for Conservation of Microbial Genetic Resource, Organization for Research and Community Development, Gifu University	27
		Tetsuya Iida	Research Institute for Microbial Diseases, Osaka University	
	B	Haruyoshi Tomita	Laboratory of bacterial drug resistance, Gunma University Graduate school of Medicine	
Cord blood cells for research	○	Tokiko Nagamura-Inoue	Department of Cell Processing and Transfusion, Research Hospital, The Institute of Medical Science, The University of Tokyo	28
		Yukio Nakamura	Cell Engineering Division, RIKEN BioResource Research Center	
Human and animal cells	○	Yukio Nakamura	Cell Engineering Division, RIKEN BioResource Research Center	29
DNA material	○	Takehide Murata	Gene Engineering Division, RIKEN BioResource Research Center	30

✳ ○ : Core Facility None : Sub-Core Facility B : Sub-Core Facility for the backup of bioresource

Information Center Upgrading Program

Subject	✳	Task	Principal Investigator	Implementing Organization	Page
Information	○	Development of the Bioresource DBs, etc.	Shoko Kawamoto	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	31
		GAIN	Tetsuro Matsuzawa	Kyoto University Institute for Advanced Study / Primate Research Institute, Kyoto University / Wildlife Research Center, Kyoto University	32
		Japan Node of GBIF	Motomi Ito	Graduate School of Arts and Sciences, The University of Tokyo	
			Tsuyoshi Hosoya	Collection Center, National Museum of Nature and Science	
		ABS Support	Mutsuaki Suzuki	NIG INNOVATION, National Institute of Genetics, Research Organization of Information and Systems	33
			Katsuya Fukami	Material Management Center, Kyushu University	
			Noriaki Murakami	Makino Herbarium, Tokyo Metropolitan University	
			Kazuo Watanabe	Gene Research Center, University of Tsukuba	
		Public Relations	Tomohiro Suzuki	Public Relations Office, National Institute of Genetics, Research Organization of Information and Systems	—
Human resource development for external verification			Chihiro Koshimoto	Japanese Association for Laboratory Animal Science	34

✳ ○ : Core Facility None : Sub-Core Facility

Genome Information Upgrading Program

Organism, etc	Principal Investigator	Organization	Focus	Project Period
Rice	Yutaka Sato	Department of Genomics and Evolutionary Biology, National Institute of Genetics	Genome sequencing of *Oryza* species	FY2019
Wheat	Shuhei Nasuda	Graduate School of Agriculture, Kyoto University	Genome Sequencing of parental accessions of the NAM population of East Asian wheat	
X. tropicalis	Hajime Ogino	Amphibian Research Center, Hiroshima University	Generation of the genome polymorphism data of *Xenopus tropicalis* inbred strains	FY2018
Zebrafish	Koichi Kawakami	Department of Developmental Genetics, National Institute of Genetics	Genetic analysis of zebrafish transgenic and inbred lines	
Drosophila	Kuniaki Saito	Genetic Resource Center, National Institute of Genetics	Sequencing genome-editing strains of Drosophila	
Silkworms	Toru Shimada	Graduate School of Agricultural and Life Sciences, The University of Tokyo	Genome re-sequencing of large body-sized strains of the silkworms suitable for pharmacological, physiological and pathological studies	
Chrysanthemum	Makoto Kusaba	Laboratory of Plant Chromosome and Gene stock, Graduate School of Science, Hiroshima University	Whole genome sequencing of the model strain for the genus Chrysanthemum using long read sequencing technology	
Mice	Toyoyuki Takada	Genetic Strains Research Center, National Institute of Genetics	Genome resequencing of Japanese fancy mouse-derived JF1/Ms strain	FY2017
Wheat	Shuhei Nasuda	Graduate School of Agriculture, Kyoto University	Garnering fundamental information on wheat genomic diversity through *de novo* sequencing of the standard Japanese wheat cultivar Norin 61.	
Mice	Toyoyuki Takada	Genetic Strains Research Center, National Institute of Genetics	Genome resequencing of Japanese wild mouse-derived MSM/Ms strain	FY2016
Rats	Mikita Suyama	Medical Institute of Bioregulation, Kyushu University	Whole genome resequencing of the representative rat strains and development of a SNP typing kit	
Silkworms	Toru Shimada	Graduate School of Agricultural and Life Science, The University of Tokyo	Genome Re-sequencing of Diverse Strains of *Bombyx mori* and *B. mandarina* (2)	
Algae	Yuu Hirose	Toyohashi University of Technology	Genome sequencing project of heterocystous cyanobacteria in the NIES collection	
Mice	Yoichi Gondo	RIKEN BioResource Center	Sequence and structure determination and open to public of reference mouse genome based on long one-molecule sequencing.	FY2015
Rats	Mikita Suyama	Medical Institute of Bioregulation, Kyushu University	Targeted genome resequencing of 20 strains of the rats	
Drosophila	Shu Kondo	Genetic Resource Center, National Institute of Genetics	Genome sequencing of diverse *Drosophila* species (II)	
Silkworms	Toru Shimada	Graduate School of Agricultural and Life Science, The University of Tokyo	Genome Re-sequencing of Diverse Strains of *Bombyx mori* and *B. mandarina*	
Lotus	Shusei Sato	Graduate School of Life Sciences, Tohoku University	Generation of high quality genome sequence of Gifu accession of *Lotus japonicus* to accelerate NBRP resource application	
Pathogenic microorganisms	Takashi Yaguchi	Medical Mycology Research Center, Chiba University	Maintenance of whole genome sequences on related species of *Aspergillus fumigatus*	
Rice	Nori Kurata	Genetic Resource Center, National Institute of Genetics	Generation of genome sequence diversity information for wild relatives of rice	FY2014
General microbes	Moriya Ohkuma	Microbe Division/Japan Collection of Microorganisms (JCM), RIKEN BioResource Center	Genome sequencing of eukaryotic microorganisms of NBRP general microbes	
Lotus	Shusei Sato	Graduate School of Life Sciences, Tohoku University	Resequencing of the NBRP collected resources intended to upgrade the genome information of *Lotus japonicus*	
Drosophila	Shu Kondo	Genetic Resource Center, National Institute of Genetics,	Genome sequencing of diverse Drosophila species	
General microbes	Moriya Ohkuma	Microbe Division/Japan Collection of Microorganisms (JCM), RIKEN BioResource Center	Genome sequencing of microbial strains for environmental and health science	FY2012
Pathogenic microorganisms	Takayuki Ezaki	GTC Genetic Resource Stock Center of Microbial Pathogens Graduate School of Medicine, Gifu University	Genome Sequencing of Opportunistic Pathogens	

Genome Information Upgrading Program

Organism, etc	Principal Investigator	Organization	Focus	Project Period
Rat	Tadao Serikawa	Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University	Whole genome sequencing of F344 rat	FY2011
Ciona intestinalis/ Oxycomanthus japonicus	Kazuo Inaba	Shimoda Marine Research Center, University of Tsukuba	Genome sequencing of the *Ciona intestinalis* inbred line	
Mice	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource Center	Completion of BAC end sequencing of the mouse C57BL/6N substrain	FY2010
Tomato	Koh Aoki	Kazusa DNA Research Institute	Micro-Tom genome sequencing	
Japanese macaques	Tadashi Isa	National Institute for Physiological Sciences, National Institutes of Natural Sciences	Japanese macaque genome sequencing	
Medaka	Kiyoshi Naruse	National Institute for Basic Biology, National Institutes of Natural Sciences	Establishment of polymorphism information of medaka inbred strains	
Mice	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource Center	BAC end sequencing of the mouse C57BL/6N substrain	FY2009
Medaka	Kiyoshi Naruse	National Institute for Basic Biology, National Institutes of Natural Sciences	Full-length cDNA resources of medaka fish	
Wheat	Yasunari Ogihara	Kihara Institute for Biological Research, Yokohama City University	Full-length cDNA resources of common wheat	
Tomato	Erika Asamizu	Gene Research Center, Graduate School of Life and Environmental Sciences, University Tsukuba	Micro-Tom BAC end sequencing	
Medaka	Kiyoshi Naruse	National Institute for Basic Biology, National Institutes of Natural Sciences	Medaka Fish Full-length cDNA Resources	FY2008
Rats	Tadao Serikawa	Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University	Rat LE/Stm BAC end sequencing	
Tomato	Koh Aoki	Kazusa DNA Research Institute	Enhancing tomato resources by sequencing Micro-Tom full-length cDNA	
Medaka	Kiyoshi Naruse	National Institute for Basic Biology, National Institutes of Natural Sciences	Full-length cDNA resources of medaka fish	FY2007
Drosophila	Ryu Ueda	Genetic Strains Research Center, National Institute of Genetics	Genome and property information for the quality control of *Drosophila* strains	
Arabidopsis	Masatomo Kobayashi	Experimental Plant Division, RIKEN BioResource Center	Sequence analysis of full-length cDNAs of *Thellungiella halophila* as new *Arabidopsis* resources	
Wheat	Yasunari Ogihara	Kihara Institute for Biological Research, Yokohama City University	Full-length cDNA resources of bread wheat	

Fundamental Technology Upgrading Program

Organism, etc	Principal Investigator	Organization	Focus	Project Period
Mice	Yumiko Saga	National Institute of Genetics	Development of degron-mediated protein knockout applicable to mouse system	FY2019-2020
Rats	Masahide Asano	Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University	Development of reproductive engineering in rats; the effective operation and the expansion of new users	
Zebrafish	Koichi Kawakami	Department of Gene Function and Phenomics, National Institute of Genetics	Development of transgenic fish lines that label and manipulate specific cell types	
Mice	Fumio Ike	Experimental Animal Division, RIKEN BioResource Research Center	Genome Sequencing of Mouse Monitoring Organisms	FY2018-2019
Japanese macaques	Katsuki Nakamura	Primate Research Institute, Kyoto University	Development of a highly sensitive detection system for Japanese monkey B virus DNA	
Chicken/Quail	Yoichi Matsuda	Avian Bioscience Research Center, Nagoya University	Development of cryopreservation methods of chicken PGCs	
Chicken/Quail	Yoshiaki Nakamura	Graduate School of Biosphere Science, Hiroshima University	Sophistication of the cryopreservation of avian germ cells.	
Silkworms	Yutaka Banno	Institute of Genetic Resources, Faculty of Agriculture, Kyushu University	Development of new cryopreservation methods for silkworm and wild silkworm	
Drosophila	Shu Kondo	Genetic Resource Center, National Institute of Genetics	Development of new technologies for stable maintenance of *Drosophila* stocks	FY2017-2018
Rice	Yutaka Sato	Genetic Strains Research Center, National Institute of Genetics	Establishment of experimental basis of genetic transformation for wild accessions of *Oryza* species	
Paramecium	Masahiro Fujishima	Graduate School of Science and Technology for Innovation, Yamaguchi University	Development of reliable cryopreservation method for *Paramecium* genus	
Drosophila	Toshiyuki Takano	Drosophila Genetic Resource Center, Kyoto Institute of Technology	Development of a new cryopreservation method for Drosophila stocks	FY2016
C. elegans	Shohei Mitani	Tokyo Women's Medical University School of Medicine	Construction of High-Performance balancers for *C. elegans*	
Rats/Zebrafish/ X. tropicalis	Takashi Yamamoto	Graduate School of Science, Hiroshima University	Development of easy protocols for efficient gene knock-in using genome editing technology	
Mice	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource Center	Fundamental technology development of genome editing for the establishment of intractable disease models	
Silkworms	Yutaka Banno	Institute of Genetic Resources, Faculty of Agriculture, Kyusyu University	Development of cryopreservation methods of the silkworm	FY2014
Mice	Fumihiro Sugiyama	Laboratory Animal Resource Center, University of Tsukuba	Development of Cre-loxP recombination atlas for Cre-driver mouse strains	
Mice	Naomi Nakagata	Center for Animal Resources & Development (CARD), Kumamoto University	Establishment of *in vitro* fertilization systems for all mouse strains	FY2012-2013
Medaka	Goro Yoshizaki	Graduate School of Marine Science and Technology, Tokyo University of Marine Science and Technology	Production of functional gametes derived from cryopreserved germ-line stem cells using a surrogate broodstock system in medaka	
Drosophila	Ryu Ueda	Genetic Resource Center, National Institute of Genetics	Development of cryopreservation method of Drosophila strains	
Rats	Tadao Serikawa	Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University	Improving the efficiency of sperm preservation technologies in rats	FY2010-2011
Mice	Yasumasa Ishida	Graduate School of Biological Sciences, Nara Institute of Science and Technology	Production of conditionally gene-disrupted ES-cell clones and establishment of a database for the inactivated genes	
Drosophila	Masa-Toshi Yamamoto	Drosophila Genetic Resource Center, Kyoto Institute of Technology	Development of a long-term stable preservation technology for Drosophila strains	FY2007-2009
Medaka	Minoru Tanaka	National Institute for Basic Biology, National Institutes of Natural Sciences	Development of standard strains for the functional analysis of medaka genes	
DNA (animal/plant/ microbial)	Masatomo Kobayashi	Experimental Plant Division, RIKEN BioResource Center	Development of long-term preservation technology for genetic resources	
Mice	Yasumasa Ishida	Graduate School of Biological Sciences, Nara Institute of Science and Technology	A novel gene-disruption strategy based on the suppression of NMD	FY2007-2008
Mice/Rats	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource Center	Development of transportation systems for mouse and rat resources	

CORE FACILITY UPGRADING PROGRAM Mice

Core Facility : Experimental Animal Division, RIKEN BioResource Research Center
Principal Investigator : Atsushi Yoshiki FAX : +81-29-836-9010
Contact site : animal@brc.riken.jp
URL : https://mus.brc.riken.jp/en/

Overview

Mice are used as model animals for human widely in the life science research and development. To meet social and research needs, the Experimental Animal Division of the RIKEN BioResource Research Center (BRC) has operated to collect, preserve, quality-control and distribute mouse models created in Japan for the study of higher biological functions and conquering diseases. Our mice are cleaned-up to specific pathogen-free state, strictly monitored for their health and genetic modifications. Genomic, gene expression and phenotypic information are added to enrich their value to establish mouse resources of the world highest standard. As an international hub, RIKEN BRC participates in the International Mouse Strain Resource, IMSR and registers strains created by Japanese scientists and disseminate the mice around the world. We have also promoted Asian/Australian networks to strengthen regional cooperation and participated with other BRC groups in the International Mouse Phenotyping Consortium (IMPC) to contribute to basic medical sciences and drug discovery by producing knockout mice for every coding gene, generating broad-based phenotypic data, and making them available to scientists around the world (*Nature* 537:508-514, 2017).

International collaboration

International Mouse Strain Resource, IMSR One-Stop Shop Database
http://www.findmice.org/

Asian Mouse Mutagenesis & Resource Association, AMMRA
http://www.findmice.org/

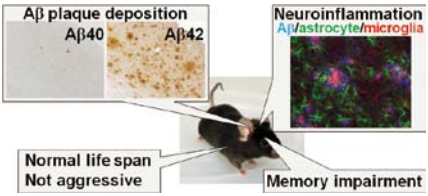
International Mouse Phenotyping Consortium, IMPC
http://www.mousephenotype.org/

Key Strains/Studies

We have approximately 8,800 mouse strains as follows: inbred mice, spontaneous and induced mutants, Cre and FLP driver strains and transgenic mice to visualize various phenomena, mice with targeted mutations such as knock-out and knock-in, congenic strains, strains with chromosomal abnormalities and chromosomal recombination, and wild-derived mouse strains.

● C57BL/6-*App*$^{tm3(NL\text{-}G\text{-}F)Tcs}$/*TcsRbrc* (RBRC06344)

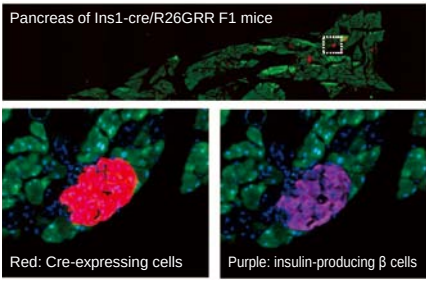
Drs. Saido, Saito, and colleagues at RIKEN Brain Science Institute have developed the next generation mouse models for Alzheimer's disease (AD) by knock-in to the *App* gene with *Swedish* (NL), *Iberian* (F) and *Arctic* (G) mutations found in familial AD patients. This mouse model well recapitulates patients' amyloid pathology (Fig.1) and is expected to become a standard model to find preventive therapies of the AD (*Nat Neurosci* 17, 661-3, 2014).



Courtesy of Drs. Takaomi C. Saido and Takashi Saito
Fig. 1. Alzheimer's disease model with human patients' mutations

● C57BL/6-*Gt(ROSA)26*$^{tm1(CAG\text{-}EGFP/DsRed)Utr}$ (R26GRR)

Dr. Sugiyama, University of Tsukuba in the FY2014 NBRP Fundamental Technologies Upgrading Program characterized Cre-driver strains such as genome-edited knockin B6-*Ins1*$^{em1(cre)Utr}$ mice (RBRC09525) and improved the technology to evaluate the tissue specificity of Cre-recombinase expression by using R26GRR mice (RBRC0487) (Fig.2, *Exp Anim* 65, 319-27, 2016).



Courtesy of Dr. Fumihiro Sugiyama
Fig. 2. Pancreatic β cell -specific Cre recombinase expression in the Ins1-cre mice

CORE FACILITY UPGRADING PROGRAM Rats

Core Facility : Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University
Principal Investigator : Masahide Asano FAX : +81-75-753-4409
Contact site : nbrp-adm@anim.med.kyoto-u.ac.jp
URL : http://www.anim.med.kyoto-u.ac.jp/NBR

Overview

The rat is the mammal which is used in many fields of research owing to its suitable size, adaptability and neurological characteristics. Recent developments including the establishment of rat ES/iPS cells and the generation of gene knockout rats using gene editing nucleases (ZFN/TALEN/Cas9) technology etc. will boost the utility of the rat as biological resource.

Various rat strains deposited to NBRP-Rat

The Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University, conducts a rat strain-based collection, preservation and distribution program and quality assurance through microbial and genetic monitoring, enhances rat strain databases and holds the Rat Resource Research Meeting to support and stimulate science in the rat research community. Riken BRC, backs up frozen embryos and sperm, and Osaka University, preserves and supplies immunodeficient rats, respectively, to support the central facility at Kyoto University as a sub center.

The NBRP-Rat has been developed with the intent of being the world's leading rat resource center. This project promotes further utilization of the rat as a research tool in many fields of science.

Key Studies

So far, approximately 900 different strains have been deposited to NBRP-Rat. The repository includes spontaneous mutants, recombinant inbred, congenic, consomic, transgenic, and knock out rats. These strains are utilized in fields as neurobiology, cardiovascular disease/hypertension, diabetes/obesity, cancer, immunology, development and metabolism.

● Severe combined immunodeficiency rats (X-SCID, SCID, FSG)

Immunodeficient rats were established using gene editing nucleases (ZFN/TALEN). These strains can act as hosts for human xenogeneic tissue grafts and stem cell transplantation.

● Reporter gene transgenic rats

GFP, DsRed, LacZ and other marker genes are important tools for the examination of many biological processes. Our repository has many of such marker strains available for various kinds of experiments with ubiquitous or organ specific marker expression.

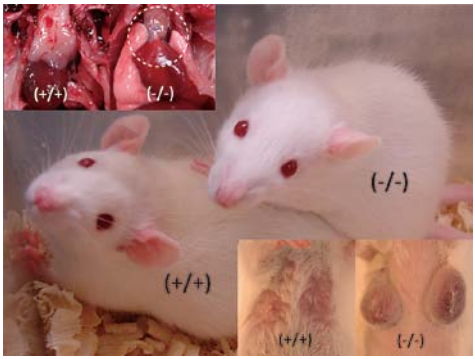


Fig.1 X-SCID Rat (+/+ : Wild type, -/- : *Il2rg* mutated). Left upper : Lack of thymus, Right lower : Xenoplantation of human tumor cells.

● KURMA (Kyoto University Rat Mutant Archive)

Sperm and DNA of 10,752 ENU mutagenized F344 G1 animals are integrated into the NBRP-Rat. This mutant archive, KURMA10K, provides gene-targeted rats as animal models for various fields in biomedical research.

Japanese macaques

Core Facility : Kyoto University Primate Research Institute
Principal Investigator : Katsuki Nakamura FAX : +81-568-65-0188
Contact site : nbrp-nihonzaru@ml.pri.kyoto-u.ac.jp
URL : https://nihonzaru.jp

Overview

The Japanese macaque is a middle-sized monkey similar to the rhesus macaque and the long-tailed macaque. These are all classified into the genus *Macaca* and belong to the *Cercopithcinae*. Monkeys of the genus *Macaca*, so-called macaques, are relatively close to humans and are indispensable experimental animals for research on higher brain functions, infections/immunology, and regenerative medicine.

