Report on Research and Other Activities of National Institute of Genetics (During 2014~2018)

国立遺伝学研究所自己評価報告書

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Preface

Director-General: Fumio Hanaoka

The National Institute of Genetics (NIG) recently celebrated its 70th anniversary since its founding and continues to strive for excellence in research, service and education. To pursue our commitment to future development, we have initiated an evaluation by an external review committee and have compiled this report which summarizes the activity of NIG during the 5 years from January 2014 to December 2018.

NIG was established in 1949 by the Japanese Ministry of Education for comprehensive studies of genetics. In 1984, it was reorganized into an Inter-University Research Institute, and the new designation established an additional official role of NIG: collaboration with researchers at universities. For this purpose, NIG now provides three services: DNA Databank of Japan (DDBJ), Advanced Genomics Services, and Bioresource Services, in addition to collaborative research. In 1988, NIG joined in the establishment of SOKENDAI (the Graduate School of Advanced Studies). NIG is in charge of the Department of Genetics of SOKENDAI and maintains a Ph.D course for fostering the next generations of researchers.

In 2004, sixteen Inter-University Research Institutes were incorporated and grouped into 4 Research Organizations. NIG chose to belong to Research Organization of Information and Systems, which consists of the National Institutes of Polar Research (NIPR), Statistical Mathematics (ISM), Informatics (NII), and Genetics (NIG). This choice reflects our institute's desire to play a central role in the integration of informatics and systems approaches in the biological systems and for strengthening research infrastructure, including open-use databases, to make use of massive genomic information.

Presently, NIG has four missions: (1) cutting-edge research in genetics and related fields, (2) collaboration with, and services to, researchers at universities, (3) graduate education and human resource development, and (4) contributions to society. It is my hope that this report will be valueable for the external evaluation of NIG.

Overview of National Institute of Genetics

Our Mission

Research

NIG conducts top-level research in life sciences leveraging on approaches and resources in Genetics. NIG also develops new research fields within the broader concept of Genetics.

Education and Career Development

NIG takes part in graduate level education. It also offers various systems to enhance research ability of young researchers.

Intellectual Infrastructure and Collaboration Research

NIG provides various research infrastructures (genetic resources and information/services) to the scientific community. It also functions as a hub for international and domestic collaborations.

Social Contribution

NIG actively disseminates the achievements from genetic research to the society. It also promotes alliance between industry and academia.

History

1949	Jun. 1	Established under the jurisdiction of the Ministry of Education, Science, Sports and Culture. Started with an administrative department and three research departments.
	Aug. 10	Prof. Kan Oguma was elected the 1st Director.
1953	Jan. 1	Three research departments were reorganized as the Departments of Morphological Genetics, Cytological Genetics and Physiological Genetics.
	Aug. 1	Department of Biochemical Genetics was added.
1954	Jul. 1	Department of Applied Genetics was added.
1955	Sep. 15	Department of Induced Mutation was added
	Oct. 1	Prof. Hitoshi Kihara was elected the 2nd Director.
1960	Apr. 30	Department of Human Genetics was added
1962	Apr. 1	Department of Microbial Genetics was added.
1964	Apr. 1	Department of Population Genetics was added.
1969	Apr. 1	Prof. Daigoro Moriwaki was elected the 3rd Director. Department of Molecular Biology was added.
1974	Apr. 1	Plant Genetic Stock Laboratory was established.
1975	Mar. 1	Dr. Yataro Tajima was elected the 4th Director.
	Oct. 1	Animal Section was added in the Genetic Stock Center.
1976	Oct. 1	Microbial Section was added in the Genetic Stock Center.
1983	Oct. 1	Dr. Ei Matsunaga was elected the 5th Director
1984	Apr. 12	Reorganized as an inter-university research institute for joint use by universities. The DNA Research Center (DNA Structure and Recombinant DNA Laboratories) and the Experimental Farm were established. The Genetic Stock Research Center was expanded into five laboratories: the Genetic Resources Laboratory was added and the Animal Section was divided into the Mammalian and Invertebrate Laboratories.
1985	Apr. 1	The DNA Synthesis and DNA Data Analysis Laboratories were added in the DNA Research Center
1987	Jan. 12	The DNA Data Bank of Japan began its operations.
1988	Apr. 8	The Radio-isotope Center was established. The Gene Library Laboratory was added in the DNA Research Center.
	Oct. 1	The Graduate University for Advanced Studies was established. The Department of Genetics, School of Life Science of the University began accepting students.
1989	Oct. 1	Dr. Jun-ichi Tomizawa was elected the 6th Director.
1993	Apr. 1	The Mammalian Development Laboratory was added in the Genetic Stock Research Center.
1994	Jun. 24	The Gene Function Research Laboratory was added in the DNA Research Center.
1995	Apr. 1	The Center for Information Biology was established.
1996	May. 11	The DNA Research Center was reorganized as the Structural Biology Center consisting of 5 laboratories (Biological Macromolecules, Molecular Biomechanism, Multicellular Organization, Biomolecular Structure and Gene Network).
1997	Apr. 1	The Genetic Stock Research Center was reorganized as the Genetic Strains Research Center consisting of 5 laboratories (Mammalian Genetics, Mammalian Development, Plant Genetics, Microbial Genetics and Invertebrate Genetics), and as the Center for Genetic Resource Information consisting of 2 laboratories (Genetic Informatics and

		Genetic Resources).
	Oct. 1	Dr. Yoshiki Hotta was elected the 7th Director
1998	Apr. 9	The Division of Early Embryogenesis was added in the Department of Developmental Genetics. The Division of Brain Function was added in the Department of Integrated Genetics.
2001	Apr. 1	The Center for Information Biology was reorganized as the Center for Information Biology and DNA Data Bank of Japan. The new center consists of 5 laboratories. The Laboratory of Molecular Classification of the former center was renamed as the Laboratory for Research and Development of Biological Databases in the new center. The Laboratory for Gene-Expression Analysis was added in the new center.
2002	Apr. 1	Two laboratories, Mouse Genomics Resource Laboratory and Model Fish Genomics Resource Laboratory, were added to the Genetic Strains Research Center.
2003	Apr. 1	The Molecular Mechanisms was added to the molecular Genetics. The Laboratry for Frontier Research was added to the Genetic Strains Research Center. Two laboratories, Comparative Genomics Laboratory and Publicity and Intellectual Propery Unit, were added to the Center for Genetic Resource Information.
2004	Apr. 1	Reorganized as Research Organization of Information and Systems, Inter-University Research Institute Corporation, together with three other national institutes.
	Dec. 1	Dr. Yuji Kohara was elected the 8th Director.
2005	Apr. 1	Intellectual Property Unit was added. Renamed as NIG INNOVATION (as of 2018 Apr.1)
2006	Apr. 1	The Center for Frontier Research was established. The Laboratory for Cell Lineage, Neural Morphogenesis and Cell Architecture was added in the new center.
2011	Oct. 1	Advanced Genomics Center was established
2012	Apr. 1	Research centers were reorganized. Intellectual Infrastructure Centers (Genetic Resource Center and DDBJ Center) and Support Centers (IT Unit, Mouse Research Supporting Unit) were established.
	Dec. 1	Dr. Isao Katsura was elected the 9th Director.
2014	Apr. 1	Office for Research Development was added.
2015	Apr. 1	Unit for Experimental Animal Care was established. Office for Female Researcher Development was added. Renamed as Office for Gender Equality (as of 2017 Apr. 1)
2018	Dec. 1	Dr. Fumio Hanaoka was elected the 10th Director.
2019	Jan. 1	The existing 5 departments, 3 research centers (Genetic Strains Research Center, Structural Biology Center and Center for Information Biology), Experimental Farm and Radio-isotope Center were abolished. Four research departments (Dept. of Informatics, Dept. of Genomics and Evolutionary Biology, Dept. of Gene Function and Phenomics and Dept. of Chromosome Science) were established. The DDBJ Center, as one of the Intellectual Infrastructure Centers, was renamed as the Bioinformation and DDBJ Center. The Support Center was reorganized. (The Radioisotope Unit was added.)

Organization

2019.1.1

Advisory Committee

Director-General Fumio HANAOKA

Advisory Board

Council for Strategy Planning ・
Council for intra-ROIS liaison and Coordination

Vice-Director

・Hironori NIKI
・Toshihiko SHIROISHI
・Hiroyuki ARAKI
・Yumiko SAGA

International Strategic Advisor /
Visiting Faculty

・Takao K HENSCH ・John F.X. DIFFLEY
・Frederic BERGER ・Didier STAINIER
・Steven HENIKOFF ・Yun-Xin FU
・Kiyoshi MIZUUCHI ・Ziheng YANG
・Feng ZHANG ・Lynn JORDE

Research Department

Department of Informatics

Biological Networks – Masanori ARITA
Genetic Informatics – Shoko KAWAMOTO
Genome Evolution – Ken KUROKAWA
Genome Informatics – Yasukazu NAKAMURA
Gene-Expression Analysis – Kousaku OKUBO
Laboratory for Research and Development of Biological Databases – Toshihisa TAKAGI

Department of Genomics and Evolutionary Biology

Evolutionary Genetics – Hiroshi AKASHI
DNA Data Analysis – Kazuho IKEO
Human Genetics – Ituro INOUE
Ecological Genetics – Jun KITANO
Population Genetics – Naruya SAITOU
Plant Genetics – Yutaka SATO
Comparative Genomics – Atsushi TOYODA

Department of Gene Function and Phenomics

Brain Function – Tatsumi HIRATA
Laboratory of Mammalian Neural Circuits – Takuji IWASATO
Laboratory of Molecular and Developmental Biology – Koichi KAWAKAMI
Mouse Genomics Resource – Tsuyoshi KOIDE
Symbiosis and Cell Evolution – Shin-ya MIYAGISHHIMA
Microbial Physiology – Hironori NIKI
Plant Cytogenetics – Ken-ichi NONOMURA
Mammalian Development – Yumiko SAGA
Model Fish Genetics – Noriyoshi SAKAI
Multicellular Organization – Hitoshi SAWA
Mammalian Genetics – Toshihiko SHIROISHI
Gene Network – Emiko SUZUKI

Department of Chromosome Science

Microbial Genetics – Hiroyuki ARAKI
Epigenomics – Tetsuji KAKUTANI
Molecular Cell Engineering – Masato KANEMAKI
Cell Architecture – Akatsuki KIMURA
Genome Dynamics – Kazuhiro MAESHIMA
Invertebrate Genetics – Kuniaki SAITO

Center for Frontier Research

Systems Neuroscience – Fumi KUBO
Chromosome Biochemistry – Yasuto MURAYAMA
Cell Dynamics and Organization – Yoshihisa ODA
Quantitative Mechanobiology – Yuta SHIMAMOTO

Intellectual Infrastructure Center

Bioinformation and DDBJ Center

・High Performance Computing Division
・Database Division

Advanced Genomics Center

・Sequencing Division
・Data Analysis Division

Genetic Resource Center

・Bioresource Management Division
・Plant Resource Development Division
・Division for development of genetic-engineered mouse resource
・Bioresource Database Division

Support Center

・IT Unit
・Radioisotope Unit
・Unit for Experimental Animal Care

NIG INNOVATION

Office for Research Development

Office for Gender Equality

Department of Administration

・General Affairs and Project Section
・Financial Affairs Section

Technical section

Outline of Departments and Centers for Research Infrastructures

Department of Informatics
Develop technologies and resources that enable users to extract actionable information from data and knowledge in life sciences.

Department of Genomics and Evolutionary Biology
Research many aspects of organisms with special reference to genome sequence analyses and their evolutionary histories.

Department of Gene Function and Phenomics
Research on genetic traits at the cellular and organismal levels and on characteristics of biological and genetic resources.

Department of Chromosome Science
Research on genetic mechanisms, such as inheritance, modifications and expression of genetic information.

Center for Frontier Research
The Center for Frontier Research provides promising young scientists with independent positions and an opportunity of developing new frontiers in genetics and related research fields. The Center thereby brings up scientists who will play crucial roles in academic fields in the future.

Bioinformation and DDBJ Center
Bioinformation and DDBJ Center collaborates with NCBI (USA) and ENA/EBI (Europe) to maintain the International Nucleotide Sequence Database Collaboration (INSDC). It also provides a public supercomputing system.

Advanced Genomics Center
This center is designed to conduct most advanced genomic researches and to provide resources based on new-generation sequencing pipeline to the community.

Genetic Resource Center
The center develops and preserves forefront bioresources of various organisms, and distributes them to domestic and overseas universities and institutes. The related information is open to the public through the databases. The center participates actively in “National BioResource Project (NBRP)” of AMED.

Research Achievements and Self Evaluation

Department of Informatics

Biological Networks Laboratory
Masanori Arita Group

Starting from November 2013 at NIG, our laboratory has been creating bioinformatics tools and standards to accelerate life sciences. In cheminformatics, we maintain internationally acknowledged databases called MassBank and LipidBank for over 10 years. In the last 5 years, we developed a software tool for non-targeted metabolomics that realizes comprehensive acquisition of MS/MS information [808]. Then through the integration with metabolome repositories, we could identify five hitherto unknown metabolites [811, 371]. The quest for better identification continues and we actively participate in international efforts for data standardization toward FAIR data principles [628, 839, 44].

In genomics, we have advanced computational classification and characterization of *Lactobacillus* and *Bifidobacterium* based on their genomic features. Using our efficient genome-annotation tool [781], we characterized functional features of the above two genera [663], and also discovered new *Lactobacillus* species such as *L. paragasseri* from a genome sequence archive [734, 785]. Most genomics works have been performed with Sokendai graduate students.

Genetic Informatics Laboratory
Shoko Kawamoto Group

We are working on research and development of databases and information systems for the National Bio-Resource Project (NBRP) since 2002. Former PI, Yukiko Yamazaki had been developing more than 20 resource organism's databases, which distribute experimental organisms for academic researcher, until her retirement in 2016 [680]. Based on each organism's database, we had been developing a search engine that allows users to conduct the cross-species search for experimental resources, by applying biological ontologies such as gene ontology, plant ontology, and disease ontology. Further, we made several organism's genome sequences available to the public via genome browser in order to increase the biological resource availability [736]. From 2017, we are in charge of the system development for Japanese Rare Disease Models & Mechanisms Network (J-RDMM) under Japan's initiative on rare and undiagnosed diseases (IRUD) project funded by the Japan Agency for Medical Research and Development (AMED).

