National BioResource Project

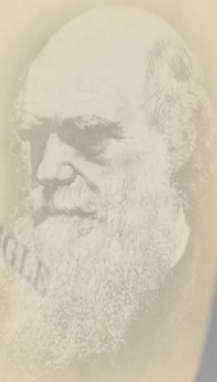
ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.



By CHARLES DARW

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)

List of NBRP Implementing Organizations

Core Facility Upgrading Program

Organism, etc	✳	Principal Investigator	Implementing Organization	Page
Mice	○	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource 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 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 Brain Science Institute	6
		Koichi Kawakami	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	
		Shinichi Higashijima	Okazaki Institute for Integrative Bioscience, 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
		Mitsuru Sakaizumi	Faculty of Science, Niigata University	
		Masaru Matsuda	Center for Bioscience Research and Education, Utsunomiya University	
	B	Hitoshi Okamoto	RIKEN Brain Science Institute	
	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	○	Ryu Ueda	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	9
		Toshiyuki Takano	Drosophila Genetic Resource Center, Kyoto Institute of Technology	
		Masayoshi Watada	Graduate School of Science and Engineering, Ehime University	
		Takeshi Awasaki	Kyorin University, School of Medicine	
Silkworms	○	Yutaka Banno	Institute of Genetic Resources, Faculty of Agriculture, Kyushu University	10
		Toru Shimada	Graduate School of Agricultural and Life Sciences, The University of Tokyo	
		Zenta Kajiura	Faculty of Textile Science and Technology, Shinsyu 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 Center	12
Rice	○	Yutaka Sato	Genetic Strains Research Center, 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 Inovation Research Center University of Tsukuba	17
		Koh Aoki	Graduate School of Life and Environmental Sciences, Osaka Prefecture Unversity	
		Kentaro Yano	School of Agriculture, Meiji University	
Chrysanthemum	○	Makoto Kusaba	Laboratory of Plant Chromosome and Gene stock, Graduate School of Science, Hiroshima University	18

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Morning glory	○	Eiji Nitasaka	Faculty of Sciences, Kyushu University	19
		Atsushi Hoshino	National Institute for Basic Biology, National Institutes of Natural Sciences	
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	Quantitative Biology Center, RIKEN	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 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	
		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 Center	
Human and animal cells	○	Yukio Nakamura	Cell Engineering Division,RIKEN BioResource Center	29
DNA material	○	Takehide Murata	Gene Engineering Division, RIKEN BioResource Center	30

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

Information Center Upgrading Program

Organism, etc	Core Facility	Principal Investigator	Implementing Organization	Page
Information	○	Shoko Kawamoto	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	31
		Tetsuro Matsuzawa	Primate Research Institute, Kyoto University	
		Motomi Ito	Graduate School of Arts and Sciences, The University of Tokyo	
		Tsuyoshi Hosoya	National Museum of Nature and Science	

List of NBRP Implementing Organizations

Genome Information Upgrading Program

Organism, etc	Principal Investigator	Organization	Focus	Project Period	Page
Mice	Toyoyuki Takada	Genetic Strains Research Center, National Institute of Genetics	Genome resequencing of Japanese fancy mouse-derived JF1/Ms strain	FY2017	32
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.	FY2017	32
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	FY2016	—
Silkworms	Toru Shimada	The University of Tokyo	Genome Re-sequencing of Diverse Strains of *Bombyx mori* and *B. mandarina* (2)	FY2016	—
Algae	Yuu Hirose	Toyohashi University of Technology	Genome sequencing project of heterocystous cyanobacteria in the NIES collection	FY2016	—
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	FY2015	—
Drosophila	Shu Kondo	Genetic Resource Center, National Institute of Genetics	Genome sequencing of diverse *Drosophila* species (II)	FY2015	—
Silkworms	Toru Shimada	The University of Tokyo	Genome Re-sequencing of Diverse Strains of *Bombyx mori* and *B. mandarina*	FY2015	—
Lotus	Shusei Sato	Graduate School of Life Sciences, Tohoku University	Generation of high quality genome sequence of Gifu accession of *Lotus japoncius* to accelerate NBRP resource application	FY2015	—
Pathogenic microorganisms	Takashi Yaguchi	Chiba University	Maintenance of whole genome sequences on related species of *Aspergillus fumigatus*	FY2015	—
Rice	Nori Kurata	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	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	FY2014	—
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*	FY2014	—
Drosophila	Shu Kondo	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	Genome sequencing of diverse Drosophila species	FY2014	—
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	FY2012	—
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	FY2011	—
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	FY2010	—
Japanese macaques	Tadashi Isa	National Institute for Physiological Sciences, National Institutes of Natural Sciences	Japanese macaque genome sequencing	FY2010	—
Medaka	Kiyoshi Naruse	National Institute for Basic Biology, National Institutes of Natural Sciences	Establishment of polymorphism information of medaka inbred strains	FY2010	—
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	FY2009	—
Wheat	Yasunari Ogihara	Kihara Institute for Biological Research, Yokohama City Universty	Full-length cDNA resources of common wheat	FY2009	—
Tomato	Erika Asamizu	Gene Research Center, Graduate School of Life and Environmental Sciences, University Tsukuba	Micro-Tom BAC end sequencing	FY2009	—

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Genome Information Upgrading Program

Organism, etc	Principal Investigator	Organization	Focus	Project Period	Page
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	FY2008	—
Tomato	Koh Aoki	Kazusa DNA Research Institute	Enhancing tomato resources by sequencing Micro-Tom full-length cDNA	FY2008	—
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, Research Organization of Information and Systems	Genome and property information for the quality control of *Drosophila* strains	FY2007	—
Arabidopsis	Masatomo Kobayashi	Experimental Plant Division, RIKEN BioResource Center	Sequence analysis of full-length cDNAs of *Thellungiella halophila* as new *Arabidopsis* resources	FY2007	—
Wheat	Yasunari Ogihara	Kihara Institute for Biological Research, Yokohama City University	Full-length cDNA resources of bread wheat	FY2007	—

Fundamental Technology Upgrading Program

Organism, etc	Principal Investigator	Organization	Focus	Project Period	Page
Drosophila	Shu Kondo	National Institute of Genetics	Development of new technologies for stable maintenance of *Drosophila* stocks	FY2017	33
Rice	Yutaka Sato	Genetic Strains Research Center, National Institute of Genetics	Development of protocols for efficient gene transfer and genome editing in wild species of rice.	FY2017	33
Paramecium	Masahiro Fujishima	Graduate School of Science and Technology for Innovation, Yamaguchi University	Development of reliable cryopreservation method for *Paramecium* genus	FY2017	34
Drosophila	Toshiyuki Takano	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*	FY2016	—
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	FY2016	—
Mice	Atsushi Yoshiki	Experimental Animal Division, RIKEN BioResource Center	Fundamental technology development of genome editing for the establishment of intractable disease models	FY2016	—
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	FY2014	—
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	FY2012-2013	—
Drosophila	Ryu Ueda	Genetic Resource Center, National Institute of Genetics, Research Organization of Information and Systems	Development of cryopreservation method of Drosophila strains	FY2012-2013	—
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	FY2010-2011	—
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	FY2007-2009	—
DNA (animal/plant/ microbial)	Masatomo Kobayashi	Experimental Plant Division, RIKEN BioResource Center	Development of long-term preservation technology for genetic resources	FY2007-2009	—
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	FY2007-2008	—

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 and plants) that are essential experimental materials for life science research. In order to meet current scientific demands, the project also aims to increase the value of bioresources via addition of genome information and development of fundamental technologies for preservation and other necessary procedures. In addition, the information center will be upgraded in order to promote dissemination of information regarding the whereabouts and biological characteristics of bioresources.

Background

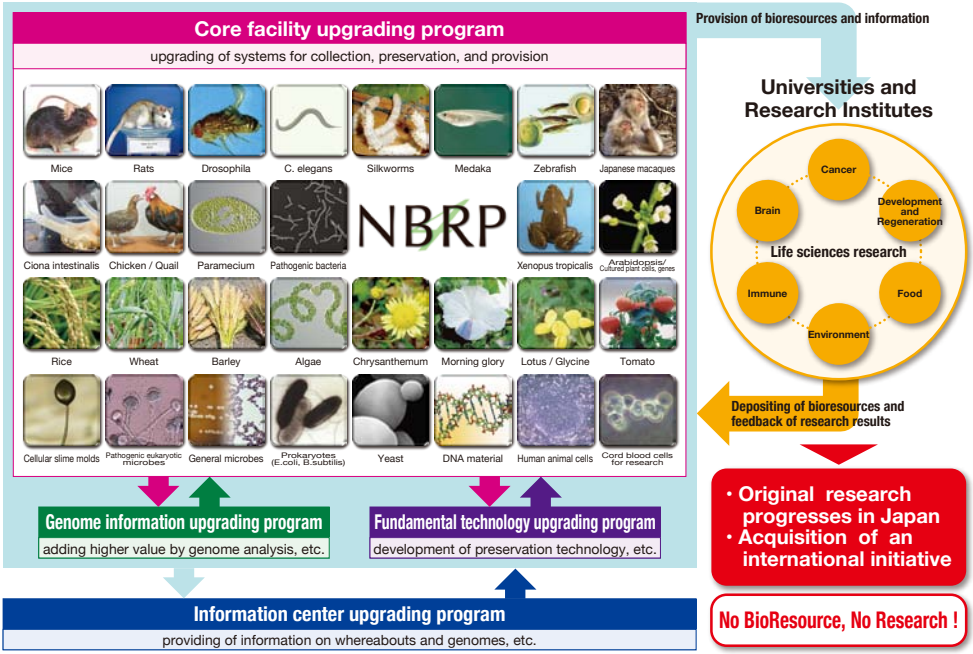
Based on the Plan for Promotion of Medical Research and Development of the Healthcare Policy approved by the Cabinet in 2014, operation of the NBRP was transferred to the Japan Agency for Medical Research and Development (AMED) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) 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 term of the NBRP (FY2017 ~ FY2021) to promote strategic collection and utilization of the bioresources.

Project Aims



CORE FACILITY UPGRADING PROGRAM Mice

Core Facility : Experimental Animal Division, RIKEN BioResource Center
Principal Investigator : Atsushi Yoshiki FAX : +81-29-836-9010
Contact site : animal@brc.riken.jp
URL : http://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, RIKEN BioResource 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(7621):508-514, 2017, *Nat Commun* 8:15475, 2017, *Nat Genet* 49:1231-1238, 2017

Objectives

- Collection to meet the social and research needs
- Quality of the world highest standard
- Role of the International Hub

International collaboration

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

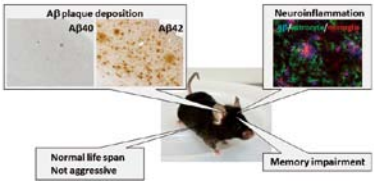
Asian Mouse Mutagenesis & Resource Association, AMMRA
http://www.findmice.org/

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

Key Strains/Studies

● 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

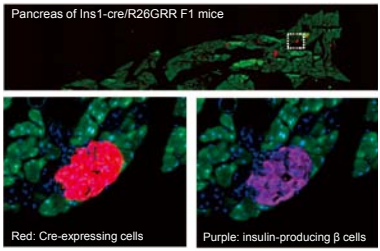


Courtesy of Drs. Takaomi C. Saido and Takashi Saito

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

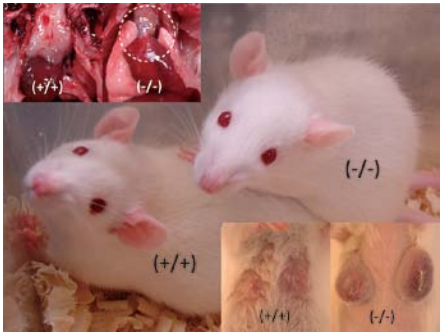
Overview

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.

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.

Various rat strains deposited to NBRP-Rat



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

Key Strains/Studies

So far, 836 different strains have been deposited to NBRP-Rat and animals have been supplied to researchers in 1,174 cases. 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.

● 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.

CORE FACILITY UPGRADING PROGRAM Japanese macaques

Core Facility : Kyoto University Primate Research Institute
Principal Investigator : Katsuki Nakamura FAX : +81-56-65-6036
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.

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. They also have less genetic mutation than other macaques that inhabit a wide area throughout 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.

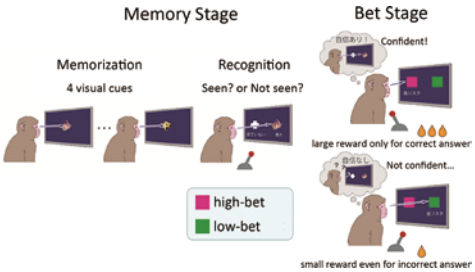
Until the start of Phase 1 of NBRP, there had been no major purpose-breeding plan for Japanese macaques. However, given future research trends, there is an obvious need for monkeys raised under supervision with records of age, growth process and genealogy. This is the reason why the current project was started as a joint effort between neuroscientists and primate researchers.

In Phase 4, the core facility, Kyoto University Primate Research Institute, keeps promoting the project, jointly with the sub center, National Institute for Physiological Sciences.