A Japanese macaques parent and child at the Primate Research Institute of Kyoto University

The Japanese macaques, which are indigenous to Japan, have often been used in the fields of neuroscience and physiology in Japan. They have a very high level of curiosity and are temperate in nature. In addition, Japanese macaques are genetically less variable and exhibit more complex cognitive functions than other macaque monkeys that commonly inhabit Southeast Asia. Because the amount of ecological, behavioral, genetic and morphological literature available concerning Japanese macaques is the largest for all monkey species, it is regarded as an extremely useful experimental animal.

In the 4th phase of NBRP, the core facility, Kyoto University Primate Research Institute, keeps promoting the project, jointly with the sub center, National Institute for Physiological Sciences. When providing Japanese macaques, we conduct the following basic tests: body weight and appearance test, tuberculin reaction test, Shigella test, salmonella test, simian varicella virus antibody test, B virus test, and simian retrovirus test. In addition, monkeys are sorted in advance according to the research purpose such as sex, age, and physical characteristics to meet the needs of researchers.

Key Studies

The following are findings obtained by studies using Japanese macaques: the direct neurophysiological evidence for psychological models of dual-task interference and capacity limitations (*Nat Neurosci* 17: 601-611, 2014), the potential contribution of the nucleus accumbens to movement control after spinal cord injury (*Science* 350: 98-101, 2015), the first demonstration of modeled vocal tics in Tourette syndrome utilizing PET imaging (*Neuron* 89: 300-307, 2016), the first report on a non-human primate that spontaneously exhibited autistic traits with rare coding variants linked to human neuropsychiatric disorders (*Sci Adv* 2: e1600558, 2016), and the discovery of the prefrontal brain areas essential for meta mnemonic decision-making via fMRI (Fig. 1-2, *Science* 355: 188-193, 2017). As such, many studies using Japanese macaques have been published in Japan.

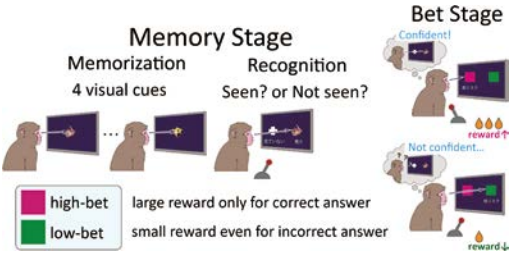


Fig.1. Monkeys were required to perform a yes/no visual memory recognition test, and to make self-confidence judgments regarding their own retrieved memory. In the bet stage, the monkeys more frequently chose “high bets” when they correctly answered the precedent test than when they failed it. ©2017 The University of Tokyo (*Science* 355: 188-193, 2017)

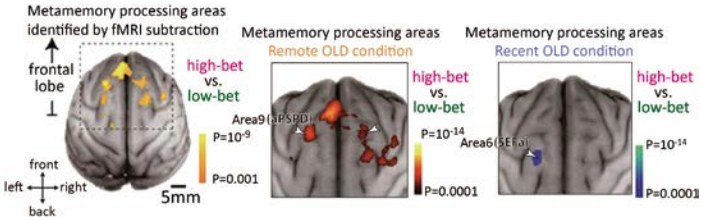


Fig. 2. By whole-brain searches via functional magnetic resonance imaging, we discovered a neural correlate of metamemory for temporally remote events in prefrontal area 9 (or 9/46d), along with that for recent events within area 6. ©2017 The University of Tokyo (*Science* 355: 188-193, 2017)

CORE FACILITY UPGRADING PROGRAM Chicken / Quail

Core Facility : Avian Bioscience Research Center, Nagoya University
Principal Investigator : Yoichi Matsuda FAX : +81-52-789-4114
Contact site : yoimatsu@agr.nagoya-u.ac.jp
URL : https://www.agr.nagoya-u.ac.jp/~nbrp/en/index.html

Overview

The chicken and quail are important model organisms in life sciences, which bridge the evolutionary gap between mammals and other vertebrates and serve as the main laboratory models for ~9,600 extant avian species. Avian Bioscience Research Center (ABRC), Nagoya University contributes to advancement of avian science research as the core facility of avian resources under NBRP.

The ABRC develops the stable system to maintain, preserve and distribute chicken and quail resources with promoting collection of bird resources available throughout Japan. We are offering high-quality resources by developing and upgrading strains under strict genetic control. Furthermore, we are working to collect new genetically modified chickens using recently developed CRISPR-Cas9 technology and develop the cryopreservation technology for germ cells. In addition, we construct the database of the resources, which is widely open to the public via the homepage, and enhance it by adding science-based information obtained using the resources. We have also generated a high quality chromosome-scale assembly of the Japanese quail genome in collaboration with the Quail Genome Consortium of Japan and published it from our homepage (http://viewer.shigen.info/uzura/index.php).

Website releasing assembly information of the Japanese quail genome

Key Strains/Studies

The ABRC distributes 37 strains and/or lines of chickens including the red junglefowl (the wild ancestor of domesticated chickens), inbred strains, and models for human diseases, and 23 lines of Japanese quail including standard lines and a variety of plumage color mutants. Moreover, we distribute transgenic chicken and quail lines that express fluorescent proteins.

● GSP

A highly inbred strain originated from the Fayoumi chicken breed native to Egypt. Skin grafts are acceptable between different individuals. The genotyping of microsatellite DNA markers revealed that 54 loci used for genetic monitoring are fixed in less than 1% heterozygous condition, indicating that this strain is very suitable for experiments for which high reproducibility and accuracy are required.

GSP

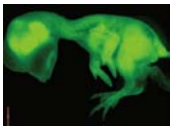
● WE

A Japanese quail line that lays white-shelled eggs, which has been maintained as a closed colony for more than 50 years. This line is used as a standard line for producing vaccine of Marek's disease and toxicity assays of chemicals including pesticides.

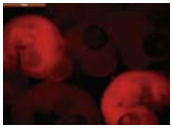
WE

● pLSi/ΔAeGFP-TG chicken and PGK:H2B-chFP-TG quail

Transgenic chicken and quail lines carrying fluorescent protein genes. The chicken and quail lines express enhanced green fluorescent protein (eGFP) and monomer cherry fluorescent protein (chFP), respectively, in the almost whole body.



pLSi/ΔAeGFP-TG



PGK:H2B-chFP-TG

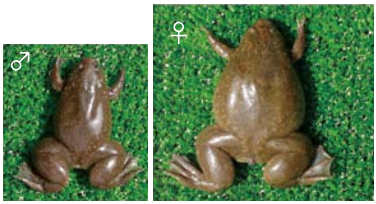
Xenopus tropicalis

Core Facility : Amphibian Research Center, Hiroshima University
Principal Investigator : Hajime Ogino FAX : +81-82-424-0739
Contact site : oginohaj@hiroshima-u.ac.jp
URL : https://xenopus.nbrp.jp/NBRP_Xenopus/NBRP_X._tropicalis_Top_Page.html

Overview

Xenopus tropicalis is a closely related species of *Xenopus laevis* that has been used widely as a model animal for developmental biology. The experimental system of *X. tropicalis* has been developed recently, by virtue of its characteristics suitable for genetic studies, such as a compact diploid genome (nearly half size of the human genome) and a short life cycle (4–6 months). The genome project has revealed that more than 79% of the genes involved in human diseases are present as orthologues in *X. tropicalis* (*Science* 328: 633-636, 2010). The gene functions can be easily examined by CRISPR-Cas9 system, which disrupts 80~99% of the target genes in founder embryos (*Genes Cells* 21: 755-771, 2016). Transgenesis also works quite efficiently with I-SceI meganuclese method, in which introduced transgenes are transmitted to offspring from the founder animals (*Nat Protoc* 1: 1703-1710, 2006).

In this project, the Hiroshima University Amphibian Research Center collects, preserves and provides living and non-living resources of *X. tropicalis* as the core facility. Waseda University, Nihon University and Yamagata University are in charge of strain preservation as the backup partner facilities. Under this arrangement, we are working together to improve the infrastructure of this new model animal, and to support the resource users for further development of amphibian genetics. As part of such activities, we are generating inbred lines, and hold technical training sessions on breeding methods, transgenesis and genome editing, and bioinformatics analysis every year.



Xenopus tropicalis (Nigerian H strain)

Key Strains/Studies

Currently our main resources are four inbred wild-type strains, Nigerian A (a derivative from the "original" Nigerian strain used for the first genome-sequencing project), Nigerian H (genetically close to Nigerian A but easier on breeding), Nigerian-BH (previously referred as "Golden", genetically close to Nigerian A but very robust), and Ivory Coast (a robust strain genetically diverged from the Nigerian group). The whole genome sequences of these four strains are available in public (https://xenopus.nbrp.jp/NBRP_Xenopus/genome_browser.html). We are also collecting transgenic lines useful for live-imaging of stem/differentiated cells (Fig. 1, *Tg(tnbb2b:GFP)1Ogino*). We are supplying 3,000 frogs and tadpoles to researchers and educators every year. Genomic DNA, RNA, and marker gene plasmids are also available as part of the resources.

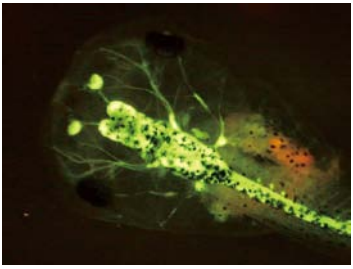


Fig. 1. A transgenic tadpole expressing GFP in the central nervous system under the control of a cis-regulatory region of *Xenopus tropicalis β-tubulin* gene.

X. tropicalis is used in various research fields, such as elucidation of the mechanisms of how zygotic transcription factors take over the blueprint of genome regulation established by maternal factors during early embryonic development (*Dev Cell* 40: 595-607, 2017), discovery of reprogramming phenomena in forelimb regeneration (Fig. 2, *Dev Biol* 432: 265-272, 2017), and elucidation of the mechanisms underlying the pathogenesis of Hermansky–Pudlak syndrome, a human hereditary disease (*Dev Biol* 426: 472-486, 2017).

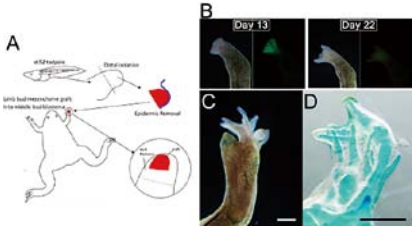


Fig. 2. The finger regenerates when juvenile limb bud mesenchyme (B: green) is transplanted to adult anterior limb blastema. (From *Dev Biol* 432: 265-272, 2017 Fig. 6 A-D)

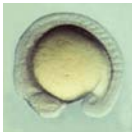
CORE FACILITY UPGRADING PROGRAM Zebrafish

Core Facility : RIKEN Center for Brain Science
Principal Investigator : Hitoshi Okamoto FAX : +81-48-467-9714
Contact site : hitoshi.okamoto@riken.jp
URL : https://shigen.nig.ac.jp/zebra/index_en.html

Overview

Zebrafish is classified as a vertebrate, and their embryos are transparent. Additionally, breeding is easy, life cycle is short, and introduction of mutation and genetic modification is easy. Therefore, they are used for studies on biological regulatory processes such as development and regeneration using molecular genetics and imaging technology. In recent years, reflecting the spirit of animal welfare, the demand as a substitute for mammalian models has also increased.

adult

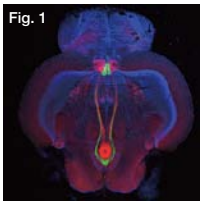


Embryo: 16 hours after fertilization

The number of zebrafish researchers in Japan is increasing. Accordingly, the number of mutant lines and transgenic lines generated in Japan is also rapidly increasing. An efficient sperm freezing technology has been developed on the "fundamental technology upgrading program" in the NBRP. Under these circumstances, the major aim of this project is to set up a system for collecting, maintaining and distributing fish lines for the following purposes: (1) to supply researchers in Japan with lines of their interests quickly. (2) to supply researchers in foreign countries with zebrafish lines created in Japan to increase Japan's contribution to the community. The RIKEN Center for Brain Science (CBS) as the core facility, and the Genetic Resource Center at National Institute of Genetics and the Exploratory Research Center on Life and Living Systems at National Institutes of Natural Sciences as partner organizations jointly maintain the system to collect, preserve, and distribute zebrafish.

Key Strains/Studies

The roles of the three institutes are as follows. RIKEN CBS: Strains with spontaneous and chemically or genetically induced mutant strains, transgenic strains, and wild-type strains. National Institute of Genetics: Transposon insertion, enhancer trap, and exon trap strains. National Institutes of Natural Sciences: Transgenic lines. Cumulatively, the number reaches approximately 6,000 lines.

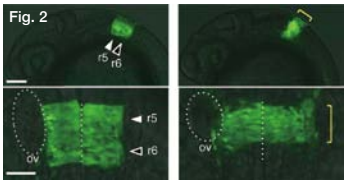


● dao:cre-mCherry; vglut2a:loxP-DsRed-loxP-GFP (RIKEN CBS)

Habebulo-raphe pathway (shown in green), a conserved neural circuit among the vertebrates, encodes the expected level of aversiveness for learning appropriate behavior to avoid the danger (Fig. 1, *Neuron* 87: 1034 1048, 2014).

● gSAIzGFFM35A; UAS:GFP (National Institute of Genetics)

We have created more than 1,000 gene trap and enhancer trap transgenic zebrafish lines that express yeast transcription factor Gal4 in specific tissues, cells, and organs. By crossing these Gal4 lines with transgenic fish lines in which a fluorescent reporter gene or an effector gene that inhibits or manipulates cell functions is placed downstream of upstream activator sequence (UAS), which is a recognition sequence for Gal4, the reporter or effector can be expressed in a tissue-, cell-, or organ-specific manner. The gSAIzGFFM35A line carries a gene-trap transposon insertion in the transcription factor mafba gene. GFP is specifically expressed in the rhombencephalon (r5, r6), and dysplasia of this region is observed in homozygous diploid embryos (Fig. 2, *Cell Rep* 24: 1562-1572, 2018).

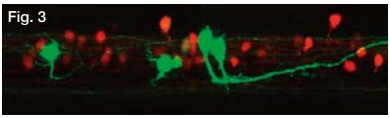


gSAIzGFFM35A; UAS:GFP Heterodiploid

gSAIzGFFM35A; UAS:GFP Homodiploid

● chx10: loxP-DsRed-loxP-GFP (National Institutes of Natural Sciences)

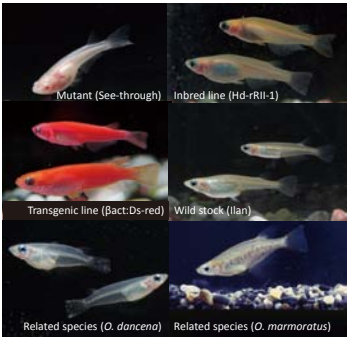
This strain uses the Cre–loxP system. Normally, DsRed is expressed in all alx-positive cells, but by using Cre, it is possible to express EGFP instead of DsRed in some (or all) alx-positive cells (Fig. 3, *J Neurosci* 26: 5684-5697, 2006).



Core Facility : National Institute for Basic Biology
Principal Investigator : Kiyoshi Naruse FAX : +81-564-55-7580
Contact site : naruse@nibb.ac.jp
URL : https://shigen.nig.ac.jp/medaka/ http://www.nibb.ac.jp/bioresources/
Facebook : https://www.facebook.com/nbrpmedaka/

Overview

Medaka, which can survive in a wide temperature range (4°C–37°C), has been used for more than 100 years as an experimental animal, and many bioresources have been accumulated by the enormous efforts of the predecessors. Furthermore, related species inhabit various environments such as freshwater or seawater. Using genetically distinct inbred strains and various strains such as wild-derived strains and related species from various regions throughout Southeast to Eastern Asia, we can study evolution in an order of millions to 10 millions of years. Genomic resources such as BAC, Fosmid, or cDNA clones are well maintained along with live resources such as inbred strains, wild stocks, related species, transgenic lines, mutants, etc. The whole genome sequence of three inbred strains is available.



Various medaka strains offered by NBRP-Medaka.

In the 4th phase of NBRP, collection, preservation, and provision of medaka resources are carried out by National Institutes for Basic Biology (NIBB) and Utsunomiya University and the backup preservation of the clone and the frozen sperm is handled by Miyazaki University and the RIKEN. These four institutions/universities will cooperate to provide the world's best medaka resources covering a wide range from primary education to cutting-edge medical and biological research. In addition, NIBB created an environment where any medaka community members can use reverse genetics techniques by providing a TILLING library and a CRISPR–Cas9 genome editing platform.

Key Strains/Studies

We preserve and provide more than 6,000 lines, including d-rR strain (males and females can be discriminated with body color), Quintet, STII, STIII lines (transparent body due to lack of most pigment cells), inbred strains (Hd-rR, HNI, Kaga, HSOK, etc.), wild stocks (wild medaka collected from Japan, China and Korea), transgenic lines (osx:mCherry/col10a1:nlGFP osteoblast/ osteoclast visualizing line, GaudiLxBBW and GaudiBBW 2.1 brainbow cassette expression line, FmpoP :RFP-Lifeact bone marrow-derived cell visualization line), closely related medaka species (Celebes medaka, Indian medaka, Javanese medaka etc.), and TILLING lines.

They are used in the following broad areas of research: identification of the second vertebrate sex-determining gene, *Dmy* and novel sex-determining genes $Gsdf^{Y}$ and $Sox3^{Y}$ (Fig. 1: *Nature* 417: 559-563, 2002, etc), identification of causal genes of mutants (body color mutants, cystic kidney disease, double anal fins, *glucocerebrosidase* (*GBA*) gene mutation *etc*.) to develop human disease models such as melanoma, Parkinson disease, etc. (Fig. 2: *PLoS Genet* 11: e1005065, 2015), discovery of a switch gene *Foxl3* determining the sex of germ cells (*Science* 328: 1561-1563, 2010; *Science* 349: 328-331, 2015), elucidation of the molecular neural basis for mate choice and social interactions (*Science* 343: 91-94, 2014), the first discovery of "face inversion effect" in non-mammalian vertebrates (Fig. 3, *elife* 6: e24728, 2017), and toxicity test using medaka embryos and adults. About 20% of the total shipments of fish is to overseas (USA, Germany, Spain, Canada, Korea, China etc.).

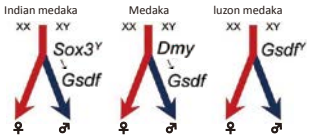


Fig. 1. Diversification of sex-determining genes in the genus *Oryzias*.

Fig. 2. Decreased function of *GBA* is a risk factor for the onset of Parkinson's disease. Unlike *GBA* deficient mice, *GBA* deficient medaka is not lethal and shows a bent posture (From *PLoS Genet* 11: e1005065, 2015, Fig. 1C).

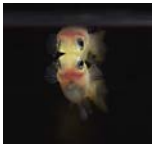


Fig. 3. The face turned upside down is reflected on the water surface. (From the University of Tokyo · Okayama University press release 'Medaka distinguishes friends by "face"' Photographed by Mr. Eiji Fujiwara in the documentary channel).

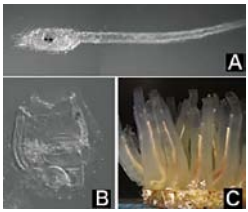
Ciona intestinalis

Core Facility : Shimoda Marine Research Center, University of Tsukuba
Principal Investigator : Yasunori Sasakura FAX : +81-558-22-0346
Contact site : sasakura@shimoda.tsukuba.ac.jp
URL : http://marinebio.nbrp.jp/
http://www.shimoda.tsukuba.ac.jp/eng-home.html

Overview

Marine invertebrates are excellent materials for various subjects of researches including embryogenesis, evolution, reproduction and neurophysiology. In marine invertebrates, ascidians are the closest living relatives of vertebrates, and share the chordate-specific characteristics including the dorsal neural tube, notochord, pharyngeal gill and endostyle/thyroid gland with vertebrates.

Ciona intestinalis is the model species of ascidians because of well-annotated genome sequence and accumulated EST/cDNA/protein resources. The genomic analyses have shown that this ascidian has the basic set of the genes for constructing chordate body plan with less redundancy of gene functions. *Ciona intestinalis* is an excellent organism to perform genetic analyses for understanding gene functions owning to its simple genome and body organization. The inland culture system, transposon-based transgenesis, mutagenesis and knockouts by genome editing have been developed in *Ciona*. By using these genetic technologies, various transgenic and mutant lines have been created which are splendid tools for studying gene functions. The mission of this Bioresource project is collecting, maintaining and supplying wild types, transgenic/mutant lines and plasmid DNAs used in *Ciona* studies.



(A) Juveniles of *Ciona intestinalis*: During the juvenile period, they actively swim in the form of tadpoles. (B) *C. intestinalis* immediately after metamorphosis: After metamorphosis, it loses its tail and enters sedentary life. (C) Adults of *C. intestinalis*.

