## NIBB Core Research Facilities

*Head*
YOSHIDA, Shosei

The NIBB Core Research Facilities were launched in 2010 to support basic biology research in NIBB. They consist of three facilities that are developing and providing state-of-the-art technologies to understand biological functions through functional genomics, bioimaging, and bioinformatics. The NIBB Core Research Facilities also act as an intellectual hub to promote collaboration among the researchers of NIBB and other academic institutions.

## Functional Genomics Facility

*Specially Appointed Associate Professor:*
SHIGENOBU, Shuji

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| *Technical Staff:* | *MORI, Tomoko* |
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The Functional Genomics Facility is a division of the NIBB Core Research Facilities organized jointly by NIBB and NIPS for promoting DNA and protein studies. The facility maintains a wide array of core research equipment, from standard machinery like ultracentrifuges to cutting edge tools such as next generation DNA sequencers, which amount to 60 different kinds of instruments. The facility is dedicated to fostering collaborations with researchers both of NIBB and other academic institutions worldwide by providing these tools as well as expertise. Our current focus is functional genomics. We also act as a bridge between experimental biology and bioinformatics through close consultation and training.

We recently largely renovated the building of the Functional Genomics Facility. For example, the Visitors Lab and the Visitors Office were newly designed so that visiting scientists can work effectively during their stay. In 2017, approximately 200 researchers visited to use our new facility and developed active collaborations, which resulted in 16 co-authored papers published.

### Representative Instruments

#### *Genomics*

The advent of next-generation sequencing (NGS) technologies is transforming today's biology by ultra-high-throughput DNA sequencing. Utilizing HiSeq2500, HiSeq1500, and MiSeq (Illumina), and PacBio RS II (PacificBio Sciences), the Functional Genomics Facility is committed to joint research aiming to explore otherwise inaccessible new fields in basic biology.

During 2017 we carried out 56 NGS projects in collaboration with NIBB laboratories as well as the researchers of other academic institutions. These projects cover a wide range of species (bacteria, animals, plants, and humans) including both model and non-model organisms, and various applications such as genomic re-sequencing, RNA-seq and ChIP-seq.

Figure 1. Next-generation sequencer

#### *Proteomics*

Three different types of mass spectrometer and two protein sequencers, as listed below, are used for proteome studies in our facility. In 2017, we analyzed approximately 750 samples with mass spectrometers and protein sequencers.

- LC-MS (AB SCIEX TripleTOF 5600 system)
- LC-MS (Thermo Fisher SCIENTIFIC Orbtrap Elite)
- MALDI-TOF-MS (Bruker Daltonics REFLEX III)
- LC-Q-TOF MS (Waters Q-TOF Premier)
- Protein sequencer (ABI Procise 494 HT; ABI Procise 492 cLC)

#### *Other analytical instruments (excerpts)*

- Cell sorter (SONY SH800)
- Bioimaging Analyzer (Fujifilm LAS 3000 mini; GE FLA9000)
- Laser Capture Microdissection System (Arcturus XT)
- DNA Sequencer (ABI PRISM 310; ABI 3130xl)
- Real Time PCR (ABI 7500)
- Ultra Centrifuge (Beckman XL-80XP etc.)