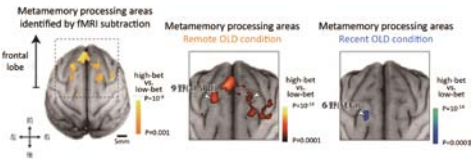
Key Strains/Studies

The following are findings obtained by studies using Japanese macaques:

- the direct neurophysiological evidence for psychological models of dual-task interference and capacity limitations (Watanabe and Funahashi, Nature Neuroscience 2014).
- the potential contribution of the nucleus accumbens to movement control after spinal cord injury (Nishimura, et al. Science 2015).
- the first demonstration of modeled vocal tics in Tourette syndrome utilizing PET imaging (McCairn, et al. Neuron 2016)
- the first report on a non-human primate that spontaneously exhibited autistic traits with rare coding variants linked to human neuropsychiatric disorders (Isoda, et al. Sci. Adv. 2016).
- the discovery of the prefrontal brain areas essential for meta mnemonic decision-making via fMRI (Miyamoto, et al. Science 2017)



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.



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.

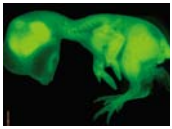
CORE FACILITY UPGRADING PROGRAM Chicken / Quail

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 : http://www.agr.nagoya-u.ac.jp/~nbrp/en/index.html

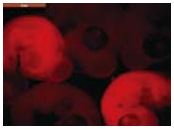
Overview

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 of the MEXT.

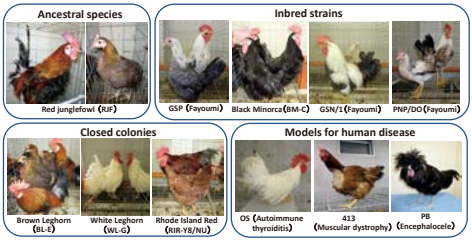
The ABRC develops the stable system to maintain, preserve and distribute chicken and quail resources. We also collect novel resources, develop them to resources of high global standard under strict genetic control, and distribute them to the community of scientists. We construct the database of the resources, 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).



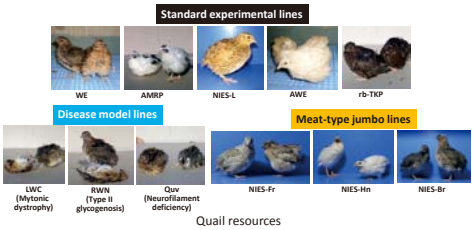
pLSi/ΔAeGFP-TG chicken



PGK:H2B-chFP-TG quail



Chicken resources



Quail resources

Key Strains/Studies

The ABRC distributes 33 strains and/or lines of chickens including the red junglefowl (the wild ancestor of domesticated chickens), inbred strains, and models for human diseases, and 22 lines of Japanese quail including standard lines and a variety of plumage mutants. Moreover, we distribute transgenic chicken and quail lines that express fluorescent proteins.

GSN/1

A highly inbred strain originated from the Fayoumi chicken breed native to Egypt. This has been maintained as a closed colony for more than 30 years. Skin grafts are acceptable between different individuals. The genotyping of microsatellite DNA markers revealed that 50 loci used for genetic monitoring are all fixed in the homozygous condition, indicating that this strain is very suitable for experiments for which high reproducibility and accuracy are required.

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.

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.

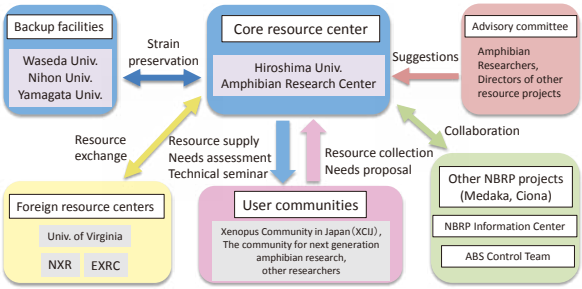
CORE FACILITY UPGRADING PROGRAM Xenopus tropicalis

Core Facility : Amphibian Research Center, Hiroshima University
Principal Investigator : Hajime Ogino FAX : +81-82-424-0739
Contact site : oginohaj@hiroshima-u.ac.jp
URL : http://home.hiroshima-u.ac.jp/amphibia/xenobiores/

Overview

Xenopus tropicalis is a recently developed amphibian model system that has characteristics suitable for genetic studies, such as a compact diploid genome (nearly half size of the human genome) and a short generation time (4–6 months). The genome project has revealed that more than 79% of the genes involved in human diseases are present as orthologues in this species. The gene functions can be easily examined by CRISPR-Cas9 system, which disrupts 80~99% of the target genes in founder embryos. Transgenesis also works quite efficiently with I-SceI meganuclese method, in which introduced transgenes are transmitted to offspring from the founder animals.

Currently our main resources are four inbred wild-type strains, Nigerian A, Nigerian H, Golden, and Ivory Coast. We are also collecting transgenics useful for live-imaging of stem/differentiated cells. We are supplying 3000~6000 frogs and tadpoles to researchers and educators every year. Genomic DNA, RNA, and marker gene plasmids are also available as part of the resources.



Core resource center, backup facilities, outside collaborators, and user communities

Key Strains/Studies

Main resources and research examples

1. Nigerian A strain

The inbred wild-type strain used for the genome-sequencing project.

2. Nigerian H strain

An easy-breeding derivative of Nigerian A.

3. Golden strain

A robust, inbred wild-type strain genetically close to Nigerian A/H.

4. Ivory Coast strain

A robust, inbred wild-type strain genetically diverged from Nigerian A/H.

- **Genome-sequencing project**

  Hellsten, U. et al. Science, 328: 633-636 (2010).

- **Analysis of genetic distances among inbred wild-type strains**

  Igawa, T. et al. PLoS One, 10: e0133963 (2015).

- **Gene targeting using CRISPR-Cas9 system**

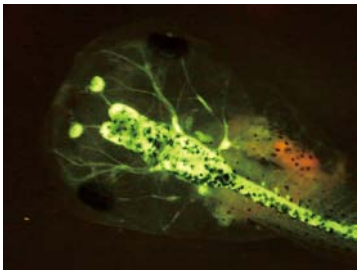
  Shigeta, M. et al. Genes Cells, 21: 755-771 (2016).

- **Transgenesis**

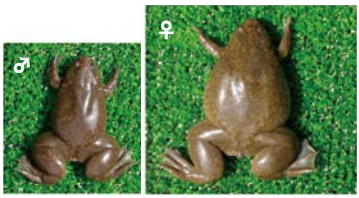
  Ogino, H. et al. Nat. Protoc. 1: 1703-1710 (2006).

- **ChIP-seq analysis**

  Yasuoka, Y. et al. Nat. Commun. 5: 4322 (2014).



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



Xenopus tropicalis **(Nigerian H strain)**

Core Facility : RIKEN Brain Science Institute
Principal Investigator : Hitoshi Okamoto FAX : +81-48-467-9714
Contact site : hitoshi@brain.riken.jp
URL : http://www.shigen.nig.ac.jp/zebra/

Overview

Zebrafish is widely used as a model vertebrate in which genetic approaches can be performed. The genomic information and techniques for embryology have been accumulated and now zebrafish plays an important role in basic biology and also a model for human diseases.

The number of zebrafish researchers in Japan is increasing. Accordingly, the number of mutant lines and transgenic lines made in Japan is also rapidly increasing. 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.

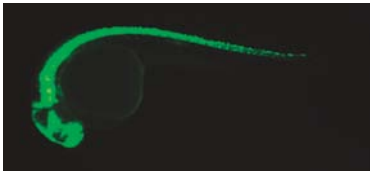
Key Strains/Studies

RIKEN (Hitoshi Okamoto)

Strain: dao:cre-mCherry; vglut2a:loxP-DsRed-loxP-GFP

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.

Amo et al., Neuron, 87 1034-1048 (2014)

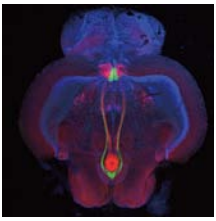


National Institute of Genetics (Koichi Kawakami)

Strain: 600 Gal4-expressing transgenic lines and UAS lines

In these lines, a modified yeast transcription factor Gal4FF is expressed in specific tissues, cells and organs. By crossing these with UAS fish, a desired gene can be expressed in a desired place.

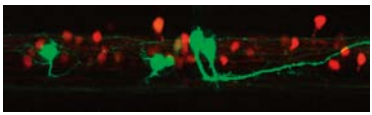
Asakawa, K. et al. Genetic dissection of neural circuits by Tol2 transposon-mediated Gal4 gene and enhancer trapping in zebrafish. Proc. Natl. Acad. Sci. USA 105, 1255-1260 (2008)



National Institutes of Natural Sciences (Shinichi Higashijima)

Strain: chx10:loxP-DsRed-loxP-GFP

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. Kimura et al., J Neurosci. May 24; 26:5684-97. 2006.



CORE FACILITY UPGRADING PROGRAM Medaka

Core Facility : National Institute for Basic Biology
Principal Investigator : Kiyoshi Naruse FAX : +81-564-55-7580
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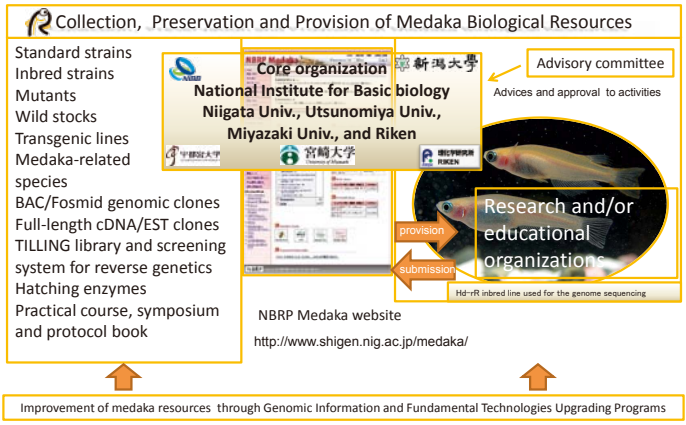
URL : http://www.shigen.nig.ac.jp/medaka/
http://www.nibb.ac.jp/bioresources/

Overview

Medaka has a history of over 100 years as an experimental animal. Many bioresources have been accumulated by the enormous efforts of the predecessors. Genomic resources such as BAC / Fosmid / 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. In the 4th term of NBRP, collection, preservation, and provision of medaka resources are carried out by National Institutes for Basic Biology (NIBB), Niigata University and Utsunomiya University and the backup preservation of the clone and the frozen sperm is handled by Miyazaki University and the RIKEN. These five 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. While looking at research and educational trends, we will advance the project management that goes a half step ahead.



Key Strains/Studies

Major possessions and research examples

● **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) ● **We are storing and providing closely related medaka species** (Celebes medaka, Indian medaka, Javanese medaka etc.).

Identification of the first sex-determining gene, *Dmy*, in non-mammmalian vertebrates, Identification of a novel gene *Gsdf* as the male initiator and male-determining gene. Determination of the medaka genome sequence, Identification of causal genes of mutants (body color mutants, cystic kidney disease, double anal fins etc.) Development of human disease models such as melanoma, Parkinson disease etc. Discovery of a switch gene determining the sex of germ cells, Foxl3, Elucidation of the molecular neural basis for mate choice and social interactions, Toxicity test using medaka embryos and adults. Currently, about 20% of the total shipments of fish is to overseas (USA, Germany, Spain, Canada, Korea, China etc.).

CORE FACILITY UPGRADING PROGRAM Ciona intestinalis (Type A)

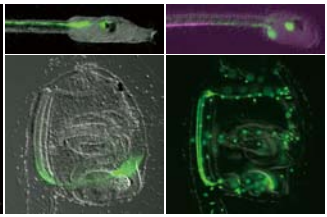
Core Facility : Shimoda Marine Research Center, Univerisity of Tsukuba
Principal Investigator : Yasunori Sasakura FAX : +81-558-22-0346
Contact site : sasakura@shimoda.tsukuba.ac.jp
URL : http://marinbio.nbrp.jp/
URL : http://www.shimoda.tsukuba.ac.jp/

Overview

Marine invertebrates are excellent materials for various subjects of researches including embryogenesis, evolution, reproduction and neurophysiology. The marine organism, *Ciona intestinalis*, has been selected as an object of the National BioResource Project.

Ciona intestinalis: Ascidians are invertebrate chordates that are the closest relatives of vertebrates. Ascidians and vertebrates share the body plan including the dorsal neural tube, notochord, pharyngeal gill and endostyle/thyroid gland. *Ciona intestinalis* is the model species of ascidians because of the determination of its 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 conduct 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 the genetic technologies, various transgenic and mutant lines have been accumulated which are splendid resources for studying gene functions. This Bioresource project involves collecting, maintaining and supplying wild types, transgenic/mutant lines and plasmid DNAs used in *Ciona* studies.

Wild type (Closed colony)



GFP and Kaede transgenic lines

The website for ordering transgenic lines

Key Strains/Studies

- **Wild type** (Closed colony), GFP-expressing marker lines, Kaede-expressing lines, enhancer trap lines, Cell cycle indicator (FUCCI) lines, Mutants, Reporter gene expression vectors, Tissue-specific TALEN expression vectors

- Acquisition of the facial sensory organs is the major event of vertebrate evolution. Ascidians possess the sensory systems homologous to vertebrate sensory organs. Using NBRP *Ciona*, the molecular mechanisms responsible for the formation of the sensory organs such as nose, were identified, to show the evolutionary history of chordates. For example, *Ciona* possesses the neurons that resembles our sensory neurons in the nose. (Abitua et al., Nature 2015; Waki et al., Nat Commun 2015)
- The nervous system of *Ciona* is simple. The CNS of *Ciona* larva possesses as many as 100 neurons. We have collected many marker lines for the neural tissues. Using NBRP resources, the mechanisms of specification, morphogenetic movement and physiological functions of neural tissues were analyzed. For example, *Ciona* AMPA-type Glutamate receptor is responsible for the formation of sensory organs and metamorphosis. (Hirai et al., PNAS 2017; Ikeda et al., 2016; Ogura et al., Dev Cell 2016; Nakamura et al., Dev Dyn 2014)

The basic use of *Ciona intestinalis* does not require any special equipment. You can culture *Ciona* in your laboratories with commercially available artificial sea water.