Key Strains/Studies

We preserve approximately 130 lines, including various fluorescent protein-expressing lines, enhancer trap lines, cell cycle visualization FUCCI lines, and mutant lines. These transgenic and mutant lines are useful for molecular studies, and they are available from NBRP. In addition, approximately 350 types of reporter constructs and tissue-specific TALEN expression plasmids can also be provided.

● Tg[MiCiβ2TBK]2

This is a transgenic strain that expresses Kaede, a coral-derived fluorescent protein, in the nervous system. The color of the Kaede protein can be changed from green to red on exposure to ultraviolet light (photoconversion activity). Therefore, we can accurately mark specific cells at a certain time and to track subsequent changes in the cells. Studies using this strain have shown that many of the glial cells that is present in the larval central nervous system remain after metamorphosis and they form the adult central nervous system including neurons in it (Fig. 1, *Nature* 469: 525-528, 2011).

● Tg[MiCiPC2K]2

This strain is one of the Kaede transgenic lines. It expresses fluorescent proteins in all neurons throughout the body. Because it emits extremely bright fluorescence in neurons, this transgenic line is an optimal strain for observing neurons and their axon trajectory. A study using this strain described the whole nerve network in the adult body. By this information, we can estimate how *Ciona* nervous systems regulate downstream tissues and organs (Fig. 2, *PLoS One* 12: e0180227, 2017).

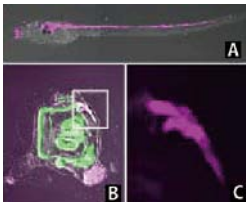


Fig. 1. Trace experiment in metamorphosis process of cells of larval nervous system using Kaede. (A) Larva: Neuronal cells were identified by red fluorescence owing to Kaede color conversion on exposure to UV light. (B) Post-metamorphosis: The presence of neural cells is identified by red fluorescence and cells that have newly emerged after metamorphosis are identified by green fluorescence. (C) (B) Magnified image of the area within the frame.

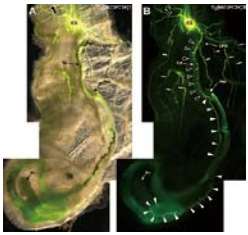


Fig. 2. Distribution of nerve cells in the sea squirt. (A) Kaede fluorescent label superimposed image of the dorsal side of a sea squirt and (B) Kaede fluorescent label image in the dark field. (From *PLoS One* 12: e0180227, 2017 Fig. 1A, B)

CORE FACILITY UPGRADING PROGRAM Drosophila

Core Facility : Genetic Resource Center, National Institute of Genetics
Principal Investigator : Kuniaki Saito Fax : +81-55-981-6825
Contact site : flyadmin@nig.ac.jp
URL : http://fruitfly.jp/
https://shigen.nig.ac.jp/fly/nigfly/

Overview

Drosophila has a 110-year history as a life science research material. In addition to the ease of mass rearing and short life cycle, it has the following advantages: 1) The genome is compact compared with the complexity of the body plan such as formation of various tissues and organs. 2) Life phenomena at an individual level can be analyzed from the functions of genes/genomes. 3) Annotation of the genome sequence is accurate, and expression data of various genes in tissues and at developmental stage are accumulated. 4) Genetic engineering methods such as modified gene introduction and conditional regulation of the expression of such genes have been developed.

Drosophila melanogaster

Keeping ~ 100 adult flies in one bottle

This project aims to comprehensively preserve and manage genetic resources such as various *Drosophila* organisms and DNA clones, and provide them widely to the research community. The core facility, National Institute of Genetics and the sub-core facilities, Kyoto Institute of Technology and Kyorin University are responsible for collecting, preserving, and providing live resources. As a result of NBRP operations in the past 15 years of the three phases, this has become world's largest stock center. While fulfilling our international responsibilities, we aim to collect resources and improve quality in response to the demands. This contributes in accelerating the advanced research activities of the user community.

Wide variety of database groups that support *Drosophila* research

Key Strains/Studies

We maintain approximately 45,000 strains, including mutant strains, genome editing related strains (FlyCas9), RNA interference (RNAi) strains, spontaneous mutant strains of *Drosophila* wild species, and close relative of *Drosophila melanogaster*. We also have approximately 260,000 different cDNA, genome DNA clones, and Cas9 plasmids. The National Institute of Genetics collects, preserves, and provides RNAi and FlyCas 9 lines; Kyoto Institute of Technology is responsible for *Drosophila* wild strains, mutant strains, genetically modified strains, and cryopreservation of selected strains; and Kyorin University is in charge of wild, mutant and transgenic strains of closely related *Drosophila* species. In *Drosophila*, approximately 70% of the 13,936 protein coding genes have homology with human genes. In addition, gene networks are also conserved. Therefore, it has been widely used as a basic research material for diseases in recent years (*Nature* 542: 246-250, 2017). In addition, in species differentiation mechanisms such as lethality, infertility, and sex ratio skewness of interspecific hybrids with closely related species, elucidation by advanced research methods of *Drosophila* is expected (*Trends Genet* 33: 68-80, 2017). *Drosophila* is also an advanced research resource for proteome analysis (*Nature Genet* 38: 1440-1445, 2006).

● y2 cho2 v1; attP40(nos-Cas9)/CyO (Cas-0001)

This is one of the transgenic lines that express Cas9 protein, and it is possible to create mutant lines with high efficiency (approximately 70%) by crossing with various guide RNA lines (Fig. 1, *Genetics* 195: 715-721, 2013).

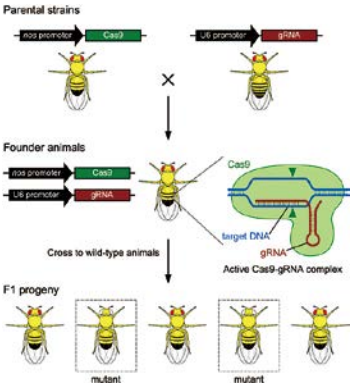


Fig. 1. Transgenic Cas9-gRNA system (From *Genetics* 195: 715-721, 2013 Fig. 1)

CORE FACILITY UPGRADING PROGRAM Silkworms

Core Facility : Graduate School of Agriculture, Kyushu University
Principal Investigator : Yutaka Banno TEL/FAX : +81-92-802-4822
Contact site : banno@agr.kyushu-u.ac.jp
URL : http://silkworm.nbrp.jp/index_en.html

Overview

The silkworms (*Bombyx mori*) can not survive themselves without human support. It is a unique genetic resource in Japan as well as valuable resource in the world because it is maintained and preserved systematically as a strain only in Japan. Because of this background, a large number of natural mutants have been discovered and become the core of current NBRP silkworms. Among the stock, mutants have been discovered one after another that can be used as models of human genetic diseases. In addition, advances in silkworm genome analysis have led to the elucidation of genes involved in insect-specific functions such as food habit and preference (selection), resistance and susceptibility to viruses, fungi, and bacteria, and diapause. Because new pesticides are expected to be developed, it is a good insect model for controlling agricultural pests. Furthermore, there are no common diseases with humans, and breeding techniques are easy and inexpensive owing to the techniques developed through sericulture. Therefore, genetically modified silkworms are used for the production of useful substances (insect factories), and as an alternative animal for experimental animals for toxicity tests and drug screening.

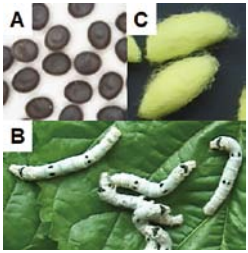


Fig. 1. Eggs (A), larvae (B), and pupae (cocoons) (C) of p50 standard strain

In this project, Kyushu University and Shinshu University collect, preserve, and provide living organisms. Gakushuin University collects, preserves, and provides cultured cells and DNA resources. In addition to providing services and support in terms of breeding methods and management techniques for researchers who have no breeding experience, we also supply silkworms for users involved in educational and cultural activities for silkworm users.

Key Strains/Studies

Kyushu University offers approximately 500 silkworm strains, including the p50 strain (Fig. 1), which is a standard strain used for genome information analysis. Shinshu University offers wild silkworms such as *Antheraea yamamai*, *A. pernyi*, and *Samia cynthia pryeri*. Gakushuin University provides more than 190,000 clones of genomic DNA libraries (Fosmid, BAC) and cDNA libraries of *B. mori* and related species, as well as cultured cells derived from the silkworm ovary, which contains PIWI-interacting RNA pathway in a complete form.

● Recent topic reported in the *Zebra* mutant

The pattern of horizontal stripes found in the larvae of *Zebra* strains is also found in several Lepidopteran larvae and is used as a warning signal to predators (Fig. 2). Recently, it has been revealed that the gene responsible for the zebra trait is *Spz3*, one of the Spätzle family genes involved in the regulation of innate immunity in humans. In silkworms, as in humans, Spz3 signaling has been shown to induce zebra-stripe melanogenesis via Toll receptors (*PNAS* 114: 8336-8341, 2017).

Fig. 2. Zebra silkworm (top) and swallowtail butterfly (bottom) (From Fig. 1 of News "A part of the immune system was diverted to stripe pattern formation of insects?" Haruhiko Fujiwara, Graduate School of Frontier Sciences, The University of Tokyo)

● Survey and use for potential genetic variation

As a result of investigating the efficiency of protein production in recombinant baculovirus AcMNPV using luciferase assay for the NBRP resources, it became clear that the production efficiency differs greatly between strains, and that this involves the locus on silkworm chromosome 3. The use of nine strains showing high luciferase activity in this study is expected to dramatically improve the production efficiency of useful proteins such as pharmaceuticals (Fig. 3, *Appl Microbiol Biotechnol* 98: 3049-3058, 2014).

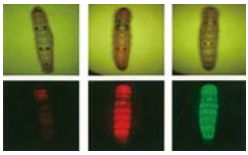


Fig. 3. Compared with general strains (left), in strains (middle and right) with high protein expression, strong fluorescence can be detected even when infected with recombinant viruses containing different fluorescent genes. (From the newsletter "Okaikosama" No. 40, 2018)

Core Facility : Tokyo Women's Medical University School of Medicine
Principal Investigator : Shohei Mitani FAX : +81-3-5269-7414
Contact site : mitani.shohei@twmu.ac.jp
URL : https://shigen.lab.nig.ac.jp/c.elegans/

Overview

C. elegans, having approximately 1,000 somatic cells, has various tissues that comprise the reproductive system, nervous system, muscle system, and digestive system and are functionally similar to those of higher animals, and cell lineage (path of differentiation from fertilized egg to adult in all cells) has been identified. In addition, the life cycle is approximately 3 days (life span is approximately 3 weeks), and almost 40% of genes encoding approximately 20,000 proteins have similar sequence and function to human genes. In addition, feeding RNA interference is available. Therefore, it is possible to efficiently inhibit gene expression simply by feeding the nematode with bacteria expressing double-stranded RNA that is complementary to the target gene.

In this project, the number of deletion mutants collected and released exceeds 8,000 by the 3rd phase. In the 4th phase, we will continue to find deletion mutants of each gene from the frozen stock of existing random mutants by whole genome sequencing to further expanding the deletion mutant resource. After purification, they are preserved, released, and provided to the applicants (Fig. 1). Furthermore, we also provide Cre recombinase transgenic strains that can be used as conditional knock-out tools and are effective for analysis of lethal mutants and fluorescence-labeled balancer strains that have been prepared based on recombination suppression within the same chromosome. These are expected to facilitate genetic analysis of *C. elegans*.

Caenorhabditis elegans

Fig. 1. Flow chart of the collection of deletion mutants

Key Strains/Studies

In addition to wild-type strains, approximately 9,100 various gene-deficient strains, 50 Cre recombinase transgenic strains, and 70 balancer strains are available.

● *lrk-1* (tm1898)

The nematode *lrk-1* gene is highly homologous to the human *LRKK2* gene, which is one of the causative genes for familial Parkinson's disease, and encodes a protein kinase. It is used in research on Parkinson's disease because it is useful for analyzing the molecular mechanism underlying neurodegenerative diseases (*J Neurosci* 37: 11085-11100, 2017).

● *pdf-1* (tm1996)

One of the leading fields of research using *C. elegans* is analysis of learning and memory. Conditioned nematodes under starvation and presence of salt exhibit learning behavior that avoids salt. However, males conditioned with hermaphrodite individuals under these conditions show salt-preferring motility to prioritize mating behavior (Fig. 2). This male-specific learning behavior involves Mystery Cells of the Male (MCM; Fig. 3), which is a male-specific interneuron derived from differentiated glia in a larval-stage male. The above-mentioned learning behavior has been found to be lost in the *pdf-1* gene mutant (tm1996), which is highly expressed in this cell (*Nature* 526, 385-390, 2015).

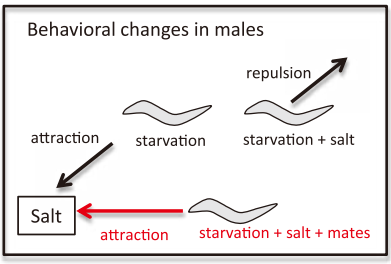


Fig. 2. Male-specific conditioned learning behavior

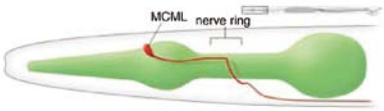


Fig.3. Diagram depicting the morphology and position of one of the bilateral pair of MCM neurons in the head of a male worm. (From *Nature* 526, 385-390, 2015 Fig. 1a)

Core Facility : Experimental Plant Division, RIKEN BioResource Research Center
Principal Investigator : Masatomo Kobayashi FAX : +81-29-836-9053
Contact site : plant@brc.riken.jp
URL : https://epd.brc.riken.jp/en/

Overview

Arabidopsis thaliana is small in size, and it is possible to obtain the next generation of seeds in three months. In addition, related information and techniques such as complete genome sequence and an efficient protocol of transformation are also available. Therefore, it is widely used as a model plant in academic studies in Japan and other countries. Cultured plant cells have traditionally been the strength of Japan in terms of resources, and are expected to be used in a wide range of research from cell biology to production of useful substances.

Arabidopsis thaliana (top) and cultured plant cells (bottom)

The RIKEN BRC Experimental Plant Division collects, preserves, and provides cultured cells and DNA clones of model plants in addition to ecotypes (wild-type strains) and gene knocked out mutants of *Arabidopsis*. In the 4th phase of NBRP, we are working on the improvement of the catalogue database with aim of enhancing international awareness and user convenience of all these diverse resource groups. In addition, as a resource with the world's highest level of reliability, we are working on establishing a quality control system, to be able to respond to resources in which innovative technologies have been employed, such as mutants produced by genome editing. We are also working with all the other NBRP resource facilities to strengthen information dissemination to the research community and support plant research for solving environmental, food, and substance production issues.

Key Strains/Studies

In *A. thaliana*, in addition to mutant libraries of both gene disruption and gene over-expression, individual mutants and transgenic strains (~200 strains) are available. We also offer ecotype strains (~530 stocks) collected from all over the world. The *A. thaliana* full-length cDNA clone (RAFL clone) is a global standard resource including approximately 21,000 clones that have been entirely sequenced. We also provide TAC clones with inserted *A. thaliana* genomic fragments and ORF clones of transcriptional factors. In addition, approximately 320,000 cDNA clones derived from eight model plants are available. We are able to offer approximately 62 plant cell lines (including transgenic lines expressing GFP) of various plant species, including *A. thaliana*.

● Bu5 (sja02900)

A. thaliana is found worldwide. Even within same species, there is a difference in osmotic tolerance. The Bu5 strain, which originates from the suburb of Goettingen in Germany, has remarkable osmotic pressure (water deficiency) resistance compared with the standard strain Col0. It was found that the responsible gene *ACQOS* identified by mapping experiments is also an important gene for plant immune response. Therefore, similar to the Bu5 strain, *A. thaliana* lacking the *ACQOS* gene acquires high osmotic tolerance; however, its disease resistance decreases. In other words, it became clear that the presence or absence of the *ACQOS* gene is a decisive factor in disease resistance and osmotic resistance (Fig. 1, *Nat Plants* 3; 17072, 2017).

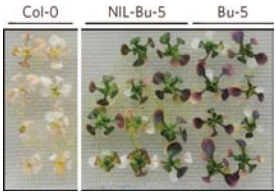


Fig. 1. Col0 standard strain (left) dies under osmotic stress, but Bu5 strain (right) can survive. The standard strain in which *ACQOS* gene was replaced with Bu5 type (center) acquired osmotic tolerance. (From *Nat Plants* 3; 17072, 2017 Fig. 1b with modifications)

● Tobacco BY2 cultured cells (rpc00001)

This cell line is the typical cultured plant cells also known as "plant HeLa cells" because they grow rapidly. New gene involved in the biosynthesis of daurichromenic acid (DCA) with anti-HIV activity was isolated from *Rhododendron dauricum*. An experiment using tobacco BY2 cultured cells has revealed that DCA is synthesized extracellularly (Fig. 2, *Plant Physiol* 174: 2213-2230, 2017).

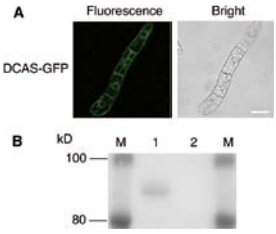


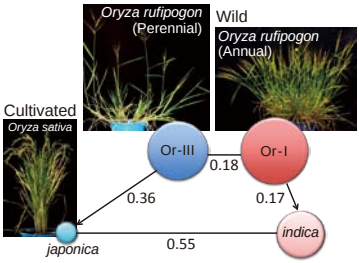
Fig. 2. (A) Fusion protein of DCA synthase and GFP expressed in BY2 cells. (B) Western blotting with GFR antibody. While GFP protein is detected in the culture medium (lane 1), it cannot be detected in the cell protein extract (lane 2). (From *Plant Physiol* 174: 2213-2230, 2017 Fig. 8 with modifications)

Core Facility : Department of Genomics and Evolutionary Biology, National Institute of Genetics
Principal Investigator : Yutaka Sato FAX : +81-55-981-6879
Contact site : yusato@nig.ac.jp
URL : https://shigen.nig.ac.jp/rice/oryzabase/

Overview

Rice is an essential food crop and is a plant that has evolved with the history of humanity. From breeding science to develop delicious and disaster resistant rice strains, to basic research, Japanese researchers have long been active in all fields related to studies in rice. Genetic resources of cultivated rice are said to be more than 140,000 strains in the world; in Japan, a total of more than 46,000 strains are preserved at the Ministry of Agriculture, Forestry and Fisheries, universities and research institutes.

Apart from these genetic resources, in NBRP-Rice, the National Institute of Genetics is in charge of collecting, preserving, and providing wild rice that is usually difficult to preserve, and Kyushu University collect, preserve, and provide experimental strains, such as mutant strains and strains with chromosome fragment substitution derived from wild rice. In the 4th phase of NBRP, to increase the added value of each strain, we are performing the following: evaluation of traits in rice, construction of molecular markers, reclassification of wild strains, and maintenance and development of integrated database (Oryzabase) including rice gene and genome information. In 2019, the operation of a cross-sectional data search system (PGR-Gateway) has been started in cooperation with the Genebank Project of National Agriculture and Food Research Organization (NARO), and now users can more efficiently access genetic information from both resources.



Genetic distance (number) between cultivated rice and their wild ancestors and size of intragroup variation (circle size)

Key Strains/Studies

We can provide approximately 19,000 lines, including wild strains, experimental strains derived from wild strains, MNU mutant strains with different genetic backgrounds such as Kin-maze, TC65, Kita-ake, and Yuki-hikari, and chromosomal segment substitution strains in which a chromosome derived from closely related wild species, such as *Oryza glaberrima*, *O. meridionalis*, *O. glumaepatula*, *O. sativa indica*, and *O. sativa japonica*, are introduced into cultivated rice.

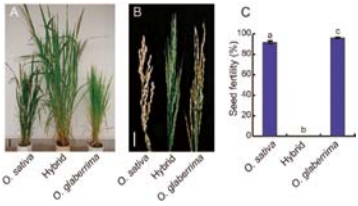


Fig. 1. In crosses between African and Asian cultivars, spikelets develop but are sterile. (From *PNAS* 115: E1955-E1962, 2018 Fig. 1)

● *Oryza glaberrima* chromosomal segments substitution strain

The African cultivar (*O. glaberrima*) has a resistant gene against unfavorable environment such as high temperature, which is not found in Asian cultivar (*O. sativa*). Because it becomes sterile in crosses between both varieties, it has been difficult to search for useful genes by hybrid cross experiments. Heavy-ion beam mutagenesis was performed in hybrid seeds between a chromosomal segment substitution strain containing S1 locus region involved in sterility and an Asian cultivar strain. Consequently, individuals in which fertility was reversed were generated and the causative gene was found to be SSP gene (Fig. 1, *PNAS* 115: E1955-E1962, 2018).