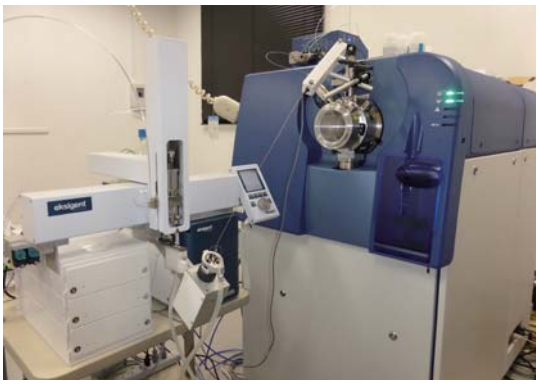

Figure 2. Triple TOF LC/MS/MS System

## Publication List on Cooperation:

〔Original papers〕


- Anbutsu, H., Moriyama, M., Nikoh, N., Hosokawa, T., Futahashi, R., Tanahashi, M., Meng, X.Y., Kuriwada, T., Mori, N., Oshima, K., Hattori, M., Fulie, M., Satoh, N., Maeda, T., Shigenobu, S., Koga, R., Fukatsu, T. (2017). Small genome symbiont underlies cuticle hardness in beetles. Proc. Natl. Acad. Sci. USA *114*, E8382–E8391.
- Fukushima, K., Fang, X., Alvarez-Ponce, D., Cai, H., Carretero-Paulet, L., Chen, C., Chang, T.H., Farr, K.M., Fujita, T., Hiwatashi, Y., Hoshi, Y., Imai, T., Kasahara, M., Librado, P., Mao, L., Mori, H., Nishiyama, T., Nozawa, M., Palfalvi, G., Pollard, S.T. Rozas, J., Sanchez-Gracia, A., Sankoff, D., Shibata, T.F., Shigenobu, S., Sumikawa, N., Uzawa, T., Xie, M., Zheng, C., Pollock, D.D., Albert, V.A., Li, S., Hasebe, M. (2017). Genome of the pitcher plant Cephalotus reveals genetic changes associated with carnivory. Nat. Ecol. Evol. *1*, 59.
- Gotoh, A., Shigenobu, S., Yamaguchi, K., Kobayashi, S., Ito, F., and Tsuji, K. (2017). Transcriptome characterization of male accessory glands in ants to identify molecules involved in their reproductive success. Insect. Mol. Biol. *32*, 382.
- Gotoh, A., Shigenobu, S., Yamaguchi, K., Kobayashi, S., Ito, F., and Tsuji, K. (2017). Transcriptome profiling of the spermatheca identifies genes potentially involved in the long-term sperm storage of ant queens. Sci. Rep. *7*, 5972.
- Hayashi, Y., Maekawa, K., Nalepa, C.A., Miura, T., and Shigenobu, S. (2017). Transcriptome sequencing and estimation of DNA methylation level in the subsocial wood-feeding cockroach *Cryptocercus punctulatus* (Blattodea: Cryptocercidae). Appl. Entomol. Zool. *52*, 643–651.
- Hayashi, Y., Oguchi, K., Yamaguchi, K., Kitade, O., Maekawa, K., Miura, T., Shigenobu, S. (2017). Male-specific molecular genetic markers in the Japanese subterranean termite *Reticulitermes speratus*. Insectes Sociaux. *64*, 357-364.
- Ihara, K., Sato, K., Hori, H., Makino, Y., Shigenobu, S., Ando, T., Isogai, E., and Yoneyama, H. (2017). Expression of the *alaE* gene is positively regulated by the global regulator Lrp in response to intracellular accumulation of l-alanine in *Escherichia coli*. J. Biosci. Bioeng. *123*, 444–450.
- Kondo, S., Wakae, K., Wakisaka, N., Nakanishi, Y., Ishikawa, K., Komori, T., Moriyama-Kita, M., Endo, K., Murono, S., Wang, Z., Kitamura, K., Nishiyama, T., Yamaguchi, K., Shigenobu, S., Muramatsu, M., Yoshizaki, T. (2017). APOBEC3A associates with human papillomavirus genome integration in oropharyngeal cancers. Oncogene. *36*, 1687-1697.
- Kudo, A., Shigenobu, S., Kadota, K., Nozawa, M., Shibata, T.F., Ishikawa, Y., and Matsuo, T. (2017). Comparative analysis of the brain transcriptome in a hyper-aggressive fruit fly, *Drosophila prolongata*. Insect. Biochem. Mol. Biol. *82*, 11–20.
- Li, B., Kamiya, T., Kalmbach, L., Yamagami, M., Yamaguchi, K., Shigenobu, S., Sawa, S., Danku, J.M.C., Salt, D.E., Geldner, N., Fujiwara, T. (2017). Role of *LOTR1* in Nutrient Transport through Organization of Spatial Distribution of Root Endodermal Barriers. Curr. Biol. *27*, 758–765.
- Matsuda, K., Mikami, T., Oki, S., Iida, H., Andrabi, M., Boss, J.M., Yamaguchi, K., Shigenobu, S., and Kondoh, H. (2017). ChIP-seq analysis of genomic binding regions of five major transcription factors highlights a central role for ZIC2 in the mouse epiblast stem cell gene regulatory network. Development. *144*, 1948-1958.
- Matsui, A., Iida, K., Tanaka, M., Yamaguchi, K., Mizuhashi, K., Kim, J.M., Takahashi, S., Kobayashi, N., Shigenobu, S., Shinozaki, K., Seki, M. (2017). Novel Stress-Inducible Antisense RNAs of Protein-Coding Loci Are Synthesized by RNA-Dependent RNA Polymerase. Plant. Physiol. *175*, 457–472.
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- Nakayama, K., Ohashi, R., Shinoda, Y., Yamazaki, M., Abe, M., Fujikawa, A., Shigenobu, S., Futatsugi, A., Noda, M., Mikoshiba, K., Furuichi, T., Sakimura, K., Shiina, N. (2017). RNG105/caprin1, an RNA granule protein for dendritic mRNA localization, is essential for long-term memory formation. Elife. *6*, e29677.
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- Suetsugu, K., Yamato, M., Miura, C., Yamaguchi, K., Takahashi, K., Ida, Y., Shigenobu, S., and Kaminaka, H. (2017). Comparison of green and albino individuals of the partially mycoheterotrophic orchid *Epipactis helleborine* on molecular identities of mycorrhizal fungi, nutritional modes, and gene expression in mycorrhizal roots. Mol. Ecol. *26*, 1652-1669.