Genome Evolution Laboratory
Ken Kurokawa Group

The Genome Evolution Laboratory was launched in April 2016 as a new laboratory in NIG. In our laboratory, we are interested in understanding about microbial genome evolution and microbial community dynamics, and we are currently reaching out in the following two major research directions; I. Facilitate the development of

an integrated database for microbes “MicrobeDB.jp” [469, 150], II. Study microbial community dynamics [498, 409, 572, 834, 571, 136, 835, 529]. Our research interests blend a background in microbial genomics and metagenomics with bioinformatics and integrated database developments that are just now allowing the prospect of illuminating microbial community dynamics. We are trying to gain a better understanding of how microbial diversity maintain as well as how it emerged [149, 398]. We are also trying to propose a new evolutionary scenario by recovering DNA information from paleontological remains [873, 664].

Genome Informatics Laboratory
Yasukazu Nakamura Group

Ultra high-throughput sequencing technologies allow biologists to obtain larger amounts of nucleotide sequence data. To facilitate for reuse such huge nucleotide data, it is necessary to create a high-quality sequence database as reference data. It is also important to equip automated annotation system that make it possible fast and accurate results for reliable sequencing analysis. Our laboratory is in charge of DNA Data Bank of Japan (DDBJ) [328] and attempts to develop advanced database management systems and to improve the quality of annotations in genome databases. We have been constructing an automatic annotation system for prokaryotes: DDBJ Fast Annotation and Submission Tool (DFAST) [780]. We are also providing several high-quality annotated genome information for important plant species such as a liverwort *Marchantia polymorpha* [43] and a japanese orange *Citrus unshu* [687].

Gene-Expression Analysis Laboratory
Kousaku Okubo Group

Our body of biomedical knowledge is developed in two steps: StepA: accumulating and exchanging situations captured in descriptions and data; and StepB: conceptualizing situations into a coherent set of dogmatic or mathematical statements that can be employ in decision-making. The overwhelming output of A, mainly due to the technological assistance by diagnostic, laboratory and communication machines, is making a stressful situation of “information over-load” or “data deluge”. Our laboratory focuses on developing new technologies to facilitate step B to enhance the return from our investment in biomedicine[586, 77].

Laboratory for Research and Development of Biological Databases
Toshihisa Takagi Group

We have developed data sharing and data analysis infrastructures to cope with the recent explosion of genome data. We have addressed a series of crucial issues for the genome data sharing, including the performance issues in database construction and genome data analysis, reproducibility of the data analysis, sustainability of database management, and security and policy issues for the personal genome data management [402, 401, 328]. We have contributed to the operation of unrestricted-access nucleotide sequence databases of International Nucleotide Sequence Database Collaboration (INSDC) [57, 402, 401, 328, 272]. In addition, we have contributed to the establishment of the controlled-access database of personal genome in Japan, Japanese Genotype-phenotype Archive (JGA) in collaboration with the National Bioscience Database Center (NBDC) in the Japan Science and Technology Agency (JST) [329, 402, 401, 328]. Our group has also constructed the controlled-access database for specific researchers, "AMED Genome group sharing Database (AGD)". Finally, we have been developing a data analysis environment for personal genomes on the NIG supercomputer along with the databases.

Department of Genomics and Evolutionary Biology

Evolutionary Genetics Laboratory
Hiroshi Akashi Group

Our research aims to identify the causes of genome evolution. We are especially interested in applying population genetics theory to large scale within- and between-species DNA data to test whether new mutations in the genome often have subtle functional and fitness effects related to fundamental biological processes such as transcription and translation. The power and robustness of our statistical approaches is critical for such analyses and method development has been a major recent focus [410, 413, 411]. We have developed methods that allow inference of ancestral and derived nucleotide states that account for biased characters and changes in biases over time, and that are accurate for within-species variation. These methods enhance the resolving power of evolutionary sequence analysis and will allow us to address key biological questions including recent fluctuations in genome-wide codon usage adaptation, relationships between chromatin structure and genome evolution, and the biophysical basis of prevalent weak selection in protein evolution [396].

DNA Data Analysis Laboratory
Kazuho Ikeo Group

We have been conducting research on molecular classification, evolution of symbiosis [891], and diseases mechanisms [652] using comparative genomics, molecular evolution, and bioinformatics. At the same time, we engaged in a Hydra strain conservation project. In the project based on external grants, we promoted NGS data analysis support to promote the use of NGS data for drug discovery in BINDS program (AMED). In Program for Basic and Clinical Research on Hepatitis (AMED), we tried analyzing transcriptome and SNPs concessions to elucidate the molecular mechanism of liver cancer onset. In CREST(JST), we worked on technology development for single cell transcriptome, especially development of data analysis method. In the SHINGAKUJYUTSU (JSPS), we are working for clarifying state transition of disease on the single cell level. The result obtained through these activities were published (51 papers) and released as databases and analysis tools. Four postdoctoral fellows and one SOKENDAI student and two additional students from other university participated in the research.

Human Genetics Laboratory
Ituro Inoue Group

Our research goal is to elucidate causalities of common diseases such as intracranial aneurysms and endometriosis and their pathogenesis. We employ next generation sequencing technologies to identify causalities of monogenic diseases as well as common diseases. Using the vast amount of genomic information at hand, we combine gene expression profiles of the response tissues together with clinical information to understand the global picture of diseases. [157, 226, 503, 707]

Ecological Genetics Laboratory
Jun Kitano Group

Our research goal is to identify molecular changes underlying naturally occurring phenotypic variation and speciation and understand how such variations arise and spread within natural populations. Because of recent advances in genomic technologies, an increasing number of candidate genomic loci or genes responsible for adaptation and speciation have been identified. Molecular changes or causative mutations, however, have been rarely elucidated. Without knowing causative mutations, we cannot understand how many mutations are important, whether each mutation is additive or epistatic, or what kind of selective pressures have acted on each mutation. To this end, we take an integrative approach across diverse disciplines using stickleback fishes (genus Gasterosteus and Pungitius) and medake fishes (genus Oryzias) as models [619, 602, 878]. Thus far, we have identified several causative genes and mutations (unpublished data). Further investigation of these mutations will lead to a better understanding of the mechanisms underlying naturally occurring phenotypic variations.

Population Genetics Laboratory
Naruya Saitou Group

We study evolution of organisms at the genomic levels through computer analyses and genome sequencing. We published a total of 20 papers during these five years. Among them, we reported human evolution with special reference to the origin and formation of people on Japanese Archipelago using modern and ancient genomes in eight papers [e.g., 251 and 271] and evolution of conserved noncoding sequences in various eukaryotic organism genomes in five papers [e.g., 36 and 143]. Saitou published “Introduction to Evolutionary Genomics Second Edition” (2018, Springer) and edited “Evolution of the Human Genome Volume I” (2017, Springer). The Google Scholar citations of the neighbor-joining method paper (Saitou and Nei, 1987) exceeded 53,000 at the end of 2018. In addition, Saitou devised and described two new methods (swift neighbor-joining method and external edge elimination) in his 2018 book.

Plant Genetics Laboratory
Yutaka Sato Group

Our group is trying to address a basic question on how do plants shape themselves and reproduce their offspring. In order to answer the question, we first aim to elucidate the mechanism of plant embryogenesis using rice as a model system [121, 233, 347]. We are focusing on processes of the patterning of apical-basal or dorsal-ventral axis formation, the organogenesis during early stages of rice embryogenesis and post embryonic development [173]. We are taking a molecular genetic approach using a series of rice embryogenesis defective mutants as well as comparative embryology and genomics approaches mainly among grass species. Secondly, we are trying to describe the mechanism generating the diversity of plant reproduction systems [727]. Our work takes an advantages of the wild accessions of *Oryza* collections at NIG; the vast diversiy in seed traits among Oryza species is powerful and convenient. We are also responsible for management, preservation, propagation, and distribution of rice genetic resources of wild rice species collected at NIG under the National BioResource Project (NBRP).

Comparative Genomics Laboratory

Atsushi Toyoda Group

The Comparative Genomics Laboratory was established in April 2008 with the task to understand basic rules of biological systems using cutting-edge DNA sequencing and analysis technologies. To date, we have employed comparative genomics approaches to identify genomic features and provide new insights into the genetic diversity of wild Oryza species and the terrestrialization process in the Chara genome [622, 562, 530]. Furthermore, through de novo sequencing of different types of algae, two silkworm species, and the organisms living in the extreme environmental conditions, we have shed light on critical mechanisms for the evolution of multicellularity, the history of domestication, and the process of cryptobiosis, respectively [118, 113, 129]. In addition, we characterized the allotetraploid origin of *Xenopus laevis* by genome comparison to the diploid *X. tropicalis* as international collaborative research [671]. Since FY 2018, we have been supporting and developing metagenomic and bioinformatic analyses to promote human microbiome research.

Department of Gene Function and Phenomics

Brain Function Laboratory
Tatsumi Hirata Group

The brain is made up of an enormous number of neurons, whose wiring patterns determine the characteristics of an animals' behavior and mental activities. The Brain Function Lab focuses on genetic mechanisms that determine the axon wiring patterns which develop through sequential steps such as neuronal migration and axon guidance. Using gene knockout mice for various axon guidance-related molecules, we revealed molecular mechanisms that control specific aspects of axon guidance and neuronal migration [437, 265, 61]. For example, in one paper [860], we provided the evidence that the famous guidance molecule netrin-1 guides hindbrain commissural axons by short-range actions but not by the long-range chemoattraction as had been believed for a long time. We also advanced the study of brain development from the evolutionary point of view [726, 534, 533]. By sharing our special techniques and materials, we performed intra-institutional [437, 655] and inter-university [561, 227, 265, 228, 61, 399, 533, 860] collaborations. Since 2015, a new assistant professor, Yan ZHU has joined the lab and started a new model involving mouse hindbrain [799, 900].

Laboratory of Mammalian Neural Circuits
Takuji Iwasato Laboratory

We aim to understand development of neuronal circuits in the mammalian central nervous system. During the last 5 years, we have published 18 papers, including 10 papers in which we are the main contributors. Our main achievements in this period are as follows: (I) We have developed the "Supernova", which is a versatile vector system for single-cell labeling and gene function studies *in vivo* [457, 382]. (II) We have developed *in vivo* imaging systems for neonatal mouse cortex and used them to reveal dynamic mechanisms of dendritic refinement of layer 4 (L4) neurons [457, 510], and unique spatial patterns and features of spontaneous activity [456, 510] in the neonatal barrel cortex. (III) By generating conditional knockout mice of the adenylyl cyclase 1 and NMDA receptor NR1 subunit, we revealed pre- and post-synaptic mechanisms of thalamocortical circuit refinement in the developing somatosensory system [722]. (IV) By generating series of knockout mice of α-chimaerin and its isoforms, we revealed that this molecule plays important roles in cognitive function [243], spine development [242] and midline barrier establishment in corticospinal axon guidance [287].

Laboratory of Molecular and Developmental Biology
Koichi Kawakami Group

We have developed *Tol2*-transposon mediated genetic methods, including transgenesis, gene trapping, enhancer trapping and the Gal4-UAS system in zebrafish [296]. By using these methods, we have performed a large-scale genetic screen and generated more than 1,500 transgenic lines expressing Gal4 in specific cells, tissues, and organs. Further, we constructed a database named zTrap which facilitates collaboration with researchers world-wide who can find transgenic fish of interests in our collection based on expression patterns. Thus, our transgenic fish serve as powerful resources to study developmental biology, organogenesis, neuroscience and human diseases [830, 295, 68, 33]. We aimed to apply these methods to analyze functional neural circuits controlling fish behaviors. First, we expressed GCaMP in various brain regions via the Gal4-UAS system, and

successfully imaged the neuronal activity during hunting behaviors in real-time [485]. Second, we expressed the neurotoxin gene to inhibit the activity of Gal4-expressing neurons and successfully identified neurons essential for fear conditioning in zebrafish [705, 372].

Mouse Genomics Resource Laboratory
Tsuyoshi Koide Group

The aim of this laboratory is to clarify the genetic and neural basis of behavior in mice. We mainly study aggression, home-cage activity, anxiety, social behavior and tameness. Tameness is a major behavioral factor for domestication. We conducted selective breeding for tameness using genetically heterogeneous wild-derived mouse stock and successfully established mice exhibiting high tameness. By using these mice, we mapped genetic loci associated with the tameness [418]. To understand how social stress affect behaviors, we analyzed social hierarchy in groups of male mice in home cage and investigated emotional behavior as well as hippocampal gene expression in the dominant and subordinate mice. We found significantly different emotional behavior and expression of genes associated with the serotonergic system between dominant and subordinate mice [180]. In order to understand genetic and neural mechanism associated with aggression, we conducted genetic mapping [747] and neurobehavioral analysis and found a neural system associate with escalated aggression [743].

Symbiosis and Cell Evolution Laboratory
Shin-ya Miyagishima Group

Several lineages of eukaryotes acquired the capability of photosynthesis through endosymbiotic events in which a cyanobacterial or photosynthetic eukaryotic cell was integrated into previously nonphotosynthetic eukaryotic cells. However, it is still unclear how the permanent endosymbiotic relationship was established by coordinated proliferation of a host and an endosymbiotic cell. By using several unicellular algae and newly developed molecular genetic tools in the red alga *Cyanidioschyzon merolae* [85, 86], we have shown the following. Chloroplast division is restricted to the S phase by the host cell cycle [591]. Alternatively, host cell cycle progression (prophase to metaphase) requires initiation of chloroplast division [718]. The G1/S transition is restricted to (subjective) evening and night when oxygenic photosynthesis in chloroplasts and respiration in mitochondria are compromised by host nuclear regulation [444]. Thus, our studies have begun to reveal how activities of eukaryotic cells and endosymbiotic organelles are coordinated by the interactive signaling between them to coordinate their proliferation.