● MNU mutagenized strain *drp7* (SG1105) in Kin-maze strain

Because the leaf surface of rice is hydrophobic, it helps the plant in maintaining gas exchange with the outside under water. The MNU-induced mutant line *drp7* cannot maintain the air layer in water, and has a reduced number of wax platelets in the cuticular layer on the leaf surface and reduced levels of hydrophobicity and photosynthetic ability in water. In addition, in the wax composition on the leaf surface, the amount of C30 primary alcohols decreases and the amount of C30 aldehydes increases. Thus, the causative gene *Leaf Gas Film 1* (*LGF1*) identified by linkage analysis was found to be involved in C30 primary alcohol synthesis (Fig. 2, *New Phytol* 218: 1558-1569, 2018).

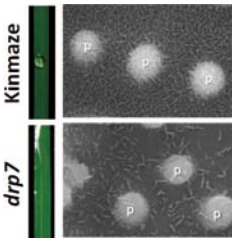


Fig. 2. Decrease in hydrophobicity of leaf surface one day after flooding (left) and decrease in the number of epicuticular wax platelet (right) under an electron microscope in *drp7* strain (bottom) (right: P = papillary projections; from *New Phytol* 218: 1558-1569, 2018 Fig 1 with modifications)

CORE FACILITY UPGRADING PROGRAM Wheat

Core Facility : Graduate School of Agriculture, Kyoto University
Principal Investigator : Shuhei Nasuda FAX : +81-75-753-6486
Contact site : nasushu@kais.kyoto-u.ac.jp
URL : https://shigen.nig.ac.jp/wheat/komugi/

Overview

Wheat is one of the world's three major crops. Wheat consists of diploid Einkorn wheat (2n = 14), tetraploid Emmer wheat (2n = 28), and hexaploid common wheat (2n = 42). Bread wheat, which is the most important staple of our diet, is an allohexaploid having three different genomes A, B, and D in one nucleus. The A genome is derived from a wild diploid wheat *Triticum urartu*, and other two genomes are from related wild weed species in the genus *Aegilops*. Such complexity of the genomic structure has been a major obstacle to whole genome sequencing of bread wheat. Recently, we successfully completed decoding the genome sequence under the initiative of the International Wheat Genome Sequencing Consortium (IWGSC) (*Science* 361: eaar7191, 2018). The core facility of NBRP-Wheat, Laboratory of Plant Genetics, Graduate School of Agriculture, Kyoto University, took part of the IWGSC. We prospect that various molecular studies in wheat will be promoted.

The complete sequence of the bread wheat genome was published in the August 17, 2018 issue of Science.

While most gene banks in the world are focusing on collection of modern cultivars of wheat, NBRP-Wheat collects, preserves, propagate, and provides wild relatives and landraces of wheat. With the completion of genome sequencing, the collections of NBRP-Wheat will be more accessible for research activities. We hope NBRP-Wheat can be regarded as one of the centers of global wheat genetic resources. In the 4th phase of NBRP, we will develop new resources and various core collections for genetic analysis. Next, we will make the resource database KOMUGI more attractive by accumulating phenotypic and genotypic data. We have started to collaborate with other gene banks in the world. One of the domestic cooperation is with the National Agriculture and Food Research Organization (NARO) Genebank, which resulted in a cross-sectional data search system (PGR-Gateway).

Key Strains/Studies

We mainly supply wild species and landraces of wheat (~6,700) and related species in the *Aegilops* and *Secale* genera (~4,200). In addition, we provide experimental strains, including Chinese Spring, a genetic standard cultivar of hexaploid wheat used for determination of the reference genome sequence. The experimental strains (~1,600 lines) include mutants, recombinant inbred lines, chromosome substitution lines, synthetic polyploids, aneuploids, alien chromosome addition/substitution lines, and other genetic strains. We terminated distribution of DNA resources at the end of the 3rd phase.

● Cultivar Chinese Spring (abbreviated as CS, LPGKU 2269), the standard cultivar of genetics and genomics of bread wheat, and Cultivar Norin 61 (abbreviated as N61, LPGKU 2305), the representative modern wheat cultivar in east Asia

The bread wheat cultivar CS is the material of decoding the reference genome sequence of hexaploid wheat. CS has been used in many research activities as the standard for many years. This is the reason why many aneuploid, chromosome deletion lines and substitution lines were created based on CS. These are stored in NBRP-Wheat. Now with the genome sequence in hand, we expect the experimental strains of CS to be actively used as research materials again.

As the first step of comparative genome analyses, we, the International wheat 10+ Genome Project, are practicing *de novo* assembly of 10 world leading hexaploid wheat varieties (Fig. 1). The Japanese team is in charge of the genome sequencing of the cultivar N61 that are currently being used in many different post-genome studies.

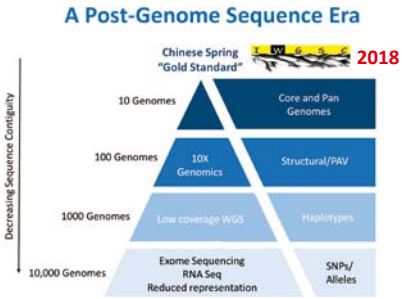


Fig. 1. Outline of wheat research in post-genomic era
It has been proposed to promote wheat sciences by determining the genomic sequence (or partial sequence) at different levels according to the research goals. The cultivar Norin 61 in the NBRP-Wheat was selected as one of the 10 wheat genomes for *de novo* sequencing, and its assembly has been completed.

Core Facility : Institute of Plant Science and Resources, Okayama University
Principal Investigator : Kazuhiro Sato FAX : +81-86-434-1249
Contact site : kazsato@rib.okayama-u.ac.jp
URL : https://shigen.nig.ac.jp/barley/

Overview

Barley is used for brewing, food, and feed, and is important as a functional food and feed with high nutritional value. There are a variety of wild and cultivated species that have the greatest wide adaptability (from Alaska to India), excluding the tropics, and resistance to environmental changes such as drought, salt, and moisture damage. In addition, because it is a diploid, it is easy to detect mutations and high quality genome sequencing has been completed (*Nature* 544: 427-433, 2017). It is used as a model plant for applying the results of plant science including the identification of useful genes.

Diversity in barley spikes

The core facility of NBRP-Barley, Institute of Plant Science and Resources, Okayama University, preserves the barley strains that have been collected and developed independently, and is one of the world's five best barley resource centers in East Asia. In the 4th phase of NBRP, the Barley DB has been updated and integrated with high-density transcript maps and SNP information based on cDNA sequences, including characterization of each strain, and will contribute to the genome and gene analysis of barley and related plants, and finally the development of new cultivars.

Key Strains/Studies

In addition to the standard genome analysis line "Haruna Nijo", it is possible to supply about 5,300 cultivated barleys, wild species, experimental lines, and a core collection of 380 strain. The core collection is a series of strains that are selected to maximize the genetic diversity of barley and improve the accessibility in genetic analysis and breeding. We also offer full-length cDNA clones of barley (Haruna Nijo: 5,000 clones) and BAC clones (Haruna Nijo: 300,000 clones, wild barley: 180,000 clones).

● Barley Core Collection and Barley BAC Library

The reduced seed dormancy period acquired during the process of barley cultivation by human has led to the emergence of pre-harvest sprouting (phenomenon of sprouting of grains on spikes) due to the high moisture condition in Japan and Northern Europe where there is a lot of rain during the harvesting period (Fig. 1). The results of genetic linkage analysis using strains with different lengths of seed dormancy and BAC clone sequencing analysis indicated that the responsible locus Qsd1 was shown to encode alanine aminotransferase (AlaAT). Furthermore, the evolutional analysis of *AlaAT* gene sequences using the barley core collection showed that wild barley near Israel (south Levant) was the origin of barley for brewing (varieties with short dormancy) and varieties with mutations imparting shorter dormancy were selected from these during malt production for beer, and were dispersed to various parts of the world (*Nat Commun* 7: 11625, 2016).

Fig. 1. Germination after 5 weeks of barley strains that differ only in the dormant (left) and non-dormant (right) allele (From *Nat Commun* 7: 11625, 2016 Fig. 1).

● Turkey 45 (T615), H.E.S.4 (I622), Maja (U053), and Sirius O.525 (U121)

Fusarium fungi that cause head blight produce toxins that are mixed into food and livestock feeds and have a harmful effect on the human body. Comparative analysis of the metabolites of fusarium blight-resistant (Maja · Sirius O.525) and susceptible strains (Turkey 45 · H.E.S.4) showed that nicotinamide mononucleotide (NMN), a metabolite related to nicotinamide mononucleotide adenyltransferase (NMNAT), was found to function as an inducer of plant resistance (Fig. 2, *Sci Rep* 7: 6389, 2017).

Fig. 2. Symptoms one week after inoculation of NMN-treated (+: right) and untreated (-: left) barley spikes with *Fusarium graminearum* (From *Sci Rep* 7: 6389, 2017 Fig. 5a)

CORE FACILITY UPGRADING PROGRAM Lotus / Glycine

Core Facility : Faculty of Agriculture, University of Miyazaki
Principal Investigator : Ryo Akashi FAX : +81-985-58-7257
Contact site : legume@brc.miyazaki-u.ac.jp
URL : https://www.legumebase.brc.miyazaki-u.ac.jp/

Overview

Leguminous plants are extremely important species that inhabit diverse environments from tropical to temperate regions, and are used for various purposes, including food. In addition, they have unique characteristics, such as diversity of seed storage proteins and symbiosis with rhizobia and mycorrhizal fungi that have the ability to fix nitrogen. Japanese trefoil (*Lotus japonicus*) is a wild perennial legume native to Japan and has a short life cycle (2–3 months). Since the genome sequence of *Lotus japonicus* was decoded, its use has been rapidly increasing in the field of basic research as a leguminous plant model. Alternatively, soybean (*Glycine max*) contains several proteins in its seeds, and also has many functional chemical components such as isoflavones, saponins, and proteins (peptides). Therefore, as one of the most important leguminous crop in the world, several basic research studies have been accumulated.

Japanese trefoil life cycle (seed, 1-month-old plant, flower, ripening pod). Upper right: Root culture system derived from *Lotus corniculatus*. Bottom: soybean [flower (bud), ripening pod, seeds of various soybean varieties].

In the 4th phase of NBRP, the *Lotus/Glycine* core facility in the University of Miyazaki comprehensively collects, maintains, and provides live and DNA resources of Japanese trefoil and soybean. The sub-core facility in Tohoku University is in charge of rebuilding LegumeBase, an integrated database for searching and providing Japanese trefoil and soybean strains. The two institutes coordinate to add characteristic information such as contents of seed components and morphogenesis of each strain, and to provide functional information to users along with high-quality resource maintenance.

Key Strains/Studies

We offer approximately 1,500 strains of Japanese trefoil (*Lotus japonicus*), including wild strains, various experimental strains, retrotransposon tag strains (LORE1), EMS (ethyl methanesulfonate)-induced mutant strains, and EMS-M2 bulk seeds. In addition, approximately 6,700 STM (Signature Tagged Mutagenesis) strains of root nodule bacteria and a root culture system (super root) derived from *Lotus corniculatus* has been conserved and can be provided. Furthermore, we can provide from our stock of approximately 1,000 soybean cell lines, including the original wild *Glycine soja* strains and cultivar for green soybean, as well as mutant strains and EMS-M2 bulk seeds. Available DNA resources include BAC and TAC clones (~27,000), cDNA clones (~160,000) in Japanese trefoil, and full-length cDNA clones (~38,000) of soybean. We also offer Japanese trefoil rhizobia DNA-plasmid clones (~4,200) and soybean rhizobia BAC and cosmid clones (~8,700).

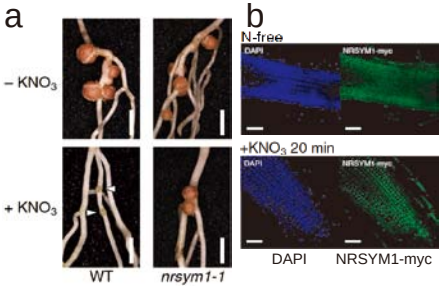


Fig. 1. a: In contrast to wild type (left), *nrsym1* mutants (right) form nodules even under nitrogen-rich conditions (bottom). Arrows indicate immature root nodules. b: At the root tip, NRSYM1 protein extranuclearly localized under nitrogen-free conditions (above) migrates into the nucleus in response to the addition of nitric acid (below), and induces the expression of target genes to suppress nodule symbiosis (From *Nat Commun* 9: 499, 2018 Fig. 1 and Fig. 8).

● EMS M2 bulk seed from Japanese trefoil

M2 seeds obtained from the M1 mutant group induced by the chemical mutagen EMS were subjected to screening under high nitrate condition, in which nodule symbiosis is suppressed in wild type. As a result of screening, *nrsym1* mutant (*nitrate unresponsive symbiosis 1*) was discovered that does not suppress root nodule symbiosis. The identified novel responsible gene *NRSYM1* was found to induce the production of peptide signal molecule CLE-RS2, which controls the number of nodules, and was identified as a factor that controls the suppression of root nodule symbiosis in response to high nitrate levels (Fig. 1, *Nat Commun* 9: 499, 2018).

Core Facility : Tukuba-Plant Innovation Research Center, University of Tsukuba
Principal Investigator : Hiroshi Ezura FAX : +81-29-853-7734
Contact site : ezura@gene.tsukuba.ac.jp
URL : https://tomato.nbrp.jp/

Overview

Many Solanaceae family plants are vegetables, and are evolutionarily distant from *Arabidopsis thaliana* (Brassicaceae family) and *Lotus japonicus* (Legumiaceae family), which are advanced in resource development and maintenance among dicotyledonous plants. Among Solanaceous plants, tomato is the most widely produced fruit vegetable in the world and contains several functional ingredients that are important for health maintenance. Conversely, the genome size is relatively small (950 Mbp), the genome sequence has been decoded, and it has many features not found in conventional model plants (such as fruit development and neutral photoperiod response). Among these, tomato is also important as a model plant to study Solanaceous plants and fruit development.

A model cultivar, Micro-Tom Japan

At NBRP-Tomato, the core facility, University of Tsukuba and the sub-core facility, Osaka Prefecture University are in charge of collecting, preserving, and providing live resources and DNA clones, respectively. The other sub-facility, Meiji University is in charge of constructing and managing various DNA information databases (MiBASE, KaFTom, and TOMATOMICS). The dwarf tomato cultivar Micro-Tom Japan has advantages as an experimental plant (small size, short life cycle, growable with weak light, genome sequence decoded, and Agrobacterium-mediated transformation). In the 4th phase of NBRP, we will prepare resources based on Micro-Tom Japan and its variants, and add genome sequences and trait characteristics information. Through this, we will achieve high quality and strive to further promote resource utilization.

Key Strains/Studies

Approximately 2,200 strains, including wild and cultivated strains, T-tag strains of Micro-Tom Japan, and EMS and gamma ray mutagenized strains (including their M3 bulk seed set), are distributed through the TOMATOMA database. Micro-Tom cDNA clones derived from fruits, leaves and roots are distributed through the omics database for tomato TOMATOMICS. The information provided by TOMATOMICS includes sequence information of approximately 36,000 ESTs and approximately 13,000 full-length cDNAs.

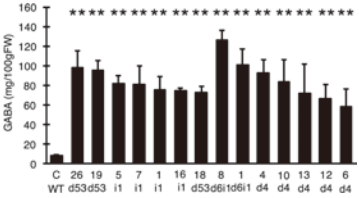


Fig. 1. Comparison of GABA concentrations in fruits of T1 generation individuals of *SlGAD3* gene modification lines, which is one of the *GAD* genes, of the flowering type (left corner) (From *Sci Rep* 7: 7057, 2017 Fig. 5)

● Micro-Tom (MT-J) (TOMJPF00001)

GABA, which is abundant in tomatoes, is noted for its suppressive effect on blood pressure elevation, and further stable and high accumulation strains are required. Therefore, we attempted to increase GABA accumulation by deleting the autoinhibitory domain of GABA biosynthetic enzyme (GAD) gene using the CRISRP-Cas9 system. Consequently, the accumulation of GABA in the fruit increased 7–10 times without decreasing the flowering rate and fruit yield (Fig. 1, *Sci Rep* 7: 7057, 2017).

● EMS treatment derived mutant (TOMJPE2753-1)

Parthenocarpy, a property to produce fruit without pollen, is an important trait for tomato, which is cultivated year-round. procera (*pro*) strain with a loss-of-function mutation at the *SlDELLA* locus exhibits parthenocarpy; however, it has problems with fruit traits. One of the EMS-induced mutant strains, TOMJPE2753-1 (*pro-2*), has a reduction-of-function mutation at the *SlDELLA* locus, and while retaining parthenocarpy, the problematic traits found in the *pro* strain are also improved. As this strain maintains high yield in the summer season, further research is expected on causality between heat resistance and parthenocarpy (Fig. 2, *Sci Rep* 8: 12043, 2018).

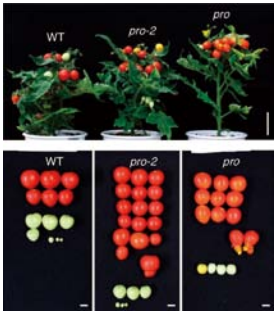


Fig. 2. Comparison of plant and fruit phenotypes of wild type (left), *pro-2* (middle), and *pro* (right) strains grown in greenhouse in summer (From *Sci Rep* 8: 12043, 2018 Fig. 6b, c)

Chrysanthemum

Core Facility : Laboratory of Plant Chromosome and Gene stock,
Graduate School of Integrated Sciences for life, Hiroshima University
Principal Investigator : Makoto Kusaba FAX : +81-82-424-0738
Contact site : akusaba@hiroshima-u.ac.jp
URL : https://shigen.nig.ac.jp/chrysanthemum/

Overview

The family *Asteraceae* is one of the most prosperous plant groups, containing more than 23,000 species. Among them, the *Chrysanthemum* genus and its closely related genera (*Chrysanthemum sensu lato*) have undergone characteristic evolution with polyploidization and hybridization. Cultivated chrysanthemum (*Chrysanthemum morifolium*) is one of the three major flower plants in the world. It is an industrially important species that accounts for one-third of cut flower production in Japan. *Chrysanthemum sensu lato* also includes many species that produce various pharmacologically active secondary metabolites, such as the *Artemisia* species.

Various chrysanthemum plants and their relatives.

NBRP-Chrysanthemum collects, preserves, and provides the world's largest number of strains of the *Chrysanthemum* genus distributed in the East Asia region. The self-incompatibility (property of producing no seeds after self-pollination) and hyperpolyploidy found in the chrysanthemum plants, are major obstacles in conducting genetic research, including developing inbred strains and breeding of cultivated varieties. The self-compatible mutant strain of a wild diploid species *Chrysanthemum seticuspe*, AEV2, which is the core facility of the NBRP-Chrysanthemum isolated by Hiroshima University, is extremely useful for overcoming these obstacles. In the 4th phase of NBRP, whole genome sequence and gene expression information of Gojo-0 line (Fig. 1), which has been established by repeating selfing of AEV2 stain, will be added. This makes it a better reference resource for cultivated chrysanthemums. Consequently, we will establish a molecular genetic research platform for the study of plants in the broad-sense *Chrysanthemum* genus.

Fig. 1. The model strain in the genus *Chrysanthemum* Gojo-0

Key Strains/Studies

Focusing on the *Chrysanthemum* genus, we provide approximately 450 wild strains and approximately 30 experimental strains such as *C. seticuspe* inbred lines and interspecies hybrids.

● XMRS10

A draft sequence of the entire genome was determined for XMRS10, a semi-pure strain derived from AEV2. The analysis of this strain revealed that *C. seticuspe* has a genome size of approximately 3 Gbp and approximately 70,000 genes. In addition, sunflower and chrysanthemum were considered to have differentiated approximately 46 million years ago (Fig. 2, *DNA Res* 26: 195-203, 2019). Controlling the flowering time of the *Chrysanthemum* genus is important in the industrial world. A common feature of the *Asteraceae* family is that a large number of small flowers combine to form one flower-like structure (capitulum). As all genetic information has been decoded, it is hoped that research on such characteristics will be further advanced, and at the same time, breeding of cultivated varieties will be more efficient. Sequence information is publicly available from Mum Garden (http://mum-garden.kazusa.or.jp/), and can be used for gene function analysis in the broad-sense chrysanthemum plants using BLAST search.

