2019-2020

Graduate School of Biostudies, Kyoto University
Master's Program in "Global Frontier in Life Science"

Guidelines for International Student Admissions

Philosophy and Admission Policy of the Graduate School of Biostudies

The field of life sciences is transforming and evolving into an advanced branch of science that will build a future for humans. With this global trend as a backdrop, the Graduate School of Biostudies was established in 1999 as Japan's first independent graduate school of biostudies with the aim of creating one of the world's top research institutions and developing bioscientists who will lead the next generation in the biostudies field. With a set of such basic units of life as "cells," "molecules," and "genes" as a common language, the Graduate School of Biostudies is home to innovative research and education activities where concepts about diverse organisms and the environments that sustain them are integrated to create new values concerning the future and respect for life.

In response to diverse social demands that call for an increasingly sophisticated and complex life sciences field, the Graduate School of Biostudies strives to develop the following human resources:

1) Researchers who explore and discover the basics of life, pursuing the cutting-edge field of biostudies at the highest level in the world;
2) Researchers and highly skilled engineers who contribute to society at public and private research institutions, endeavoring to protect the global environment and maintain human health, well-being, and fulfillment; and
3) Educators and highly skilled practitioners who possess broad knowledge of diverse vital phenomena of living organisms and contribute to society through education, industry, mass media, and the public sector.

In April 2011, the Graduate School of Biostudies launched "Global Frontier in Life Science", an educational program as a part of K.U. PROFILE (Kyoto University Programs for Future International Leaders: http://www.opir.kyoto-u.ac.jp/kuprofile/ e/index.html). This program, "Global Frontier in Life Science", is held entirely in English, including the entrance examinations, lectures, experiments and discussions.

The Graduate School of Biostudies seeks international as well as domestic students who hope to join this program. In particular, the School welcomes those who show a respect for life and a desire to create a comprehensive and cutting-edge area within the life sciences field beyond existing disciplinary boundaries.

Admission examinations for the Master's program in "Global Frontier in Life Science" consist of: 1) a documentation screening and 2) an oral examination (interview). **Please note that applicants are NOT required to be physically present in Japan for the examination.**

The academic year starts on October 1, 2019 or April 1, 2020.

I. "Global Frontier in Life Science"

The Graduate School of Biostudies launched "Global Frontier in Life Science", an educational program for Doctoral and Master's students, as a part of K.U. PROFILE (Kyoto University Programs for Future International Leaders: http://www.opir.kyoto-u.ac.jp/kuprofile/e/index.html). This program, "Global Frontier in Life Science", is held entirely in English, including the entrance examinations, lectures, experiments, and discussions. Up to ten applicants will be accepted.

II. Division/Laboratories and Enrollment

The Graduate School of Biostudies consists of two divisions, which are made up of 41 laboratories. Details of each laboratory are described on pp. 9 - 27 (tentative) of these guidelines and the Graduate School of Biostudies website (http://www.lif.kyoto-u.ac.jp/). Applicants can apply for up to two laboratories. **Thus, applicants must contact the lab heads and fully discuss potential research activities and availability before filing the application.**

III-1. Eligibility Requirements for Applicants expecting to start from October 1, 2019

Applicants must match one of the following requirements by September 30, 2019:

1. Individuals with any nationality who have completed (or are expected to complete by September 30, 2019) 16 years of education in foreign countries. This includes individuals who have completed an equivalent of 16 years of education but have less than 16 years due to skipped (advanced) grades.
2. Individuals, other than Japanese nationals, who graduated (or are expected to graduate by September 30, 2019) from a Japanese university.
3. Individuals who have received (or are expected to receive by September 30, 2019) a degree equivalent to a bachelor's degree by completing a curriculum with a term of enrollment of at least three years (including completion of such a curriculum by studying relevant subjects in Japan via a correspondence course provided by a school in a foreign country and completion of a curriculum at an educational facility that has been accredited as having an approved curriculum under the educational system of said country and is designated by the Minister of Education, Culture, Sports, Science and Technology) at a university or other school in a country other than Japan (only those universities or schools for which the overall conditions of education and research activities have been assessed by a party authorized by the government of said country or an organization concerned, or those corresponding to such entities as designated by the Minister of Education, Culture, Sports, Science and Technology).
4. Individuals, other than Japanese nationals, who are recognized by the Graduate School of Biostudies to have completed an education equivalent to a university degree of Japan and are at least 22 years old by September 30, 2019.
5. Individuals with Japanese nationality who are determined by the Graduate School of Biostudies to have completed an education in foreign countries equivalent to a university degree of Japan or had school education that were mainly given in English, and are at least 22 years old by September 30, 2019.

Those who are applying under requirement 4 or 5 must undergo a preliminary eligibility screening process before applying.