Microbial Physiology Laboratory
Hironori Niki Group

Bacteria and yeast are important model organisms to elucidate the fundamental mechanisms of cell proliferation. Our laboratory studies the mechanisms behind the cell division cycle and adaptations to external stresses under environments. We focused on compaction of chromosomal DNA as a nucleoid inside a tiny bacterial cell during cell division. Bacterial condensin is an essential factor for packaging of a nucleoid to properly segregate into daughter cells. We found that bacterial condensin topologically loads on DNA, and preferentially binds to single-stranded, rather than double-stranded, DNA [519]. In a bacterial cell, bacterial condensin loads on

rDNAs that are located near replication origins [867]. In addition, we study hyphal development and growth by using a new model organism, *Schizosaccharomyces japonicus* that is closely related to the fission yeast *S. pombe* [517]. However, *S. japonicus* is dimorphic yeast and non-pathogenic. We established new investigative methodologies to investigated *S. japonicus* [20, 22, 96] and have revealed that several biological processes conserved in *S. pombe* as well as some that are not conserved[21, 536].

Plant Cytogenetics Laboratory
Ken-ichi Nonomura Group

This laboratory aims to unveil genetic mechanisms driving plant reproduction; including meiotic cell-fate decision, meiosis, reproductive organ development and meristem maintenance. In the last five years, we reported that the Argonaute protein MEL1 associates with 21- and 24-nt non-codingRNAs (phasiRNAs) in rice reproductive organs [335, 334] and is required for meiotic chromatin modifications [379]. The 24-nt phasiRNAs were produced in tapetal cells surrounding male meiocytes [587, 588]. These results imply the nature of phasiRNAs in non-cell autonomous regulation of meiotic events. We also revealed a DNA consensus bound with MEL2, the rice protein required for meiosis entry [453]. In meristem research, we analyzed KNOX proteins and cofactors in rice and maize [807, 805, 383].

Furthermore, this laboratory is responsible for the maintenance of rice genetic resources with Plant Resource Development division. For this purpose, molecular markers were developed [516] and genetic diversity of natural populations was explored [592].

Mammalian Development Laboratory
Yumiko Saga Group

We use mouse genetics to elucidate molecular mechanisms involved in several developmental processes such as germ cell development and somitogenesis. Recent achievements are as follows: (I) Germ cells are first specified as primordial germ cells (PGCs) in the early embryonic stage. However, it is largely unknown what factor is responsible for sexual fate determination in germ cells. We demonstrated that two factors (STRA8 and SMAD4) work as sex determinants since female germ cells lacking both *Smad4* and *Stra8* develop as male gonocyte-like cells in ovaries [843]. (II) In the male germ cells, an RNA binding protein NANOS2 is essential to promote male pathway. We have identified DND1, another RNA binding protein, as a partner of NANOS2 to recruit target RNAs [844, 724, 285]. (III) NANOS2 is also required for sustainable spermatogenesis in adult testes. We showed mechanisms of NANOS2 action in spermatogonial stem cells (SSCs) and demonstrated how NANOS2 expression is regulated in SSCs [899, 898]. (IV) Previously we identified a transcription factor Mesp2 and the target gene *Ripply2* as factors required for somite segmentation. We found that Ripply2 directly binds Tbx6 (an enhancer of *Mesp2*) to degrade it to define the segmental border [896].

Model Fish Genetics Laboratory
Noriyoshi Sakai Group

Our lab focuses on germ cell development in zebrafish. To analyze molecular mechanisms to regulate germ cells efficiently, we developed techniques to recapitulate the entire process of spermatogenesis entirely in cell culture, from spermatogonial stem cell propagation to differentiation of functional sperm, [306]. This culture

technique was applied for spermatogonia of the endangered endemic cyprinid *Gnathopogon caerulescens* [146]. We also established subcutaneous grafting methods of a fragment of the hyperplastic testis and a whole body of the embryo for *in vivo* assay, which enable continuous growth of the hyperplastic testis and development of embryonic lethal mutants beyond the lethal stage to the spermatogenic stage [305]. Furthermore, we investigated the meiotic process and found formation of a clear telomere bouquet structure and initiation of synapsis from the telomere region in zebrafish spermatocytes, unlike the mouse [639]. In addition, we established a new inbred zebrafish line from the AB line by complete sib-pair mating for more than 20th generations. The inbred line, ABM, is healthier and more readily maintained compared to the previously established IM line.

Multicellular Organization Laboratory
Hitoshi Sawa Group

The relationship between cell size and cell cycle was reported only in *Xenopus*. We showed in *C. elegans* embryos that cell cycle duration and cell size exhibited a power law distribution as in *Xenopus*. However, the absolute powers in *C. elegans* were different from that in *Xenopus* and depends on cell types [30]. PIGN is known to be an enzyme for glycosylphosphatidylinositol (GPI)-anchor biosynthesis in the endoplasmic reticulum (ER). We showed that independent of this enzymatic activity, PIGN functions to prevents protein aggregation in ER in *C. elegans* and in mammalian cells [197]. The adenomatous polyposis coli (APC) protein is a tumor suppressor that inhibits canonical Wnt signaling and stabilizes microtubules by binding to their plus ends. We have shown in *C. elegans* embryo that APC on the cell cortex attenuates spindle-pulling forces to prevent excess movements of centrosome during asymmetric division [712].

Mammalian Genome Laboratory
Toshihiko Shiroishi Group

1. Mechanism and evolution of enhancers regulating tissue-specific *Shh* expression
We identified remote enhancers that regulate *Shh* expression specifically in various different endodermal tissues by genetic analyses of spontaneous mouse mutants and gene-modification methodologies including genome editing. Furthermore, we conducted comparative analyses of the enhancer sequences across a wide-range of vertebrates and experimental analyses with mice and medaka fishes, and we found that evolution of the *Shh* enhancers has been involved in morphological change of respiratory laryngeal structure in vertebrates [637].

2. Mechanism of mouse speciation
Reproductive isolation promotes speciation. A good example is hybrid male sterility observed in mouse, which may be caused by genetic incompatibility between diverged genetic factors in two mouse subspecies. Genetic factors responsible for the sterility are disproportionately located on the X chromosome. Our studies showed that evolutionary divergence of transcriptional regulation causes genetic incompatibilities in the hybrid males, and results in reproductive isolation [567].

Gene Network Laboratory

Emiko Suzuki Group

Our laboratory is studying molecular and cellular mechanisms of tissue development and function, using *Drosophila melanogaster* as a model system. We have been focused on two lines of projects. The first topic is epithelial cell competition for the homeostasis of normal tissue development. We found new mechanisms for cell competition and also found special epithelial areas, tumor hot spots, in which abnormal outcome of cell competition leads to tumors [767]. The second line of research focuses on formation and function of neuronal circuits. By studying the taste system, we identified the neurons crucial for the connection between sensory inputs and the feeding motor system, and the neurons which connect sensory inputs and higher order neurons involved in the reward system associated with olfaction. We also carried out many collaborative projects including 28 NIG Collaborative Research Programs (NIG-JOINT) on neuronal functions, offering our expertise of electron microscopy for the analyses of subcellular structures [669, 710].

Department of Chromosome Science

Microbial Genetics Laboratory
Hiroyuki Araki Group

We have studied eukaryotic chromosome DNA replication using budding yeast as a model organism and have made some important discoveries. First, we solved the crystal structures of the Sld3 and Sld7 proteins, which form a complex working at the initiation step of DNA replication, and revealed that two Sld3 molecules are connected by two Sld7 molecules in an anti-parallel manner. This structure suggests simultaneous loading of Sld3 onto a pair of helicase cores, Mcm2-7, preloaded on replication origins [235, 236]. Second, we analyzed assembly of replication proteins at origins and revealed new mechanisms, which include automatic splitting of a pair of Mcm2-7 after the assembly and formation of a replicative helicase, Cdc45-Mcm2-7-GINS (CMG) complex [169, 454]. Thirdly, we showed that DNA polymerase modulates the activity of CMG helicase to pause the replication fork at the barrier [168]. This finding suggests a novel regulation of the CMG helicase activity by DNA polymerase when the replication forks face barriers on chromosome.

Epigenomics Laboratory
Tetsuji Kakutani Group

In Arabidopsis mutants defective in DNA methylation, diverse transposable elements (TEs) were mobilized, indicating that DNA methylation is important for immobilizing them (Miura et al 2001 *Nature*; Tsukahara et al 2009 *Nature*). *VANDAL21*, one of the TEs immobilized by DNA methylation, encodes a protein with anti-silencing effect; that protein, called VANC, induces loss of DNA methylation, expression of encoded genes and mobilization of *VANDAL21* (Fu et al 2013 *EMBO J*). We have shown that this anti-silencing system is sequence-specific and that the proteins and targets coevolve to differentiate the sequence specificity [184]. An important remaining question is how this anti-silencing is accomplished, after sequence-specific binding of this protein.

Silent epigenetic marks, such as DNA methylation and methylation of lysine 9 of histone H3 (H3K9me), are found not only in promoters but also in internal regions (body) of transcription units. Despite its prevalence, the biological significance of gene body silent modifications remains enigmatic. We showed that H3K9me-associated removal of H3K4 monomethylation (H3K4me1) in gene bodies mediates transcriptional silencing. Mutations in an Arabidopsis H3K9 demethylase gene *IBM1* induce ectopic H3K9me2 accumulation in gene bodies, with accompanying severe developmental defects (Saze et al 2008 *Science*). Through suppressor screening of the *ibm1*-induced developmental defects, we showed that gene-body H3K9me2/H3K4me1 mediates heterochromatin silencing and epigenome differentiation [207].

Molecular Cell Engineering Laboratory
Masato Kanemaki Group

Our group pioneered auxin-inducible degron (AID) technology to rapidly degrade a degron-fused protein of interest in nonplant cells. To apply this technology to control endogenous proteins in human cells, we developed a new method to tag endogenous genes using the CRISPR–Cas9 genome editing and generated conditional cells of RAD21 cohesin and DHC1 dynein [513]. The plasmids for making AID mutants were deposited at Addgene and NBRP, which have distributed more than 2000 plasmids to researchers all over the world. We published a review paper to promote the use of degron technologies [512]. We also used the AID technology to reveal a backup mechanism to deal with a failure in DNA replication and showed a pathway to form mitotic chromosomes [514, 101].

Cell Architecture Laboratory
Akatsuki Kimura Group

This laboratory aims to understand how the spatial organization of cells is accomplished in terms of genetics, mechanics, and self-organization. For this purpose, we combine genetics with quantitative microscopy and mechanical modeling of cells, using *Caenorhabditis elegans* as a primary model organism. A major question is how nanometer-sized macromolecules can measure micrometer-sized cellular spaces. We have revealed how the cell nucleus finds the center of the cell [779] and discovered scaling relationships between the nuclear size and chromosome compaction [122] and between nuclear size and chromosome mobility [24]. We also succeeded in constructing a mechanical model that accounts for the relationship between eggshell shape and the cell arrangement within the eggshell [856]. Another question is how the macromolecules in a cell behaves collectively. As a collective behavior, we focus on cytoplasmic streaming, and have succeeded in constructing mechanical models of actin-based [531] and microtubule-based [313] streaming.

Genome Dynamics Laboratory
Kazuhiro Maeshima Group

How is the long strand of genomic DNA organized in the cell? For the past 5 years, using various imaging technologies, we have been contributing to change people's view on chromatin structure from a static regular one to a more irregular and dynamic one [387, 393]. By combining super-resolution imaging and single nucleosome tracking, we revealed that chromatin forms numerous dynamic compact domains that act as functional units of the genome [538]. This compact organization seems to generate a spring-like force that resists various mechanical stresses [684]. Furthermore, to better understand the chromatin environments in living cells and given the ease with which chromatin structure and dynamics can be modulated in the cellular environment by free cations and macromolecular crowding, we developed new imaging methods and visualized free Mg^{2+} behavior [391] and density of total materials [202] in living cells, shedding new light on the nature of chromatin and how it is regulated.

Invertebrate Genetics Laboratory

Kuniaki Saito Group

The genome-sequencing project stimulated many studies that revealed conservation and difference of the genetic systems in many model organisms. The fruit fly *Drosophila* that has 14,066 genes in its genome was studied extensively in genetics and reverse genetics. However, biological function of a half of its genes is still obscure. To develop a genetic resource for comprehensive analyses of fly genes, we are establishing RNAi and knock out mutants. By mid2018, we comprehensively generated fly lines that can knock down 10,000 genes using RNAi and knock out 2,500 genes by the CRISPR/Cas9 system. These strains are open to all researchers globally and are widely utilized for studying gene functios [225, 339]. As a result of collaborations, more than 20 research papers were published. These achievements demonstrate our substantial contribution to the fly research community and the development of a promising approach to clarify complex systems of genetic networks underlying fly genome function.

Center for Frontier Research

The Center for Frontier Research is an “incubation” system to foster human resources and new research fields. Promising young scientists conduct research as principal investigators (tenure-track associate professors) to explore new frontiers in genetics and related areas, taking advantage of NIG’s research infrastructure and support systems. Those who obtain tenure establish new research divisions in NIG to lead the new fields that they contributed to creating.

During the tenure-track period of 5 years each faculty is provided ample laboratory facilities, generous funding (a total of 36 million JPY of research funds as well as a postdoctoral fellow and a technician position) and limited service and teaching duties. Before finishing the term, the tenure evaluation is conducted based on the candidate’s potential to lead a new research field. The criteria could be fulfilled by a discovery of a new phenomenon, concept, technique, or molecule that foreshadows a new research field, followed by a demonstration of the path to the establishment of such a field.

In the past five years, four CFR members succeeded to obtain tenure and were appointed as professors of new Labs in NIG. In addition, four new members (including one female scientist) were selected through a highly competitive selection process (international recruitments).