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## Symbiogenomics

*"Nothing, it seems, exists except as part of a network of interactions." (Gilbert & Epel, 2008)*

Every creature on the earth exists among a network of various biological interactions. For example, many multicellular organisms, including humans, harbor symbiotic bacteria in their bodies: some of them provide their hosts with essential nutrients deficient in the host's diet and others digest foods indigestible by the host alone. In spite of numerous examples of symbioses and its intriguing outcomes, the genetic and molecular basis underlying these interactions remains elusive. The goal of our group is to establish a new interdisciplinary science "Symbiogenomics", where we aim to understand the network of biological interactions at the molecular and genetic level. To this end, we take advantage of state-of-the-art genomics such as next-generation sequencing technologies.

### I. Genomic revelations of a mutualism: the pea aphid and its obligate bacterial symbiont

Aphid species bear intracellular symbiotic bacteria in the cytoplasm of bacteriocytes, specialized cells for harboring the bacteria. The mutualism is so obligate that neither can reproduce independently. The genome sequence of the pea aphid, *Acyrthosiphon pisum*, in consort with that of bacterial symbiont *Buchnera aphidicola* illustrates the remarkable interdependency between the two organisms. Genetic capacities of the pea aphid and the symbiont for amino acid biosynthesis are complementary. The genome analysis revealed that the pea aphid has undergone characteristic gene losses and duplications. The IMB antibacterial immune pathway is missing several critical genes, which might account for the evolutionary success of aphids to obtain beneficial symbionts. Lineage-specific gene duplications have occurred in genes in a broad range of functional categories, which include signaling pathways, miRNA machinery, chromatin modification and mitosis. The importance of these duplications for symbiosis remains to be determined. We found several instances of lateral gene transfer from bacteria to the pea aphid genome. Some of them are highly expressed in

bacteriocytes.

We recently discovered a novel class of genes in the pea aphid genome that encode small cysteine-rich proteins with secretion signals that are expressed exclusively in bacteriocytes of the pea aphid, and named these bacteriocyte-specific cysteine-rich proteins (BCR). The BCR mRNAs are first expressed at a developmental time point coincident with the incorporation of symbionts strictly in the cells that contribute to the bacteriocyte, and this bacteriocyte-specific expression is maintained throughout the aphid's life. Some BCRs showed an antibiotic activity. These results suggest that BCRs act within bacteriocytes to mediate the symbiosis with bacterial symbionts, which is reminiscent of the cysteine-rich secreted proteins of leguminous plants that also regulate endosymbionts. Employment of small cysteine-rich peptides may be a common tactic of host eukaryotes to manipulate bacterial symbionts.