CORE FACILITY UPGRADING PROGRAM Drosophila

Core Facility : Genetic Resource Center, National Institute of Genetics
Principal Investigator : Ryu Ueda Fax : +81-55-981-6825
Contact site : rueda@nig.ac.jp
URL : http://www.shigen.nig.ac.jp/fly/nigfly/index.jsp

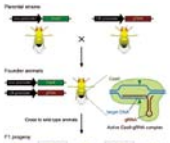
Overview

The purposes of this program are to comprehensively maintain, manage, and widely distribute to research communities the genetic resources of Drosophila, such as (1) mutant strains including genome-editing strains (FlyCas9) and RNAi of *Drosophila melanogaster*, which are useful as a basis or platform for life science studies, and (2) mutant strains of the wild species of Drosophila or related species of Drosophila melanogaster, which are important for evolution and biodiversity studies. To this end, five organizations —the National Institute of Genetics, Kyoto Institute of Technology, Ehime University, Kyorin University, and Miyazaki University— are to constitute a consortium for the joint project. By the third stage in the next 15 years, the consortium aims to assume international responsibility as the fully developed, world's largest stock center by collecting the resources and improving the quality according to the needs of the times; thus we will contribute to the acceleration of leading-edge research activities in user communities.

Stock maintenance and trains

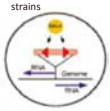
Drosophila melanogaster

Drosophila culture: Culture bottle & fly stocks in incubator



Genome-editing related strains

D. melanogaster basic strains



NP, Cas9, DrosDel, FRT, RNAi, many others

Other species Mutant & standard strain

Some examples among extensive database

Key Strains/Studies

National Institute of Genetics

● RNAi mutant strains (18,351 for 9,989 genes) ● FlyCas9 strains (33 strains) Kyoto Institute of Technology (Total 29,200 strains) ● Basic strains (3,700 strains) ● NP strains (4,200 strains) ● GS strains (6,800 strains) ● FRT-lethal strains (1,200 strains) ● MARCM strains (2,200 strains) ● DrosDel strains (1,700 strains) ● Imaging strains (1,300 strains) ● Humanized strains (800 strains) ● Others (7,300 strains)

Ehime University

● Japanese wild-type strains (59 species, 909 strains) ● Asian wild-type strains (47 species, 196 strains) ● Others (69 species, 425 strains)

Kyorin University

● Regional strains (wild type, except for *D. melanogaster* (70 species, 783 strains)) ● Mutant strains (except for *D. melanogaster* (12 species, 432 strains)) ● Transgenic strains (2 species, 32 strains)) ● Genome-sequenced species (11 species, 15 strains)

Powerful model system for the study of human diseases.

More than 70% of human disease-related genes are conserved between mammals and *D. melanogaster*, allowing us to clarify a molecular pathway using *D. melanogaster* (Nature 542: pp. 246-250, 2017; Trends Genet. 33: pp391-398, 2017).

Speciation Study

By applying the advanced *Drosophila* research techniques to the classical evolutionary studies such as lethality, sterility and sex ratio distortion resulted in terms of interspecific hybrids between closely-related species, understanding of the causative genes and the speciation mechanisms can be anticipated (Trends Genet. 33: pp68-80, 2017; Science 350: pp. 1552-5, 2015; Genome Res. 24: pp. 797–808, 2014; Dev. Cell 27: pp. 412-24, 2013).

CORE FACILITY UPGRADING PROGRAM Silkworms

Core Facility : Graduate School of Agriculture, Kyushu University
Principal Investigator : Yutaka Banno TEL/FAX : +81-92-624-1011
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URL : http://www.shigen.nig.ac.jp/silkwormbase/

Overview

The Mendel's laws of genetics were rediscovered and recognized widely in the early 20th century. During that period, Japan was the most developed country in sericulture in the world and reared 40 billion silkworms per year. Several spontaneous mutants of silkworm were found in various places in Japan, which were introduced to some universities and research centers across the country. These mutants are the core resources of NBRP silkworms. These genetic resources have been contributing to the development of sericulture and genetics. Recently, it was recognized that some silkworm mutants could be used as models for some human genetic diseases. For example, skunk, which is a silkworm mutant, can be used as a model for the human genetic disease, isovaleric acidemia; because skunk lacks the same gene homolog with a gene responsible for isovaleric acidemia, which codes for a metabolic enzyme. Lemon lethal, another silkworm mutant, shows the same symptoms as that of Parkinson's disease. This mutant can be kept alive after administering dopamine. We can also artificially develop a new silkworm mutant, which shows classic symptoms of diabetes. These silkworm mutants may be promising in drug development for some human genetic diseases. Therefore, silkworms can be used for medical and pharmaceutical research as an alternative animal model for detecting human genetic diseases because it would be remarkably inexpensive compared with mammals. We support the beginners of silkworm use with rearing and other techniques. We also supply silkworms to users in the field of education and cultural activity as well as to researchers.

Roles of organizations participating in NBRP silkworms

- Kyushu University: Collection, maintenance, and supply of silkworm strains.
  - We collected approximately 800 strains, which is the largest number in the world. We will develop novel useful mutants for research.
  - We established a method of safe and efficient maintenance of silkworm resources via cryopreservation using germplasm and sperm against disasters or accidents.
  - We supply silkworm strains all year round, including winter, and also supply mulberry leaves, as the need arises.
- Shinshu University: Collection, maintenance, and supply of wild strains.
  - Collection, maintenance, and supply of wild strains, such as *Antheraea yamamai*, *A. pernyi*, and *Samia cynthia pryeri*.
- University of Tokyo: Collection, maintenance, and supply of genome resources and cultured cells.
  - Upgrading and efficient maintenance of cDNA clones and genomic DNA libraries (Fosmid, BAC), and improving accessibility. Maintenance and supply of cultured silkworm cells from Phase 4.

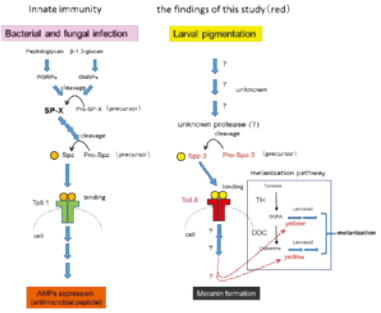
Key Strains/Studies

● p50 strain used as standard strain of academic material. ● Spontaneous mutants, showing various phenotypes (photos). ● Wild silkmoths inhabiting Japan ● Cultured cell lines of silkworm ● Lethal mutant strains as models of human genetic diseases

Various phenotypes of larval marking and cocoon color

Zebra marking

The silkworm mutant Zebra has a black stripe in each segment (right figure). A stripe pattern is often used for an aposematic or camouflage coloration to predators. Recently, a Spätzle family gene spz−3 was clarified to be responsible for the Zebra locus. Spätzle is known as a ligand of Toll receptor, which function in the innate immunity was revealed by novel prize winners in 2011, Dr. Hoffman and others. The recent report suggests that the spz−3 signal is received by Toll−8, which further induces melanization in the Zebra pattern. This result indicates that a part of innate immunity is co−opted to control the melanisation process in the larval pigmentation. Since there are many spz/Toll family genes in human cells, it is possible that some of them is related to melanaization in skin and hair. KonDo et al. (2017) PNAS, vol. 114, (31), 8336.

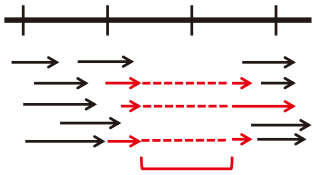


Core Facility : Tokyo Women's Medical University School of Medicine
Principal Investigator : Shohei Mitani FAX : +81-3-5269-7414
Contact site : mitani.shohei@twmu.ac.jp
URL : http://shigen.lab.nig.ac.jp/c.elegans/

Overview

One of the objectives of Phase 4 National BioResource Project of the AMED (Japan Agency for Medical Research and Development), which began in FY 2017, is to advance the collection, preservation, and provision of nematode strains for gene function analyses. The nematode *C. elegans* is a good model organism for life science research. Genome information has elucidated all the gene composition of chromosomes. Using the information, we have collected more than 8,000 deletion mutant strains. In the Phase 4 project, we continue to support genetic research on *C. elegans* by collecting and provision of deletion mutants, using the genome information. we will add Cre-recombinase transgenic strains, which are useful for conditional knockout analyses, and balancer strains, which are useful for maintenance and analyses of lethal and sterile mutants. Using these biological resources, genetic research is expected to be expedited very much.

Project management: The core facility for this project, Tokyo Women's Medical University School of Medicine collects deletion mutants by whole genome sequencing. After collection of the mutants (Fig. 1), we will distribute strains to the requesting researchers (Fig. 2).



Identification of deletions by whole genome sequencing

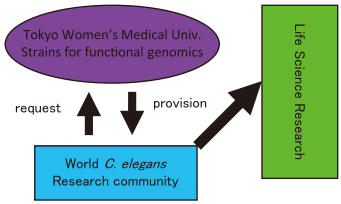
⬇

Confirmation of deletions by PCR and Sanger sequencing

⬇

Collection of deletion mutants

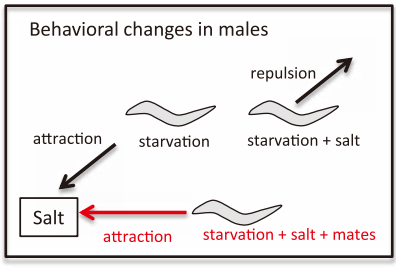
Research system using *C. elegans* strains



Key Strains/Studies

pdf-1 (tm1996)

One of the leading fields of research using *C. elegans* is analysis of learning and memory. Sammut *et al* (Nature **526**, 385 (2015)) used a pdf-1 (tm1996) mutant and showed that the gene is required for male sex-specific learning that animals are attracted to salt even if conditioned with salt and without food (Figure). Authors demonstrated that this learning is regulated by neurons MCM which are derived from glia by transdifferentiating to neurons at the larval stage.



Arabidopsis / Cultured plant cells, genes

Core Facility : Experimental Plant Division, RIKEN BioResource Center
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URL : http://epd.brc.riken.jp/en/

Overview

The small size and short life cycle of Arabidopsis make it an excellent model plant for experimental research. Since the sequencing of its genome was completed in December 2000, development and distribution of research resources such as gene-disrupted mutants and full-length cDNA clones are supported by the collaborative works of international research communities. In addition, plant researchers are now utilizing the growing pool of Arabidopsis research findings to the betterment of society, such as the improvement of food production. The RIKEN BioResource Center (BRC) is contributing to efforts for tackling challenges related to food, the environment, and materials production not only by supplying researchers with seeds of gene-disrupted mutants, full-length cDNA clones, and other Arabidopsis stocks, but also by enhancing its resource databases, organizing technical trainings, and engaging in other productive efforts to aid plant research. RIKEN BRC also supports research involving cultured plant cells and plant genes by storing and supplying model plant resources developed in Japan, and by disseminating information to research communities through coordination with other organizations participating in NBRP.

Key Strains/Studies

- **Arabidopsis transposon-tagged mutants (approx. 16,000 lines) and FOX mutants (approx. 20,000 lines)**

  These can be used as gene-disrupted mutants and over-expression mutants, respectively.

- **Arabidopsis full-length cDNA (RAFL) clones (approx. 250,000 clones, including about 21,000 completely sequenced clones)**

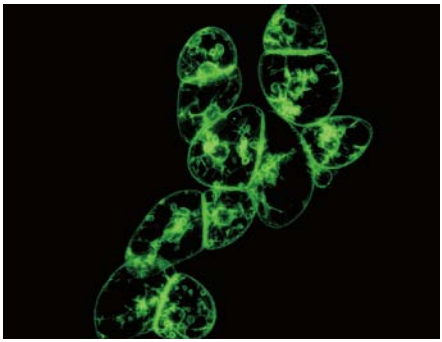
  These are standard resources used around the world.

- **Arabidopsis T87 cultured cells**

  These are the most frequently used Arabidopsis cells.

RIKEN BRC supplies its plant resources to approx. 2,000 laboratories and research groups in Japan and abroad for use in a broad range of research. One example is the research groups in Nara Institute of Science and Technology and Duke University, which utilize Arabidopsis full-length cDNA clones in research of key proteins that regulate differentiation and development of root tissues in Arabidopsis. The research results were published from Nature Plants in Feb. 2017.

Flower of agamous mutant



Tobacco BY-2 cells transformed with GFP

CORE FACILITY UPGRADING PROGRAM Rice

Core Facility : Genetic Strains Research Center, National Institute of Genetics
Principal Investigator : Yutaka Sato FAX : +81-55-981-6879
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URL : http://www.shigen.nig.ac.jp/rice/oryzabase/

Overview

Japan has some of the world's most valuable collections of rice genetic resources. The NBRP-Rice collects, preserves, and provides a wide variety of genetic resources of wild and cultivated rice as well as valuable information of them for rice researchers. Specifically, the following efforts will be made aiming to meet different needs in current research areas of rice science.

(1) Preservation and provision of worldwide collection of wild rice species (23 species, 1,700 accessions). Characterization and reclassification of the wild accessions. Development of DNA markers to classify the wild rice species.

(2) Collection of experimental rice strains derived from wild species such as chromosome segment substitution lines (CSSLs) and monosomic alien addition lines.

(3) Collection of MNU-induced mutants derived from several varieties.

(4) Open laboratory supporting TILLING analysis to identify mutations in MNU-induced mutants

(5) Creation and management of ORYZABASE database for releasing rice resource and genomics information

The National Institute of Genetics functions as the core facility, managing all projects and handling the practical aspects of the wild species rice projects. Kyushu university is responsible for collecting mutants induced by the chemical (MNU) and CSSL series of wild species.