Systems Neuroscience Laboratory
Fumi Kubo Group

Animals generate a range of behaviors depending on visual information that they receive from the outside world. Using zebrafish as a model, our lab studies the neural circuit mechanisms by which visual inputs produce goal-directed behavioral outputs. In particular, we aim to understand the roles of genetically defined neuron types and their circuit connectivity underlying the visually guided behaviors. Our approaches include behavioral, genetic and optical techniques, as well as quantitative data analyses. In our lab, started in Dec 2017, we have established an infrastructure for imaging neural activity of larval zebrafish *in vivo* using two-photon microscopy, combined with simultaneous visual stimulation. We have developed optogenetic tools to analyze the function and morphology of single neurons *in vivo* [72]. Furthermore, we have applied these optogenetic methods to a visual processing circuit to reveal the function and connectivity of the underlying neural circuit (Kramer et al., in preparation).

Chromosome Biochemistry Laboratory
Yasuto Murayama Group

Our laboratory studies the molecular mechanism that enables proper organization and faithful segregation of chromosomes. The ring-shaped structural maintenance of chromosomes (SMC) complexes are major architects of chromosomes, which topologically entrap DNA. SMC complexes play vital roles in chromosome condensation, sister chromatid cohesion, DNA repair and transcriptional regulation. They are thought to organize chromosomes by tethering more than one DNA strand by topological embrace. Using purified proteins, we have successfully reconstituted topological DNA binding by cohesin, the SMC1-SMC3 complex which mediates sister chromatid cohesion as well as higher-order chromosomal structures in interphase. Our studies

provide important molecular insights into DNA entry into and exit out of the cohesin ring. In addition, we have also demonstrated DNA-DNA tethering by cohesin [480]. The biochemical approaches provide an unprecedented opportunity to understand fundamental mechanisms of how SMC proteins organize chromosome architecture [481].

Cell Dynamics and Organization Laboratory
Yoshihisa Oda Group

Cell polarization and patterning are fundamental processes essential for a range of cellular activities. We have been focused on the plant metaxylem vessel cell differentiation, in which pitted cell wall patterns are established at the cell surface through formation of plasma membrane domains occupied with ROP GTPases as a model of intracellular patterning. We have revealed that the plasma membrane domains are generated in a cell-autonomous manner via a reaction-diffusion mechanism [489]. The size and shape of the plasma membrane domains are regulated by two novel proteins that have opposite effects on the interaction between the plasma membrane and microtubules [656, 713]. We also found that a novel tethering protein complex mediates microtubule-dependent targeting of exocytotic vesicles to promote cell wall development at the outside of the plasma membrane domains [547, 828]. In addition to these studies, we revealed the mechanisms underlying cell fate determination of vascular cells [553] and pith parenchyma cells [81].

Quantitative Mechanobiology Laboratory
Yuta Shimamoto Group

Our laboratory studies how cells generate, sense, and respond to mechanical force to properly function. It has been widely recognized that mechanical force plays essential roles in regulating cellular processes. However, examining forces in cells has been challenging, as existing methods are limited in their physical access to the intracellular space without perturbing cell's physiology. In the past five years, we have been developing quantitative micromanipulation tools (e.g., force-calibrated microneedles, optical tweezers), integrating microscopy imaging and reconstitution assays to examine the mechanical integrity of the mitotic apparatus, the protein machinery essential for proper segregation of chromosomes during cell division [49, 737, 738]. We also applied our methods to analyze the mechanical properties of other subcellular organelles, such as the cell nucleus [684] and the endoplasmic reticulum [313], revealing unprecedented roles in governing subcellular processes. Our approach further enabled us to build quantitative physical models, which elucidate how these structures generate and respond to force while maintaining overall integrity.

Intellectual Infrastructure Center

Bioinformation and DDBJ Center

Head: Masanori Arita

I. Overview

The DNA Data Bank of Japan (DDBJ) Center is engaged in four major activities. (1) Since 1987 it has been a member of the International Nucleotide Sequence Database Collaboration (INSDC), a public resource for life sciences that includes the National Center for Biotechnology Information (NCBI) of the USA and the European Bioinformatics Institute (EBI). (2) The DDBJ provides supercomputing services to Japanese researchers in the life sciences, especially for biological sequence analyses. Each year, more than 600 registered users from 130 institutions use our computing service. (3) The DDBJ develops software tools to accelerate research efforts. To keep our computing environment useful and up-to-date, its interface and application tools are constantly updated and refactored. Computation nodes can be also reserved for the smooth performance of scheduled analyses (paid service). (4) Our outreach and educational activities include lectures and workshops. Below we summarize our activities of the past five years.

II. Activities (2014 – 2018)

A. *Management of INSD databases and other repositories*

As of December 2018, the DDBJ Center hosts multiple public databases (**Table 1**). Six are INSDC databases and two, the Genomic Expression Archive (GEA) and the Japanese Genotype-Phenotype Archive (JGA) are outside the INSDC. The INSDC policy guarantees free and unrestricted access to DNA data; it does not fully apply to personal genomes and expressions. However, with the exception of personal information, the three host institutions (DDBJ, NCBI, and EBI) seek to exchange as much (meta) data in each database as possible to support scientific endeavors through global coordination. The database content is searchable on our web interface at https://www.ddbj.nig.ac.jp/.

Table 1. Database categories of INSDC and the two coordinated repositories

	Annotated/ Assembled sequences	**Capillary reads**	**NGS reads**	**Study**	**Sample**	**Assembly**	**Functional genomics**	**Genotype and phenotype**
NCBI	GenBank	Trace Archive	SRA	BioProject	BioSample	Assembly	GEO	dbGaP
EBI	European Nucleotide Archive (ENA)						ArrayExpress	EGA
DDBJ	DDBJ	Trace Archive	SRA	BioProject	BioSample	Assembly	GEA (2018 -)	JGA (2013 -)

The submission trend for annotated sequences is shown in **Table 2**. There is a mild but steady shift from traditional web-based- to large-scale submissions (denoted as mass data). Most data submissions to DDBJ come from Japan. Others are from Asian and middle-eastern countries. Altogether, these sources account for a little less than 10% of all INSDC submissions. Statistics of internet access to DDBJ, obtained via domain names in 2018, show that about 50% access come from companies ('.com' and '.net'), 20% from '.jp' (Japan), 7% from '.gov' (US government), and 23% from anonymous origins or unknown addresses.

Table 2. The number of DDBJ submissions for annotated sequences

	Web Submission		Mass Data Submission	
	Submitters	Submissions	Submitters	Submissions
2018.Jan ～ Dec	2268	3979	350	2716
2017.Jan ～ Dec	2124	3555	346	1410
2016.Jan ～ Dec	2387	4105	346	986
2015.Jan ～ Dec	2417	4110	327	970
2014.Jan ～ Dec	2499	4034	352	920

Besides submissions from researchers, patent-related DNA- and amino-acid sequences are handled by INSDC in collaboration with patent offices in Japan, the USA, and Europe. DDBJ also cooperates with the Korean Bioinformation Center to publish data from Korean patent offices. Integrated submissions to the three host institutions and patent information are published quarterly in the DDBJ release.

In the last decade, the availability of next-generation sequencers (NGS) has drastically changed the landscape of the life sciences. INSDC has provided the Sequence Read Archive (SRA) for NGS data since 2009; its size now exceeds 4 petabytes (PB). To streamline associated metadata, INSDC started the BioProject database for project information and the BioSample database for biological source- and material information. The size trend of the public DRA (the SRA at DDBJ) is shown in **Table 3**. Its size decreased in 2018 because storage shortage forced us to stop mirroring NCBI/EBI SRA data in April 2017. We have prepared an additional 30 PB of storage and the mirroring will restarted in 2019.

Table 3. DDBJ SRA file size

	DRA file size
2018. Jan	3.88 PB (1.07 fastq + 2.81 SRA)
2017. Jan	3.68 PB (1.06 fastq + 2.62 SRA)
2016. Jan	2.44 PB (0.655 fastq + 1.78 SRA)
2015. Jan	1.35 PB (0.27 fastq + 1.08 SRA)
2014. Jan	0.92 PB (0.25 fastq + 0.67 SRA)

The other important trend is the rapid accumulation of personal genomes. As personal information must not be copied across countries without permission, each institution controls access to submitted data by restricting user access. In October 2013, DDBJ started the Japanese Genotype-Phenotype Archive (JGA) in collaboration with the National Bioscience Database Center (NBDC), which organizes access guidelines and data-sharing policies for Japan (http://humandbs.biosciencedbc.jp/en/guidelines). Under these policies, JGA offers restricted access similar to the Database of Genotypes and Phenotypes (dbGaP) at the NCBI and the European Genome-phenome Archive (EGA) at EBI. The size increase in personal genomes in JGA is slower than expected (**Table 4**), probably due to the data-sharing policies of funders of research in Japan.

Table 4. Cumulative growth of JGA data

	Archived numbers (parentheses show the number of available data)		
	study	sample	file size (T bytes)
2018. Jan	123 (72)	204130	106.19
2017. Jan	82 (30)	8785	46.3
2016. Jan	46 (20)	6199	14.32
2015. Jan	10 (5)	6199	14.32
2014. Jan	Not available		

B. *Management of the NIG supercomputer*

The DDBJ Center hosts a sequence analysis platform on its supercomputing system. The UNIX-based system is comprised of 554 general-purpose calculation nodes (64-GB memory each), 10 *de novo* assembly nodes (2-TB memory each), and one 10-TB memory node. Over 200 software tools, mainly designed for sequence analysis, are pre-installed on the system. Its use by small-scale users is free (up to 30 TB of disk space). Users exceeding this threshold must pay a prorated volume fee. Users are required to renew their application every budget year, indicate the specific purpose of usage, and submit their publication records. All user names, affiliations, purposes, and publications are available on our website [https://sc.ddbj.nig.ac.jp/ja/report (in Japanese only)]. Because the Japanese law, the Foreign Exchange and Foreign Trade Act, prohibits the export of supercomputers, the system is available to Japanese researchers and their colleagues only. The number of registered users is listed in **Table 5**; the number increases toward the end of our budget year. The number of users becomes lowest at the time of our supercomputer application in April because accounts are closed if their owners do not apply for their continuation. We estimate the average number of active users to be 600. The total number of user institutions is 130.

The supercomputer traffic is highly congested; the CPU occupancy by assembly nodes surpasses 70% throughout the year (up-to-date information is available online at https://sc.ddbj.nig.ac.jp/ja/statistics). Since 2017, the DDBJ Center offered several paid services such as scheduled priority data processing and the secure analysis platform for private genomes. The price list for these services is available on our homepage [https://sc.ddbj.nig.ac.jp/ja/application (in Japanese)].

Table 5. Trend of registered users and number of published research papers

	Login user (standard)	Login user (large scale)	DDBJ usage	Maintenance	Total	Research papers reported by users
2018 Dec	616	199	88	18	921	35 (partial data)
2017 Dec	557	182	92	15	846	95
2016 Dec	549	165	88	14	816	83
2015 Dec	519	139	83	15	756	43
2014 Dec	380	105	82	13	580	53

In addition to ssh login services, the supercomputer resources can be accessed via two web services. The DDBJ Pipeline and the MiGAP annotation system provide web interfaces to analyze genome sequences from web browsers. In 2018 the cumulative number of user accounts of these web systems exceeded 3000 (**Table 6**). Both web services ceased at the end of budget year 2018 to increase the transparency of user control and to cope with staff changes. Upon their termination, the DDBJ Center provides alternative web services, i.e. the DFAST annotation system for small bacterial genomes and the Maser one-stop platform for NGS data, on a stand-alone server.

Table 6. Cumulative number of web service users

	MiGAP users	DDBJ Pipeline users	Total
2018 Dec	1000	1824	2824
2017 Dec	908	1622	2530
2016 Dec	767	1363	2130
2015 Dec	667	952	1619
2014 Dec	537	694	1231

C. *Development of software tools to accelerate research*

The computing environment of DDBJ has been constantly updated. In 2017, DDBJ started the Group Cloud service (DGC) to provide a secure database system for a private use (a paid service). The first instance of this service was the AMED Genome group sharing Database (AGD), on which private genome data are shared among restricted users; traditional person-by-person access restrictions apply. To analyze private genomes in JGA or AGD, in September 2018 DDBJ started to offer a secure computing environment specifically designed for private information (a paid service). DDBJ also installed a 15-PB hard disk and a 15-PB tape archive to accommodate the increase in data.

By the end of budget year 2018, our computation facility will be updated. The new system specifications include 204 general-purpose computing nodes (136 AMD EPYC with 512 GB-, 52 Intel Xeon with 384 GB-, and 16 NVIDIA GPU with 384 GB memory), 10 de novo assembly nodes (3-TB memory each), one 12-TB memory node, and 10 PB of Lustre file storage.

D. *Education and outreach*

Each year, the DDBJ Center organizes at least three lecture series. The full list is available at https://www.ddbj.nig.ac.jp/training.html. Since 2015, DDBJ has collaborated with the Database Center for Life

Science (DBCLS), the Protein Data Bank Japan (PDBj), and the NBDC in organizing an annual all-in-one training course for beginners. In 2017, DDBJ started to organizes a new lecture course, the "DDBJ-Supercomputer Training & Educational Program" (D-STEP). It trains intermediate- to upper level data scientists to handle omics data in life sciences.

In commemoration of its 30th anniversary in 2017, DDBJ organized the NIG International Symposium "Life, Environment, and Evolution Revealed by Genomes" (https://www.ddbj.nig.ac.jp/ddbj3). Support came from different sources including Mishima City and six companies. Invited and oral presentations and poster sessions from eight neighboring high schools attracted 293 participants in the course of three days. Video lectures are available online from TogoTV at DBCLS.

Between March and July of 2017, the Shizuoka Shinbun newspaper published 16 articles on the 30-year history of DDBJ. All lecture materials and database statistics are available on our website (https://www.ddbj.nig.ac.jp/activities.html).

III. Staff and organization

The DDBJ staff includes 4 full-, 2 associate-, and 4 assistant professors and 13 annotators/curators. In 2017, the job title "annotator" was changed to "curator" and 3 curators were chosen as "coordinators" to organize DDBJ activities. Since 2017, attendance management is processed online. Faculty members communicate with all curators through regular interviews and self-evaluation sheets. Budget information is provided in our annual report available on our website.