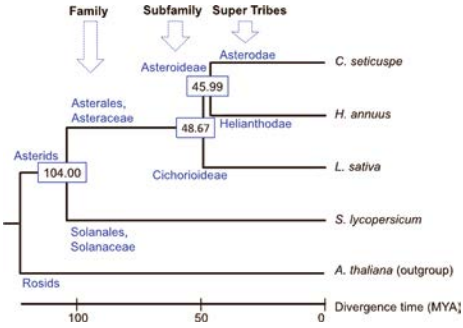


Fig. 2. A phylogenetic tree based on the 2,280 common single-copy genes of the four *Asterids* species and *A. thaliana*. (From *DNA Res* 26: 195-203, 2019 Fig. 4)

Morning glory

Core Facility : Faculty of Sciences, Kyushu University
Principal Investigator : Eiji Nitasaka FAX : +81-92-802-4330
Contact site : nitasaka.eiji.358@m.kyushu-u.ac.jp
URL : http://mg.biology.kyushu-u.ac.jp/

Overview

The Japanese morning glory (*Ipomoea nil*) is a bioresource that was developed in Japan along with more than a century of knowledge amassed from its applications in genetics, physiology, natural product chemistry, and other research fields. It has several strong advantages for various areas of plant science, such as its highly homogeneous genome, which is the result of its high selfing rate and its restricted origin, as well as various mutants related to flower color and morphology induced by its highly active transposons. It is also an excellent model for plant physiology such as photoperiodic flowering, because it has high photoperiod sensitivity. Moreover, near-complete genome sequences of the Japanese morning glory were published in 2016 (*Nat Commun* 7, 13295, 2016). It is expected to grow in importance for its usefulness in applied research, including its use in ornamental horticulture, and its use as a model organism for the sweet potato, which is a member of the same genus.

Examples of mutants with a variety of flower colors, patterns, and morphology.

NBRP-Morning glory collects, preserves, and provides live and DNA resources through its core facility, Kyushu University and the sub-core facility, National Institute for Basic Biology. In the 4th phase of NBRP, to increase added value of our resources, we will enhance the integrated database of strain characteristic information and genomic information, and support it to develop as a Japan's leading bioresources.

Key Strains/Studies

Most of the mutant strains maintained in the NBRP originate from the late Edo period, and transposons of the *Tpn1* family are mutagens. In addition to these, we provide approximately 3,000 strains, including recombinant inbred strains and strains from natural populations worldwide and *Ipomoea* species. The DNA resources include BAC libraries comprising approximately 100,000 clones of Tokyo Kokei Standard strains, cDNA libraries comprising approximately 60,000 EST clones, and petal-specific expression vectors.

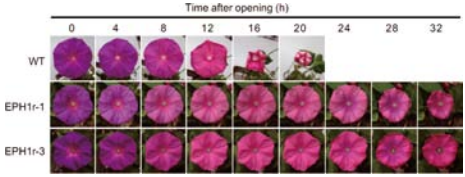


Fig. 1. Life extension of petals of *EPH1* knockdown strain (From *Plant J* 79: 1044-1051, 2014 Fig. 1a).

● Violet: Q0079

Suppression for petal senescence is an important floricultural trait that helps to preserve the vase life of cut flowers. Violet is extremely sensitive to short-day photoperiod, and reproducible transformation conditions have also been established. In the knockdown (RNAi) strain of the *EPHEMERAL1* (*EPH1*) gene, which is a member of NAC transcription factor family involved in leaf aging, the lifespan of morning glory petals was doubled (Fig. 1, *Plant J* 79: 1044-1051, 2014). A similar phenotype was also observed in strains in which the *EPH1* gene mutation was introduced by the CRISPR-Cas9 system (*Plant Physiol Biochem* 131: 53-57, 2018).

● Tokyo Kokei Standard strain (TKS: Q1065) and 19 strains of dwarf mutant *contracted* (*ct*)

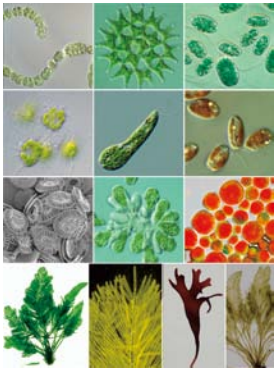
Tokyo Kokei Standard strain is highly inbred, and the transposition of endogenous transposon is also suppressed. The *ct* mutant has small cotyledons and leaves with thick and dark green mesophyll. After completion of genome sequencing of Tokyo Kokei Standard strain, genetic linkage map and the physical map were integrated. This has revealed that the *ct* allele phenotype is due to the suppression of gene expression by a transposon inserted in the *CYP90C1* gene, which is involved in the biosynthesis of brassinosteroids (a group of plant hormones that promote elongation growth) (Fig. 2, *Nat Commun* 7, 13295, 2016).

Fig. 2. The *ct* strains of the three different alleles and wild-type (TKS) strain at 8 days of seeding (From *Nat Commun* 7, 13295, 2016 Fig. 3a)

CORE FACILITY UPGRADING PROGRAM Algae

Core Facility : National Institute for Environmental Studies (NIES)
Principal Investigator : Masanobu Kawachi FAX : +81-29-850-2587
Contact address : kawachi.masanobu@nies.go.jp
URL : https://shigen.nig.ac.jp/algae/ (NBRP Algae Official Website; NIG)
http://mcc.nies.go.jp/ (Microalgae; NIES)
http://ku-macc.nbrp.jp/ (Macroalgae; Kobe University)

Overview



A wide variety of algal resources

"Algae" is a generic term for organisms that perform oxygen-producing photosynthesis, which exclude land plants but include a wide range of organisms such as prokaryotes, protists, and plants. Algae inhabit not only ordinary water environments but also extreme environments such as hot springs. Particular algal species also occur in areas with arid conditions, high salinity, and ice. Therefore, they are expected to have diverse biological functions. Consequently, algae are used in a wide range of fields, including those focused on research on evolution, photosynthesis and metabolic functions, energy, drug development, and environmental issues.

In NBRP-Algae, the National Institute for Environmental Studies and Kobe University collect, preserve, and provide microalgal strains and seaweed strains, respectively. Hokkaido University is involved in backup of important strains. In the 4th phase of NBRP, three institutions collaborated with each other for establishing a quality control system and collecting new important strains such as genome-analyzed strains and model organism candidate strains. Additionally, to increase the values of algal resources, we collected novel and useful information on strains, including morphology, photosynthetic pigment data, fatty acid composition, genomic information, and so on. We then upload all the data collected on our homepages to make them available to the world. We strive to provide the world's highest level of algal resources.

Key Strains/Studies

At present, we provide 3,897 strains belonging to 1,286 species (21 phyla, 63 classes, and 602 genera as of January 2019). We have a variety of species and strains, including model organisms for photosynthesis, cell division and evolutional researches from various aspects, phylogenetically and taxonomically important species, harmful species causing environmental problems, test strains for bioassay, and strains producing biomass or other useful substances, used in various research fields.

● *Chlamydomonas eustigma* (NIES-2499)

To elucidate the environmental adaptation mechanism of algae found in strong acidic environments, a comparative genomic analysis was performed between *C. eustigma*, an acidophilic species, and its related species, *C. reinhardtii*, a neutrophilic species. Consequently, their characteristic genes and metabolic pathways became clear because of the following reasons: increased expression of heat shock proteins and cell membrane proton ATPase, disappearance of fermentation (organic acid production) genes, acquisition of phosphagen kinase–amidinotransferase energy shuttle buffer system by horizontal gene transfer, and duplication of arsenic detoxification gene (Fig. 1, *PNAS* 114: E8304–E8313, 2017).

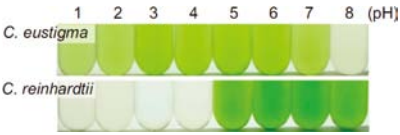


Fig. 1. Comparison of the growth ability of the acidophilic *Chlamydomonas eustigma* strain (top) and the neutrophilic *C. reinhardtii* strain (bottom) in culture for 24 h under various acidic conditions (*PNAS* 114: E8304–E8313, 2017, Fig. 1c).

● *Volvox rousseletii* (NIES-4029)

Volvox species are green, multicellular organisms comprising a large number of cells with flagella. Each cell is functionally differentiated, and an individual shows a harmonious photoresponsive behavior; however, its molecular mechanisms remain unknown. Using the zombie *Volvox* method which removes the entire cell membrane of *V. rousseletii*, it has become clear that the front and rear flagella of the organism share roles of steering and driving force via calcium ions (Fig. 2, *PNAS* 115: E1061–E1068, 2018).

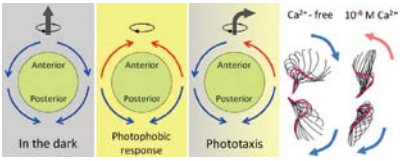
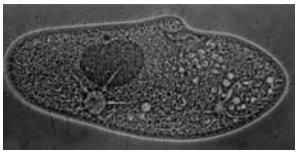


Fig. 2. The direction of the water flow by the front and back flagella under different light conditions (left) and change in movement of the front and back flagella in the presence or absence of calcium ions by the zombie *Volvox* method (right) ("*Volvox*'s flagella discovered to be functionally differentiated-revealed by zombie *Volvox* experiment", Tokyo Institute of Technology Press Release, with modifications).

CORE FACILITY UPGRADING PROGRAM Paramecium

Core Facility : Graduate School of Science and Technology for Innovation, Yamaguchi University
Principal Investigator : Masahiro Fujishima FAX : +81-83-933-5712
Contact site : nbrpcm@yamaguchi-u.ac.jp
URL : http://nbrpcms.nig.ac.jp/paramecium/

Overview



A phase contrast microscope image of a *P. caudatum*

The *Paramecium* genus is a group of protists belonging to the *Ciliophora* phylum. They are large (150-300 μm) among unicellular organisms and easy to culture or manipulate under a microscope; therefore, they are used as model organism of eukaryotic cells for various basic researches (such as endosymbiosis, intermediate host of pathogenic bacteria, infection prevention, aging, ciliary movement, binucleation, sexual cell recognition, conjugation, deviated codons, phagocytosis, circadian clock, osmotic pressure control, environmental adaptation, taxis, ion channels, learning, and water purification). In addition, genome sequences of macronuclei (vegetative nuclei) have been decoded in several species (*Nature* 444: 171-178, 2006; *Genetics* 197: 1417-1428, 2014), and various genetic approaches have been developed.

Yamaguchi University, the core facility of NBRP-*Paramecium*, preserves and provides 24 species which are the largest number in the world. In the 4th phase of NBRP, we aim to develop high-quality *Paramecium* resources that will become an international standard, while providing stable supply through the development of cryopreservation technology and adding each strains' information such as syngen (conjugable isogenic population), mating type (sex), collection site, and phenotypic characteristics. We are also working to disseminate research using *Paramecium* resources by providing the strains with their endosymbiotic bacteria or algae, and holding exhibitions and technical workshops.

Key Strains/Studies

Although 47 *Paramecium* species are stated, only 29 species are still collectable. NBRP-*Paramecium* provides approximately nine species (~40 strains) from preserved 24 species (~800 strains). We also provide a variety of monoclonal antibodies against *Paramecium* species and their endosymbionts.

● Ai253 (*Paramecium caudatum* PC121100A)

Ciliates such as *P. caudatum* have a property of gathering at the interface of a solid with sufficient nutrient sources and stable environment. The behavior of *P. caudatum* near the wall surface (solid-liquid interface) was analyzed by fluid dynamics simulation. We found that the duration of sliding behavior in the vicinity of the wall surface can be explained only by two factors: Cell shape (elliptical shape) and reduction of propulsive force (characteristics of mechanical stimulus response) due to the decreased movement of cilia on the wall contact side (Fig. 1, *Commun Integr Biol* 11: e1506666, 2018).

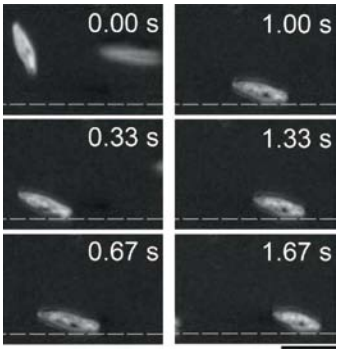


Fig. 1. Sliding behavior of *P. caudatum* on solid surface (dashed line). Bar (lower right) = 200 μm. (From *Commun Integr Biol* 11: e1506666, 2018 Fig. 1B with modifications)

● Yad1g1N (*Paramecium bursaria* PB031010B) and Yad1w (*P. bursaria* PB031012B)

P. bursaria has symbiotic *Chlorella* species within a cell (secondary symbiosis: endosymbiosis between eukaryotic cells) (Fig. 2). A comprehensive gene expression analysis was conducted by the RNA-Seq between the Yad1g1N, which is a strain with symbiotic *Chlorella* species, and Yad1w, which is a strain without the symbiotic algae. Consequently, we found that the expression levels were different for 6,698 genes out of the 10,557 genes identified. They included genes encoding stress response proteins and genes with the antioxidant activity (*BMC Genomics* 15: 183, 2014). Elucidation of the secondary symbiosis mechanism using these strains is still ongoing (*Symbiosis* 71: 47-55, 2017; *Symbiosis* 75, 51-59, 2018).

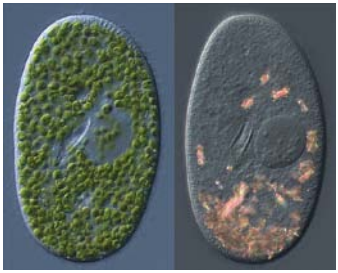


Fig. 2. *P. bursaria* cells with (left) and without (right) symbiotic *Chlorella variabilis*.

Cellular slime molds

Core Facility : RIKEN Center for Biosystems Dynamics Research
Principal Investigator : Yoichiro Kamimura FAX : +81-6-6155-0112
Contact site : ykamimur@riken.jp
URL : https://nenkin.nbrp.jp/

Overview

Dictyostelia, known as cellular slime mold, is unicellular amoebae that feed on bacteria and proliferate by fission. One of their key features is that when they are placed under starvation stress, they aggregate to form multicellular structures that develop into fruiting bodies composed of spore balls, or sorus, and supporting stalks (Fig. 1). Experimental strains, such as AX2, can be grown axenically and genetically modified. Their whole genome sequence data and various expression vectors are also available. Therefore, cellular slime molds are used as a model organism in basic science fields such as cell biology, developmental biology, biophysics, and mathematical biology. They are also used in the fields of medical science and drug discovery as infection hosts for pathogenic bacteria and organisms producing useful physiologically active substances. Recently, similar to *E. coli* and yeasts, cellular slime molds are used as a working platform for molecular biology experiments and as an experimental system for evaluation.

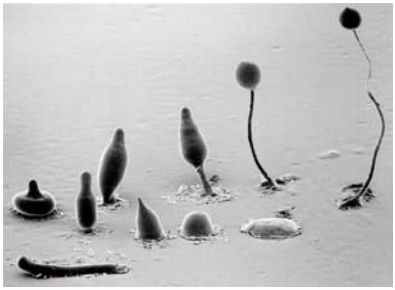


Fig. 1. Life cycle of *Dictyostelium discoideum* (photograph taken with scanning microscope; from DictyBase photo collection). Right: fruiting body, Lower left: slug.

In NBRP-Cellular slime molds, the core facility, RIKEN Center for Biosystems Dynamics Research (BDR) collects, preserves, and provides of strains and DNA resources. The sub-core facility, University of Tsukuba, conducts training courses in addition to the preservation of these resources. In the 4th phase of NBRP, we will develop high-quality resources that become international standards and add characteristic information of each strain. In addition, we are promoting public relations such as displaying actual cellular slime molds and issuing newsletters to increase new users.

Key Strains/Studies

We can provide four groups of wild strains (*parvisporids* · *heterostelids* · *rhizostelids* · *dictyostelids*) and mutant strains (~1,100 strains) mainly of *Dictyostelium discoideum*. We also provide expression vectors, gene knock-out constructs, and plasmid vectors (~420 clones), including All in one CRISPR-Cas9 vector (*Sci Rep* 8: 8471, 2018).

● Ax2 (*D. discoideum* S00001)

Left-right asymmetry is a basic feature of body plan. It has been suggested to be attributable to the chirality of cells. We analyzed the movement of cellular slime molds using newly developed Riesz Transform Differential Interference Contrast Microscopy (RT-DIC). Consequently, we found that the cells tend to move clockwise on a two-dimensional substrate, and the radially extending cell protrusions tend to rotate right-spirally in a three-dimensional substrate (Fig. 2, *Nat Commun* 8: 2194, 2017).

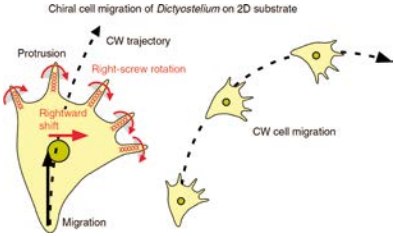


Fig. 2. Schematic diagram of the clockwise motion of cellular slime molds on 3D and 2D substrates (From *Nat Commun* 8: 2194, 2017 Fig. 8d)

● KAx3 (*D. discoideum* S00184)

In the soil, single-celled cellular slime molds are preyed by nonparasitic nematodes. However, they escape from predation by forming fruiting bodies. Accordingly, we investigated the response and effects of the cellular slime molds against *Meidogyne incognita*, one of the root-knot nematodes infesting and damaging many plants, including grains. Consequently, we have found that chemicals released from fruiting bodies have a repelling effect that is potent enough to protect plant roots from *M. incognita* (Fig. 3, *PLoS One* 13: e0204671, 2018).

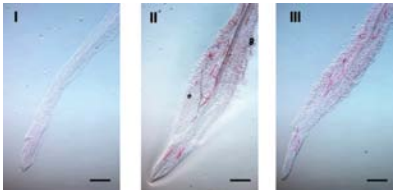


Fig. 3. Preventive effect of extracts from the fruiting bodies of cellular slime molds on infestation of *Lotus japonicus* roots with root-knot nematodes (red). Distance from the cellular slime mold fruiting body extract is closer in the order of I to III. (From *PLoS One* 13: e0204671, 2018 Fig. 5b)

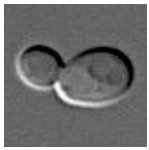
CORE FACILITY UPGRADING PROGRAM Yeast

Core Facility : Graduate School of Science, Osaka City University
Principal Investigator : Taro Nakamura FAX : +81-6-6605-2576
Contact site : nbrpombe@sci.osaka-cu.ac.jp (Taro Nakamura)
bygrc@bio.eng.osaka-u.ac.jp (Minetaka Sugiyama)
URL : http://yeast.nig.ac.jp/

Overview

Yeast is an important eukaryotic model organism. Particularly, for *Schizosaccharomyces pombe*, a fission yeast, and *Saccharomyces cerevisiae*, a budding yeast, various experimental methods and research resources for genetic, biochemical, and molecular biology studies have been developed, including recombinant DNA technology. There are several examples of mechanisms that have been elucidated based on yeast research, such as cell cycle, intracellular protein transport, and autophagy. In addition, yeast is the first eukaryotic organism for which the genome project was completed. It has rich databases of genome, transcriptome, proteome, and other omics information, and plays a leading role in post-genome research. Alternatively, applied studies are also actively conducted in brewing and fermentation industries.

Fission yeast



Budding yeast

Visualization of the nuclear division (fission yeast)

Visualization of the vacuolar membrane (budding yeast)

In NBRP-Yeast/YGRC (Yeast Genetic Resource Center), the core facility, Osaka City University and the sub-core facility, Osaka University collect preserve, and provide various resources of fission yeast and budding yeast, respectively. The other sub-core facility, Hiroshima University is in charge of backing up the above resources. Through these activities, YGRC has become one of the top international yeast resource centers. In the 4th phase of NBRP, while continuing the existing activities, we aim to enrich genome-wide resources and high-demand timely resources to further improve the quality of our resources.

Key Strains/Studies

In fission yeasts, we can provide approximately 15,000 strains, including cell division- and sexual reproduction-related mutants, gene knock-out strains, GFP fusion gene expression strains, and conditional lethal mutant strains. We also can offer yeast strain sets according to the applications. In DNA resources, we can provide full-length cDNA clones (~1,600 clones), genomic DNA clones (~59,000 clones), genomic DNA and cDNA libraries, and various plasmid vectors (~1,700 clones).

For budding yeasts, approximately 13,400 strains are available, including mutant strains related to cell cycle, cell wall synthesis, autophagy, and meiosis specific DNA recombination; ribosome synthesis related strains; series of genome-wide chromosome partial duplicated strains; series of double knock-out strains of various sets of protein phosphatase genes; conditional mutant collection by auxin induction degron method; DNA barcode strain collection; and model budding yeast mutant strains other than *S. cerevisiae*. Additionally, we offer genome-wide single gene overexpression resource named gTOW6000 (~5,800 strains) and various plasmid vectors (~5,800 clones).

● Autophagy-related vectors (pRS316[GFP-ATG8], pRS416GAL1[ATG13], pRS416GAL1[ATG13-8SA], pRS315[mCherry-ATG8])

The kinase complex of Atg1 and Atg13 is essential for starvation-induced macroautophagy. Both kinases are regulated by phosphorylation, but the enzyme responsible for Atg13 dephosphorylation has not been identified. By analyzing Ptc2 and Ptc3, which are phosphatases involved in various pathways, we found that these enzymes act to promote macroautophagy by dephosphorylating Atg1 and Atg13 (Fig. 1. *PNAS* 116: 1613-1620, 2019).