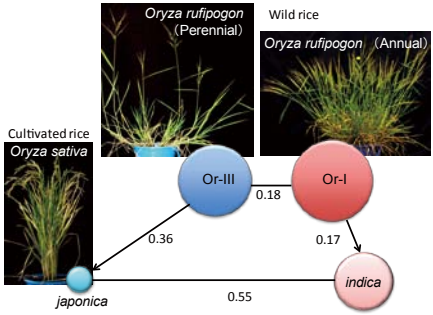
Locality map and details of wild rice accessions

Key Strains/Studies

- **Wild species rice strains**
  (approx. 1,700 strains)
- **MNU-induced mutant strains**
  (approx. 9,500 strains)
  (derived from Kinmaze, TC65, Kitaake, & Yukihikari)
- **Others including CSSLs of wild species**
  (approx. 5,000 strains)

Recent topics

NBRP-Rice preserves a wide range of wild rice species collected from around the world. Comparative genome analysis of these wild accessions and cultivars have revealed the origin of cultivation in the middle area of the Pearl River in southern China (Huang et al., Nature 490: 497–501, 2012).



Genetic diversity and population differentiation in cultivated rice and its wild progenitor

Core Facility : Graduate School of Agriculture, Kyoto University
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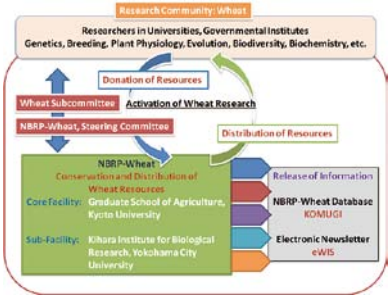
Overview

Wheat includes bread wheat, which is used to make bread and udon noodles, and macaroni wheat, which is used to make macaroni and other forms of pasta. The NBRP Wheat project stores and supplies wild species, landraces, and experimental strains of wheat and related species. It also collects and stores wild species and landraces that have not yet been archived, and stores and supplies EST and TAC clones of wheat. The project is implemented by the Graduate School of Agriculture, Kyoto University (core facility) and the Kihara Institute for Biological Research, Yokohama City University (sub-facility). The Wheat Subcommittee, which is organized by scientists who conduct wheat researches in Japan, supports the core team's work. The project's wheat resources can be requested online. The project members are also focusing on the characterization of DNA markers for use in gene isolation, and will release the resulting data in the NBRP section of the KOMUGI database.



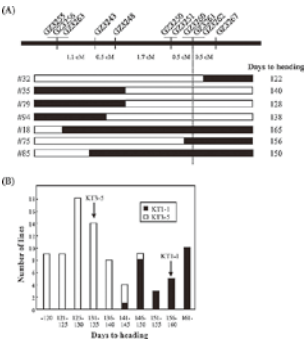
NBRP-Wheat, Project Implementation System

Key Strains/Studies

● Bread wheat aneuploids, ancestral species, landraces, full-length cDNA clones

Bread wheat is an allohexaploid species carrying three genomes (A, B, and D genomes) derived from diploid ancestral species. The main body of our genetic stocks is the aneuploids, the chromosome structural mutants, and the alloplasmic lines of a standard hexaploid wheat cultivar 'Chinese Spring'. Recent major advancement of wheat science is the exploration of genome sequence of the Chinese Spring wheat, which was has been led by the International Wheat Genome Sequencing Consortium (IWGSC). The draft sequences of the genes locating on each chromosome arm are currently available (IWGSC (2014) Science 345, DOI: 10.1126/science.1251788). In parallel, the BAC-based physical maps of wheat chromosomes are under construction and efforts are to be made to determine the sequences of the BAC contigs. Japanese team is in charge of the chromosome 6B (Kobayashi et al. (2015) BMC Genomics 16, DOI: 10.1186/s12864-015-1803-y). The genetic stocks of NBRP-Wheat are fully utilized in these genome projects.

On 18 July 2014, the IWGSC published in the international journal Science a draft sequence of the bread wheat genome.



A gene conferring early heading phenotype has been identified by utilizing the genome information of cereals.

The availability of genome-information of wheat and barley as the reference sequences has been changing the research environment in wheat. Gene identification by utilizing genome information is a feasible approach. The 'Early mutant' of a diploid what is known for its early heading nature for a long time and stored in a collection of induced mutants in NBRP-Wheat. Now we discovered that a deletion of a circadian clock gene *Phytoclock1* is responsible for the early heading phenotype (Mizuno et al. (2012) Genes Genet. Syst. 87, DOI: 10.1266/ggs.87.357).

Barley

Core Facility : Institute of Plant Science and Resources, Okayama University
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Overview

Barley is an important crop plant that serves many purposes, including malting, food, and animal feed. Diverse genetic resources of wild and cultivated barleys have been preserved, and a large range of experimental strains have been developed, particularly mutant strains. BAC libraries and cDNA resources have been developed for genomic analysis of barley, which is sequenced in high resolution.

Okayama University's Institute of Plant Science and Resources, preserves and supplies barley strains collected or developed originally, BAC libraries, and cDNA clones. The project also supplies filters for efficient selection of BAC clones and pooled DNA samples for PCR analysis. Moreover, the project distributes the world's first full length cDNA clones of barley (developed in the NBRP genome analysis program), and publishes their nucleotide sequences.

Diversity in barley spikes

Key Strains/Studies

- **Database publication and supply of approx.6,000 strains, including Haruna Nijo, a standard strain for genomic analysis**
- **cDNA clones: 5,000 (Haruna Nijo)**
- **BAC clones: 300,000 (Haruna Nijo) and 180,000 (wild barley)**

Haruna Nijo full length cDNA sequences are contributed to estimate gene regions on the draft barley genome sequence. 15 million SNPs are detected among haplotypes including Haruna Nijo sequenced by Okayama University. (IBSC 2012 Nature)

Barley is now being analyzed its agriculturally important genes, and the development of techniques for isolating and selecting those genes has a key challenge for researchers. Mutant lines and information to identity their responsible genes are provided from NBRP barley. The Okayama University project team has mapped Haruna Nijo and wild barley segregating populations approx. 3,000 markers generated from 3' EST resources. Among the loci segregating in the population, a major seed dormancy has been cloned and analyzed its function. The nucleotide sequence of dormancy is identified by using cDNA information and two sets of BAC libraries provided from NBRP barley. Strains from NBRP barley were also used for the molecular evolutionary analysis and the process of selection on short dormancy barley strains by brewing uses is also shown.

Germination after five weeks on dormant (left) and non-dormant (right) types of barley (Sato et al. 2016 *Nature Communications*)

CORE FACILITY UPGRADING PROGRAM Lotus / Glycine

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Overview

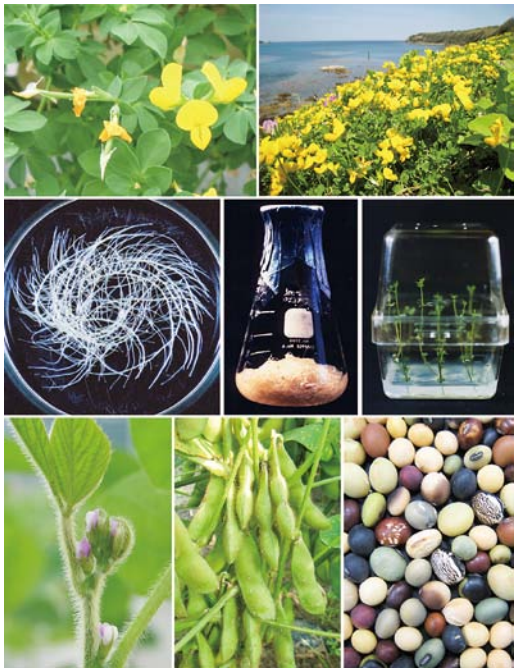
Legumes are cultivated and used as a vital source of protein from the tropics to the temperate zones, and they are also an important resource for research on such topics as the accumulation of secondary metabolites and symbiosis with microorganisms. *Lotus japonicus* (Japanese trefoil) is a perennial legume that grows naturally throughout many parts of Japan. It is widely used as a model plant for legumes because of such advantages as its small genome and short life cycle. Soybeans (*Glycine max*) have been grown as an important crop since ancient times, and a large amount of basic research has been conducted on them over the years. The *L. japonicus* resources and information that have been collected and developed are indispensable for improving the efficiency of a great variety of soybean- related research, including studies aimed at increasing soybean yields based on symbiosis with *Rhizobium*, and at enhancing the nutritional functions of soybeans.

This program features a new structure beginning from this year of 2017. As the representative institution, the University of Miyazaki handles the collection, preservation, and distribution of all resources, and supervises the project as the representative institution. Tohoku University, as a sub-institution, carries out the restructuring of resource information. We will rebuild and expand the fundamental information of collected resources towards strengthening maintenance of high quality resources and provision of functional information to users.

Key Strains/Studies

This project has preserved approximately 4,000 plant resources. The *L. japonicus* collection is mainly 3 experimental strains, 200 wild strains and Superroot derived from *Lotus corniculatus*, and a database is being built up based on this collection. The project has also preserved a variety of soybean strains, including wild strains and recombinant inbred lines. This project has collected more than 220,000 BAC, TAC and cDNA clones derived from *L. japonicus* Miyakojima MG-20 and soybean full-length cDNA clones derived from Norin No. 2.

The experimental strains, Gifu B-129 and Miyakojima MG-20, which are mainly used in research pertaining to root nodules (where the plant has a symbiotic relationship with microorganisms) and mycorrhiza formation. A number of important genes have been isolated through such research.



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

Overview

Tomato is an excellent model plant for studying fruit development. Tomato is considered as a model species of Solanaceae, and its genome sequence has determined by international consortium. In order to fully utilize the genome information, the core facility, University of Tsukuba, and a sub-facility, Osaka Prefecture University and Meiji University, launched on the tomato resource development program within the framework of the National BioResource Project. The University of Tsukuba, Osaka Prefecture University and Meiji University take charge of developing plant resource, DNA-level resource and resource database respectively.

Key Strains/Studies

The University of Tsukuba maintains more than 17,000 lines such as tomato wild varieties, tomato transgenic lines, and Micro-Tom mutant lines which were generated by ethylmethanesulfonate (EMS) treatment and gamma-ray irradiation (Figure 1 and 2). These materials are available through database 'TOMATOMA' that was developed by a collaboration with the National Institute of Genetics. Osaka Prefecture University maintains 627,312 clones such as full-length cDNA clones, tomato BAC clones and tomato promoter clones. The full-length cDNA clones are also available upon request. Information of full-length cDNA sequences are available at full-length cDNA database KaFTom, EST database MiBASE and integrated omics database TOMATOMICS, which were developed by Meiji University and Kazusa DNA Research Institute. In 2016-2017, several papers using our resource were published in *Cell* 169.6 (2017): 1142-1155, *Nature Biotechnology* 35.5 (2017): 441-443, *Plant physiology* 171.3 (2016): 1821-1836.

Figure 1. A model cultivar, Micro-Tom Japan

Figure 2. Mutant population based on Micro-Tom Japan

Chrysanthemum

Core Facility : Laboratory of Plant Chromosome and Gene stock,
Graduate School of Science, Hiroshima University
Principal Investigator : Makoto Kusaba FAX : +81-82-424-0738
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URL : http://shigen.nig.ac.jp/chrysanthemum/index.jsp

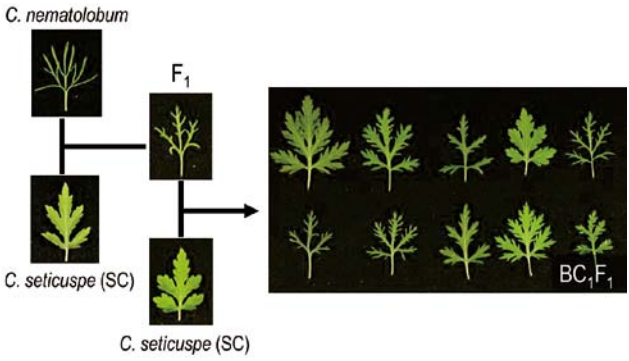
Overview

Various *Chrysanthemum* plants and related species.

Asteraceae, which consists of more than 23,000 species, is one of the largest families in angiosperm and distributed worldwide except Antarctica. Among its members, the genus Chrysanthemum has evolved in the Eurasian continent and its surrounding regions and contains autoploid species from diploid to decaploid endemic to Japan. The cultivated chrysanthemum is unsuitable for genetic analysis due to its autohexapolidy and self-incompatibility. We discovered a self-compatible mutant from a natural population of the diploid *Chrysanthemum* species *C. seticuspe*. We have developed a model strain by selfing this mutant. The model strain is useful to elucidate various properties in cultivated chrysanthemum at molecular level because its flowering and inflorescence morphological properties resemble those of the cultivated chrysanthemum and the transformation method has been established. Furthermore, because hybridization between *Chrysanthemum* species is easy, *C. seticuspe* is expected as a platform for molecular analysis of genetic diversity in the genus *Chrysanthemum*. NBRP Chrysanthemum resources include chrysanthemum and related species with various morphology and characteristics. These bioresources are maintained in the field, pots, or *in vitro* to be provided to researchers and breeders.

The model strain in the genus *Chrysanthemum* Gojo-0

Key Strains/Studies



***C. nematolobum* (left) and the progeny of an interspecific hybrid with the self-compatible *C. seticuspe* (right).**

The progeny of interspecific hybrid between *C. nematolobum*, a diploid species with very narrow leaf, and the self-compatible *C. seticuspe* show segregation in leaf morphology.