Faculty

Professors	Masanori Arita	(2013 -; Head, 2018 -)
	Yasukazu Nakamura	(2009 -)
	Toshihisa Takagi	(2009 - 2018; Head, 2012 - 2017)
	Kosaku Okubo	(2003 - ; Head 2009 - 2011)
Associate Professors	Osamu Ogasawara	(2003 -)
	Nozomu Sakurai	(2018 -)
Assistant Professors	Yasuhiro Tanizawa	(2018 -)
	Kazuo Hara	(2016 - 2017)
	Takeshi Kawashima	(2017 -)
	Eri Kaminuma	(2009 - 2017)

Curator (* … coordinator)

Yoshihiro Okuda Ph. D	(2016 -)
Toshiaki Tokimatsu Ph. D	(2016 -)
Shiho Mukaida Ph. D	(2016 - 2017)
Hideo Aono	(2001 -)
Asami Fukuda	(2005 -)
Yuichi Kodama Ph. D *	(2008 -)
Takehide Kosuge Ph. D *	(2002 -)
KyungBum Lee Ph. D	(2006 -)
Jun Mashima Ph. D *	(1999 -)
Toshihisa Okido Ph. D	(2001 -)
Katsunaga Sakai Ph. D	(2002 -)
Haru Tsutsui	(1995 -)
Noriko Furuya Ph. D	(2013 - 2014)

IV. Timeline of major DDBJ activities

Event	2014	2015	2016	2017		2018	
ICM host	DDBJ	NCBI	EBI	DDBJ		NCBI	
Collaboration	DBCLS branch started in Mishima	All-in-one lecture course with NBDC, PDBj, and DBCLS	Semantic web database with DBCLS			Personal genome with Tohoku Medical Megabank	
JGA	Online submission started	Security update (file transfer)				Off-premise server at Tohoku Medical Megabank	
GEA	(preparation)		Mirroring of ArrayExpress			Online submission started	
Paid service	(preparation)			Group Cloud (AGD)	Advanced reservation		Platform for personal genomes
Outreach	(regular lecture courses (3 per year)			30th anniversary symposium			DS Workshop

Advanced Genomics Center

Head: Ken Kurokawa

I. Overview

With the rapid development of Next-generation sequencing technologies (NGS) and of technologies to analyze these DNA sequences, human genome project was succeeded in completing the whole genome sequence of human. This project triggered an independent field of science “Genomics” which is likely to lead to new opportunities for all life science fields. Due to further development of current sequencing technologies, genomes of diverse organisms, from bacteria to humans, are decoded and new biological discoveries are successively brought about on the basis of their genome information. Also, not only the genome of a single organisms but also the genomes from the environmental samples such as soil, water, and human feces are being deciphered (i.e. metagenomics, eDNA). In addition, integrated analysis of heterogeneous data such as biological information and environmental information is also developing, and genome information become effectively utilized not only for life science but also variety fields of research. In these situations, the NIG Advanced Genomics Center (AGC), which was established in 2011, is expected to accelerate the genome science by providing cutting-edge technologies to research communities through its service cores that specialize in genome analysis, bioinformatics, and multi-omics analysis. To answer the heavy demand of genome analyses from the universities and research communities, the AGC promotes activities focusing on the following five missions, 1. Continual development of advanced genomics technologies, 2. Development of bioinformatic technologies, 3. Promotion of collaborative research, 4. Promotion of open science and open data, 5. Education on advanced genomics. Projects for the AGC support are selected from the applications which are based on NIG-Joint program. The major criteria for successful applications are as follows, 1. Applications that are expected to produce outcome exceeding the initial plan of the applicant's project by receiving the AGC support, 2. Applications that contain challenging tasks that require advanced technologies, 3. Applications that contain request for advanced technologies that are not available in commercial service.

II. Major research tasks on the AGC

In addition to the NIG-joint program, the AGC is promoting the following four research projects through provision of public funds.

A. National BioResource Project (AMED)(from FY2011)

The major purpose of this project is to collect, preserve, and provide bioresources (such as experimental animals and plants) that are essential experimental materials for life sciences research. The role of the AGC is to analyze genome sequences of bioresources.

B. Platform for Advanced Genome Science (MEXT)(from FY2016)

The mission of this project is to advance technologies in genomics and bioinformatics and to provide them for a wide range of research projects that are supported by the KAKENHI. The AGC is the analysis center for this project.

C. Human Microbiome Project (AMED)(from FY2017)

This program is aim to achieve a better understanding of the molecular mechanisms of host-microbiome interactions and symbiosis. The AGC is the analysis center for this project.

D. Promotion of Microbiome Research (ROIS)(from FY2018)

This project is aimed at strengthening the function of the AGC to support rapidly developing microbiome research. Establish a research platform for metagenomics by circulating “3A cycles” (Analysis - Accumulation - Application), and contribute to the enhancement of the international competitiveness of universities and industries in microbiome research.

III. Sequencing facilities

As mentioned above, NGS technologies are essential in genome science. However, NGS technologies advance at remarkable rates, and the equipment often becomes obsolete in about 3 years. Therefore, in order to provide advanced genomics techniques, it is necessary to keep equipment up-to-date. Unfortunately, this is a major hurdle for universities and laboratories. The AGC has always upgraded or introduced NGS to the latest version (e.g., HiSeq2000 (2011), HiSeq2500 (2012), PacBio RSII (2014), PacBio Sequel (2015), GridION (2017), NovaSeq6000 (2018))(Table 1), and has been achieving technologies advances in order to full use of NGS

Table 1. Sequencing facilities in the AGC

Machine	Num	Type	Performance		
			Sequence length	Data volume	Running time
ABI 3730xl	2	Capillary	~800bp	~77kb	2h
NovaSeq 6000	1	DNA synthesis	~150bp	~6Tb	48h
HiSeq 2500	3	DNA synthesis	250bp	~300Gb	60h
MiSeq	1	DNA synthesis	300bp	~15Gb	6.5h
PacBio RSII	1	Single molecule	~15kb	~1Gb	6h
PacBio Sequel	1	Single molecule	~15kb	~8Gb	6h
GirdION	1	Single molecule	~1Mb	~8Gb	48h

IV. Data productivity of the AGC

By utilizing the next-generation sequencers, we have produced a vast amount of sequence data of genomes from bacteria to human (Figure 1). These data are analyzed using NIG supercomputer, and these are released to the world through DDBJ.

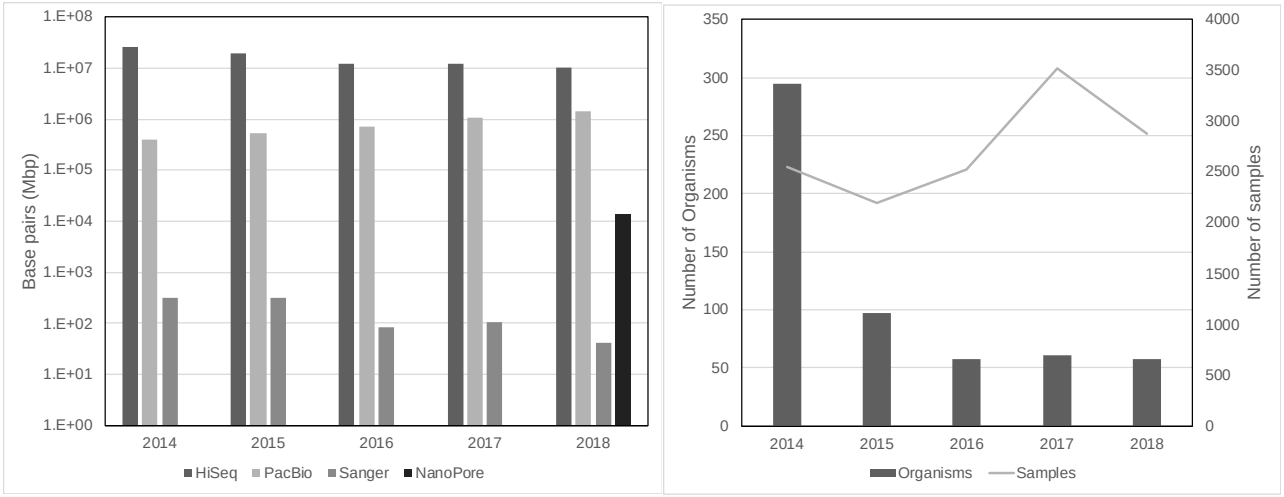


Figure 1. Total amount of sequenced base (left), number of organisms and samples (right).

V. Publications through the AGC activities

2018: Genome analysis of California poppy (Papaveraceae)(Plant Cell Physiol.). 18 publications in total.

2017: Elucidation of the evolutionary mechanism of gene expression on Stickleback (Evolution). 18 publications in total.

2016: Genome analysis of Xenopus laevis (Nature), Genome analysis of morning glory (Nat. Commun.), Genome analysis of Bearbear (Nat. Commun.). 15 publications in total.

2015: Genome analysis of Acytostelium subglobosum (Slime mold)(BMC Genomics), High resolution analysis of Marmoset genome (Science. Rep.). 14 publications in total.

2014: Sex chromosome analysis of Stickleback (PLoS Genet.), Development of genome assemble software (Genome Res.), Genetic analysis of Killifish sex determination (Nat. Commun.). 15 publications in total.

Genetic Resource Center

Head: Hironori Niki

I. Overview

The Genetic Resource Center is composed of two divisions of "Bioresource Division" and "Database Division." The Bioresource Division takes responsibility for the development, preservation, and distribution of forefront bioresources of various organisms including *E.coli*/*B.subtilis*. Rice, Mouse, *Drosophila*, Zebrafish, *C. elegans*, and Hydra, and of collected wild species of those organisms. The Database Division makes the above information available to the public through websites shown below. The BRC/NIG participates activity in the "National Bioresource Project (NBRP)" under the organization of Japan Agency for Medical Research and Development (AMED) and takes a role for management, *E.coli*/*B.subtilis*. Rice, Mouse, *Drosophila*, Zebrafish as the central or sub-central organization for each organism in the project. Furthermore, the Database Division also contributes to NBRP as the national center of bioresource information, by taking responsibility for the development and management of the relevant database.

Bioresource Management Division

E. coli & *B. subtilis* Resource (Prof. Hironori Niki)
Drosophila Resource (Prof. Kuniaki Saito)
Hydra Resource (Associate Prof. Kazuho Ikeo)
Mouse Resource (Prof. Toshihiko Shiroishi)
Rice Resource (Prof. Yutaka Sato)
Zebrafish Resource (Prof. Kouichi Kawakami)
Gene Library (Project Prof. Yuji Kohara)

Plant Resource Development Division

(Associate Prof. Kenichi Nonomura)

Division for Development of Genetic-Engineered Mouse Resource

(Prof. Yumiko Saga)

Bioresource Database Division

(Associate Prof. Shoko Kawamoto)

II. Bioresource Management Division

A. *E. coli* & *B. subtilis* Resource (Prof. Hironori Niki)

An international resource center for representative model Gram-positive and-negative bacteria, *Escherichia coli*, and *Bacillus subtilis* have been established in NIG. Now the center for prokaryotes has collected and stored the most extensive genetic resources of *E. coli* and *B. subtilis* in the world. We provide for all life science and applied sciences researchers globally. We further promote the collection and preservation of more helpful *E. coli* and *B. subtilis* resources for researchers. For the resource collection, it is crucial for careful selection and checks on genetic resources of both the model organisms from researchers. We mostly chose resources that

were described in published scientific papers. To improve the collected resources qualitatively, we carried out a whole-genome sequencing for bacterial strains. The whole genome data are opened as the genetic information of the strain.

The resources distributed by the center are all non-pathogenetic strains, *E. coli* strains are derived from strain K12, and *B. subtilis* strains are derived from the strain 168. We provide gene mutants, DNA clones of bacterial genes, phages, and cloning vectors. Also, A whole set of genome-wide mutant libraries are supplied for researches: the Keio collection is a set of single-gene deletion mutants of *E. coli* K12 (3,909 strains), BKS is a set of single-gene deletion mutants of *B. subtilis* 168 (3,974 strains).

The number of the stocked resources

	2014	**2015**	**2016**	**2017**	**2018***
E.coli/B.subtilis etc.	56,733	60,817	60,888	64,997	65,067

*Sep. 2018

The number of requests for resources

		2014	**2015**	**2016**	**2017**	**2018***	Total
Domestic	orders	231	218	523	263	144	1,379
	strains	41,195	50,336	72,157	39,140	28,466	231,294
International	orders	218	166	144	141	52	721
	strains	169,532	118,259	111,675	116,178	39,709	555,353
Total	orders	449	384	667	404	197	2,100
	strains	210,727	168,595	183,832	155,318	68,175	786,647

*Sep. 2018

B. *Drosophila* Resource (Prof. Kuniaki Saito)

The international resource center for "*Drosophila*" in NIG comprehensively maintains, manages, and globally distributes to research communities the genetic resources, such as mutant strains including genome-editing (FlyCas9) and RNAi strains of *Drosophila melanogaster*, which are useful as a basis or platform for life science studies. We have collected new resources that meet the current and the future needs of users, which were gathered from the expanding and diversifying community through the mailing list, the web sites, the *Drosophila* Board meeting, and domestic international scientific conferences. We also manage the consortium of National Bioresource Project for *Drosophila*, which consists of the five institutions, NIG, Kyoto Institute of Technology, Ehime University, Kyorin University, and Miyazaki University, and control collaborative roles as the internationally acclaimed stock centers in Japan. To encourage and support the use of collected resources, we analyzed and opened the whole-genome sequencing data for *Drosophila* wild-type strains.

We provided RNAi and genome-editing strains (>35,000 strains in the latest 5 years) and plasmid vectors related to CRISPR/Cas9 system (>130 plasmids in the latest 5 years) to contribute to the acceleration of leading-edge research activities in user communities.