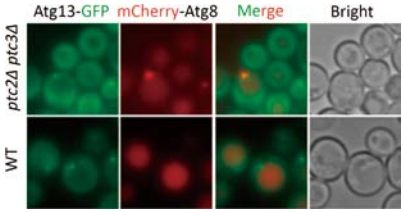


Fig. 1. Decreased pre-autophagosome structures (Atg13 protein aggregation: green spots) and vacuolar fusion of autophagosome (red) in the *ptc2/3* double mutant under rapamycin-induced autophagy (From *PNAS* 116: 1613-1620, 2019 Fig. 3b)

Prokaryotes (E. coli, B. subtilis)

Core Facility : Genetic Resource Center, National Institute of Genetics
Principal Investigator : Hironori Niki FAX : +81-55-981-6826
Contact site : genkaku@nig.ac.jp
E. coli URL : https://shigen.nig.ac.jp/ecoli/strain/
B. subtilis URL : https://shigen.nig.ac.jp/bsub/

Overview

Escherichia coli *Bacillus subtilis*

Escherichia coli, a prokaryote, is widely used as a research material. A great deal of biological knowledge and experimental methods related to genetics, biochemistry, and molecular biology is accumulated. Many basic genes common to the biogenic of eukaryotes, including humans, are also conserved in *E. coli*. Therefore, *E. coli* is expected to remain an extremely important resource as a model organism for all living organisms. Furthermore, *E. coli* has another important aspect as a production bacterium at industrial level. *Bacillus subtilis* is a gram positive soil bacterium. It is an important model organism of prokaryotic cells as it has biological characteristics different from *E. coli*, which is a gram-negative enteric bacterium. *B. subtilis* is also used for industrial production of various degradative enzymes.

In NBRP-Prokaryotes, the core facility, National Institute of Genetics collects, preserves, and provides *E. coli* and *B. subtilis* resources, phages, and antibodies developed in Japan. The sub-core facility, Kyushu University is in charge of backing up the resources. In the 4th phase of NBRP, information of actual mutation sites in strains and plasmid physical maps will be released to increase the added value of each resource, and information on genes, strains, and gene maps will be integrated to improve the convenience of the database.

Key Strains/Studies

The resources being distributed are all non-pathogenic strains, and *E. coli* and *B. subtilis* resources are derived from K12 strain and 168 strain, respectively. In *E. coli*, we provide mutant strains (~15,000 strains, including comprehensive gene deletion strains and transposon-disrupted strains) and gene clones (~19,000 clones with His tag or GFP). We also can provide cloning resources (~470 vectors and ~80 host strains), including host strain for iVEC ultra simple cloning (*J Bacteriol* 201: e00660-18 2019), as well as phages and antibodies. For *B. subtilis*, following resources can be provided: gene mutation/knock-out strains [~7,200 strains, including a collection of ~4000 genes of drug cassette substitution type DNA barcode strains (*Cell Syst* 4: 291-305.e7, 2017)], chromosomal deletion strains (~350 strains), and gene clones (~4,400 clones).

● *E. coli* Keio Collection

5-Fluoropyrimidines (e.g., 5-FU) are anticancer drugs effective for colon cancer; however, their efficacy varies among patients, and the mechanism of action of these drugs is unclear. To investigate the contribution of gut microbiota on drug efficacy, nematodes-*E. coli*-5-FU interactions were analyzed as a model system. The analysis revealed that 5-FU does not act directly on nematodes, but exerts its effect by acting on the metabolism of vitamin B6, B9, and ribonucleotides in *E. coli* (Fig. 1 *Cell* 169: 442–456.e18, 2017).

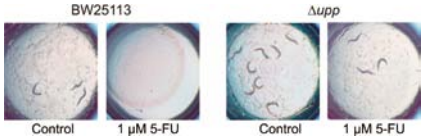


Fig. 1. Relevant genes and mechanisms in *E. coli* were screened through viability evaluation of nematodes treated with 5-FU in media containing normal strain (right: BW25113) and comprehensive gene-deleted strains of *E. coli* [left: (*Δupp*) for example] (From *Cell* 169: 442-456.e18, 2017 Fig. 1A).

● Cell division- and rDNA-related mutants of *Bacillus subtilis*

The condensin complex, which is essential for nucleoid formation in *B. subtilis*, is induced in the *Spo0J-parS* region near the origin of DNA replication. However, these deletion mutants did not show any impairment in nucleoid separation. Alternatively, aberrant cells containing non-separated nucleoids are observed in mutants that have one copy of rDNA among the multiple ribosomal RNA loci (rDNAs) near the replication origin. Analysis of rDNA has revealed that condensin binds to rDNA and that at least two copies of rDNA are required for normal nucleoid separation (Fig. 2, *Cell Rep* 21: 1347-1360, 2017).

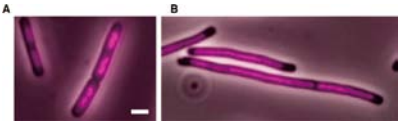


Fig. 2. *Spo0J* gene deletion strain (left) and double deletion strain of *spo0J* and rDNA (one copy only) (right) of *Bacillus subtilis*. In the double deletion strain, the nucleoid (reddish purple: DAPI staining) is elongated. (From *Cell Rep* 21: 1347-1360, 2017 Fig. 6A, B).

General Microbes

Core Facility : Microbe Division/Japan Collection of Microorganisms (JCM),
RIKEN BioResource Research Center
Principal Investigator : Moriya Ohkuma FAX : +81-29-836-9561
Contact site : inquiry.jcm@riken.jp
URL : https://jcm.brc.riken.jp

Overview

Microorganisms are characterized by species diversity. In addition to our living environment, microorganisms inhabit various environments, including symbiosis with hosts and extreme environments in terms of temperature, pH, barometric pressure, salt concentration, humidity, and radiation. These diverse functions of microorganisms have been used in a wide range of research, including ecosystem maintenance, environmental remediation, and production of food and drugs.

In NBRP-General microbes, RIKEN BRC-JCM (Japan Collection of Microorganisms) collects, preserves, and provides diverse microbial strains. In quality control of these strains and the entire operation, we strive to ensure credibility by conducting under the international quality management standard ISO9001 certification. We help rescue microbial resources which are valuable but are facing a difficulty to be preserved at some laboratories. We also collaborate with NBRP-Pathogenic eukaryotic microbes and NBRP-Pathogenic bacteria to complement microbial resources required for research and development. In the 4th phase of NBRP, while enriching the information related to the strains such as physiological characters, genomes, and related publications in our catalogue database, we will strive to improve the convenience of the database for promoting microbial research in the world.

Top: Certified ISO9001
Photos, upper left: *Bifidobacterium longum subsp. longum* inhibiting infection of enteric pathogens.
Upper right: *Lactococcus lactis subsp. lactis* stimulating entire immune system (Gram-stained image).
Lower left: Avermectin-producing *Streptomyces avermitilis*, isolated by the Novel Prize laureate Prof. Ōmura.
Lower right: *Cryptococcus terricola* producing biodiesel from starch.

Key Strains/Studies

A total of approximately 19,000 strains of various non-pathogenic microbial strains belonging to bacteria (including lactic acid bacteria and actinomycetes), archaea, yeast, and filamentous fungi are released. We maintain a large number of type strains representing species equivalent to approximately half of internationally recognized bacteria, archaea, and yeast, and strains isolated in the fields of fermentation and biotechnology. We also provide anaerobic bacteria and extremophiles that are difficult to culture. A large number of microorganisms useful for health research such as for human and animal indigenous microbiota, and those useful in biotechnology fields such as for food, agriculture, drug discovery, bioenergy, substance production, and environmental remediation, are available. In addition, we have self-decoded the genome sequence information of approximately 500 strains of bacteria, archaea, and fungi. This information is available in our home page.

● *Aquificae* bacteria, including *Thermosulfidibacter takaii* (JCM 13301)

The reductive TCA cycle is one of the oldest carbon assimilation pathways required for the biosynthesis of organic compounds. In *thermosulfidibacter*, a thermophilic, hydrogen-oxidizing, sulfur-reducing bacteria isolated from the deep sea, no known carbon-fixing enzymes involved in reductive TCA cycle were found by whole genome sequence analysis. Using transcriptome, proteome, trace metabolome analyses and so on, it was found that the responding direction of the TCA cycle was flexibly changed depending on the available carbon source with same enzymes. These results suggest that life may have come to being as something which flexibly change metabolism depending on the abundance of available inorganic and organic carbon sources (*Science* 359: 559-563, 2018).

Apart from this report, many research results using NBRP resources have been reported, such as the discovery that peptides in natto have pneumococcus-specific antibacterial activity (Fig. 1, *AMB Express* 7: 127, 2017) and development of a single culture medium suitable for the culture of several human enteric bacteria (*Biosci Biochem Biotech* 81: 2009-2017, 2017; *Int J Biochem Cell Biol* 93: 52-61, 2017).

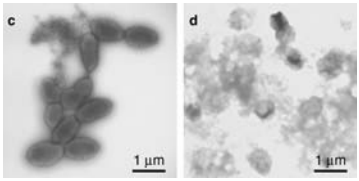


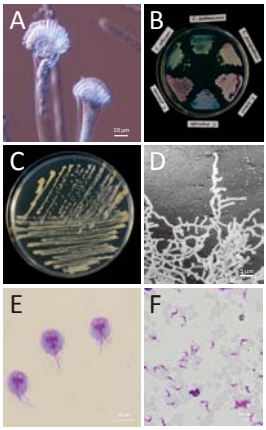
Fig. 1. Pneumococci are lysed in the presence of a natto-derived peptide (right). (From *AMB Express* 7: 127, 2017 Fig. 5c, d).

Core Facility : Medical Mycology Research Center, Chiba University
Principal Investigator : Takashi Yaguchi FAX : +81-43-226-2486
Contact site : bioresource@ml.chiba-u.jp (pathogenic fungi and actinomycetes; Chiba Univ.)
protozoa@tm.nagasaki-u.ac.jp (pathogenic protozoa; Nagasaki Univ.)
URL : https://pathogenic-microbes.nbrp.jp/

Overview

The need for infectious disease control is increasing nowadays. In addition to education and basic research on infectious diseases, research for new diagnostic reagents and drug development requires high-quality resources of pathogenic microorganisms.

In NBRP-Pathogenic eukaryotic microbes, the core facility, Medical Mycology Research Center of Chiba University, collects, preserves, and provides pathogenic fungi and actinomycetes. The sub-core facility, Nagasaki University Institute of Tropical Medicine collects, preserves, and provides pathogenic protozoa. We receive the deposit of clinical isolates through cooperation with medical institutions and support of clinical sites (e.g., identification of bacterial isolates, implementation of drug susceptibility tests, and cooperation on detection of pathogenic factors), and again provide them by adding molecular, morphological, physiological, and clinical information to users as reliable pathogenic strains. We aim to establish a collection that can reliably respond to any infections caused by pathogenic eukaryotic organisms in the future. This project also provides microorganisms in the form of DNA and inactivated forms to research institutions that are not able to handle pathogenic microorganisms as living cells. In the 4th phase of NBRP, while continuing the existing activities, we will focus on collecting clinically important species, and development of genomic information. By providing high value-added resources, we will contribute to basic and applied research in the field of medicine.



Fungi A) *Aspergillus fumigatus*, B) Various *Candida* (cultured at 25°C for 3 days). Middle row: *Actinomycetes*, C, D) *Nocardia farcinica*. Bottom row: Protozoa E) *Giardia intestinalis*, and F) *Trypanosoma brucei*.

Key Strains/Studies

We offer the following strains: fresh clinical isolates of fungi and actinomycetes, all species of highly pathogenic fungi (including Class III pathogens) and other major pathogenic fungal species (~ 15,000 strains), standard strains of pathogenic actinomycetes, mainly in the *Nocardia* genus (~ 2,700 strains), and human infectious protozoal strains (~ 350 strains).

● Azole-resistant *Aspergillus fumigatus* clinical isolate (IFM61567), *etc*.

Azoles are important therapeutic agents for aspergillosis due to *Aspergillus fumigatus* infection. However, situation is becoming serious as azole-resistant strains are spreading. As a result of screening for azole-resistance-related genes. *atrR* gene-deleted strains of azole-resistant *A. fumigatus* clinical isolates were highly susceptible to azoles (Fig. 1, *PLoS Pathog* 13: e100609, 2017).

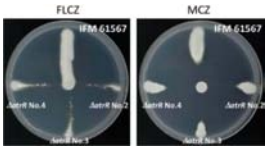


Fig. 1. Colony growth of the atrR gene-deficient strain (3 · 6 · 9 o'clock direction) is suppressed more than the resistant clinical strain (12 o'clock direction) when azoles (FLCZ and MCZ) are added to the center of the plate (From *PLoS Pathog* 13: e100609, 2017 Fig. 10A).

● *Plasmodium yoelii* 17XL strain (Py003) *etc*.

EBL family proteins are secreted from malaria parasites and bind to the molecules on the erythrocyte surface. A transgenic line of *Plasmodium yoelii* (a malaria parasite that infects rodents) in which the *ebl* gene expression was suppressed by the Tet-Off system, could not bind to erythrocytes and showed reduced invasion of erythrocytes and proliferation therein. (Fig. 2, *Parasitol Int* 67: 706-714, 2018).

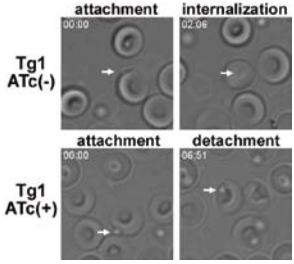


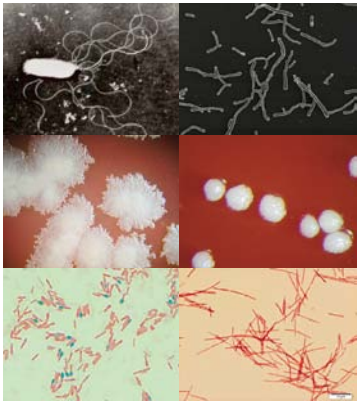
Fig. 2. *Plasmodium yoelii* binds to and invades an erythrocyte when EBL is expressed (upper), but binding to the erythrocyte is not maintained when expression is suppressed (lower) (From *Parasitol Int* 67: 706-714, 2018 Fig. 5a with modifications).

Core Facility : Center for Conservation of Microbial Genetic Resource, Organization for Research and Community Development, Gifu University
Principal Investigator : Kaori Tanaka FAX : +81-58-230-6154
Contact site : g_cmr@gifu-u.ac.jp
URL : https://pathogenic-bacteria.nbrp.jp/

Overview

To counteract against emerging and re-emerging infectious diseases that are ongoing and are expected to continue, as well as rapidly progressing gene mutations and development of drug resistance, development of high-quality and excellent bioresources critical for these studies and a core institution that manages and provides these bioresources along with useful supplementary information is necessary.

Regarding NBRP-Pathogenic bacteria, the core facility, Gifu University collects, preserves, and provides bacteria causing infectious diseases and opportunistic infections in various fields. The sub-core facility, Osaka University collects, preserves, and provides bacteria responsible for enteric infections. In addition, the other sub-core facility, Gunma University is responsible for backing up these resources. The three organizations coordinate with each other to develop a more stable preservation system and to offer strains with useful information, including pathogenic factors, biochemical characteristics, drug susceptibility and resistance. In addition, we will conserve valuable bacteria resources deposited by researchers. To improve user convenience, we will create a database of preservation methods and culture methods for provided strains. We will work to support people involved in education, research, and development related to infectious diseases and pathogens.



A wide variety of pathogenic bacteria resources

Key Strains/Studies

Gifu University owns more than 20,000 bacterial strains including over 80% of strains pathogenic to human. We preserve phylogenetically related anaerobes and aerobic non-fermenting gram-negative bacteria. We also collect BSL2-3 specified pathogens, opportunistic pathogens, attenuated strains for educational purpose, and drug-resistant strains. The collection also includes variants within bacterial species, such as serotypes, which are important in the field of infectious diseases. Osaka University owns standard strains and clinical isolates mainly of pathogenic *E. coli*, *Vibrio bacteria*, and other enteropathogenic bacteria. A total of approximately 8,000 strains are publicly available on the NBRP Pathogenic Bacterial Database. As this project provides pathogenic microbes, we may ask ordering institutions to provide facility information or may place restrictions on database search, depending on bacterial species. If you are interested in such bacteria, please consult with our representative in advance.

● POR1: TDH (thermostable direct hemolysin)-negative strain derived from *Vibrio parahaemolyticus* clinical strain (RIMD2210633)

Vibrio parahaemolyticus is a major cause of food poisoning by fish and shellfish. T3SS2, which is a type III secretion system to inject effector proteins into host cells, is considered as the main virulence factor for gastroenteritis; however, the function of VopL, one of its effector proteins, in host infection was unknown. Analysis using the *vopL* gene deletion strains, which were prepared from POR1 strain, revealed that VopL inhibits the migration of the regulatory subunit of NADAPH oxidase (NOX) from the cytoplasm to the cell membrane and reduces reactive oxygen species production by destroying the normal cytoskeleton function by actin (Fig. 1, *PLoS Pathog* 13: e1006438, 2017).

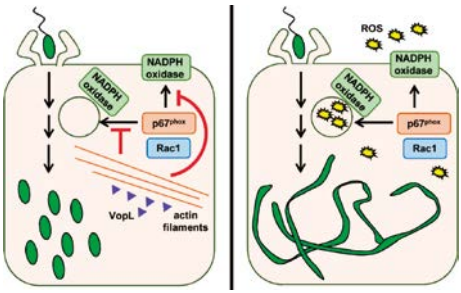


Fig. 1. Schematic diagram of suppression of reactive oxygen species production in host by VopL.
Left) Normal strain (green) suppresses NOX activity and proliferates. Right) In the *vopL*-deficient strain, reactive oxygen species (yellow) induce elongation of intracellular bacteria (suppression of cell division) and reduce proliferation. (From *PLoS Pathog* 13: e1006438, 2017 Fig. 8)

Cord blood cells for research

Core Facility : Department of Cell Processing and Transfusion, Research Hospital, The Institute of Medical Science University of Tokyo (IMSUT)
Principal Investigator : Tokiko Nagamura-Inoue FAX : +81-29-836-9130
Contact site : cellbank@brc.riken.jp
URL : https://cell.brc.riken.jp/en/

Overview

Human cord blood cells (CBCs) have been known as the source of hematopoietic stem cell transplantation for severe hematologic diseases like leukemia, and they are now widely used for research purposes in the medical and biological studies of regenerative medicine, drug development, epidemiology, infection, genetics and environmental studies.

This project provides frozen CBCs for research use, to researchers through the RIKEN BioResource Research center (BRC). The research CBs are collected with written consent in hospitals participating in this project, then transferred to the processing facility, The Institute of Medical Science, The University of Tokyo, Cell resource center (IMSUT CRC), where CBCs are processed, cryopreserved, and transferred to RIKEN BRC. Through the RIKEN BRC, research CBCs shall be provided to the researchers in need.

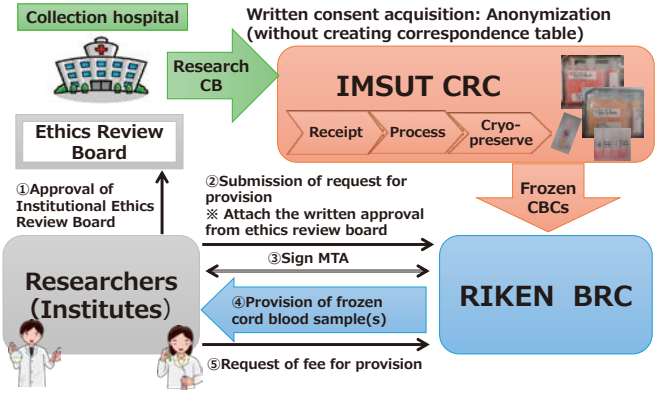


Fig. 1. Flow chart of collection, cell processing, cryopreservation, and provision of human CBCs for research, and method of application for use thereof

Key samples / Studies

All samples in this bank are frozen after processing. Nucleated cell samples contain whole white blood cells in cord blood. Mononuclear cell samples primarily consist of lymphocytes and monocytes, but also contain CD34-positive cells. CD34-positive cell samples carry representative markers of hematopoietic stem cells, attracting attention not only in hematopoietic stem cell transplantation research and blood differentiation research but also in regenerative medicine as a source of iPS cells. For frozen cord blood, infection test [HBs-Ag, HBc-Ab, HCV-Ab, HIV-I/II-Ab, HTLV-1-Ab, Syphilis (TPHA)] and sterility test are conducted.

● Examples of research results using this bank

Important issues such as recurrence and metastasis remain unsolved even with immunotherapy, which has recently been proven to be an effective treatment modality against cancer. Immunotherapy with NKT cells is expected to comprehensively activate innate and acquired immunity, it may be useful for treatment of any type of cancer. In fact, activated NKT therapy through NKT cell-specific antigen presentation by the glycolipid α-galactosylceramide (GC) (*via* GC-pulsed dendritic cells) has succeeded in substantially extending the survival of cancer patients in clinical research. Furthermore, among the GC derivatives, a synthetic glycolipid called RK that induces more potent antitumor effects has been developed. In an *in vitro* system using NKT cells differentiated from cord blood cell-derived iPS cells (NKT-iPS cells), RK-pulsed dendritic cells show significant improvements in multiple antitumor-related indices of NKT cells compared with GC-pulsed dendritic cells. In addition, long-term antitumor effects were also observed in mice (Fig. 2, *Front Immunol* 8: 1206, 2017).