CORE FACILITY UPGRADING PROGRAM 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. Moreover, near-complete genome sequences of the Japanese morning glory were published in 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. Under the NBRP Morning Glory project, Kyushu University (core organization) and the National Institute for Basic Biology (sub-organization) are building up stock centers for the mutant strains, DNA clones, mutated gene information, and other resources. It is expected that the Japanese morning glory will become one of Japan's leading bioresources.

An *efp* mutant with defects in anthocyanin accumulation (left). A wild-type (right).

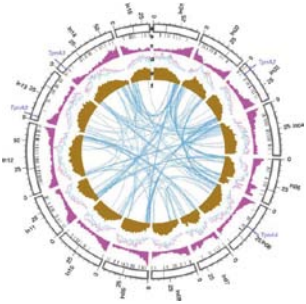
Key Strains/Studies

Tokyo Kokei Standard (TKS)

Dr. Yo Takenaka of the National Institute of Genetics selected this strain as a wild-type Japanese morning glory, and developed into a standard strain through repeated selfing. This strain was used in the genome project and to construct the DNA clones supplied in this project. The transposition of *Tpn*-transposons is suppressed.

Violet

This is widely used as a standard strain for plant physiology research. It bears flower buds that are highly sensitive to short-day conditions. It includes the mutations *magenta* (*mg*) and *dragonfly* (*dg*). This strain can be used for mapping of mutations using nucleotide polymorphisms between TKS and Violet.



Schematic drawing of morning glory genome: 15 surrounding open lines correspond to pseudo chromosomes.

The genome sequence of the Japanese morning glory (TKS strain) was decoded. It covers 98% of the 750 Mb genome and has one of the highest quality in fully sequenced plant genome. Scaffolds were combined into 15 pseudo chromosomes using RAD markers created by the polymorphisms between TKS and Africa strain. The candidate gene for *contracted* mutation were also identified with the information of classical genetic map and this genome. (Hoshino et al. Genome sequence and analysis of the Japanese morning glory Ipomoea nil. Nature Commun. 7, 13295, 2016)

contracted (*ct*): A plant hormone (brassinosteroid) biosynthesis mutant.

Core Facility : National Institute for Environmental Studies (NIES)
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Contact address : kawachi.masanobu@nies.go.jp
URL : http://www.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

Algal bioresources include evolutionarily diverse organisms, such as prokaryotic cyanobacteria, photosynthetic eukaryotes except for the so-called land plants, as well as non-photosynthetic relatives (protozoa) (Fig. 1 & 2). These algae are also used for a wide-rang of researches such as life sciences, evolutionary and environmental studies. Selected algae are designated as model organisms, which are used for specific researches (for example photosynthesis and sexual reproduction). The National Institute for Environmental Studies (core facility: collection, preservation and supply of microalgae, collection acronym: NIES), the Kobe University (sub-facility: collection, preservation and supply of macroalgae, collection acronym: KU-MACC), and the Hokkaido University (sub-facility: backup of algal bioresouces) aim to be culture collections with the highest quality algal bioresources by collecting important species, adding valuable information to the strains maintained, and creating a quality control system.

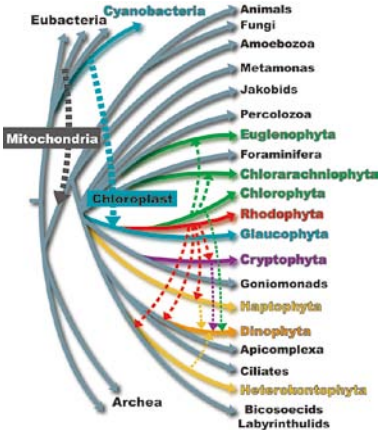

Fig. 1. Tree of life
Various phylogenetic groups are found in the eukaryotes. Colored branches indicate the algal groups, and the broken lines designate the organisms from which the chloroplast originated. The chloroplasts of Chlorophyta, Rhodophyta, and Glaucophyta are all originated from cyanobacteria. In contrast, the chloroplasts of the other algal groups are originated from particular chlorophyte or rhodophyte.

Key Strains/Studies

A diverse collection of algae including approximately 4,000 strains are available for the purposes of education, research and development, and have been used for a diverse range of researches as follows:

- **Model organisms (photosynthesis, sexual reproduction, cell division, etc.):** *Thermosynechococcus elongatus* (NIES-2133/BP-1), *Cyanidioschyzon merolae* (NIES-3377/10D), *Chlamydomonas reinhardtii* (NIES-2235/C-9), *Ectocarpus siliculosus* (KU-1371).
- **Evolutionarily important species:** *Mesostigma viride* (NIES-296), charophyte (NIES-1601).
- **Harmful algal species:** *Microcystis aeruginosa* (NIES-44), *Chattonella marina* (NIES-3).
- **Test strains for bioassay:** *Pseudokirchneriella subcapitata* (NIES-35), *Cyanobium* sp. (NIES-981).
- **Commercially useful strains:** *Botryococcus braunii* (NIES-836), *Porphyridium* sp. (NIES-1035), *Chlorella vulgaris* (NIES-227).

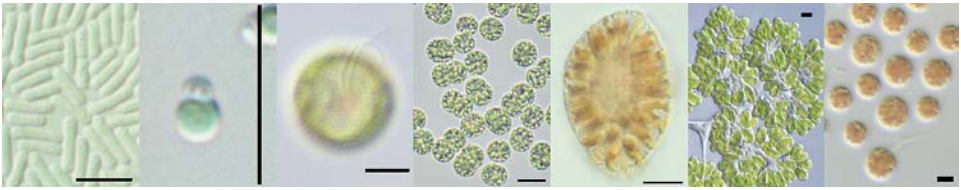

Fig. 2. Light micrographs of various algal resources.
From left side. *Thermosynechococcus* (NIES-2133), *Cyanidioschyzon* (NIES-3377), *Mesostigma* (NIES-296), *Microcystis* (NIES-44), *Chattonella* (NIES-3), *Botryococcus* (NIES-836), *Porphyridium* (NIES-1035). Scale bar = 10 μm.

Paramecium

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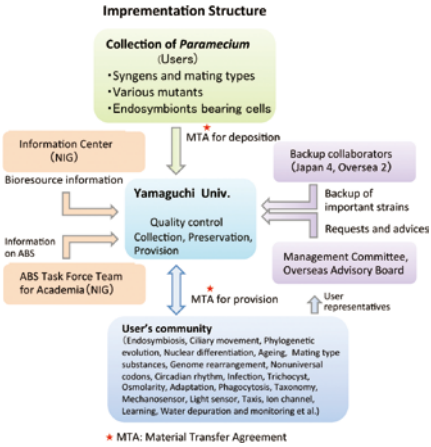
Overview

The ciliate *Paramecium* species are model organisms used for various researches on eukaryotes. Although 47 species are described, only 29 species are currently collectable from fields. NBRP *Paramecium* maintains over 740 strains belonging to 24 species. In addition, this project is responsible for the preservation of *Paramecium* species. Important strains, which are highly demanded by users, have been maintained by backup of Japan and overseas researchers in preparation for disasters.

NBRP *Paramecium* is acting as a core facility for this bioresource in the world, and provide related information of each strain. Strains that have been used for genome or transcriptome studies and those bearing endosymbionts are also available. The spread of shares and use is done through website updates, various exhibitions, and technical lecture meetings.



Collected species (24)	Sept. 2017
P. caudatum	*P. primaurelia*
P. multimicronucleatum	*P. biaurelia*
P. jenningsi	*P. triaurelia*
P. nephridiatum	*P. tetraurelia*
P. bursaria	*P. pentaurelia*
P. putrinum (= *P. trichium*)	*P. sexaurelia*
P. duboscqui	*P. septaurelia*
P. calkinsi	*P. octaurelia*
P. woodruffi	*P. novaurelia*
Not yet collected species (5)	*P. decaurelia*
P. polycaryum	*P. undecaurelia*
P. africanum	*P. dodecaurelia*
P. schewiakoffi	*P. tredecaurelia*
P. chlorelligerum	*P. quadecaurelia*
P. buetschlii	*P. sonneborni*

Key Strains/Studies

- ***P. caudatum* strain My43C3d (NBRP PC121015B)**
- ***P. multimicronucleatum* strain M03c4 (NBRP PM024002A)**
- ***P. tetraurelia* strain 51 (NBRP PA040011A)**
- ***P. tetraurelia* strain d4-2 (NBRP PA040015A)**

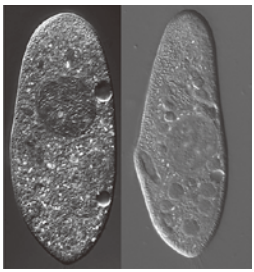
Macronuclear genomes of these four strains of three species were sequenced (Aury, JM et al. Nature 444, 171–178, 2006; McGrath CL et al. Genetics 197, 1417–1428, 2014).

- ***P. caudatum* strain RB-1 (NBRP PC042001A)**

Interactions between *Paramecium* species and a pathogenic bacterium *Legionella pneumophila* were studied (Watanabe K et al. Scientific Reports 6, Article number: 24322, 2016).

- ***P. bursaria strain* Yad1g1N (NBRP PB031010B)**

Infection process between *P. bursaria* and its symbiotic *Chlorella variabilis* was clarified, and gene expressions of the host cell with and without the symbiotic alga were compared (Kodama Y, Fujsihima M. In, *Biocommunication in ciliates*, (Eds, Witzany G, Nowacki M), Springer, pp. 277–304, 2016; Kodama Y. et al. BMC Genomics, 2014, 15:183).



P. caudatum cells bearing *Holospora obtusa* (left) and *H. undulata* (right).

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

Cellular slime molds

Core Facility : Quantitative Biology Center, RIKEN
Principal Investigator : Yoichiro Kamimura FAX : +81-6-6155-0112
Contact site : ykamimur@riken.jp
URL : http://nenkin.nbrp.jp/

Overview

Cellular slime molds are 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 and supporting stalks. They are used as a model organism for research on development, cell division, cell motility, mathematical biology, and so forth. They are also employed as a resource for medical research because of several useful features, such as: they can serve as hosts for pathogenic microorganisms and they serve novel physiological active substances.

This project is being implemented by RIKEN QBiC and the University of Tsukuba with the goals of developing a world-class collection of high-quality cellular slime mold resources and providing a broad range of services to answer the needs of researchers in Japan. As part of this endeavor, the project members engage in the following activities:

(1) Collection, preservation, and supply of various strains
(2) Collection, preservation, and supply of genes and vectors
(3) Hosting of training courses for new users

Cellular slime molds are easy to culture, and most molecular biology techniques can be applied to them. Moreover, they are haploid for most of their life cycle. Even laboratories with no prior experience in working with cellular slime molds will find them readily usable as a secondary resource.

Key Strains/Studies

Dictyostelium discoideum

NC4, KAX3, AX2, AX4, and V12 strains, and genetically manipulated strains

Other strains available:

Dictyostelium mucoroides, Dictyostelium purpureum, Polysphondylium pallidum, Acytostelium subglobosum, and more

Gene expression vectors:

D. discoideum expression vectors with various tags

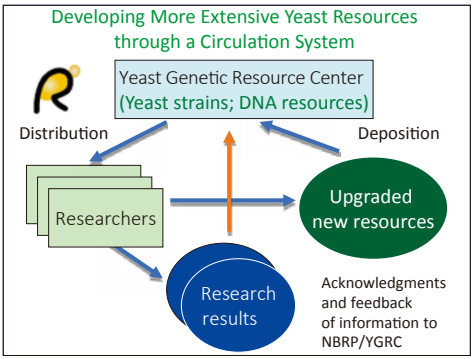
D. discoideum AX4 is the strain that was used to analyze that species' genome and EST. KAX3 and AX2 are widely used for studies on cell motility, chemotaxis, cell division, and so on, in molecular biology, cell biology, and biophysical analysis, and many development-related genes have been identified. Furthermore, collected new naturally-isolated strains are under investigation for novel physiological active substances.

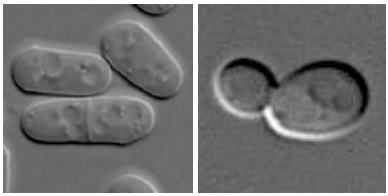
CORE FACILITY UPGRADING PROGRAM Yeast

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.lab.nig.ac.jp/nig/

Overview

Yeast is an important eukaryotic model organism. This is especially true of the fission yeast *Schizosaccharomyces pombe* and the budding yeast *Saccharomyces cerevisiae*, which are making significant contributions to research in a variety of areas within the life sciences. Upgrading bioresources and expediting their distribution are essential to successful research. Through phases 1 - 3 of the NBRP, the Yeast Genetic Resource Center (YGRC) has become one of the top international yeast resource centers. In phase 4 of the NBRP, YGRC will aim to possess various high-quality resources, such as genome-wide and highly-demanded resources. The project will be managed by the Graduate School of Science, Osaka City University (fission yeast) and the Graduate School of Engineering, Osaka University (budding yeast). The Center for Gene Science, Hiroshima University, handles the preservation of "Back-up" resources in order to ensure their safe storage. The "Yeast Genetic Resource Center Steering Committee" is functioning effectively as a contact point between the project and resource users.