The number of the stocked resources

	2014	2015	2016	2017	2018*
Drosophila melanogaster, etc.	25,987	27,121	27,774	29,438	29,790

*Sep. 2018

The number of requests for resources

		2014	2015	2016	2017	2018*	Total
Domestic	orders	85	106	113	151	69	524
	strains	698	2,324	2,186	3,709	2,411	11,328
International	orders	255	278	253	252	107	1,145
	strains	4,475	7,136	4,231	3,967	4,193	24,002
Total	orders	340	384	366	403	176	1,669
	strains	5,173	9,460	6,417	7,676	6,604	35,330

*Sep. 2018

C. Hydra Resource (Associate Prof. Kazuho Ikeo)

Hydra is a popular model organism because of its strong regenerative capacity and its primitive nervous system termed nerve net. Hydra has been used not only for research but also for educational purposes at high schools and universities. The stock strains maintained at NIG originates from the collection of domestic strains by Dr. T. Sugiyama with later inclusion of foreign strains and transgenic strains from other research groups. The distribution of strains to institutions, schools and individuals has been performed at constant levels for years, however, in recent years, use of strains constructed by genome editing has become more popular than the use of mutant strains. Since there are requests to maintain transgenic strains, we have added such strains to the stock to make it more updated. At the same time, it is expected to increase the use of symbiotic lines for environmental problems and evolutionary research. However, more efforts are needed to keep the project.

The number of the stocked resources

	2014	2015	2016	2017	2018*
Hydra	214	180	195	195	195

*Sep. 2018

The number of requests for resources

		2014	2015	2016	2017	2018*	Total
Domestic	orders	15	16	28	11	4	74
	strains	35	48	96	17	6	202
International	orders	4	2	2	3	2	13
	strains	14	25	24	5	2	70
Total	orders	19	18	30	14	6	87
	strains	49	73	120	22	8	272

*Sep. 2018

D. Mouse Resource (Prof. Toshihiko Shiroishi)

The NIG mouse bioresource project aims to improve the value of mouse genetic resources collected and preserved by NIG for many years and to disseminate the genetic resources for research community. Our collections include inbred strains derived from wild mice belonging to different mouse sub-species, and consomic strains, in which every chromosome of a classical inbred strain C57BL/6J is replaced by the counterpart of Japanese wild mouse-derived MSM/Ms strain. We distribute all these resources for research community every year. In addition, we have sequenced whole genome of ten inbred strains established from wild mice, which are collectively referred to as “Michima Battery” and preserved in the NIG mouse bioresource project. Furthermore, we have developed a database named “NIG_MoG” (Mouse Genome) that provides information of genome polymorphisms between the reference sequence of C57BL/6J and those of “Mishima Battery”. Now, NIG_MoG is accessed by many world-wide users.

The number of resources provided

Strain	**2014**	**2015**	**2016**	**2017**	**2018**
Molossiuns	103(0)	75(84)	105(0)	73(412)	64(80)
Inbred	7(0)	0(0)	0(0)	0(0)	0(0)
Congenic	0(0)	4(0)	0(0)	0(0)	0(0)
Wild	0(0)	2(0)	0(0)	3(0)	1(0)
Mutant	0(0)	0(0)	6(0)	0(80)	0(0)
Consomic	23(0)	110(0)	52(0)	103(0)	19(0)
Others	0(171)	0(0)	15(0)	16(0)	45(0)
Total	133(171)	191(84)	178(0)	195(492)	129(80)

Class of user	**2014**	**2015**	**2016**	**2017**	**2018**
National Univ.	91(83)	72(0)	75(0)	14(0)	10(0)
National Inst.	10(0)	5(84)	0(0)	6(84)	0(0)
Public Inst.	7(0)	102(0)	53(0)	148(0)	64(80)
Private Univ.	25(0)	0(0)	0(0)	4(80)	0(0)
Industry	0(0)	0(0)	24(0)	0(328)	10(0)
High School	0(0)	0(0)	9(0)	7(0)	0(0)
Oversea	0(88)	12(0)	5(0)	16(0)	45(0)
Total	133(171)	191(84)	178(0)	195(492)	129(80)

*Parenthesis is the number of frozen embryos.

E. Rice Resource (Prof. Yutaka Sato)

An international resource center for the valuable collections of rice genetic resources have been established in NIG. Our center collects, preserves and provides wide varieties of genetic resources, such as wild and cultivated accessions of rice in addition to experimental strains. We also provide information on these resources from our database to rice research community. Following effort have been made to meet various research needs in different research areas in 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 that classify the

wild rice species.

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

(3) Characterization of genomes of the collection of wild rice species using NGS.

(4) Operation and management of Oryzabase database for releasing rice resources and genome information.

By the support of National Bioresource Project, we are in charge of increasing the use of our genetic resources. In order to accomplish this aim, we are conducting the advertisement through Oryzabase, issues of Newsletters and open-field tour at NIG.

The number of the stocked resources

	2014	**2015**	**2016**	**2017**	**2018***
NIG rice resources	7,280	7,556	8,442	10,599	11,799

*Sep. 2018

The number of requests for resources

		2014	**2015**	**2016**	**2017**	**2018***	Total
Domestic	orders	24	10	19	53	10	116
	strains	518	99	350	1,318	78	2,363
International	orders	4	5	3	10	1	23
	strains	73	90	384	372	2	921
Total	orders	28	15	22	63	11	139
	strains	591	189	734	1,690	80	3,284

*Sep. 2018

F. Zebrafish Resource (Prof. Kouichi Kawakami)

Zebrafish is an important model animal for basic biology in vertebrates and also for disease modeling and drug discovery. The zebrafish resouce center offers unique zebrafish resources that have been generated in NIG. One is a collection of transgenic zebrafish generated by Kawakami lab by using the transposon-mediated transgenesis and gene/enhancer trap methods. These transgenic fish can be used to visualize and manipulate specific cells, tissues and organs genetically. The other is a zebrafish inbred line generated by Sakai lab. This line should be useful for standardized experiments.

For the past 15 years, Kawakami lab has been performing a large-scale gene trap screen and collected more than 1,000 lines that express Gal4 in spatially and temporally restricted fashions. From the zebrafish resource center, to date more than 2,000 lines have been shipped to researchers world wide.
Further, the transposon system developed by Kawakami lab can be applied not only to zebrafish but also to other vertebrate systems including mouse, chick, frog, and mammalian culture cells such as ES and iPS cells, and have been distributed to more than 2,000 labs world wide.

These activities have led to more than 100 collaborative publications [578, 830, 79, 756, 832, 761, 815, 551, 829, 845, 660, 324, 35, 627, 345, 116, 870, 344, 41, 568, 170, 38, 605, 455, 261, 677, 705, 894, 203, 141, 620, 555, 893, 90, 125, 827, 872, 153, 296, 406, 374, 381, 239, 68, 866].

Lines generated and collected for the last 5 years:

2014	60	Total: 920
2015	60	Total: 980
2016	60	Total: 1040
2017	65	Total: 1105
2018	65	Total: 1170

Lines (transgenic fish) shipped out for the last 5 years:

2014	255	(Japan:69, Abroad:255)
2015	264	(Japan:103, Abroad:161)
2016	248	(Japan:75, Abroad:173)
2017	112	(Japan:28, Abroad:84)
2018	161	(Japan:27, Abroad:134)

Lines (inbred line) shipped out for the last 5 years:

2014	2	(Japan:0, Abroad:2)
2015	2	(Japan:0, Abroad:2)
2016	2	(Japan:0, Abroad:2)
2017	0	(Japan:0, Abroad:0)
2018	0	(Japan:0, Abroad:0)

Transposon system distributed for the last 5 years:

2014	153	(Japan:49, Abroad:104), Total:1792
2015	116	(Japan:21, Abroad:95) , Total:1908
2016	92	(Japan:14, Abroad:78) , Total:2000
2017	66	(Japan:20, Abroad:46) , Total:2066
2018	113	(Japan:28, Abroad:85) , Total:2179

The databases:

zTrap（zebrafish gene trap and enhancer trap database）
http://kawakami.lab.nig.ac.jp/ztrap/
zeBrain（zebrafish brain atlas）
http://zebrain.nig.ac.jp/zebrain/
ZIGS（Zebrafish inbred line database）
http://zigs.nig.ac.jp

G. Gene Library (Project Prof. Yuji Kohara)

We are storing and distributing the following genomic/cDNA clones: 1) the ordered genomic clones of *E. coli*, 3,400 clones and the mini-set 476 clones (Cell, 50, 495 (1987)), 2) the nematode *C. elegans* cDNA clones, 140,000 clones, most of which are full-length and are added the information on their expression patterns (available at NEXTDB https://nematode.lab.nig.ac.jp/), 3) full-length cDNA and BAC/fosmid clones of various organisms of animals, plants and microorganisms that have been analyzed at the former DNA sequencing center of this institute. Thus far, more than 100,000 *E. coli* genomic clone have been distributed to 28 countries since 1987. The requests for the *E. coli* clones and the various organisms clones are almost vanishing, thus the distribution will be terminated. Stating in 1994, more than 40,000 *C.elegan*s cDNA clones have been distributed to 26 countries, and, although the requests are reducing, the clones are still actively used world wide for various research.

1) *E. coli* ordered genomic clones

Year	2014	2015	2016	2017	2018	Total*
Number of requests	1	0	0	0	0	847
From Japan	1	0	0	0	0	241
From other countries	0	0	0	0	0	606
Number of shipped clones	476	0	0	0	0	101,588
To Japan	476	0	0	0	0	18,158
To other countries	0	0	0	0	0	83,429
Number of shipped countries	1	0	0	0	0	28

* total number from the start of distribution

2) *C. elegans* cDNA clones

Year	2014	2015	2016	2017	2018	Total*
Number of requests	65	52	39	38	19	8,564
From Japan	17	12	7	10	2	1,278
From other countries	48	40	32	28	17	7,286
Number of shipped clones	290	260	185	168	80	40,255
To Japan	62	37	11	45	3	8,264
To other countries	228	223	174	123	77	31,991
Number of shipped countries	9	9	10	11	7	26

* total number from the start of distribution

III. Plant Resource Development Division

(Associate Prof. Ken-ichi Nonomura)

This division aims to support for domestic and overseas researchers to grow and/or develop non-transgenic and transgenic plant resources at NIG, using the open fields, greenhouses, controlled growth chambers and equipment. It is also in charge of the mission to conserve rice genetic resources, including about 4,000

accessions of world's landraces and a thousand or more of wild rice relatives in cooperation with the Plant Genetics laboratory and the Plant Cytogenetics laboratory, in the support of the National Bioresource Project (NBRP). For the last five years, the division has supported 22 researches in total as NIG-Joint programs, and consequently, 16 scientific papers with the results obtained by means of our supports have been published.

IV. Division for Development of Genetic-Engineered Mouse Resource

(Prof. Yumiko Saga)

This division was newly established to support mouse researches inside and outside of NIG. The major tasks of this division are (1) making a new mouse line, (2) preserving mouse lines already established, (3) cleaning of mice for introducing new lines to our mouse facility (SPF grade). Especially, we have good technologies to create new mouse lines using genetic manipulation such as microinjection, ES-mediated gene-knockout. Current development of Cas9-technology made possible to generate new mouse models quickly, thus further demands are rising.

We just started to accept requests from outside of NIG from 2017. We charge a researcher for some costs. Mouse cleaning includes re-establishing lines via frozen embryos, frozen sperm and from live animals. The number of chimera production is very high since it includes F0 chimera analyses without delivery.

Number of requests from inside and outside of NIG

Contents of orders	2016(NIG)	2017(NIG)	2017(outside)
Mouse cleaning	10	13	N/A
Embryo freeze	17	10	N/A
Sperm freeze	31	22	N/A
Transgenic mouse production	4	2	3
Transgenic mouse production via Cas9	8	8	4
Gene modification into ES cells	34	16	2
Chimera mouse production via ES cells	32 (3 clones/each)	39 (3 clones/each)	2
Other works	4	15	0

V. Bioresource Database Division

(Associate Prof. Shoko Kawamoto)

This division is responsible for the developing and maintaining the information systems for the genetic resource center, including overall information of the National BioResource Project (NBRP) other than in NIG. To support the distribution of resources provided by the resource center, we have developed web applications for the information retrieval and online ordering system of the resources. There are 21 resource organisms databases that we have developed: mice, fly, *C.elegans*, Silkworms, Medaka, Zebrafish, *C.intestinalis*, Tropical clawed frog, Rice, Wheat, Barley, Chrysanthemum, Morning glory, Lotus/Glycine, Tomato, Paramecium, cellular slime molds, Algae, *E.coli*, *B.subtilis*, Yeast. Among these organisms, we also provided 12 species genome sequences via the genome browser for the researcher. From our portal site(http://nbrp.jp), the resource user can be accessed to 6.5 million bioresources and 30,000 reference papers related to NBRP resources through the integrated cross-referenced search. The average number of users per month in our website reached 80,000

unique IP addresses (FY2017), and users are gradually increasing. In order to make it convenient for the foreign academic researchers, we developed an electronic material transfer agreement system for the *E.coli* and fly, so that resource user can order resources through our web site and don't need to exchange paper contract.

The number of the records in the databases

FY	2014	2015	2016	2017	2018*
Total	6,372,927	6,517,277	6,530,479	6,535,055	6,543,821

*Sep. 2018

The number of monthly average users of the websites

FY	2014	2015	2016	2017	2018*
Total	66,894	62,077	64,514	80,645	83,657

*from Apr. to Sep. 2018

Joint Research and Research Meeting (NIG-JOINT), and International Symposium

In order to give researchers opportunities to use NIG facilities and equipment and to encourage collaborative research that leverages our infrastructure, “Joint Research” and “Joint Research Meeting” have been conducted between researchers from inside and outside of NIG.

Originally, joint research was categorized into two groups: Collaborative Research (A), which supports only travel expenses to visit NIG, and Collaborative Research (B), which supports both travel and research expenses. To further promote collaborative researches from foreign institution and universities, Collaborative Research (A2) which is applicable only to foreign researchers was newly founded in 2015 and renamed to “International Joint Research” in 2017. In addition, the English name of Collaborative Research has been changed to unique name “NIG-JOINT” in 2017, so that publications of Collaborative Research can be easily searchable and recognized.

Joint Research Meeting and International Symposium support travel expenses (other expenses for International Symposium) for participants in scientific meetings that are held among researchers from inside and outside of NIG. These scientific gatherings have been contributing to scientific community by facilitating discussions and collaborations.