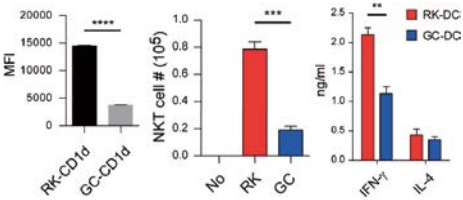


Fig. 2. Comparison of NTK cell activity indices between RK and GC
Left: Mean fluorescence intensity (MFI) of CD1d (dendritic cell surface antigen), Middle: Vα24+CD3+NKT cell count, Right: INF-γ and IL-4 concentrations in culture medium (From *Front Immunol* 8: 1206, 2017 Fig. 2 with partial modifications)

Core Facility : Cell Engineering Division, RIKEN BioResource Research Center
Principal Investigator : Yukio Nakamura FAX : +81-29-836-9130
Contact site : cellqa.brc@riken.jp (Regarding materials and methods)
cellbank.brc@riken.jp (Regarding deposit or provision)
URL : https://cell.brc.riken.jp/en/

Overview

Advances in genetic engineering techniques such as gene cloning by PCR technology and development of mutant mice by combining ES cells and homologous recombination technology have dramatically driven progress in functional analysis of genes in the late 20th century. In addition, reprogramming of cells by nuclear transfer technology and ES cell culture technology have led to revolutionary iPS cell technology in the 21st century. After “era of freely manipulating genes,” “era of freely manipulating cells” has arrived. Consequently, the types of cell materials are also drastically increasing.

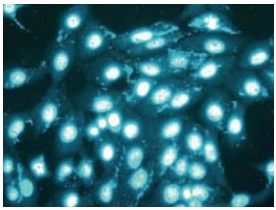


Fig. 1. DNA staining of cells. Not only nuclei but also cytoplasm are stained due to mycoplasma infection.

RIKEN BRC Cell Engineering Division is focusing on accepting deposition, preserving, and distributing high-quality and diverse cell materials. Increased use of cell materials can lead to frequent cell line mix-ups and mycoplasma contamination (Fig. 1), and results from experiments with such materials can be inaccurate and non-reproducible. In our division, we have developed a highly reliable system that provides cell specimens which are confirmed to be free of these problems. We are also working to incorporate cutting-edge technologies such as animal species identification using DNA sequencing. To reduce human error in quality control, we have introduced a quality control system under ISO9001 certification (Fig. 2). In addition, we are working to enrich additional information, including characteristics and culture methods of various cell lines such as cancer cells and human disease-specific iPS cells.

Fig. 2. Accreditation by ISO9001

Key Strains/Studies

We can provide following cells: Human cell lines including cancer cells and general cell lines derived from various animal species (~2,400 lines); cell lines for gene analysis consisting of healthy Japanese-derived immortalized cell lines, Sonoda-Tajima collection cells (mainly from various races and ethnic groups in South America), and Goto collection cells [derived from Werner syndrome patients] (~400 lines); and stem cell lines (~5,400 lines) including human somatic stem cells (human cord blood and mesenchymal stem cells), ES cells (human, marmoset, rabbit, and mouse), and disease-specific iPS cells and healthy human iPS cells (~3,100 and 480 lines, respectively) and animal iPS cells.

Fig. 3. von Kossa staining of ST2 cells.
In ST2 medium supplemented with mature osteoclast secreted microvesicles (mOC-SEVs), calcification of cells (brown) is observed (middle panel). However, in the mOC-SEVs-supplemented medium pretreated with RANKL extracellular domain protein, no calcification of cells is observed (lower panel). (From *Nature* 561: 195-200, 2018 Fig. 1F)

● Mouse osteoclast precursor-like cell RAW264 (RCB 0535) and osteoblast-like cell ST2 (RCB 0224)

RANK and its ligand RANKL mediate osteoclast maturation via osteocytes. Experiments with RAW264 and ST2 cells have demonstrated that they also act to promote bone formation by osteoblasts via osteoclasts and play a central role in linking bone resorption and bone formation. Furthermore, an antibody designed to bind to the RANKL extracellular domain and promote osteoblast activation was found to suppress bone resorption simultaneously with promoting bone formation in osteoporosis model mice (Fig. 3, *Nature* 561: 195-200, 2018).

● iPS cells derived from patients with amyotrophic lateral sclerosis (ALS) (HPS0251, HPS0252, HPS0292)

SOD1 mutation is one of the causes of ALS. The SOD1 mutant binds to the endoplasmic reticulum DERL1 protein and eventually causes motor neuron death. Derivatives of SOD1-DERL1 binding inhibitors, which were discovered from screening by the TR-FRET method, inhibited death of ALS motor neurons induced from ALS patient-derived iPS cells carrying SOD1 gene mutations. Furthermore, when these derivatives were administered to transgenic mice with the mutant SOD1 gene, delayed onset and prolonged survival were also observed (*Nat Commun* 9: 2668, 2018).

CORE FACILITY UPGRADING PROGRAM DNA material

Core Facility : Gene Engineering Division, RIKEN BioResource Research Center
Principal Investigator : Takehide Murata FAX : +81-29-836-9120
Contact site : dnabank.brc@riken.jp
URL : https://dna.brc.riken.jp/en/

Overview

Genetic material such as genomic and cDNA clones of human, animal and microbe origin, and genetic research tools such as genome editing vectors, fluorescent/ luminescent protein genes and viral vectors are one of the most important and fundamental bioresources for the life science. Genetic materials and tools are now widely utilized in numerous life science research fields not only in basic researches such as analyses of gene function and control mechanisms of gene expression but also in applied researches such as development of various therapies and drugs as well as material production.

RIKEN BioResource Research Center (BRC) Gene Engineering Division has been engaging in the collection, preservation, quality control and distribution of cutting-edge genetic materials and tools developed mainly by Japanese researchers. To provide scientific community with genetic materials and tools of the highest quality with assured reproducibility of experimental results, we perform rigorous quality control by testing growth, restriction enzyme mapping and nucleotide sequencing of clones. The Material Transfer Agreement is used for each transfer of genetic materials and tools to protect the intellectual property rights of developers and to define the responsibility of users. We have also opened a path of the academic use of advanced genetic materials and tools such as genome editing vectors and fluorescent/luminescent protein genes owned by commercial entities. Relevant information such as characteristics of bioresources and methodologies are provided via the web of the RIKEN BRC. For the best use of genetic resources, technical seminars and training courses are also given.

Genetic tools such as fluorescent protein (upper left) and comprehensive clones such as human cDNA and mouse BAC clones are collected and preserved. After quality test, we distribute them to researchers worldwide.

Key Genetic Materials and Tools

Comprehensive libraries such as cDNA clones corresponding to allmost all human genes, EST clones of mouse, common marmoset, clawed frog and ascidians, BAC clones covering almost entire genome of mouse, rat, Japanese macaque and Drosophila, and ORF clones of fission yeast and thermophile *T. thermophilus*. The clones can be searched in our web site and KEGG (Kyoto Encyclopedia of Genes and Genomes) database. By the collaboration within our center, we provide genomic DNA of microorganisms and mouse strains. Furthermore, we provide cutting-edge genetic tools such as near-infrared luciferase Akaluc, Fucci expression vectors for monitoring cell cycle progression in living cells, organelle markers, knock-in vectors for the regulation technology of protein degradation by the auxin degron method, expression vectors, plasmid clones for genome editing and gene transduction.

● Our Recommended Genetic Tool : pMRX-IP-GFP-LC3-RFP-LC3ΔG (cat# RDB14600)

In order to visualize autophagosome and observe autophagy, MAP1LC3 (LC3) fused with fluorescent proteins as a probe are used. However, the fluorescence of the probe attenuates during autophagy progresses and it is not suitable for quantitative assay of autophagy. Dr. Noboru Mizushima and his colleagues at the University of Tokyo developed a new probe that can expresses GFP-LC3 and RFP-LC3ΔG (lacking glycine (G) at the LC 3 end) simultaneously at equimolar amounts (Fig.1, *Mol. Cell*, 64 (4): 835-849., 2016). As autophagy progresses, the fluorescence of GFP-LC3 decays whereas that of RFP-LC3ΔG remains in the cytoplasm as an internal standard. Therefore, the activity of autophagy can be evaluated by the fluorescence intensity ratio of GFP/RFP. Using this probe, autophagic flux was measured in embryos and tissues of mouse and zebrafish as well as cultured cells. This is also suitable for analysis of large number of samples.

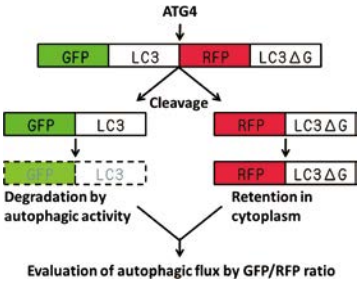


Fig. 1. Fluorescent protein probes introduced into cultured cells and animals can be used to quantitatively monitor autophagy activity (From *Mol Cell* 64: 835-849, 2016 Fig. 1 with partial modifications)

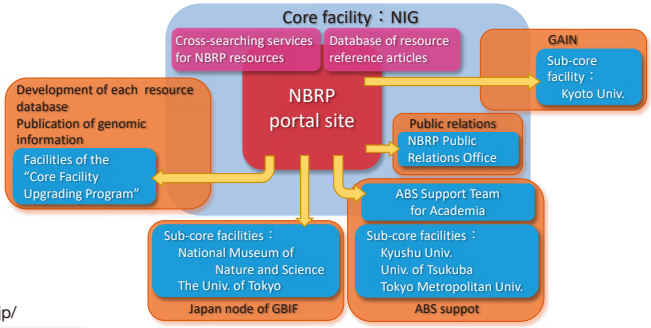
Core Facility : Genetic Resources Center, National Institute of Genetics
Principal Investigator : Shoko Kawamoto FAX : +81-55-981-6886
Contact site : nbrp@shigen.info
URL : https://nbrp.jp/

Overview

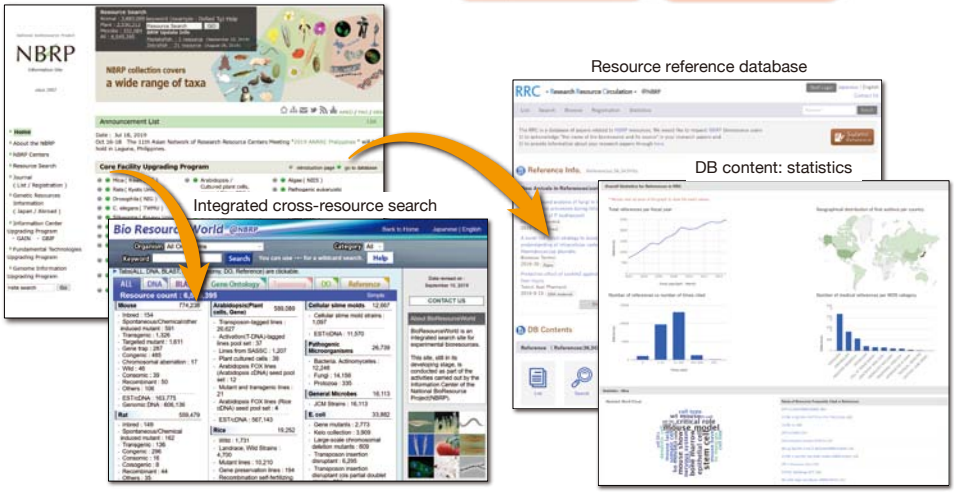
The Information Center Upgrade Program promotes the following five efforts by seven organizations: (1) NBRP information center activity, (2) the Great Ape Information Network (GAIN), (3) the Japan Node of the Global Biodiversity Information Facility (GBIF), (4) the Access and Benefit Sharing (ABS) Support Team for Academia, and (5) public relations activities for NBRP.

NBRP information center's primary task is the development of bioresource databases (1). The information center is located at the National Institute of Genetics (NIG) and supports the development and operation of information disclosure sites and resource distribution sites for each species of the Core Facility Upgrading Program. Bioresource users can search 6.54 million resource data, and 36,000 scientific articles that have used or cited these resources by cross-searching service. The center also supports the release of genomic information obtained from the bioresources sequenced by the Genomic Information Upgrading Program. The information center is also working together with GAIN (2) and GBIF (3). In addition, the ABS Support Team for Academia and the NBRP Public Relations Office have been opened in the NIG. ABS Support Team for Academia works as a general contact office for ABS-related matters in cooperation with sub-core facilities (4). NBRP public relations promotes the appropriate use of NBRP resources, we will cooperate with organizations participating in all of the NBRP programs to develop activities of public relations (5).

The organization of the Information Center Upgrading Program



NBRP portal site https://nbrp.jp/



INFORMATION CENTER UPGRADING PROGRAM Information (GAIN)

Sub-Core Facility : Kyoto University Institute for Advanced Study / Primate Research Institute, Kyoto University / Wildlife Research Center, Kyoto University
Principal Investigator : Tetsuro Matsuzawa FAX : +81-568-62-2428
Contact site : gain@pri.kyoto-u.ac.jp
URL : https://shigen.nig.ac.jp/gain/

Overview

Research using great apes is extremely important for understanding human nature. The *Hominidae* family is currently classified into four genera (*Hominidae Homo*, *Hominidae Pan*, *Hominidae Gorilla*, and *Hominidae Pongo*) in terms of biology and law. To understand human beings, it is essential to understand the other three genera in the *Hominidae* family. Alternatively, they are endangered species. The so-called Washington Convention prohibits international commercial trading of these species. Therefore, chimpanzees, gorillas, and orangutans in Japan are extremely valuable in terms of species conservation and academic research.

The Gain website https://shigen.nig.ac.jp/gain/

The Great Ape Information Network (GAIN) project collects and manages information, such as the history, family, genome, behavior, and other materials about all individuals of valuable endangered species such as great apes in Japan, including individuals in zoos. By providing them for joint use by researchers all over the country, we promote the development of academic research and conduct activities to promote the welfare and conservation of great apes.

INFORMATION CENTER UPGRADING PROGRAM Information (GBIF Japan Node)

①Sub-Core Facility : Collection Center, National Museum of Nature and Science
Principal Investigator : Tsuyoshi Hosoya
②Sub-Core Facility : Graduate School of Arts and Sciences, The University of Tokyo
Principal Investigator : Motomi Ito
Contact site : http://gbif.jp/v2/en/contact/index.html
URL : http://www.gbif.jp/

Overview

Ecosystems on the earth are constructed by various organisms that interact with each other. As a species on earth, humans benefit from biodiversity in many ways, from food, clothing, and shelter to economic activities. To maintain biodiversity for the future, it is necessary to understand the mechanisms and preserve the biodiversity.

The JBIF website http://gbif.jp

To share biodiversity information in the world and create a mechanism that anyone can freely access, the Global Biodiversity Information Facility (GBIF) conducts the following activities: (1) development of biodiversity information infrastructure to be used for research and policy decision purposes, (2) accumulation and provision of biodiversity information, (3) development of information accumulation and analysis tools, and (4) support of activities and development of skills related to biodiversity information. GBIF Japan Node (JBIF) promotes the use of biodiversity data in Japan and disseminates its presence to the world. The National Museum of Nature and Science provides biodiversity information utilizing the network of natural history museums. The University of Tokyo is in charge of collecting domestic and foreign information and standardizing the proves of dissemination of biodiversity information.

Core Facility : Genetic Resources Center, National Institute of Genetics
General contact office : ABS Support Team for Academia, NIG INNOVATION Mutsuaki Suzuki
①Sub-Core Facility : Material Management Center, Kyushu University
Principal Investigator : Katsuya Fukami
②Sub-Core Facility : Makino Herbarium, Tokyo Metropolitan University
Principal Investigator : Noriaki Murakami
③Sub-Core Facility : Gene Research Center, University of Tsukuba
Principal Investigator : Kazuo Watanabe
Contact site : abs@nig.ac.jp, msuzuki@nig.ac.jp
TEL : +81-55-981-5831 FAX : +81-55-981-5832
URL : http://nig-chizai.sakura.ne.jp/abs_tft/en/

Overview

● Nagoya Protocol Implementation (compliance with laws and regulations on access and utilization of genetic resources from overseas)

To access overseas plants, animals and microorganisms, it is inevitable to observe relevant national laws of provider countries. The Nagoya Protocol on Access and Benefit Sharing (ABS) was brought into effect in 2014 to effectively share benefits among countries that provide genetic resources and those that use genetic resources. On August 20, 2017, Japan became the 99th party of the Nagoya Protocol, and domestic measures (ABS guidelines) were launched on the same day. Relevant laws and regulations of each country are on the way to be developed, and contracts with providers (mutual agreed terms: MAT) and permission from the provider country government (prior informed consent: PIC) are required to use the genetic resources of those countries. However, there might be some cases in which individual researchers may not be able to solve because the scope, enforcement, and development status of laws and regulations related to ABS differ from country to country, and ABS procedure is still unclear.

● Implementation system of support and enlightenment

In Japan, with the three cooperative institutions of Kyushu University, University of Tsukuba, and Tokyo Metropolitan University, National Institute of Genetics is developing a system to support the procedures of the permit (PIC) and the contract with the provider (MAT) as part of the NBRP Information Center Upgrading Program. The three institutions are in charge of the following tasks: The Material Management Center, Kyushu University is in charge of supporting the acquisition of genetic resources in the field of biotechnology and the development of tools such as contract templates; Gene Research Center, University of Tsukuba is in charge of supporting genetic resource acquisition, considering the role of genetic resources in the field of breeding and horticulture and the related seed banks; Makino Herbarium, Tokyo Metropolitan University is in charge of supporting the acquisition and use of genetic resources in the field of biodiversity research based on studies of ABS-related case studies in Asia.

The ABS Support Team for Academia, NIG INNOVATION at the National Institute of Genetics supports universities and research institutes for acquiring genetic resources from overseas as a general contact office for ABS-related matters in Japan. In addition, we have established a website to post ABS information database, comprehensive search site, and related materials. We also conduct visiting free seminars and provide email and phone consultations (please use the contact information above). Furthermore, as a university system construction WG, we are examining the university system construction with partner schools consisting of Tokyo University of Marine Science and Technology, Mie University, Nagasaki University, Nagoya University and others.

Website for the ABS Support Team for Academia

● International activities related to overseas genetic resources

We participate in and discuss at international conferences such as the Conference of the party (to cope with issues such as digital sequence information).

Core Facility : Japanese Association for Laboratory Animal Science
Principal Investigator : Chihiro Koshimoto FAX : +81-3-3814-3990
Contact site : saegusa@jalas.jp
URL : http://www.m-kenshou.org/

Overview

Human Resources Development Workshop for External Verification (left) and a briefing session on external verification (right)

Although animal experimentations are crucial as a research platform for life science development, it is necessary to conduct them properly based on social consensus. “Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Academic Research Institutions” issued by the Ministry of Education, Culture, Sports, Science, and Technology requires the animal research conducting institutions to disclose information and undergo external verification by third parties to assure the rational use of experimental animals. The Japanese Association of Laboratory Animal Facilities of National University Corporations and the Japanese Association of Laboratory Animal Facilities of Public and Private Universities have jointly established a technical committee, and conducted external verification of animal experimentation. Fulfilling social accountability by ensuring transparency of animal experimentations in Japan is important for appropriate use of animal resources developed by NBRP. However, specialists who can review the state of animal experimentation in each institution objectively are not enough because they are required to have high level of expertise and experience. For this reason, it is necessary to strengthen the implementation system of external verification for animal experimentation. The purpose of this project is to considerably increase the number of specialists who can objectively verify the appropriateness of animal experiments conducted in research institutions including universities from the outside point of view, and to strengthen the external verification function as a mechanism to give assurance transparency and appropriateness of animal experimentation to the society.

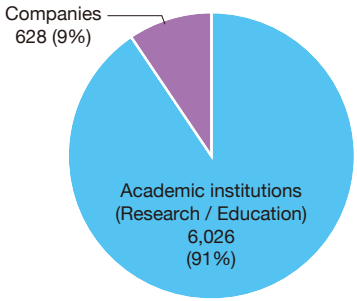
Therefore, several types of educational workshops to train specialized personnel to promote external verification are organized concurrently with an orientation meeting on the external verification of animal experimentation for research institution in Japan widely.

Outcomes of NBRP Activities

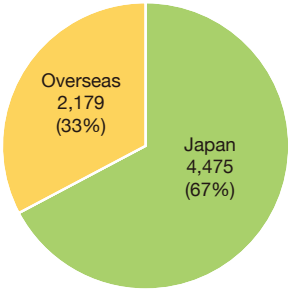
In the past four years (FY2015–FY2018), the average number of depositors of bioresources was **658** per year, and the average number of users was **6,654** per year. Many individuals related to research, education, and business have used NBRP.