Figure 1. Pea aphids and the bacterial symbiont, *Buchnera*. Adult aphids (Left). A developing viviparous embryo which symbionts are infecting (Right). Scale bar = 20 um.

## Publication List:

### 〔Original papers〕


- Anbutsu, H., Moriyama, M., Nikoh, N., Hosokawa, T., Futahashi, R., Tanahashi, M., Meng, X.-Y., Kuriwada, T., Mori, N., Oshima, K., Shigenobu, S., *et al*. (2017). Small genome symbiont underlies cuticle hardness in beetles. Proc. Natl. Acad. Sci. USA *114*, E8382–E8391.
- Hayashi, M., Shinozuka, Y., Shigenobu, S., Sato, M., Sugimoto, M., Ito, S., Abe, K., and Kobayashi, S. (2017). Conserved role of Ovo in germline development in mouse and *Drosophila*. Sci. Rep. *7*, 40056.
- Ota, R., Morita, S., Sato, M., Shigenobu, S., Hayashi, M., and Kobayashi, S. (2017). Transcripts immunoprecipitated with Sxl protein in primordial germ cells of *Drosophila* embryos. Dev. Growth Differ. *59*, 713–723.


### 〔Review article〕


- Mergaert, P., Kikuchi, Y., Shigenobu, S., and Nowack, E.C.M. (2017). Metabolic integration of bacterial endosymbionts through antimicrobial peptides. Trends Microbiol. *25*, 703–712.

## SPECTROGRAPHY AND BIOIMAGING FACILITY

*Specially Appointed Associate Professor:*
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*Technical Staff:* *KONDO, Maki*
*TANIGUCHI-SAIDA, Misako*
*Technical Assistant:* *ICHIKAWA, Chiaki*
*ISHIKAWA, Azusa*

The Spectrography and Bioimaging Facility assists both collaborative and core research by managing and maintaining research tools that use "Light". The facility also provides technical support through management of technical staff assisting in the advancement of collaborative and core research projects, as well as academic support to researchers by Dr. Y. Kamei (refer to the Collaborative Research Group Research Enhancement Strategy Office section). Among its tools are advanced microscopes for biology and the Okazaki Large Spectrograph for photobiology. The Okazaki Large Spectrograph is the world's largest wide spectrum exposure mechanism, capable of producing a range of wavelengths from 250 nm (ultraviolet) to 1,000 nm (infrared) along its 10 meter focal curve; allowing exposure to strong monochromatic light. The facility's microscopes, which are cutting edge devices such as confocal and multi-photon excitation microscopes, are used by both internal and external researchers as vital equipment for core and collaborative research projects.

### Representative Instruments: Okazaki Large Spectrograph (OLS)

The spectrograph runs on a 30 kW Xenon arc lamp and projects a wavelength spectrum from 250 nm (ultraviolet) to 1,000 nm (infrared) onto its 10 m focal curve with an intensity of monochromatic light at each wavelength more than twice as much as that of the corresponding monochromatic component of tropical sunlight at noon (Watanabe *et al*., Photochem. Photobiol. *36*, 491-498, 1982). The spectrograph is dedicated to action spectroscopical studies of various light-controlled biological processes.

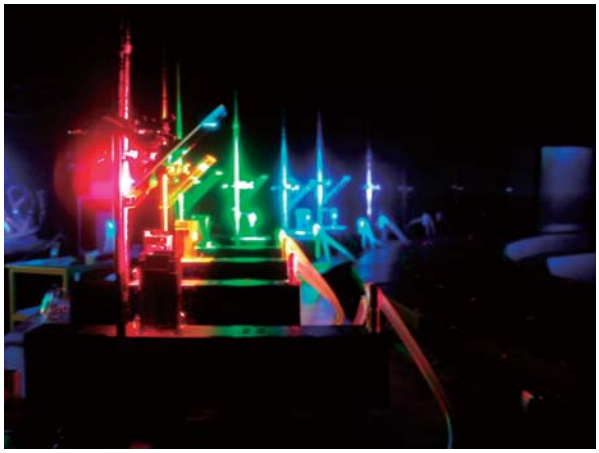

Figure 1. An example of experiments using the Large Spectrograph. Various color rays (monochromatic light from right side and reflected by mirrors) were irradiated simultaneously to samples in cooling chambers.