As shown in the following chart (plus one International Symposium every year), NIG has been continuously supporting a number of scientists for joint research and research meetings to help advertising the importance of NIG as an Inter-University Research Institute.

	Collaborative Research(A)/ NIG-JOINT(A)	Collaborative Research(B)/ NIG-JOINT(B)	Collaborative Research (A2)/ NIG-JOINT(I)	Collaborative/ Joint Research Meeting	Total
2014	87	8	-	18	113
2015	63	7	5	13	88
2016	68	5	6	13	92
2017	92	6	5	18	121
2018	91	4	5	19	119

Education and Outreach

Graduate education

Achievements of graduate education

Graduate Education at NIG

The NIG functions as the "Department of Genetics of SOKENDAI (The Graduate University for Advanced Studies)" and offers the graduate programs for 5 years and 3 years, both of which award a PhD degree upon successful completion. The objective of education is to foster graduate students to become independent scientists who can conduct their original research in various fields of life sciences related to genetics. For this objective, students receive research-based education by NIG faculty members with the aid of rich facilities and resources. NIG also accepts graduate students affiliated to other universities as "Special Collaborative Research Students", who can take part in the educational programs of the Department of Genetics.

Education Philosophy

The Department of Genetics embraces the idea that every single student gets the attention of the entire faculty from various disciplines. This is enabled by the extremely high ratio of faculty to students (~1.4 faculty/student) at NIG. The selection of students involves all the NIG faculty members. After admission, each student is supported by a special "Progress Committee" organized by 1~4 faculty members outside the student's host lab. With the support of the Progress Committee, students complete assignments and activities set each semester throughout the program, and by doing so, develop their ability and skills that are necessary to become an independent researcher.

General Admission

Applicants to the general admission have decreased for the past 10 years (Table 1). This decrease is apparently due to the overall decline of young Japanese population because other Japanese universities face exactly the same problem. A bright side of the situation is the high enrolment ratio (enrolled/admitted), which has continued throughout the history of our graduate program. This means that our graduation programs have a strong competitive advantage and that the applicants have a specific motivation to study at NIG under expert guidance of the faculty. As explained above, our programs aim to educate a small number of students, catering to the needs of individual students, so that the official number of enrollment is only 9 students per year (5-year and 3-year courses combined). Thus, we did not compromise the student quality to preserve the numbers, but rather have maintained the selection standard accepting fewer students.

Table 1 The number of students accepted in different types of admission

General admission

Year of exam taken	2009		2010		2011		2012		2013		2014		2015		2016		2017	
	5-year course	3-year course	5-year course	3-year course	5-year course	3-year course	5-year course	3-year course	5-year course	3-year course	5-year course	3-year course	5-year course	3-year course	5-year course	3-year course	5-year course	3-year course
Applicants	16	4	14	11	17	3	15	2	8	11	11	5	7	2	11	1	4	1
Admitted	7	4	6	6	11	3	8	1	5	7	4	3	3	1	6	0	2	1
Enrolled	6	4	5	6	8	3	6	1	4	7	4	3	3	1	6	0	2	1

IGP (international graduate program)

Year of exam taken	2009	2010	2011	2012	2013	2014	2015	2016
	5-year course only	5-year course only	5-year course only	5-year course only	5-year course only	5-year course only	5-year course only	5-year course only
Applicants	33	10	12	12	11	14	17	11
Admitted	3	3	4	2	3	5	3	4
Enrolled	1	1	3	1	1	0	0	1

EA-MEXT/NIG-GS (international students)

Year of exam taken	2015	2016	2017
	5-year course only	5-year course only	5-year course only
Applicants	6	22	24
Admitted	2 (2)	4 (3)	6 (3)
Enrolled	2	3	2

The numbers in parentheses are supporded by MEXT schollarship

Admission of International Students

We made an effort to expand the potential pool of students by reaching out globally. Since 2007, we have offered an international graduate program (IGP) that accepts international graduate students with full financial support (Table 1). Because this IGP program was designed to recruit students competitively with Western universities, the selection schedule was not appropriate for recruiting students supported by Japanese Government (MEXT) scholarship. In fact, in the exams of 2013 and 2014, we failed to fill the two scholarship slots for international students promised by MEXT in the newly adopted International Priority Graduate Program (2014-2018) with collaboration of SOKENDAI Life Science Departments. To counteract the situation, we created a new admission path for international students in an optimized schedule for awarding MEXT Scholarship (EA-MEXT). This EA-MEXT targets international students who prioritize the Department of Genetics for their graduate studies. The candidates are selected together with those in the general admission, so that it is clear and easy to set the selection level of EA-MEXT equal to or higher than that of the general admission. The EA-MEXT selection started in 2015, and afterward has effectively recruited international students who fulfill requirements for the MEXT scholarship (Table 1). In 2017, we unified the two different recruiting paths for international students, IGP and EA-MEXT, and then renamed it to NIG Global Scholar (NIG-GS).

Admission of Special Collaborative Research Students

Special Collaborative Research Students technically belong to other universities but perform their PhD study at NIG under the guidance of NIG faculty. The accepted numbers show a slight increasing trend in recent years (Table 2). Based on the equal treatment policy for students who conduct PhD study at NIG regardless of affiliation, NIG started financial support for qualified Special Collaborative Research Students by Research Assistant (RA) employment equivalent to SOKENDAI students in 2017. The Students are also eligible to live in the student dormitory since 2016.

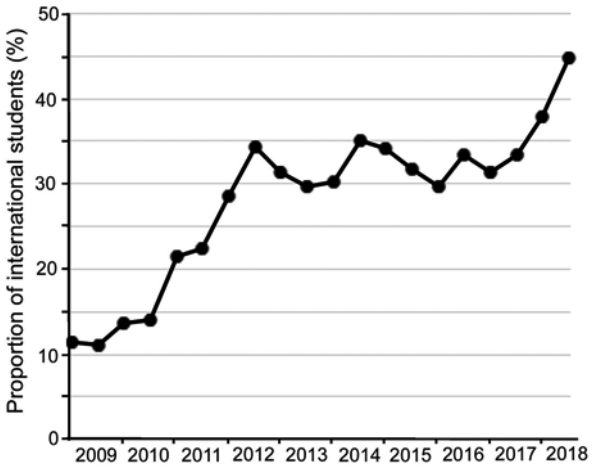
Table 2 The number of special collaborative research students accepted each year

Year	2009	2010	2011	2012	2013	2014	2015	2016	2017
Admitted	3	4	3	5	6	10	9	7	6

Globalization of the Graduate Program

The proportion of international students at the Department of Genetics has greatly increased for the past years (Fig.1). Currently, more than 40% of the students are international students, whose national origins are diverse: India, Malaysia, America, Pakistan, China, Taiwan, Kazakhstan, Philippine, Ghana, etc. Many students got to know about NIG by NIG intern program. As will be explain later, this intern program is hugely popular among international undergraduate students and quite effective to increase the publicity of our graduate program.

Fig.1 Proportion of international students



The Department of Genetics has prepared a good environment for both Japanese and international students to actively study together. All the lectures are now given in English with fully-equipped Syllabi in English and Japanese dual-languages. Students present and discuss their research in English on every occasion such as open presentation for a Master's degree, progress poster presentation or PhD defense. To train their scientific presentation skills, NIG faculty members developed "NIG method" education program for scientific presentations based on the longtime observation and analyses of student presentations, which will be touched upon later. This program is taught by the NIG English Instructor, Todd Gorman, as a year-round course.

Our graduate programs enable international students to complete without any knowledge of Japanese language. All the required information is provided in English. The support members of the Education Office are proficient in English. The daily life of an international student is supported by a Japanese tutor who is appointed from SOKENDAI students. Upon request, one-to-one Japanese language classes are provided by a qualified teacher for free. Mental health counseling sessions on a regular basis are provided at NIG by a specialist who can communicate in Japanese and English.

PhD Degree Conferment

The numbers of PhD awarded in recent years are shown in Table 3. The PhD thesis is evaluated by five members including internal three or four faculties and one or two external experts. Internal members are usually selected from the student's Progress Committee, and therefore well aware of the student's performances and capabilities through the program period. The PhD evaluation processes exclude the student's supervisor, allowing fair, objective evaluation and criticism. To guarantee the quality of PhD thesis, pre-examination started in 2017. In the pre-examination, the Progress Committee reads a manuscript of the PhD thesis and makes a decision on whether it can go ahead to the PhD evaluation or should be waited for revision.

Table 3 The number of PhDs awarded each

Year	2009	2010	2011	2012	2013	2014	2015	2016	2017
PhD	11	8	9	6	3	5	6	7	12
RONPAKU	0	0	1	0	1	0	0	0	0

Lectures and Courses

Lecture courses were reorganized in 2015-2017. The main purpose of this change is to make it clear for students what they should learn in the graduate program in relation with the degree criteria. After the reorganization, attendance of each course is much increased.

SOKENDAI promotes inter-department multi-disciplinary education programs. The Department of Genetics installed remote lecture systems in two lecture rooms, so that the students can freely attend lectures provided by NIPS (Department of Physiological Sciences), NIBB (Department of Basic Biology) or ESB (Department of Evolutionary Studies of Biosystems) in geographically distant locations. Using the systems, the Department of Genetics also broadcasts our lectures to other departments. The mutual collaboration in education among departments is effective to promote broad perspectives in students.

Student Dormitory

A student dormitory was built on campus in 2011 and the second one in 2016. Currently, 20 Sokendai Students and 3 Special Collaborative Research Students live in the dormitory. Such in-kind support is cost effective and highly appreciated by students. Unfortunately, the rooms will be almost occupied at the end of 2018, and some students may have to be evacuated depending on their financial situations.

Financial Support

The Department of Genetics employs graduate students (excluding JSPS fellowship, IGP and MEXT scholarship holders) as Research Assistants (RA). The salary is about 600,000 yen/year.

Travel Support for International Meetings and Courses

In 2016, the Department of Genetics launched travel support for students who give a presentation at international meetings. So far 14 students have been supported and presented their studies abroad. The Department also offers support for students to take a high-profile education course provided by research organizations; if a student is accepted to participate in a course provided by Marine Biological Laboratory, Cold Spring Harbor Laboratory, EMBO or Welcome Genome Campus, the tuition and travel costs will be supported. One student was supported to participate in a course in 2017.

Awards

Funded with a generous donation by Professor Emeritus Hiroko Morishima, the following two awards were established; 1) The Morishima Award, started in 2012, is given to students who receive a PhD degree with outstanding performance. Seven students have been awarded so far. 2) Hiroko Morishima Progress Award, started in 2017, is given to students at each Student Poster Presentation to appreciate their eager effort in research. Twelve students have been awarded so far.

Student Requests and Responses

In 2015, one-to-one interviews were conducted for all the students. To collect requests and problems from students on regular basis, we made a student survey page, in which students can enter any problems, concerns

or requests anytime anonymously or onymously. The issues brought up are individually addressed by the Education Research Committee. Because most problems stemmed from information shortage from faculty to students, student information page was also constructed. With this page, all the students can now share the same detailed information promptly provided by the Education Research Committee or Education Office.

Education: Outreach

Close Network of Research Groups

NIG is famous for active interactions and discussions among the in-house researchers. Because each research group is small, many groups have joint lab meetings with other labs, and collaborations between groups are very common. Younger scientists and students also actively and freely visit other research groups to acquire new techniques and knowledge, which is another advantage of small groups. NIG also hosts various types of researchers, such as postdoctoral fellows, collaborative researchers and visiting scientists from abroad. Interacting and networking with researchers with diverse levels and backgrounds is an ideal way for younger people to develop broad and balanced views as mature scientists.

The NIG Postdoctoral Fellow program

We employs young promising researchers as NIG postdoctoral research fellows and involve them in research activities at the institute for a limited amount of time, aiming at further development of research at NIG and fostering researchers with excellent research ability.

NIG Postdoctoral Research Fellow (NIG Postdoc) Result of Recruitment

Fiscal Year	Number of Applicants	Number of Candidates Interviewed (Those who passed the Preliminary Screening)	Number of Successful Candidates (Those who passed the Secondary Screening)	Acceptance Rate
2018	16	8	4	25.0%
2017	9	6	4	44.4%
2016	17	9	5	29.4%
2015	14	9	5	35.7%
2014	13	8	5	38.5%

Average Age of Successful Candidates in 2018: 29.3 years old (as of date arrival at post)

NIG Colloquia

Seminars are held every Friday by researchers at the institute to discuss their progress during the past year. Presentations are made not only by faculty, but also by fifth year graduate students as a part of their D5 Progress Report.

Biological Symposia

Biological Symposia are held throughout the year, featuring distinguished speakers in many areas of biological sciences, from universities and institutions worldwide.

The NIG INTERN program

We accept four to seven undergraduate and postgraduate students from overseas every summer. The intern students work in an assigned laboratory for 6 to 8 weeks and give an oral presentation at the end of the program. We got more than 400 applications last year and have hosted 29 students in total from India, Serbia, Philippines, UAE, UK, USA, Kazakhstan, Russia, Spain, Vietnam, Sweden, Mongols, Belarus, and Taiwan in the last 5 years. Among these intern students, three of them became SOKENDAI students and are currently studying at NIG.

Short Internship for Domestic Students

NIG (the Department of Genetics) offers a week-long internship program for domestic undergraduate students. There are the spring course that is held in the fixed time during the spring vacation (February-March) and the flexible course scheduled on an as-requested basis. Undergraduate students from various universities across Japan apply and are accepted in this program (see the table below). During the program, students conduct experiments individual host labs and join various activities undertaken at NIG such as seminars, journal clubs or student gatherings. This program assists in the development of young researchers and helps to increase awareness of NIG among undergraduate students (the vast majority of students who go on to graduate studeis in Japan remain at their undergraduate institutes).

The number of applicants and students accepted in the program

Year & Time	2014		2015		2016		2017	
	spring	flexible	spring	flexible	spring	flexible	spring	flexible
Applicants	29	4	18	3	18	7	14	8
Accepted	12	4	14	3	9	6	10	8

International Strategic Advisor/Visiting Faculty

NIG selects and invites outstanding researchers from abroad as an international strategy advisor or visiting professor. The aim is to gain advice on the operation of the institute and to gain strong research cooperation.