Fission yeast Budding yeast

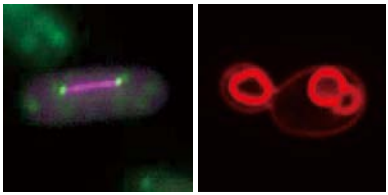
Key Strains/Studies

- **Fission yeast** (approx. 23,100 strains; approx. 103,000 DNA clones)

Mutant strains related to sexual reproduction and mitotic division; GFP-fusion gene library; sequenced full-length cDNA and genome DNA clone sets; various cDNA and genome libraries; temperature-sensitive mutant set; cold-sensitive mutant set

- **Budding yeast** (approx. 27,300 strains; approx. 6,200 DNA clones)

Mutant strains related to cell cycle and cell wall synthesis, autophagy and meiosis-specific DNA recombination; auxin-induced degron resources; genome-wide segmental chromosome duplication series; gTOW6000 resources; ribosome biogenesis-related resources; DNA barcode strains; Mutants and DNA resources related to biologically important budding yeasts other than *S. cerevisiae*; double disruptant series of protein phosphatase genes



Visualization of the nuclear division (fission yeast)

Visualization of the vacuole membrane (budding yeast)

1. Analyses of intracellular protein localizations and protein dynamics have been conducted using GFP-fusion genes.
2. An analysis using full-length cDNA clone sets to clarify the yeast transcriptome is well under way and the results look very promising.

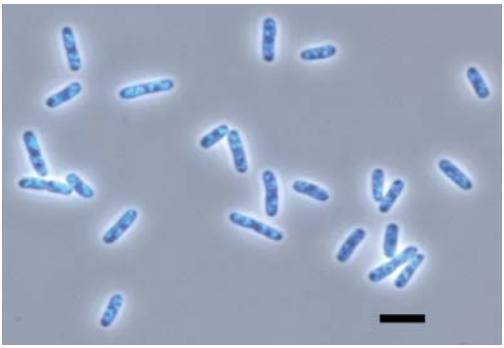
Prokaryotes (E. coli, B. subtilis)

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: http://www.shigen.nig.ac.jp/ecoli/strain/
B. subtilis URL: http://www.shigen.nig.ac.jp/bsub/

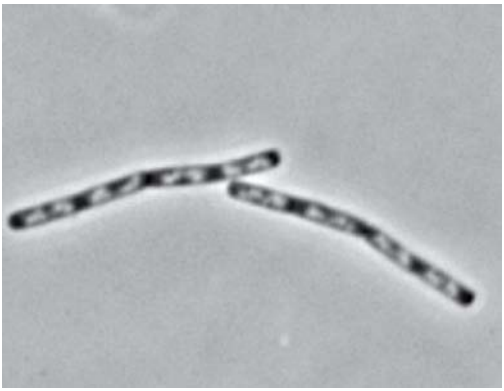
Overview

The National Institute of Genetics collects and preserves *Escherichia coli* and *Bacillus subtilis* resources developed in Japan, and supplies them to institutions that engage in basic research. Resource orders are handled through the webpage for each species, so users can request delivery of their desired strains by filling out the necessary information online. Delivery is made to domestic addresses within one week of ordering. Fees of strains and DNA are shown in tour web home page. Shipping fees are usually born by the user. In addition, in order to receive resources, the leader of the research project must sign a materials transfer agreement (MTA) with the National Institute of Genetics. For certain resources that are genetically modified organisms, users also need to obtain a permit for handling the organism.

The National Institute of Genetics acts as the core organization for this NBRP project, and sub-organization Kyushu University handles the preservation of resources in order to ensure their safe storage.



Escherichia coli



Bacillus subtilis

Key Strains/Studies

The resources distributed by this project are all nonpathogenic strains. *E. coli* strains are derived from strain K12, and *B. subtilis* strains are derived from strain 168. The project's collection consists of *E. coli* gene clones with GFP- or His-tag on expression vectors. The *E. coli* resources are largely divided into the following three groups.

- **Mutant *E. coli* strain resources** (exhaustive collection of gene-knockout mutants, transposon-insertion mutants, etc.)
- **Cloned genetic resources** (GFP-tagged and untagged ASKA clones)
- **Cloning vector** (465 types) and host resources

The *B. subtilis* resource collection consists of nearly 2,500 gene-disrupted strains created mainly by the Ogasawara Laboratory of the Nara Institute of Science and Technology (Kobayashi et al., 2003). The disrupted genes of all strains are being checked by PCR. The strains that pass this quality control check have been released and distributed as they become available. The host stain for the seamless cloning is now available.

CORE FACILITY UPGRADING PROGRAM General Microbes

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

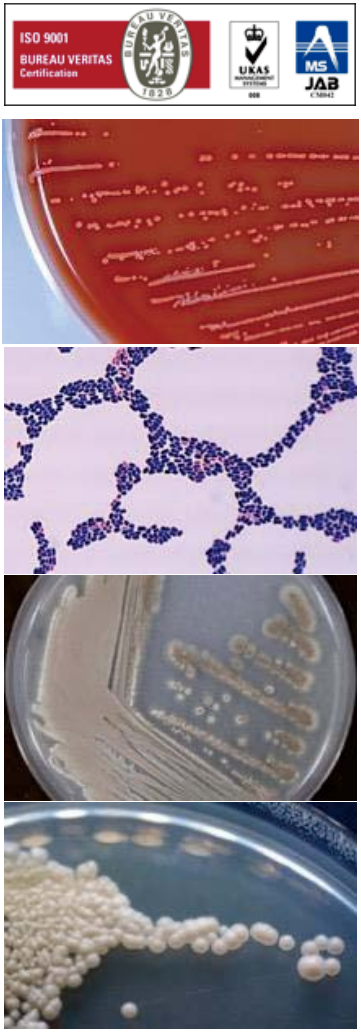
Overview

Microorganisms have a wide variety of functions owing to their species diversity and have been frequently utilized for researches in health and environmental sciences, biotechnology, and various fields of sciences. We collect, preserve, and distribute diverse microbial strains, particularly focusing on type strains representing microbial species and well-characterized strains appeared in scientific publications. We are trying to enrich information related to the strains such as physiological characters, genome, and related publications in our catalogue database, and to improve its accessibility. As a result, we contribute much to research advances involved in microorganisms. Many of our distributions went abroad and to profit organizations, which proves our international high-level status and our contribution to applied sciences and developments. Annually we receive a large number of strain depositions, but many of them have problems such as their authenticity. Therefore, we are extensively checking the quality of strains at the time of deposit receptions or distributions with gene sequences tests or others. These activities are conducted under the quality management system certified by ISO9001 international standard to establish reliability to our strains and to our institute.

Key Strains/Studies

Microbial strains of diverse species are available, which are comprised of bacteria including lactic acid bacteria and actinomycetes, archaea, eukaryotic microorganisms including yeasts and filamentous fungi. We particularly focus on well-characterized type strains. Our collection includes commensal microorganisms of human or animals and key microorganisms in ecosystems including extreme environments, which are useful for researches in health and environmental sciences, respectively. Our collection also contains strains useful for researches in various fields of biotechnology and applied sciences for food, agriculture, bioenergy, biomaterials, biochemicals, bioremediation, and so on.

A large number of original papers and patent applications have been published by users. These outcomes are exhibited through the information site of NBRP and our homepage, and in our database of individual microbial strains as well.



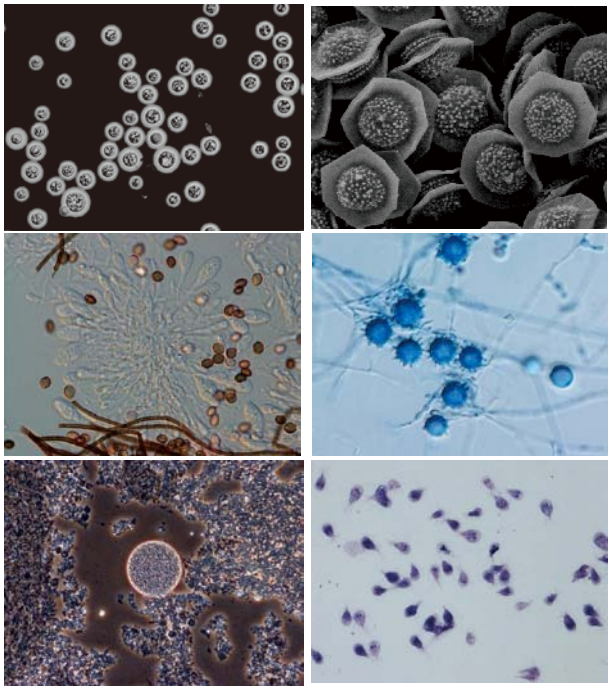
Top: Certified ISO9001
Photos, top: *Bifidobacterium longum* subsp. *longum* JCM 1217 inhibiting infection of enteric pathogens
Middle upper: *Lactococcus lactis* subsp. *lactis* JCM 5805 stimulating entire immune system (Gram-stained image)
Middle lower: Avermectin-producing *Streptomyces avermitilis* JCM 5070, isolated by the Novel Prize laureate Prof Ōmura
Bottom: *Cryptococcus terricola* JCM 24518 producing biodiesel from starch.

Pathogenic eukaryotic microbes

Core Facility : Medical Mycology Research Center, Chiba University
Principal Investigator : Takashi Yaguchi FAX : +81-43-226-2790
Contact site : yaguchi@chiba-u.jp URL : http://www.pf.chiba-u.ac.jp
Kenji Hirayama, Nagasaki University Contact site: hiraken@nagasaki-u.ac.jp

Overview

This project is carried out by Chiba University's Medical Mycology Research Center (pathogenic fungi/actinomycetes) and Nagasaki University's Institute of Tropical Medicine (pathogenic protozoa). Together, they cooperate in various efforts to support education and research pertaining to infectious diseases and pathogens. Specifically, they are developing a system for collection, preservation, and distribution of pathogenic microorganisms, and they supply reliable strains of pathogenic microorganisms that are backed by high-level information. They also contribute to efforts aimed at conquering infectious diseases. For some institutes are not able to deal with living pathogenic microorganisms, we distribute their DNA or killed ones.



Key Strains/Studies

● Pathogenic fungi, actinomycetes and protozoa:

All species of highly pathogenic exogenous fungi (including type 3 pathogens), other principal pathogenic fungi species, standard strains of pathogenic actinomycetes (mainly *Nocardia*), and human infecting protozoa (including information of strains preserved by other institutions).

Research contributions: The project's resources have been used as, among other applications: (1) strains for whole genomic analysis, strains for creation of DNA chips for identification of pathogenic microorganisms, (2) standard strains for proposing new species, (3) comparative strains for drug susceptibility testing of clinical isolates, (4) resources for drug development by pharmaceutical companies, (5) strains for creation of MALDI-TOF MS for identification of pathogenic microorganisms, and (6) resources for student experiments.

Pathogenic bacteria

Core Facility : Center for Conservation of Microbial Genetic Resource, Organization for Research and Community Development, Gifu University
Principal Investigator : Kaori Tanaka FAX : +81-58-230-6184
Contact site : g_cmr@gifu-u.ac.jp
Tetsuya Iida : iida@biken.osaka-u.ac.jp
Haruyoshi Tomita : tomitaha@gunma-u.ac.jp

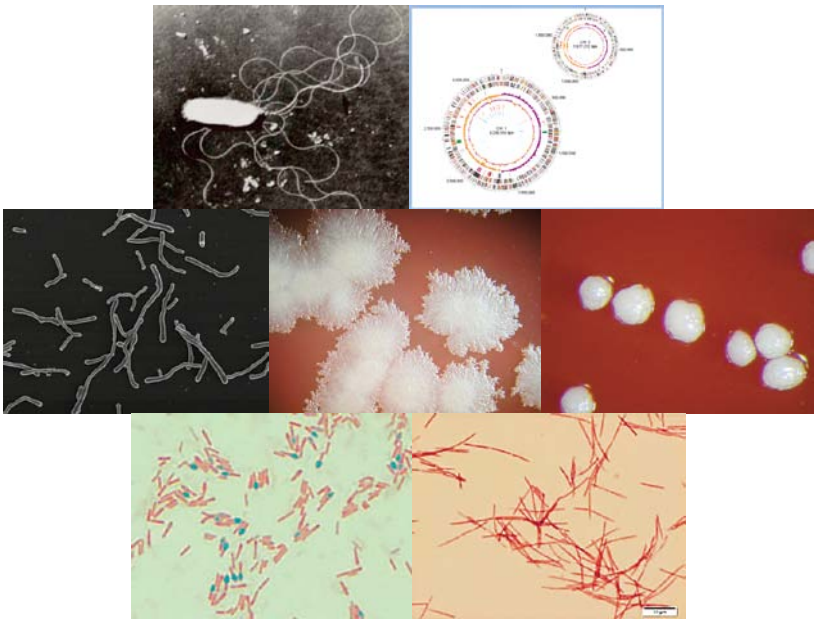
Overview

The tasks of this project are collecting, preserving, and providing of bacteria, which are related to infectious diseases and human health. This project is carried out by Gifu University, Center for Conservation of Microbial Genetic Resource (GCMR) (bacterial pathogens in various infection, opportunistic bacteria), Osaka University, Research Institute for Microbial Diseases (bacterial pathogens in various intestinal infection), and Laboratory of Bacterial Drug Resistance, Gunma University Graduate School of Medicine (backup facility). We collaborate to provide a more stable preservation system and a collection with useful strain information on use. We support people who do education, research, and development of tools, related to infectious diseases and bacterial pathogens. We also take over the collection of researchers who retire and preserve their precious genetic resources.

Key Strains/Studies

Over 80% of bacterial species that are pathogenic in humans are preserved in this project. In addition, the collection also includes varieties in bacterial species such as serotype important for infectious disease studies. We plan to collect more valuable species and variants in the future, including drug-resistant strains and zoonotic pathogens.

Research contributions: The project's resources have been used: (1) for preparing DNA chips for identification of pathogenic microorganisms, (2) as whole genome analysis strains, (3) as standard strains in the proposal of new bacterial species, (4) as quality control strains for susceptibility test of clinical isolating bacteria, (5) for education, (6) for discovery and development of new antibacterial agents by pharmaceutical companies.