III-2. Eligibility Requirements for Applicants expecting to start from April 1, 2020

Applicants must match one of the following requirements by March 31, 2020:

1. Individuals with any nationality who have completed (or are expected to complete by March 31, 2020) 16 years of education in foreign countries. This includes individuals who have completed an equivalent of 16 years of education but have less than 16 years due to skipped (advanced) grades.
2. Individuals, other than Japanese nationals, who graduated (or are expected to graduate by March 31, 2020) from a Japanese university.
3. Individuals who have received (or are expected to receive by March 31, 2020) a degree equivalent to a bachelor's degree by completing a curriculum with a term of enrollment of at least three years (including completion of such a curriculum by studying relevant subjects in Japan via a correspondence course provided by a school in a foreign country and completion of a curriculum at an educational facility that has been accredited as having an approved curriculum under the educational system of said country and is designated by the Minister of Education, Culture, Sports, Science and Technology) at a university or other school in a country other than Japan (only those universities or schools for which the overall conditions of education and research activities have been assessed by a party authorized by the government of said country or an organization concerned, or those corresponding to such entities as designated by the Minister of Education, Culture, Sports, Science and Technology).
4. Individuals, other than Japanese nationals, who are recognized by the Graduate School of Biostudies to have completed an education equivalent to a university degree of Japan and are at least 22 years old by March 31, 2020.
5. Individuals with Japanese nationality who are determined by the Graduate School of Biostudies to have completed an education in foreign countries equivalent to a university degree of Japan or had school education that were mainly given in English, and are at least 22 years old by March 31, 2020.
6. Individuals, other than Japanese nationals, who will be enrolled at least 3 years in a Japanese university by March 31, 2020 and are recognized by the Graduate School of Biostudies as having acquired sufficient credits with excellent academic records.

Those who are applying under requirement 4 or 5 must undergo a preliminary eligibility screening process before applying.

IV. Eligibility Screening

Applicants filing under eligibility requirement 4, 5, or 6 above are required to contact the Student Affairs Section (Kyomu gakari) of the Graduate School of Biostudies to request that the designated application form for preliminary eligibility screening to be sent at any time, but no later than April 11 (Thu), 2019. Submit the following preliminary eligibility screening documents via email to the Student Affairs Section of the Graduate School of Biostudies (150kyomu@adm.lif.kyoto-u.ac.jp) by JST 5:00 p.m., April 18 (Thu), 2019 at latest. When filing the admission application, applicants cannot in principle apply for any laboratory other than the one or two specified in the documents being submitted for the eligibility screening.

The screening results will be sent by e-mail to the applicants as soon as the decision is made, at latest on May 9 (Thu), 2019.

1. Documents for the Eligibility Screening

When filing under eligibility requirement 4 or 5

(1) Application form for the eligibility screening **(designated form)**	This form is provided upon request.
(2) Academic transcript	Submit an academic transcript prepared and sealed by the university last attended. (The transcript does not need to be sealed if it is made of a material that prevents photocopying.)
(3) Research progress report **(designated form)**	Present a brief, objective statement on the progress of the applicant's research in the field of specialization. This form is provided upon request.
(4) Details of previous studies **(designated form)**	Submit a certificate of research work content prepared and sealed by the institution to which the applicant belongs. This form is provided upon request.
(5) A valid score for GRE General Test or Subject Test (See **Note** below)	Any scores of the Subject Test are optional. Acceptable test includes: Biology/ Biochemistry, Cell and Molecular/Biology/Chemistry/Physics.
(6) Others	Documents or printed materials that support academic or scientific achievements, if any, such as books, research articles, or academic presentations.

When filing under the eligibility requirement 6

(1) Application form for the eligibility screening	This form is provided upon request. **(designated form)**
(2) Letter of recommendation	Submit a letter of recommendation prepared and sealed by the university in which you are/were enrolled. Note that recommendation letters must be written on the letterhead of the institution to which the recommender belongs and are valid only when the recommender's handwritten signature and full contact addresses (including Email address) are provided.
(3) Academic transcript	Submit an academic transcript prepared and sealed by the university in which you are/were enrolled. (The transcript does not need to be sealed if it is made of a material that prevents photocopying.)
(4) Statement of personal objectives **(designated form)**	This form is provided upon request.
(5) A valid score for GRE General Test or Subject Test See **Note** below)	Any scores of the Subject Test are optional. Acceptable test includes: Biology/ Biochemistry, Cell and Molecular/Biology/Chemistry/Physics.

Note

1) For applicants who hold a GRE* General Test or Subject Test score for Biology/Biochemistry, Cell and Molecular Biology/Chemistry/Physics, those scores can be provided as supplemental supporting information.

***GRE:** Graduate Record Examination http://www.ets.org/gre
Designated Institution (DI) Code: 3814 Kyoto U

2) Successful applicants filing under the eligibility requirement 6, expecting to matriculate in April, 2020, must submit an academic transcript for the 2019 academic year to the Student Affairs Section (Kyomu gakari) of the Graduate School of Biostudies by February 20 (Thu), 2020. Otherwise successful applicants whose transcripts demonstrate a failure to meet the admissions standards of the Graduate School of Biostudies may be refused admission.
Successful applicants filing under eligibility requirement 6 must also submit a certificate of withdrawal by March 31 (Tue), 2020; thus, they cannot obtain a bachelor's degree at the university currently attended.