International Strategic Advisor

HENSCH, Takao K	International Strategic Advisor (Professor, Center for Brain Science, Harvard University)	2018
BERGER, Frederic	International Strategic Advisor (Senior group leader, Gregor Mendel Institute	2018
MIZUUCHI, Kiyoshi	International Strategic Advisor (NIH Distinguished Investigator, National Institutes of Health)	2017
HENIKOFF, Steven	International Strategic Advisor (Member, Fred Hutchinson Cancer Research Center)	2017
STAINIER, Didier	Visiting Professor (Director, MAX Planck Institute)	2016
EXCOFFIER, Laurent	Visiting Professor (Professor, University of Bern)	2016
YANG, Ziheng	Visiting Professor (Professor, University College London)	2016

Visiting Faculty

HENIKOFF, Steven	Visiting Professor (Member, Fred Hutchinson Cancer Research Center)	2018
MIZUUCHI, Kiyoshi	Visiting Professor (Distinguished Investigator, NIDDKD, NIH)	2018
FU, Yun-Xin	Visiting Professor (Professor, School of Public Health, University of Texas Health Science Center at Houston)	2018
YANG, Ziheng	Visiting Professor (Professor, University College London)	2018
ZHANG, Feng	Visiting Associate Professor (Assistant Professor, McGovern Institute for Brain Research at MIT)	2016-2018

DIFFLEY, John F.X.	Visiting Professor (Associate Research Director, The Francis Crick Institute)	2016-2018
STAINIER, Didier	Visiting Professor (Director, MAX Planck Institute)	2016-2018
JORDE, Lynn	Visiting Professor (Professor, University of Utah School of Medicine)	2016-2018
YANG, Ziheng	Visiting Professor (Professor, University College London)	2016-2017
ZENG, Hongkui	Visiting Professor (Senior Director, Allen Institute for Brain Science)	2015-2017
EXCOFFIER, Laurent	Visiting Professor (Professor, University of Bern)	2015-2017
ZILBERMAN, Daniel	Visiting Associate Professor (Associate Professor, University of California, Berkeley)	2015-2017
BELMONT, Andrew S.	Visiting Professor (Professor, University of Illinois at Urbana-Champaign)	2014-2016
DEKKER, Job	Visiting Professor (Professor, University of Massachusetts Medical School)	2014-2016
SHERRATT, David	Visiting Professor (Professor, Oxford University)	2014-2015
ROTHSTEIN, Rodney	Visiting Professor (Professor, Columbia University Medical Center)	2014-2015
ENGERT, Florian	Visiting Professor (Professor, Harvard University)	2014-2015
LONG, Manyuan	Visiting Professor (Professor, University of Chicago)	2014-2015
SASAKI, Hiroyuki	Visiting Professor (Professor, Kyushu University)	2014-2015
FURLONG, Eileen E. M.	Visiting Professor (Joint Head of Unit and Senior Scientist, EMBL)	2014
von HAESELER, Arndt	Visiting Professor (Scientific Director of the Center for Integrative Bioinformatics Vienna)	2014
MARTIENSSEN, Robert A.	Visiting Professor (Howard Hughes Medical Institute, Cold Spring Harbor Laboratory)	2014

Lecture courses organized by DDBJ

Each year, the DDBJ Center organizes three lecture courses. The full list is available at https://www.ddbj.nig.ac.jp/training.html. There are three types of programs. The “DDBJing” program provides practical information to submit / access INSD databases and to use the NIG supercomputer. Most lectures were provided as hands-on style of max 20 beginners. The All-in-One program is a joint lecture with the Database Center for Life Science, the Protein Data Bank Japan, and the National Bioscience Database Center. This is the most introductory program covering the activities of the four research institutions. For intermediate- to upper level scientists, DDBJ provides the “DDBJ-Supercomputer Training & Educational Program” (D-STEP) since 2017. This program focuses on the analysis of omics data and attracts much attention.

Location of the lecture courses. Parentheses are number of participants. Okinawa events are organized by invitation.)

	2014	2015	2016	2017	2018
DDBJing	Mishima (?), Tokyo (?)	Tokyo (20), Okinawa* (?), Tokyo (20)	Mishima (14)	Okinawa* (60)	Hiroshima (37)
All-in-One		Osaka	Osaka	Mishima	Tokyo
D-STEP				Mishima (25)	Mishima (20), Yokohama (100)

International Training Course for Bio-Resource

NIG organized international training courses for bio-resources. In 2015, a training course for “zebrafish imazing and transgenesis” was held with participants from all over the world under the direction of Prof. Kawakami. In 2015 and 2016, international researchers visited Kawakami lab and performed genetic screens to find zebrafish that will be useful for their research (“self-screen” course). In 2017, a training course for “Drosophila subspecies classification” was held under the direction of Prof. Saito. Thus, NIG is aiming to promote international

collaborations and establish a basis of international activities.

Activities to Promote International Interaction and Cooperation

An important mission of NIG is to strengthen interactions among researchers worldwide. The research infrastructure provided by the three “Intellectual Infrastructure Centers” as well as international collaborations and international symposia are the major mechanisms for this mission. Such activities resulted in the establishment of Memoranda of Understanding (MOU) between NIG and partner institutions (Table 1). As these activities will be detailed in other parts of this report (section 4,5), this section will focus on the international atmosphere of NIG and globalization of the Japanese scientific community.

[Atmosphere] As an international hub for research in genetics, NIG hosts many researchers and students from the world (Table 2). All faculty searches are fully open to international researchers, and as of January 2019 NIG faculty include two international (non-Japanese) members. NIG graduate program is internationally renowned, and more than 40% of the current students are international students (section 6). As such NIG adopts an “English as common language” policy. All educational programs, and almost all seminars conducted in English. All notices sent from the Department of Administration are Japanese-English bilingual, and English translations of some administration documents have been prepared and are posted on the homepage.

The Internationalization Promotion Committee, established in 2010, strives to maintain and enrich this international environment (https://www.nig.ac.jp/jimu/soken/info-int/HelpDesk.html). For example, the English Help Desk provides various supports to new international members, e.g. visa issues, setting up life in Mishima, and finding medical and child-care. The committee also supports various social activities to enhance internationalization, and arranges free Japanese lessons to those who are interested in acquiring Japanese proficiency. These activities help create a true international environment at NIG to nurture researchers who can flourish in the global scientific community.

[Globalization] NIG also assists globalization of the scientific community through disseminating the educational program for scientific communication developed by NIG faculty, dubbed as “NIG Method”. This program, which is used in the scientific presentation course at NIG, has won critical acclaim from the attendants including international students, postdocs and faculty members, for its effect on simultaneously developing English presentation ability and scientific thinking (section 6). To share this resource with the research community, in 2014 NIG initiated activities to disseminate this program through seminars, workshops and invited lectures (Table 3). Through facilitating communication between researchers, we hope to strengthen international and interdisciplinary collaborations and thereby expand the output of the scientific community as a whole.

Table 1 Memorandum of Understanding established during 2014-2018

date	Partner institution (country)
2015.7.24	The University of Melbourne (Australia)
2015.10.16	University of the Philippines, Diliman (Philippines)
2018.5.11	College of Life Science, National Taiwan University (Taiwan)
2018.6.1	The Brain Research Institute, Monash Sunway (Malaysia)
2018.6.1	Universiti Kebangsaan Malaysia (Malaysia)
2018.6.1	National Science and Technology Development Agency by National Center for Genetic Engineering and Biotechnology (Kingdom of Thailand)
2018.6.18	College of Pharmacy, Kyungpook National University (Republic of Korea)

Table 2 Biological Symposia

year	Total number	Speakers from abroad
2014	80	59
2015	60	35
2016	72	42
2017	50	25
2018	64	43

Table 3 Introductory seminars, workshops and lectures on the scientific presentation educational program "NIG Method" (2014-2018)

category	Number of institutions (total number of events)[4]
SOKENDAI Departments	14[1] (17[2])
Universities in Japan (other than SOKENDAI)	18 (25)
Academic Societies/Groups	4
Private Companies	1
Institutions outside Japan	5 (6)
Open workshops[3]	(4)

Notes

1. The number of SOKENDAI Departments to which NIG provided seminars, workshops or lectures. This number does not include the Department of Genetics (NIG) itself.

2. Four of these correspond to lectures in SOKENDAI Freshman course, an event attended by all new incoming students. Five are full courses on scientific presentation offered at other departments of SOKENDAI, taught by the NIG English instructor, Todd Gorman.

3. These workshops were organized by NIG and were open to researchers in other institutions.

4. Of a total of 51 events held in Japan, 10 were offered in English to accommodate international audience.

Office for Research Development

Director: Yasushi Hiromi

The Office for Research Development (ORD) was established in 2014 as part of the ROIS recruitment of University Research Administrators (URAs) under MEXT's "Program for Promoting the Enhancement of Research Universities". While the objective of this program in a university would be to enhance the research capacity of the university organization itself, NIG has set ORD's objective to "contribute to enhancing research capacity of NIG as well as the entire scientific community", because ROIS's mission is to assist Universities and their researchers. ORD aims to elevate scientific output through enhancing the research capacity of individual researchers, in and out of NIG. Staff members of ORD are all former or current faculty members of NIG, and can act as a soundboard for researchers with new results and ideas. ORD also designs and organizes seminars, and workshops aimed at enlightening and stimulating the way that research is conducted.

ORD also takes part in the institutional research (IR) for NIG and ROIS, and public relations of NIG, collaborating with NIG's Department of Administration, NIG Innovation, as well as URAs stationed in the ROIS headquarters and other institutions of ROIS. Major activities in the past 5 years are summarized in Table 1.

Table 1 Major activities of ORD (2014-2018)

Category	Activities (number of cases/events)
Enhancing Research Activities	Advising/commenting from a scientific viewpoint ・Manuscripts[1] (43) ・Grant applications[1] (95) ・Presentations[2] (24) Workshops/seminars (16) Seminars and Workshops to disseminate the Educational Program on Scientific Presentation developed at NIG[3] (53)
Institutional Research (IR)	Acknowledgement study of NIG collaboration grant system [2015] Study on female applicant ratio in NIG faculty searches [2016] Follow-up study of RPD researchers -- toward career support of female researchers [2016] Report on the contributions of ROIS to the Japanese scientific community[4] [2017]. Historical Survey "Research infrastructure function of NIG -- Establishment and development of DDBJ"[5] [2017] Annual compilation of reports of institutional output (publications, research infrastructure services, graduate education)
Public Relations	NIG homepage renewal/update[6] Press Release of research outputs[7] (71) Annual NIG Brochure production[8] Annual events such as NIG Open House, Public Lecture, Introductory session of the NIG graduate program: co-organize and publicize

Notes

1. These activities are done as a group discussion of the applicant and the three ORD staff members, thereby providing diverse viewpoints.

2. This activity, called Presentation DOJO, is carried out by a group of volunteer members of NIG (mostly assistant professors), organized by ORD. https://sites.google.com/site/nigrest/

3. Details of this program can be found in section 6,7.

4. This report includes contributions of various research infrastructure provided by each institution (Resource-Sharing), as well as funded collaborations with ROIS researchers (Joint-Research). The compilation work was done in collaboration with other URAs of ROIS. The report was sent to 758 Universities in Japan to improve ROIS functions based on the feedback.

5. Shizuoka Shimbun (SBS) 2017.3.31-7.10.

6. ORD organized homepage renewal in 2014, and since has been responsible for its updating and maintenance. https://www.nig.ac.jp/nig/

7. Prior to 2015 NIG faculty had been sending out press release only sporadically. ORD established a faculty-ORD collaboration system for preparing press release, and dramatically increased the dissemination of NIG's research output through media coverage.

8. https://www.nig.ac.jp/nig/about-nig/annual-report

NIG INNOVATION

Director: Mutsuaki Suzuki

NIG INNOVATION (a section for technology transfer management) has had a successful achievement from FY 2013 to FY 2018 (as of 5th March 2019). Our total income through technology transfer has increased year by year and reached more than ¥ 113 million in these five years. It is noteworthy that the income for FY2018 (as of 5th March 2019) has already come to a record level of ¥ 35 million, more than three times of the income for FY2013.

This great leap has been achieved because we have concluded an unprecedented number of collaborative research agreements with industries in FY2018. We also have changed the name of our department to “NIG INNOVATION” to centralize the technology transfer activities more in FY2018.

Other highlights are the close collaboration with local community. We have provided average 30 laboratory tours, courses, lectures and visiting lectures to the local government and schools in the past five years and built a trustful and long-term partnership.

Office for Gender Equality

Director: Tatsumi Hirata

The Office for Female Support was established at NIG in 2014 and then renamed as the Office for Gender Equality in 2017. Initiatives and achievements made by the Office are as follows:

1. A multi-purpose nursery room was made in the main building in July 2015. Anyone who works or studies at NIG can use the room upon request.
2. In-house temporary childcare is provided in the multi-purpose nursery room to NIG employees when public childcare service are closed. Since Aug, 2016, 29 employees have used this service in total 16 days.
3. To raise the money for the in-house temporary childcare, a donation fund was created in Apr 2017. This fund has received donations from 9 people so far.
4. A career-building seminar was held in Izu-nagaoka on March11-12, 2017. Both male and female researchers engaged in active discussion and exchanged valuable information.
5. Requests about childcare and working rules received from NIG employees were submitted to ROIS and Mishima City Office in July 2018.
6. The homepage of the Gender Equality Office was renewed in Aug 2018.
7. Childcare support for participants of NIG meetings was launched in Dec 2018.
8. A childcare assistance program by NIG, started in 2009, allocates a lab assistant to a female faculty member who is rearing a child to the 6th grade. Another program by ROIS, started in 2014, allocates a lab assistant to a researcher including post-doc who has difficulty in family care. The number of NIG researchers supported by the two programs is shown in the table.

Year	2014	2015	2016	2017	2018
NIG program	1	2	3	4	5
ROIS program	−	1	3	2	3

Publication Lists

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