The NIBB Collaborative Research Program for the Use of the OLS supports about 10 projects every year conducted by both visiting scientists, including foreign researchers, as well as those in NIBB.

Action spectroscopical studies for various regulatory and damaging effects of light on living organisms, biological molecules, and artificial organic molecules have been conducted.

### Microscopes

This facility also has Bioimaging machines such as wide-field microscopes (Olympus IX-81 and BX-63), confocal microscopes (Olympus FV1000, Nikon A1R, Nikon A1Rsi and Yokogawa CSU-X1 with EM-CCD camera), multi-photon microscopes (Olympus FV1000-MP, FV1200-MPs, Leica TCS-SP8 MPs) and other advanced laser microscopes with special aims (Light-sheet Microscope and Infrared Laser-Evoked Gene Operator microscope: IR-LEGO) for users in NIBB and collaborative guest researchers. We began two new types of Collaborative Research Program from 2016. One is a new category of the NIBB Collaborative Research for Integrative Bioimaging using machines and bioimage processing/analysis techniques, and the other is the Advanced Bioimaging Support Program (ABiS) of the Grant-in-aid for Scientific Research on Innovative Areas.

The light-sheet microscope was developed by Dr. Ernst Stelzer's group at the European Molecular Biology Laboratory (EMBL). This microscope can realize high-speed z-axis scanning in deeper tissue by illuminating a specimen from the side with a light sheet (more information is given in Dr. Nonaka's section: Lab. for Spatiotemporal Regulations). Dr. Shigenori Nonaka conducted and supported about 10 projects as Collaborative Research Programs for Integrative Bioimaging. The IR-LEGO was developed by Drs. Shunsuke Yuba and Yasuhiro Kamei at the National Institute of Advanced Industrial Science and Technology (AIST). This microscope can induce a target gene of interest by heating a single target cell *in vivo* with a high efficiency irradiating infrared laser. Details are described in the next section. The IR-LEGO was also used for about 10 Collaborative Research projects, including applications for animals and plants.

### Workshop and Symposium

In 2017 we held the 5$^{th}$ biological image processing training course with the Department of Imaging Science, CNSI. We also have been holding a "Bioimaging Forum" every year which discusses Bioimaging from various directions such as microscopy, new photo-technology, and computer science. This year we held the 11$^{th}$ NIBB Bioimaging Forum focused on adaptive optics for microscopy. In addition, we held three symposiums focused on new emerging model animals, next generation research using amphibians, and Biothermology: heat and temperature in biology.

### Publication List on Cooperation

〔**Original papers (Selected)**〕

● Homma, N., Harada, Y., Uchikawa, T., Kamei, Y., and Fukamachi, S.