The current activities and their results are shown below.

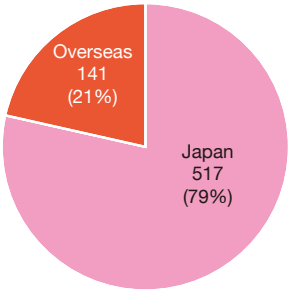
● Percentage of average annual users by organization type (past 4 years)



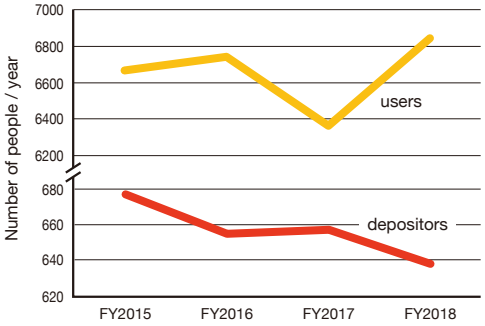
● Percentage of average annual users in Japan and overseas (past 4 years)



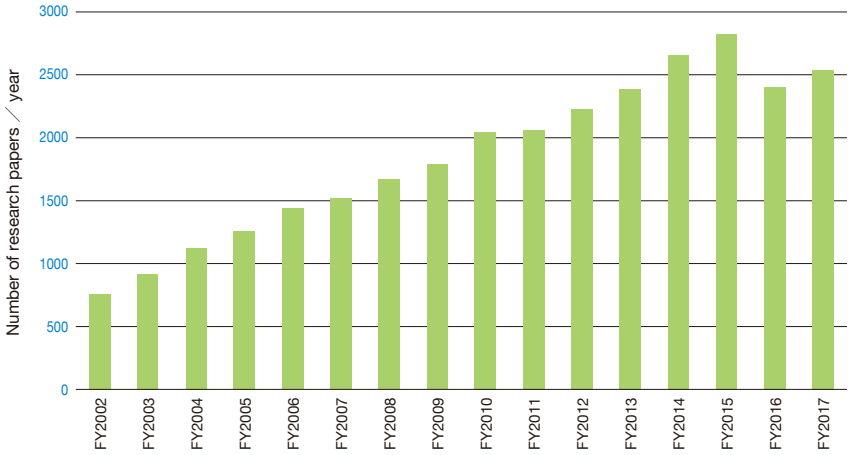
● Percentage of average annual depositors in Japan and overseas (past 4 years)



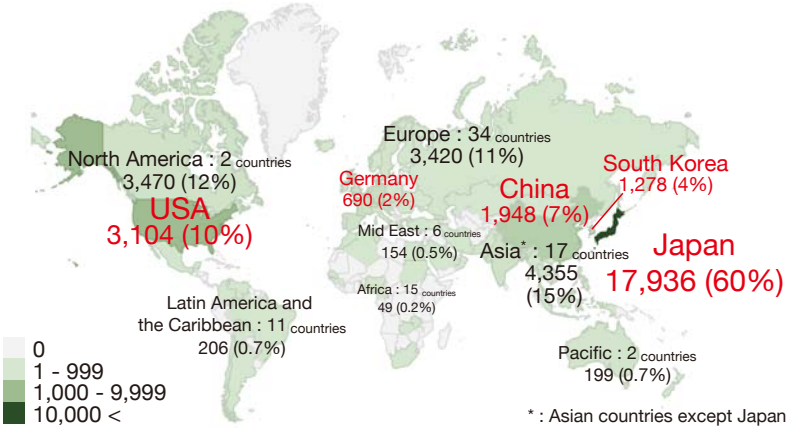
● Trends in the number of users and depositors (past 4 years)



● Trends in the number of research papers published using NBRP resources from the start of NBRP to FY2017



● Global distribution of authors (first authors) of papers on research outcomes using NBRP resources (as of June 2019)



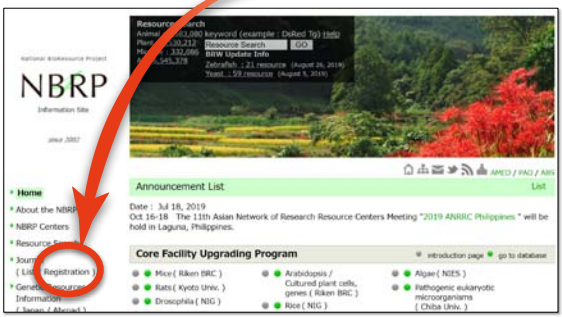
Feedback of research outcomes using NBRP resources

● Collection of research paper information

Accumulation of research outcome using bioresources can further enhance the value of the bioresources. NBRP is collecting such research outcomes, and integrating them into the NBRP database. Therefore, we would like to request the bioresource users 1) to describe "the name of the bioresource and its supplier" in the research papers and 2) to send the paper information to the NBRP Core Facility, upon publication of research outcome using the NBRP resources.

Please visit to the "Research Paper Online Registration Site" for easy feedback of such information.

Please click "Journal (List / Registration)", on the top page of https://nbrp.jp/



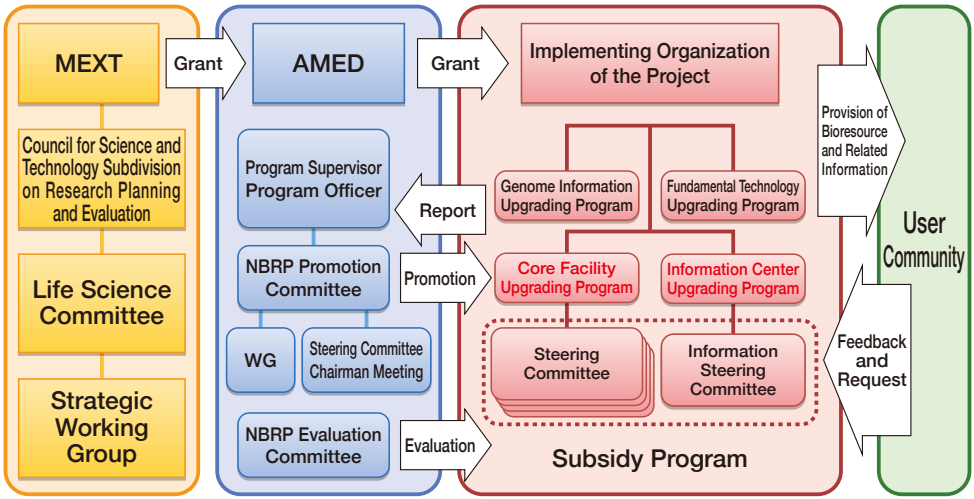
● Deposit of bioresources

It is important for the development of life science research in Japan to make the newly developed and collected bioresources continuously available to research communities. In this project, these resources will be deposited with the appropriate institutes for implementation of the "Core Facility Upgrading Program" (see p1–p30). These institutions will do the work of reproducing, sending, and documenting the resources needed to provide research communities on your behalf.

Depositors can add various conditions for using the deposited resources, such as citation of published articles, restrictions on purpose of use, and requirement of separate license agreement for commercial use.

For consultation on deposit, please contact an appropriate institute for implementation of the "Core Facility Upgrading Program".

Project Implementation System



NBRP Program Supervisor (PS)

NBRP-PS coordinates the operation of the project and the cooperation and promotion of each program.

Name	Affiliated organization
Yuji Kohara	Director, Database Center for Life Science Research Organization of Information and Systems Inter-University Research Institute Corporation

NBRP Program Officer (PO)

NBRP-PO assists the PS and promotes the operation of each task.

Name	Affiliated organization
Yuichi Obata	Special Advisor, RIKEN BioResource Research Center (BRC)
Satoshi Tabata	Vice President / Director, Kazusa DNA Research Institute
Tetsuya Hayashi	Professor, Graduate School of Medical Sciences, Kyushu University

NBRP Promotion Committee

The NBRP Promotion Committee formulates the promotion policy of the project, makes plans for dissemination activities, and provides guidance and communication to the operating institutions.

Position	Name	Affiliated organization
Chairman	Yuji Kohara	Director, Database Center for Life Science Research Organization of Information and Systems Inter-University Research Institute Corporation
Vice-Chairman	Yuichi Obata	Special Advisor, RIKEN BioResource Research Center (BRC)
	Kiyotaka Okada	Professor, Faculty of Agriculture, Ryukoku University
	Makoto Kawase	Professor, Faculty of Agriculture, Tokyo University of Agriculture
	Kazuo Shinozaki	Director, RIKEN Center for Sustainable Resource Science (CSRS)
	Toshihiko Shiroishi	Director, RIKEN BioResource Research Center (BRC)
	Satoshi Tabata	Vice President/ Director, Kazusa DNA Research Institute
	Tetsuya Hayashi	Professor, Graduate School of Medical Sciences, Kyushu University
	Hiroo Fukuda	Vice President/ Trustee, The University of Tokyo

Changes in bioresources developed by NBRP and core facilities (from the 1st phase to the 4th phase)

Bioresource (Core facility)	1st Phase 2002~2006	2nd Phase 2007~2011	3rd Phase 2012~2016	4th Phase 2017~2021
Mice (RIKEN BRC)	✓	✓	✓	✓
Mice: ENU mutagenesis (RIKEN GSC)	✓			
Rats (Kyoto University)	✓	✓	✓	✓
Japanese macaques (National Institute for physiological Sciences)	✓	✓	✓	
Japanese macaques (Kyoto University)				✓
Chicken / Quail (Nagoya University)			✓	✓
Xenopus tropicalis (Hiroshima University)	✓	✓	✓	✓
Zebrafish (RIKEN CBS : Former name is RIKEN BSI - FY2017)	✓	✓	✓	✓
Medaka (Nagoya University)	✓			
Medaka (National Institute for Basic Biology)		✓	✓	✓
Ciona intestinalis / Oxycomanthus japonicus (University of Tsukuba)		✓		
Ciona intestinalis (University of Tsukuba)			✓	✓
Drosophila (Kyoto Institute of Technology)	✓	✓		
Drosophila (National Institute of Genetics)			✓	✓
Silkworms (Kyushu University)	✓	✓	✓	✓
C. elegans (Tokyo Women's Medical University School of Medicine)	✓	✓	✓	✓
Arabidopsis / Cultured plant cells, genes (RIKEN BRC)	✓	✓	✓	✓
Rice (National Institute of Genetics)	✓	✓	✓	✓
Wheat (Kyoto University)	✓	✓	✓	✓
Barley (Okayama University)	✓	✓	✓	✓
Lotus / Glycine (University of Miyazaki)	✓	✓	✓	✓
Tomato (University of Tsukuba)		✓	✓	✓
Chrysanthemum (Hiroshima University)	✓	✓	✓	✓
Morning glory (Kyushu University)	✓	✓	✓	✓
Algae (National Institute for Environmental Studies)	✓	✓	✓	✓
Paramecium (Yamaguchi University)			✓	✓
Cellular slime molds (University of Tsukuba)		✓	✓	
Cellular slime molds (RIKEN BDR : Former name is RIKEN QBiC - FY2017)				✓
Yeast (Osaka City University)	✓	✓	✓	✓
E.coli (National Institute of Genetics)	✓			
Prokaryotes (E.coli, B.subtilis) (National Institute of Genetics)		✓	✓	✓
General microbes (RIKEN BRC)		✓	✓	✓
Pathogenic microorganisms (Chiba University)	✓	✓	✓	
Pathogenic eukaryotic microbes (Chiba University)				✓
Pathogenic bacteria (Gifu University)				✓
Cord blood stem cells for research (Tokai Univ. FY2012, 13→The Univ. of Tokyo FY2014 -)			✓	
Cord blood cells for research (The University of Tokyo)				✓
Human ES cells (Kyoto University)	✓	✓		
Human and animal cells (RIKEN BRC)	✓	✓	✓	✓
DNA (Animals and microorganisms) (RIKEN BRC)	✓			
DNA material (RIKEN BRC)		✓	✓	✓
Total number of bioresources	**24**	**27**	**29**	**30**

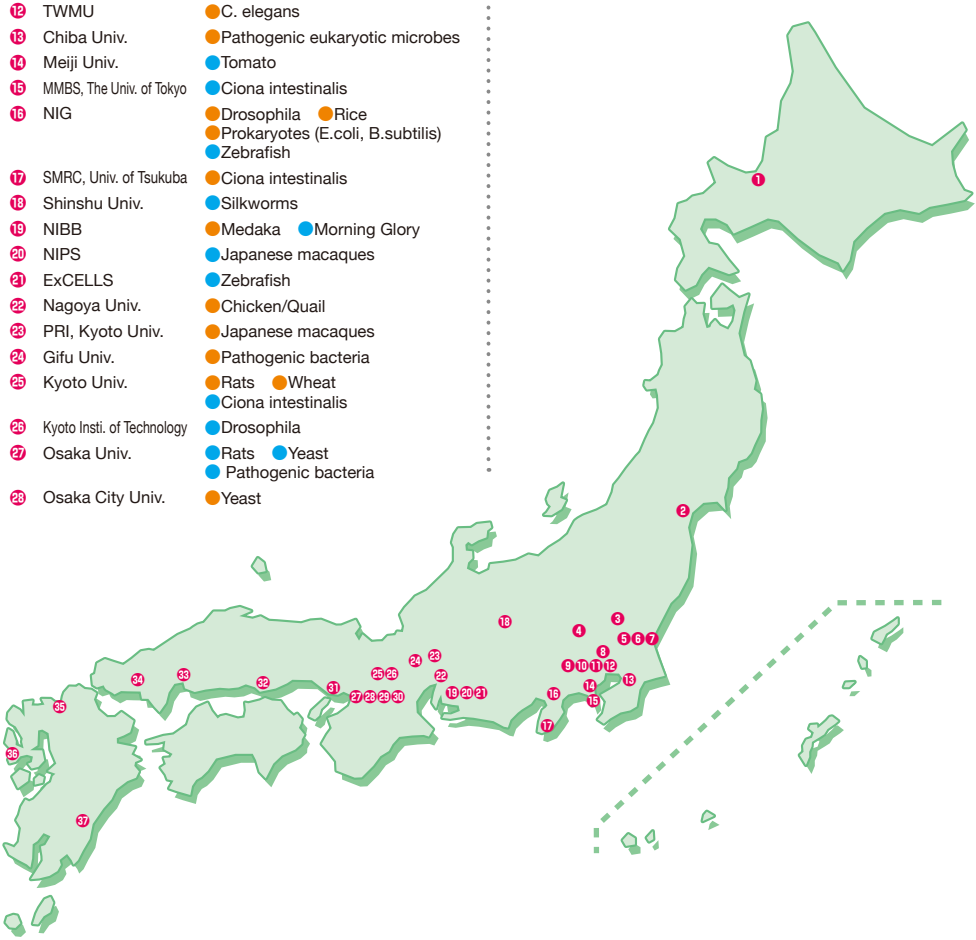
History of NBRP

1996	July	The First Science and Technology Basic Plan was decided at the Cabinet.
2001	January	RIKEN BioResource Center was established in Tsukuba.
2002	April	National BioResource Project (NBRP) was started and led by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan, as a part of Research Revolution 2002 (RR2002).
	April	Beginning of the first phase of NBRP (22 resources). The project was composed of the Core Facility Upgrading Program and the Information Center Upgrading Program.
2003	April	Two resources were added to the Core Facility Upgrading Program.
	December	The NBRP exhibition was held at the 26th Annual Meeting of the Molecular Biology Society of Japan (continued every year). The exhibition was also held in the meetings of other academic societies.
2006	June	Publication of "Report for the Bioresources Upgrading Strategy", prepared by the Working Group on Bioresources Upgrading Strategy of the Life Science Committee.
2007	April	Beginning of the second phase of NBRP (27 resources).
	April	The Genome Information Upgrading Program and the Fundamental Technology Upgrading Program were added to NBRP.
	December	MEXT and the NBRP Promotion Committee visited the implementation organizations of the NBRP with the aim of engaging in discussions with principal investigators and directors of the organizations ("Site Visit").
2008	March	The second phase NBRP Kick-off Symposium, titled "Bioresources that Open the Future of Life Sciences", was held.
2009	April	NBRP, which was a MEXT project, began to be operated under the Grant for Promotion of Shared Use of R&D Facilities.
	August	Submission of the "Report on Database Upgrading and Dissemination of Outcome Information at NBRP" and the "Report on Desired Forms of Provision Fee and Protection of Intellectual Properties at NBRP" by the working group.
2010	February	Notification of "Basic Principles for Handling and Shipping Costs at NBRP".
	October	The 2nd International Meeting of Asian Network of Research Resource Centers was held in Tsukuba.
2011	June	Publication of "Report on Future Vision on Bioresources Upgrading" by the Life Science Committee.
	August	Following the Great East Japan Earthquake, the "Symposium on Disaster Mitigation on Bioresources" was held.
2012	January	The 10th anniversary open symposium to report the achievements of NBRP was held.
	April	Beginning of the third phase of NBRP (29 resources).
	November	The symposium "Challenges in the Third phase of NBRP" was held.
2013	October	The 5th International Meeting of Asian Network of Research Resource Centers was held in Hayama.
	December	Publication of "A Report on Desired Implementation of the Nagoya Protocol" (Ministry of the Environment).
2015	January	The open symposium to present about the achievements of NBRP (at the middle of the third phase) was held.
	April	The Operation of NBRP was transferred from MEXT to the Japan Agency for Medical Research and Development (AMED).
2016	May	The report "Desired Future Bioresource Upgrading" was prepared by the Life Science Committee.
	October	The 8th International Meeting of Asian Network of Research Resource Centers was held in Kyoto.
2017	April	Beginning of the fourth phase of NBRP (30 resources).
	December	The fourth phase NBRP Kick-off Symposium, titled "Research outcomes in basic and applied research using NBRP bioresources", was held.

NBRP Network of Japan

● Core facilities ● Sub-core facilities

1	Hokkaido Univ.	● Algae
2	Tohoku Univ.	● Lotus/Glycine
3	Utsunomiya Univ.	● Medaka
4	Gunma Univ.	● Pathogenic bacteria
5	Univ. of Tsukuba	● Tomato ● Cellular slime molds
6	NIES	● Algae
7	RIKEN BRC	● Mice ● Arabidopsis/Cultured plant ● cells, genes ● General microbes ● Human and animal cells ● DNA material ● Rats ● Cord blood cells for research
8	RIKEN CBS	● Zebrafish
9	Kyorin Univ.	● Drosophila
10	The Univ. of Tokyo	● Cord blood cells for research
11	Gakushuin Univ.	● Silkworms
12	TWMU	● C. elegans
13	Chiba Univ.	● Pathogenic eukaryotic microbes
14	Meiji Univ.	● Tomato
15	MMBS, The Univ. of Tokyo	● Ciona intestinalis
16	NIG	● Drosophila ● Rice ● Prokaryotes (E.coli, B.subtilis) ● Zebrafish
17	SMRC, Univ. of Tsukuba	● Ciona intestinalis
18	Shinshu Univ.	● Silkworms
19	NIBB	● Medaka ● Morning Glory
20	NIPS	● Japanese macaques
21	ExCELLS	● Zebrafish
22	Nagoya Univ.	● Chicken/Quail
23	PRI, Kyoto Univ.	● Japanese macaques
24	Gifu Univ.	● Pathogenic bacteria
25	Kyoto Univ.	● Rats ● Wheat ● Ciona intestinalis
26	Kyoto Insti. of Technology	● Drosophila
27	Osaka Univ.	● Rats ● Yeast ● Pathogenic bacteria
28	Osaka City Univ.	● Yeast
29	Osaka Prefecture Univ.	● Tomato
30	RIKEN BDR	● Cellular slime molds
31	Kobe Univ.	● Algea
32	Okayama Univ.	● Barley
33	Hiroshima Univ.	● Xenopus tropicalis ● Chrysanthemum ● Yeast
34	Yamaguchi Univ.	● Paramecium
35	Kyushu Univ.	● Silkworms ● Morning Glory ● Rice ● Prokaryotes (E.coli, B.subtilis)
36	Nagasaki Univ.	● Pathogenic eukaryotic microbes
37	Univ. of Miyazaki	● Lotus/Glycine ● Medaka



■Contact Information / Regarding the project operation

Japan Agency for Medical Research and Development
Department of Research Infrastructure, Division of Biobank
21F Yomiuri Shimbun Bldg., 1-7-1 Otemachi, Chiyoda-ku,
Tokyo 100-0004, JAPAN
Phone: +81-3-6870-2228
E-mail: national-bioresource@amed.go.jp
URL: https://amed.jp/

■Contact Information / Regarding the contents of this booklet

National Institute of Genetics
Public Relations Office of National BioResource Project
1111 Yata, Mishima, Shizuoka 411-8540, Japan
Phone: +81-55-981-6876
E-mail: nbrp-pr@nig.ac.jp
URL: https://www.nbrp.jp

2019.10