Cord blood cells for research

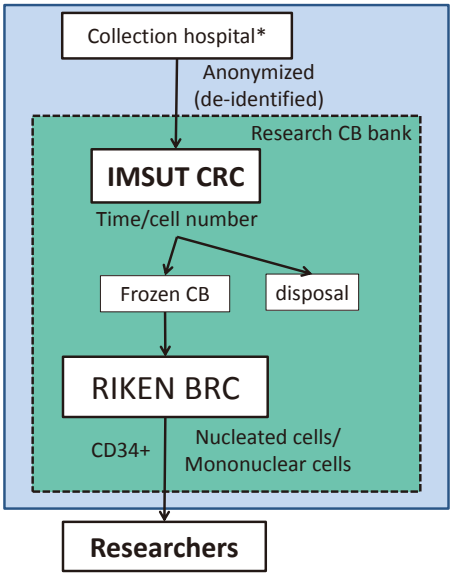
Core Facility : Department of Cell Processing and Transfusion, Research Hospital,
The Institute of Medical Science University of Tokyo (IMSUT)
Principal Investigator : Tokiko Nagamura-Inoue FAX : +81-29-836-9130
Contact site : cellbank@brc.riken.jp
URL : http://www.brc.riken.jp/lab/cell/hcb

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 Bioresouce 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.

Flow chart of research cord blood



*In the hospital collecting both clinical and research CBs, CBs are selected for clinical and the remaining ones are for research use in NBRP.

Key Strains/Studies

● Mononuclear cells (CBF)

- providing form: cryotubes (4 in one set) or plastic Bag
- cell numbers > 1×10^7/tube or > 1×10^8/bag
  ※the users can choose sets from the same donor or different donors
- method: Ficoll sedimentation
- neutrophils less than 20% at freezing

● Nucleated cells (HCB)

- providing form: plastic bags
- cell numbers > 3×10^8/bag
- method: HES sedimentation

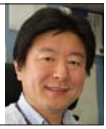
● CD34positive cells (C34)

- providing form: cryotube
- cell numbers > 1×10^5/tube
- method: immunomagnetic beads separation
- CD34purity > 90%

※frozen CBs are checked for infectious agents (HBs-Ag, HBc-Ab, HCV-Ab, HIV-I/II-Ab, HTLV-1-Ab, Syphilis (TPHA,RIA)), and proved to be sterile.

Human and animal cells

Core Facility : Cell Engineering Division, RIKEN BioResource 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 : http://www.brc.riken.jp/lab/cell/english/



Overview

Cell lines are a relatively easy-to-use research material, which can be used by anyone at any time and any place. They are also an extremely convenient research material because they can multiply virtually forever in a test tube. This convenience, however, is a double-edged sword. Researchers who are just starting out often become involved in cell culturing and this frequently gives rise to problems such as "cell line mix ups," "mycoplasma contamination (Fig. 1)," and so forth. When specimens affected by these problems end up being used in research, it results in work that is inaccurate and unreproducible. Scientifically valid conclusions thus cannot be obtained. In our division, we have developed a highly reliable system that provides cell specimens which are confirmed to be free of these problems. We invite all researchers considering new research projects to obtain cells from our ISO 9001 certified facility. (Fig. 2).

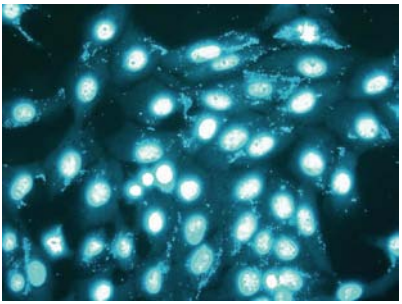


Fig. 1. DNA staining of cells. Not only nuclei but also cytoplasm are stained due to mycoplasma infection.

Fig. 2. Accreditation by ISO9001

Key Strains/Studies

(1) General Cell Lines

- Human Cancer Cell Lines, Human Primary Cells
- Animal Cell Lines (Mouse, Rat etc.)

(2) Cells for Genome Research

- Cells of Healthy Japanese
- Sonoda-Tajima Collection (Various Racial and Ethnic Background)
- Cells of Patients (Werner Syndrome, Breast Cancer etc.)

(3) Stem Cell Bank

- Human Somatic Stem Cells (Umbilical Cord Blood, Mesenchymal Stem Cells)
- Embryonic Stem Cells (Human, Common Marmoset, Mouse)
- Induced Pluripotent Stem Cells (Human, Mouse, Rabbit)
- Disease-specific iPS cells (Human)

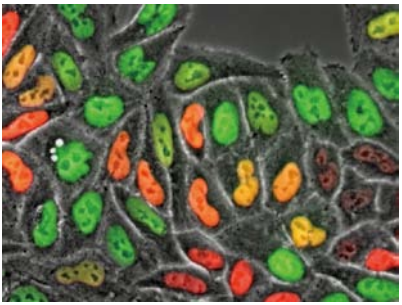


Fig. 3. A subline of HeLa (HeLa/Fucci) expressing a cell cycle marker

There are already an enormous number of studies that have been completed using the division's cultured cells. Please refer to the information that is available at the following URL: http://www.brc.riken.jp/lab/cell/english/

A human cancer cell line, HeLa, was generated in 1952 as the world first human cancer cell line and induced the following generation of many human cancer cell lines derived from various cancers around the world. HeLa cell line is still very frequently used in the community such as the HeLa/Fucci cells which express a cell cycle marker (Fig.3).

DNA material

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

Overview

Genetic experimental materials, such as plasmid and viral vectors, genomic and cDNA clones, have become one of the most important and fundamental research tools for life sciences. Genetic materials are now widely utilized in numerous fields of life sciences, 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 novel diagnostic and therapeutic methods, drug discovery and material production. The Gene Engineering Division of RIKEN BioResource Center (BRC) has been engaging in the collection, preservation, quality control and distribution of genetic materials developed mainly in Japan by individual scientists and by various national projects.

Recently, genetic materials can be prepared easily by means of, for example, polymerase chain reaction. However, such materials often contain accidental mutations and produce dubious experimental results. To provide domestic and international scientific community with genetic materials of the highest quality and reproducibility, the Gene Engineering Division performs rigorous quality control by testing growth and propagation, restriction enzyme mapping and nucleotide sequencing of clones. Relevant information such as characteristics and methodologies is provided via the web site of the RIKEN BRC. For the best use of genetic resources, training courses of advanced technologies are also given.

The Material Transfer Agreement is used for each transfer of genetic materials to protect the intellectual property rights of developers and to define the responsibility of users. We have opened a path of the academic use of genetic materials produced by using advanced research tools owned by commercial entities. Deposition of genetic materials in the RIKEN BRC frees researchers from time consuming preparation and distribution of materials to fellow researchers. Furthermore, deposition increases chance of collaboration and citation of research papers. Your deposition of genetic resources in RIKEN BRC Gene Engineering Division and use of these resources are most appreciated.

Key Strains/Studies

● Deposited clones from researchers around the world

[Genomic (BAC) and cDNA clones of human, model animals and microorganisms]

Numerous clones developed by individual researchers, and large sets of genetic materials from the core facilities of NBRP and other National Projects are available. The KEGG (Kyoto Encyclopedia of Genes and Genomes) database of pathways and orthologs among human, mouse and fission yeast are now linked to our clones and can be searched by users.

● Ready for use genetic materials

[Recombinant adenoviruses, promoter and reporter constructs, and expression vectors]

Users can readily perform their experiments using our genetic materials without re-constructing in an expression vector. For example, luciferase reporters to study signal cascades of Hedgehog, Notch, and Wnt/β-catenin as well as promoter constructs from 300 human genes are available.

INFORMATION CENTER UPGRADING PROGRAM Information

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

Overview

The Information Center Upgrade Program promotes the following five efforts by seven organizations: (1) development of bioresources databases, (2) development of the Great Ape Information Network (GAIN), (3) serving as the Japan node of the Global Biodiversity Information Facility (GBIF), (4) the ABS (Access and Benefit Sharing) Task Force team for academia, and (5) public relations activities for NBRP. The main purpose of the Information Center is to broadly support life science research by promoting the effective use of bioresources through consolidation and provision of information regarding the locations of bioresource collections, scientific knowledge related to these resources, genomic data, and other essential information. Therefore, we have enabled the integrated cross-referenced search of 6.5 million bioresources, and constructed a reference database of 28,000 papers related to NBRP resources.

(1) NBRP portal site http://www.nbrp.jp/
(2) Great Ape Information Network (GAIN) http://shigen.nig.ac.jp/gain/
(3) Japan node of the Global Biodiversity Information Facility (GBIF) http://www.gbif.jp
(4) RRC database https://rrc.nbrp.jp/

Key Strains/Studies

National Institute of Genetics -Development of bioresources databases and promoting the effective use of bioresources.
-ABS task force team -NBRP Public Relations
www.nbrp.jp

Portal site

Integrated cross search

Resource Reference Database

Sub Core Facility

Kyoto Univ.
Development Great Ape Information Network - GAIN -

Natl. Museum of Nature and Science
Publication of biodiversity information based on the network of natural historical museums

Tokyo Univ.
Collection and standardization of biodiversity information and its metadata through local and international networks

Kyushu Univ.
Tsukuba Univ.
Tokyo Metropolitan Univ.

ABS (Access and Benefit Sharing) Task Force team for academia support universities and researchers in order to facilitate access to genetic resources.

GENOME INFORMATION UPGRADING PROGRAM

Genome resequencing of Japanese fancy mouse-derived JF1/Ms strain

Core Facility : Genetic Strains Research Center, National Institute of Genetics
Principal Investigator : Toyoyuki Takada FAX : +81-55-981-6817
Contact site : ttakada@nig.ac.jp
URL : http://molossinus.lab.nig.ac.jp/msmdb/index.jsp

Overview

The laboratory mouse is one of the most important bioresources for studying principles underlying higher-order biological phenomena and etiologies of human diseases. National Institute of Genetics (NIG) has established a series of mouse experimental strains named “Mishima Battery” since 1970’s. These strains have very remote genetic status from the commonly used laboratory mouse strains such as C57BL/6J (B6), and show very unique phenotypes. The mouse strains in “Mishima Battery” are now distributed to the science research community via RIKEN BioResource center and NIG, and contribute to broad range of life science. In our previous study, we found that many the classical laboratory strains have genomic segments with extremely high sequence similarity to those of JF1/Ms (JF1), which is a member of “Mishima Battery” and belongs to Japanese subspecies, M. m. molossinus. It suggested that ancestor of JF1 could be origin of the molossinus-derived genome in the classical laboratory strains. In this program, to collect more precise information of structure and copy number variations in the JF1 genome for the reference genome of B6, we will employ further resequencing by the SMRT-sequencing on the PacBio genome sequencing platform as collaboration with Comparative Genomics Laboratory and Advanced Genomics Center, NIG, and Joint Support-Center for Data Science Research, ROIS. Upcoming resequencing data will be open to the research community via public domain database, “NIG_MoG”.

GENOME INFORMATION UPGRADING PROGRAM

Garnering fundamental information on wheat genomic diversity through de novo sequencing of the standard Japanese wheat cultivar Norin 61.

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 : http://www.plant-genetics.kais.kyoto-u.ac.jp

Overview

We will determine the genome sequence of a Japanese wheat variety Norin 61, which enable comparative genome analyses of the wheat cultivars. International Wheat Genome Sequencing Consortium organized the International 10 Wheat Genomes Project aiming of comparative genomics of wheat. We will utilize the genomic sequence of Norin 61, together with those of other cultivars, for determining the Pan Genome sequence of wheat varieties (Figure 1).

Genome information is the most fundamental resource of life sciences. The high precision genome sequence of Norin 61 decoded in our project will be a common basic resource for both basic and applied researches. It will also add values of genomic information to the Nested Association Mapping population, which NBRP-Wheat is currently developing using Norin 61.

Based on the genomic information of Norin 61, the resource database KOMUGI is to be enriched so that researchers can access the information from nucleotide sequences to genetic resources in one-stop.

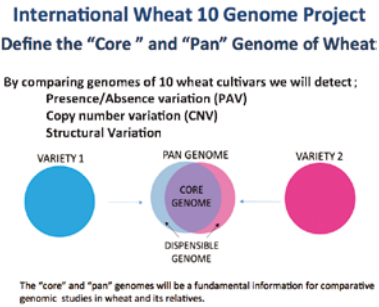


Figure 1 The high precision genome sequence of Norin 61 decoded in our project will be a common basic resource for both basic and applied researches.

FUNDAMENTAL TECHNOLOGY UPGRADING PROGRAM

Development of new technologies for stable maintenance of *Drosophila* stocks

Core Facility : National Institute of Genetics
Principal Investigator : Shu Kondo FAX : +81-55-981-6825
Contact site : skondo@nig.ac.jp
URL : https://shigen.nig.ac.jp/fly/nigfly/

Overview

Currently, there are no effective ways of preserving *Drosophila* strains other than continuously culturing them as live stocks. Accordingly, there is always an unpredictable risk of stocks getting lost due to various possible accidents during culture. For instance, most *Drosophila* stocks are maintained in combination with a balancer chromosome. Recent studies revealed that rare recombination occurs between a balancer and a mutant chromosome, resulting in loss of the desired mutation. Thus, it is important to establish a more reliable way to maintain stocks. To address these issues, we propose to develop the following technologies: (1) A method to cryopreserve primordial germ cells. (2) New balancer chromosomes that completely suppress genetic recombination. Cryopreservation will greatly expand the capacity of our stock centers, allowing us to collect and distribute many more useful stocks. In addition, we will be able to stop culture of live stocks that are rarely requested by putting them into cryopreservation, which will greatly reduce the labor and space for maintaining live stocks and streamline the operation of the stock centers.