(2017). Protanopia (red color-blindness) in medaka: a simple system for producing color-blind fish and testing their spectral sensitivity. BMC Genetics *18*, 10.
- Ishikawa, T., Kashima, M., Nagano, A.J., Ishikawa-Fujiwara, T., Kamei, Y., Todo T., and Mori, K. (2017). Unfolded protein response transducer IRE1-mediated signaling independent of XBP1 mRNA splicing is not required for growth and development of medaka fish. eLife *6*, e26845.
- Li, C., Sako, Y., Imai, A., Nishiyama, T., Thompson, K., Kubo, M., Hiwatashi, Y., Kabeya, Y., Karlson, D., Wu, S. H., Ishikawa, M., Murata, T., Benfey, P.N., Sato, Y., Tamada, Y., and Hasebe, M. (2017). A Lin28 homologue reprograms differentiated cells to stem cells in the moss Physcomitrella patens. Nat. Commun. *8*, 14242.
- Nakano, M., Arai, Y., Kotera, I., Okabe, K., Kamei, Y., and Nagai, T. (2017). Genetically encoded ratiometric fluorescent thermometer with wide range and rapid response. PLoS ONE *12*, e0172344.
- Nakayasu, T., Yasugi, M., Shiraishi, S., Uchida, S., and Watanabe, E. (2017). Three-dimensional computer graphic animations for studying social approach behaviour in medaka fish: Effects of systematic manipulation of morphological and motion cues. PLoS ONE *12*, e0175059.
- Osanai, Y., Shimizu, T., Mori, T., Yoshimura, Y., Hatanaka, N., Nambu, A., Kimori, Y., Koyama, S., Kobayashi, K., and Ikenaka, K. (2017). Rabies virus-mediated oligodendrocyte labeling reveals a single oligodendrocyte myelinates axons from distinct brain regions. Glia *65*, 93-105.
- Shimmura, T., Nakayama, T., Shinomiya, A., Fukamachi, S., Yasugi, M., Watanabe, E., Shimo, T., Senga, T., Nishimura, T., Tanaka, M., Kamei, Y., Naruse, K., and Yoshimura, T. (2017). Dynamic plasticity in phototransduction regulates seasonal changes in color perception. Nat. Commun. *8*, 412.
- Suzuki, M., Sato, M., Koyama, H., Hara, Y., Hayashi, K., Yasue, N., Imamura, H., Fujimori, T., Nagai, T., Campbell, R.E., and Ueno, N. (2017). Distinct intracellular Ca2+ dynamics regulate apical constriction and differentially contribute to neural tube closure. Development. *144*, 1307-1316.
- Taniguchi, A., Kimura, Y., Mori, I., Nonaka, S., and Higashijima, S.-I. (2017). Axially-confined in vivo single-cell labeling by primed conversion using blue and red lasers with conventional confocal microscopes. Dev. Growth Differ. *59*, 741-748.

〔**Original paper (E-publication ahead of print)**〕

- Nakamoto, M., Shibata, Y., Ohno, K.. Usami, T., Kamei, Y., Taniguchi, Y., Todo, T., Sakamoto, T., Young, G., Swanson, P., Naruse, K., and Nagahama, Y. Ovarian aromatase loss-of-function mutant medaka undergo ovary degeneration and partial female-to-male sex reversal after puberty. Mol. Cell Endocrinol. 2017 July 13.

### ● *Research activity by Y. Kamei*

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| *Specially Appointed Associate Professor:* | *KAMEI, Yasuhiro* |
| *NIBB Research Fellow:* | *SAKAMOTO, Joe* |
| *Visiting Scientist:* | *HATTORI, Masayuki* |
| *Technical Assistant:* | *NAKAGAWA, Mami* |

Our research group promotes two cutting-edge microscope projects; "observation" and "manipulation" using optical and biological technologies. The aim of our "observation project" is deep-seeing in living organisms using adaptive optics (AO) which were well-developed in the field of astronomy as a key technology of large telescopes such as the Subaru telescope in Hawaii. Although observation using telescopes on the earth may be disturbed by fluctuations in the atmosphere, AO technology can cancel this disturbance. On the other hand, living materials have particular refractive

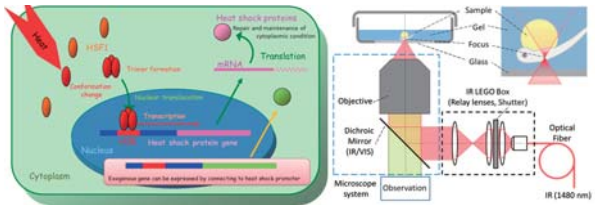


Figure 1. Schematic illustration of heat shock response of cells (left) and an infrared laser-evoked gene operator (IR-LEGO) microscope system.

indexes, therefore, some organelles act as disturbances of the ideal optical path for microscope observation just like the atmosphere does for telescopes. AO technology can also compensate for this disturbance by sensing and correcting wave fronts using a wave front sensor and deformable mirror. Hence, we developed a custom-made wide-field microscope equipped with an AO system for observation of living organisms in collaboration with Dr. Tamada in NIBB and Dr. Hayano in the National Astronomical Observatory of Japan (NAOJ) and got high-resolution bright field and fluorescent images of living cells. Our results indicated that improvement of optical resolution was restricted to a small area which is called the "isoplanatic patch".

Second, the aim of our "manipulation project" is to control gene expression *in vivo*. Gene function analysis must be evaluated at the cell level *in vivo*. To achieve spatiotemporal-controlled gene expression we employed one of the stress responses, the heat shock response. The heat shock promoter is the transcription regulation region of heat shock proteins and all organisms have this mechanism. Positioning the target gene downstream of the promoter, we can induce the target gene expression by local heating.

Infrared (IR) beams can heat water molecules, which are the main constituent of cells, hence, we can heat a single cell by irradiating IR to a target cell using a microscope. We have developed a microscope, IR laser evoked gene operator (IR-LEGO), specialized for this purpose (Figure 1). The IR-LEGO microscope can irradiate an IR laser to a single cell *in vivo* such as in *C. elegans*, *Drosophila*, medaka, zebrafish, *Xenopus* and *Arabidopsis*, to induce the heat shock response at a desired timing. In 2015, additionally, we confirmed the system was effective in the moss *Marchantia polymorpha* and in the newt *Pleurodeles waltl*.

Optimal heating induces the heat shock response and subsequent gene expression, while an excess results in cell death. Hence, we must precisely control laser heating. We evaluated time course and spatial heating profiles, and the results presented that temperature of the target area rose rapidly and kept a constant level dependant on IR laser power, additionally, the heated area was adequately as small as a typical cell size.

With this in mind, we tried to induce gene expression in various species. At first, we reported an IR-LEGO experiment in living *C. elegans*. Target gene expression in a target cell could be induced with only 1 s-IR irradiation. Whereas the optimal power range which can induce gene induction without cell damage was limited. Excess laser power resulted in cell death or cessation of cell division. We confirmed that an optimal irradiation, e.g. 11 mW for 1 s, induced physiological gene expression in the target cell and subsequent

cell division or morphogenesis underwent normal development. Next, we tried the experiment in other animals, such as, medaka, zebrafish and *Xenopus*, and the higher plant, *Arabidopsis*, since all organisms have a heat shock response system. We succeeded in local gene induction in all the species as expected. Moreover, this system can be combined to the cre/loxP recombination technique for long-term gene expression (Figure 2).

As mentioned above, excess irradiation resulted in cell damage, so we utilized the system to ablate target cells with strong pulsed irradiation. In collaboration with National Taiwan University, we used the system for neuronal regeneration study in zebrafish and revealed that a kind of neuronal precursor cell played an important role within the neuron regeneration step the in zebrafish spinal cord (Zeng *et al*. Biol. Cell 2016). In addition, the IR-LEGO system can be utilized for biothermology, a new field thinking about temperature or heat in biological systems, because spatiotemporal micrometer order local heating is difficult without this system. Now we are trying to estimate thermal properties of cells and biomaterials *in vivo* using a newly developed thermo-probe (Nakano *et al*. PLoS One 2017) and the IR-LEGO microscope system.

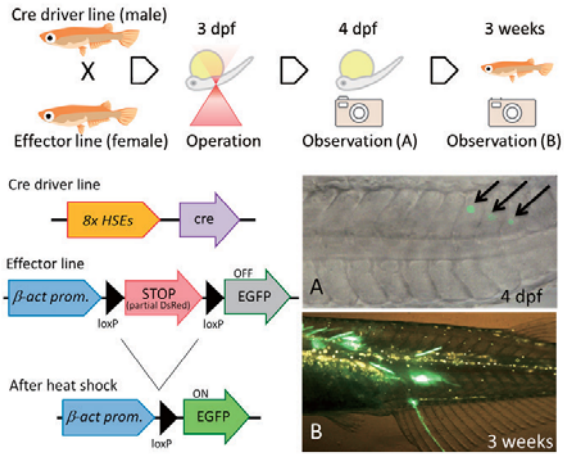


Figure 2. Long-term gene expression system with cre/loxP recombination system and its example of practical experiment in medaka embryo to adult.