FUNDAMENTAL TECHNOLOGY UPGRADING PROGRAM

Development of protocols for efficient gene transfer and genome editing in wild species of rice.

Core Facility : Genetic Strains Research Center, National Institute of Genetics
Principal Investigator : Yutaka Sato FAX : +81-55-981-6879
Contact site : yusato@nig.ac.jp
URL : http://www.shigen.nig.ac.jp/rice/oryzabase/

Overview

Wild species of rice are often difficult to grow and harvest. Due to these difficulties, not many molecular genetic experimental protocols specific to wild species are developed so far and this is a limitation to prevail the usage of wild rice species. In order to increase the user of our resources, it is important to propose to potential users the easy and solid ways to handle wild rice resources. Now, in this program, we aim to establish a system of genetic transformation of wild rice species and confirm CRISPR/cas9 based genome editing is also applicable to them.

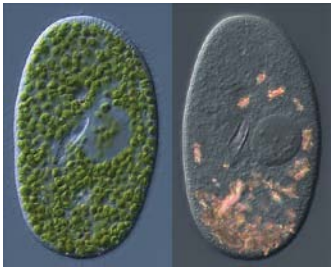
During the course of genome editing in plants, Agrobacterium mediated gene transfer is a necessary step. In case in rice, tissue culture and regeneration is required in this step. However, the established process of the tissue culture and regeneration is only suitable to domesticated species and a part of wild species relatively close to domesticated ones. Thus, it is necessary to establish conditions applicable to varieties of wild species of rice and confirm that it is possible to modify genetic traits of wild species of rice by CRISPR/cas9. This will help to attract new users of NBRP RICE.

Development of reliable cryopreservation method for *Paramecium* genus

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

In ciliate *Paramecium* genus, several cases of successful cryopreservation with DMSO and liquid nitrogen have been reported in *P. aurelia* and *P. caudatum*. However, practical application as a reliable technology has not yet been established. The reason is that the survival rate after thawing is unstable and low. Therefore, long-term preservation of *Paramecium* species is carried out by using a test tube, adding culture medium once a month at low temperature (about 10 °C) and to make cells slowly growing. The lifespan of *Paramecium* is determined by the number of cell divisions after conjugation. In case of *P. caudatum*, its life span is about 700 fissions. Since *P. caudatum* can divide three times in a day at 25 °C, its life span will be exhausted within 8 months after conjugation. At 10 °C, we can preserve *Paramecium* cells for several years, but cannot stop aging. Therefore, in order to use strains of a specific period of the life cycle, it is essential to develop a cryopreservation method that allows us to obtain living cells stably at high survival rate after thawing. The aim of this research project is to develop the new method in collaboration with Dr. Yuki Kodama of Shimane University, Dr. Mihoko Takahashi of Tsukuba University and Dr. Nobuyuki Haga of Ishinomaki Sensyu University.



Photomicrographs: *P. bursaria* with (left) and without (right) symbiotic algae.

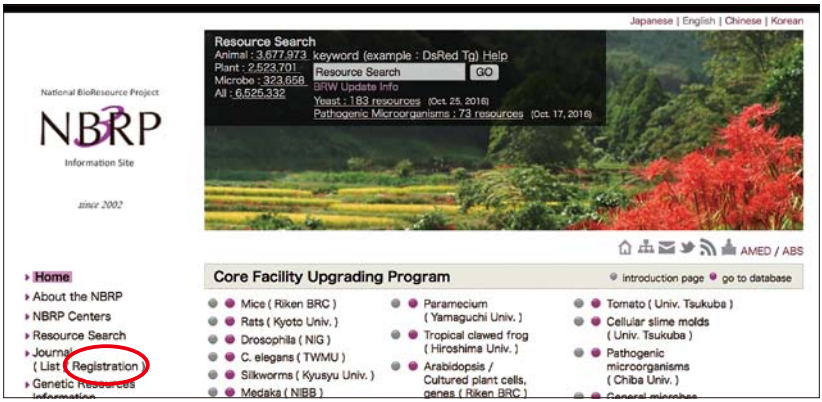
NBRP needs feedback from the users.

Accumulation of research outcome using bioresources can further enhance the value of the bioresouces. 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” (see below) for easy feedback of such information.

Please click “Journal (List / Registration)”, on the top page of

http://www.nbrp.jp/



How to order and about handling/shipping costs

How to order:

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

About handling and shipping costs:

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

Support for the Japanese academic field, concerning the Nagoya protocol on overseas genetic resources

To access overseas plants, animals and microorganisms, it is inevitable to observe relevant national laws of provider countries. In 2014, the Nagoya Protocol on Access to Genetic Resources and Benefic Sharing (ABS: Access and Benefit Sharing) took effect, followed by Japan's entry as the 99th party to the Protocol on August 20, 2017 and the simultaneous start of the domestic measure (ABS Guidelines). Other countries, in recent years, are also developing their national regulations on ABS. There is therefore, a growing need for serious attention to ABS.

We support universities and other institutions in establishing their systems for ABS, and engage in activities for supporting access to genetic resources.

1. Support and promotion for establishment of universities' systems

We hold free visit seminars, give advice, and make posters, leaflets, and handbooks for system establishment.

2. Support for access to genetic resources

We provide consultation services by e-mail and telephone. For the support, we work together with the cooperative institutions.

3. International activities related to overseas genetic resources

We cooperate with overseas authorities and participate in CBD/COP etc. (to respond to such an issue as digital sequence information).

As the cooperative institutions for the issue, we work with Material Management Center in Kyusyu University, Gene Research Center in University of Tsukuba, and Makino Herbarium in Tokyo Metropolitan University. We also work with the members of the system establishment working group including Tokyo University of Marine Science and Technology, Mie University, and Kyoto University.

Contact: Mutsuaki Suzuki ABS Task Force Team for Academia, Intellectual Property Unit, National Institute of Genetics, Research Organization of Information and Systems

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TEL: +81-55-981-5831 **FAX**: +81-55-981-5832

URL: http:www.idenshigen.jp (English version: http://nig-chizai.sakura.ne.jp/abs_tft/en/)

Mutsuaki Suzuki

Website for the ABS Task Force Team for Academia

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.

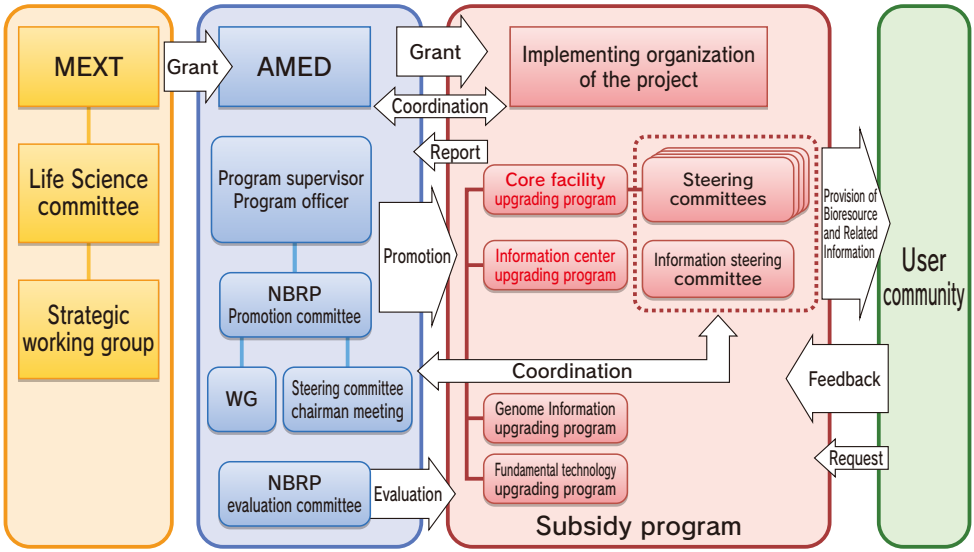
(3) Fundamental technology upgrading program:

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 bioresourcesthat are gathered at the core facilities, and public relations of the NBRP through its home page is upgraded.

Project Implementation System



NBRP Promotion Committee

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	Director, RIKEN BioResource Center (BRC)
	Kiyotaka Okada	Professor, Faculty of Agriculture, Ryukoku University
	Makoto Kawase	Professor, Social and International Studies Global Commons, University of Tukuba
	Kazuo Shinozaki	Director, RIKEN Center for Sustainable Resource Science (CSRS)
	Toshihiko Shiroishi	Vice-Director · Professor, National Institute of Genetics (NIG)
	Satoshi Tabata	Vice President, Kazusa DNA Research Institute
	Tetsuya Hayashi	Professor, Graduate School of Medical Sciences, Kyushu University
	Hiroo Fukuda	Professor, Graduate School of Sciences, The University of Tokyo

NBRP Network of Japan

1. Hokkaido University
2. Tohoku University
3. Niigata University
4. Utsunomiya University
5. Gunma University
6. Tsukuba University
7. NIES
8. Riken BRC

9. Riken BSI
10. Kyorin University
11. University of Tokyo
12. TWMU
13. Chiba University
14. Meiji University
15. Misaki Marine Biological Station, The University Tokyo
16. National Institute of Genetics

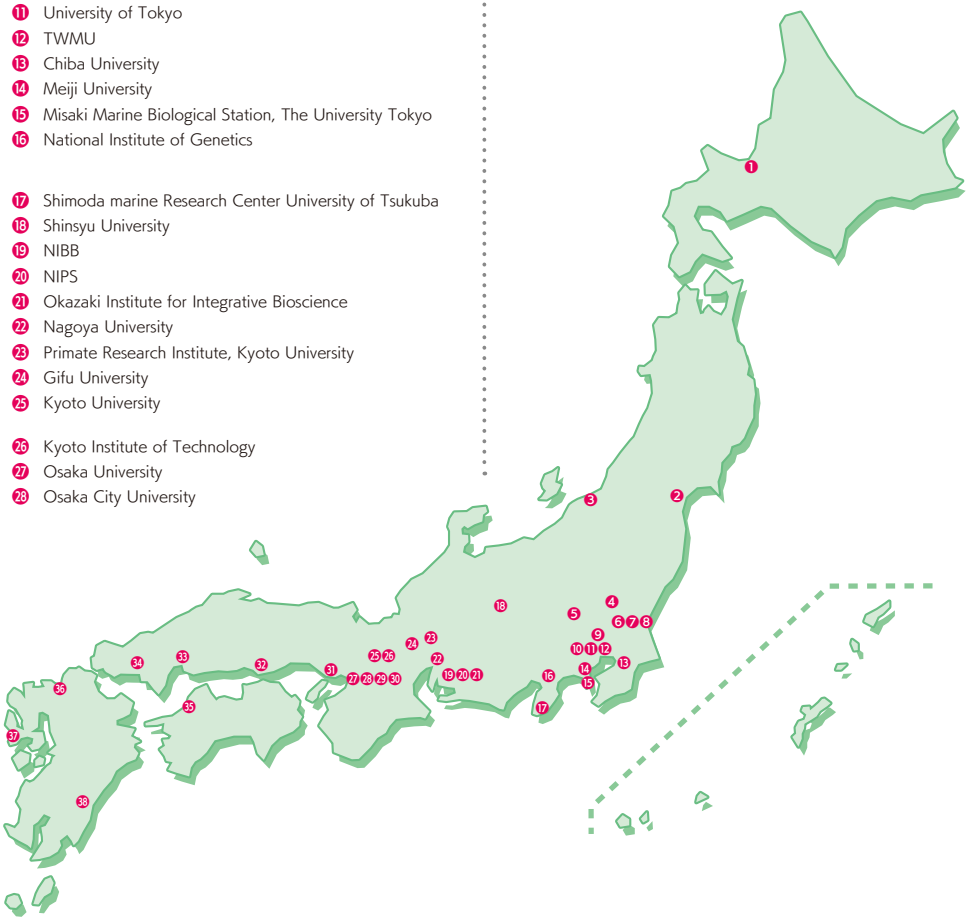
17. Shimoda marine Research Center University of Tsukuba
18. Shinsyu University
19. NIBB
20. NIPS
21. Okazaki Institute for Integrative Bioscience
22. Nagoya University
23. Primate Research Institute, Kyoto University
24. Gifu University
25. Kyoto University

26. Kyoto Institute of Technology
27. Osaka University
28. Osaka City University

29. Osaka Prefecture University
30. Riken QBiC
31. Kobe University
32. Okayama University
33. Hiroshima University

34. Yamaguchi University
35. Ehime University
36. Kyushu University

37. Nagasaki University
38. Miyazaki University



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 term 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 th Molecular Biology Society of Japan (continued every year). The exhibition was also held in the meetings of other academic societies.
2006	June	"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 term 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 term NBRP Kick-off Symposium, titled "Bioresources that Open the Future of Life Sciences".
2009	August	"Report on Database Upgrading and Dissemination of Outcome Information at NBRP" by the working group.
	August	"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 (Tsukuba)
2011	June	"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 .
	April	Beginning of the third term of NBRP (29 resources)
	November	The symposium "Challenges in the Third Term of NBRP" was held.
	October	The 5th International Meeting of Asian Network of Research Resource Centers (Hayama)
2013	December	"A Report on Desired Implementation of the Nagoya Protocol" (Ministry of the Environment)
2015	January	The open symposium to present about the achivements of NBRP (at the middle of the third term).
	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 (Kyoto)
2017	April	Beginning of the fourth term of NBRP (30 resources).

■Contact Information / Regarding the project operation

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