## Publication List:

### 〔Original papers〕


- Hattori M., Tamada Y., Murata T., Oya S., Hasebe M., Hayano Y., and Kamei Y. (2017). Artificial testing targets with controllable blur for adaptive optics microscopes. Optical Engineering *56*, 080502.
- Homma, N., Harada, Y., Uchikawa, T., Kamei, Y., and Fukamachi, S. (2017). Protanopia (red color-blindness) in medaka: a simple system for producing color-blind fish and testing their spectral sensitivity. BMC Genetics *18*, 10.
- Ishikawa, T., Kashima, M., Nagano, A.J., Ishikawa-Fujiwara, T., Kamei, Y,, Todo T., and Mori, K. (2017). Unfolded protein response transducer IRE1-mediated signaling independent of XBP1 mRNA splicing is not required for growth and development of medaka fish. eLife *6*, e26845.
- Ishikawa, T., Toyama, T., Nakamura, Y., Tamada, K., Shimizu, H., Ninagawa, S., Okada, T., Kamei, Y., Ishikawa-Fujiwara, T., Todo, T., Aoyama, E., Takigawa, M., Harada, A., and Mori, K. (2017). UPR transducer BBF2H7 allows export of type II collagen in a cargo- and developmental stage-specific manner. J. Cell Biol. *216*, 1761-1774.
- Nakano, M., Arai, Y., Kotera, I., Okabe, K., Kamei, Y., and Nagai, T. (2017). Genetically encoded ratiometric fluorescent thermometer with wide range and rapid response. PLoS ONE *12*, e0172344.
- Shimmura, T., Nakayama, T., Shinomiya, A., Fukamachi, S., Yasugi, M., Watanabe, E., Shimo, T., Senga, T., Nishimura, T., Tanaka, M., Kamei, Y., Naruse, K., and Yoshimura, T. (2017). Dynamic plasticity in phototransduction regulates seasonal changes in color perception. Nat. Commun. *8*, 412.


### 〔Original paper (E-publication ahead of print)〕


- Nakamoto, M., Shibata, Y., Ohno, K.. Usami, T., Kamei, Y., Taniguchi, Y., Todo, T., Sakamoto, T., Young, G., Swanson, P., Naruse, K., and Nagahama, Y. Ovarian aromatase loss-of-function mutant medaka undergo ovary degeneration and partial female-to-male sex reversal after puberty. Mol. Cell Endocrinol. 2017 July 13.

## Data Integration and Analysis Facility

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The Data Integration and Analysis Facility supports research activities based on large-scale biological data analysis, such as genomic sequence analysis, expression data analysis, and imaging data analysis. For this purpose, the facility maintains high-performance computers with large-capacity storage systems. On the basis of this system, the facility supports development of data analysis pipelines, database construction and setting up websites to distribute the data worldwide as well as providing users' basic technical support. In addition to computational analysis, the Data Integration and Analysis Facility supports NIBB's information infrastructure, the maintenance of the network systems in the institute and computer/network consultation for institute members.

### Representative Instruments

Our main computer system is the Biological Information Analysis System (BIAS) (Figure 1), which consists of a high-performance cluster system (SGI Rackable server C2112-4RP; 40 nodes/800 cores, 96GB memory/node), a shared memory parallel computer (HP ProLiant DL980 G7; 80 cores, 4TB memory), a high-throughput storage system (DDN SFA7700; 480TB), and a large capacity storage system (DELL PowerEdge R620; 720TB). All subsystems are connected via a high-speed InfiniBand network so that large amounts of data can be processed efficiently. Some personal computers and color printers are also available. On this system, we provide various biological databases and data retrieval/analysis programs, and support large-scale data analysis and database construction for institute members and collaborative researchers. Especially, we have supported the construction and maintenance of published databases of various model organisms including XDB (*Xenopus laevis*), PHYSCObase (*Physcomitrella patens*), DaphniaBASE (*Daphnia magna*), The Plant Organelles Database, and MBGD (microbial genomes).

The facility also provides network communication services. Most of the PCs in each laboratory, as well as all of the above-mentioned service machines, are connected by a local area network, which is linked to the high performance backbone network ORION connecting the three research institutes in Okazaki. Many local services, including sequence analysis services, file sharing services, and printer services, are provided through this network. We also maintain a public World Wide Web server that hosts the NIBB home page (http://www.nibb.ac.jp/en).


Figure 1. Biological Information Analysis System

### Research activity by I. Uchiyama

Assistant professor I. Uchiyama is the principal investigator of the Laboratory of Genome Informatics, which currently focuses on microbial comparative genomics studies. For details, please refer to the laboratory page (p. 69).