V. Application Fee

Application fee: 10,000 yen
Payment period: From May 1 (Wed) to May 16 (Thu), 2019 JST

Only payments marked as made within this period will be valid; those made outside this period will be invalid. Once received, application fees will not be refundable under any circumstances.

[Payment methods]

1. **Payment by Credit Card (only for applicants residing outside Japan).**
Applicants residing outside Japan should pay the application fee (10,000 yen) and Service Fee (500 yen). Please access the URL below titled "Examination Settlement Service (EXSS)" and complete the payment process following the instructions provided during the designated payment period. For details, please refer to a separate sheet titled "Payment Methods for Application Fees with Convenience Store or Credit Card". Note that the Application Completed page must be printed out and submitted along with the other application documents (see section VI below).

EXSS: https://www3.univ-jp.com/kyoto-u/en/bio/

2. **Payment with Convenience Store (only for applicants residing inside Japan).**
Applicants residing inside Japan should pay the application fee (10,000 yen) and Service Fee (500 yen). Please access the URL below titled "Examination Settlement Service (EXSS)" and complete the payment process following the instructions provided during the designated payment period. For details, please refer to a separate sheet titled "Payment Methods for Application Fees with Convenience Store or Credit Card". Note that the Application Completed page must be printed out and submitted along with the other application documents (see section VI below).

EXSS: https://www3.univ-jp.com/kyoto-u/en/bio/

3. **Payment by bank transfer (only for applicants residing inside Japan).**

Applicants residing inside Japan should pay the application fee (10,000 yen) by bank transfer with the following procedures.

Payment at a bank window in Japan

(1) **Enter the applicant's name in the appropriate spaces (three spaces) on the Application Fee Payment Request Form (available upon request via regular mail). Take the form to a bank without separating any of its portions (payment through the post office or Japan Post Bank is not available) and make your payment. Please note that payment via the Internet is not accepted.**

(2) No transfer fee is charged if payment is made at the head office or a branch office of Mitsui Sumitomo Banking Corporation. If payment is made at any other bank, you shall be responsible for the cost of transfer.

(3) After making your payment, make sure that the bank's receipt seal is stamped on the "Evidence of Application Fee Payment" and the "Application Fee (and Transfer Fee) Receipt" returned from the bank. Paste the "Evidence of Application Fee Payment" (left portion) on the "Form for Affixing Evidence of Application Fee Payment". Please retain the copy of the "Application Fee (and Transfer Fee) Receipt" with revenue stamp attached for your records.

Payment via ATM

Bank Name	Branch	Type of Account	Account No.	Recipient's Name
Mitsui Sumitomo Bank 三井住友銀行	Kyoto 京都支店	Ordinary (*futsu*) 普通	8089428	Kyoto University 国立大学法人 京都大学

(1) Enter the applicant's name as the payer in the appropriate space in the ATM so that the university will be able to identify by whom the amount was deposited in the university's account.

(2) Extra charge for deposit via ATM must be paid by the applicant.

(3) Submit the receipt of the deposit to be issued with the ATM and make a photocopy of the receipt for yourself.

VI. Application Documents

(1) Admission application form, photograph card, examination card	**Use the provided form.** Fill in the blanks and paste a photo to each of the two indicated places. Make sure the photos present your full-face and frontal view, without a hat or cap, and are taken within the past three months.
(2) Research achievement (Questions for application screening)	**Use the provided form.** Fill in the boxes in the designated form. Do not exceed to write expanding the original size of the boxes. The sizes are fixed. Please write in Times New Roman 12 point.
(3) Academic transcript	Submit an academic transcript prepared and sealed by the university you are currently attending or from which you have graduated.
(4) Graduation certificate (or certificate of expected graduation)	Submit a certificate prepared by the university you are currently attending or from which you have graduated.

(5) Recommendation letters	At least two letters are required. (Mandatory) Letter of recommendation 1: Written by a faculty member of your current educational institution, who can evaluate your academic performance and potential for success in the Master's program. The letter must be written on the letterhead of the respective institution and must include the recommender's contact information and hand-written signature.
	(Choose at least one, as appropriate) Letter of recommendation 2: Written by the faculty supervisor of the applicant at the university to which you belong or from which you graduated, who can evaluate your research and your potential to become a productive scientist. The letter must be written on the letterhead of the supervisor's institution and must include the supervisor's contact information and hand-written signature. Letter of recommendation 3: If you are employed at a public agency or company at the time of application, submit a letter of recommendation from your immediate supervisor, with his/her hand-written signature. The letter must include your supervisor's contact information and be written on the letterhead of the agency/company to which he/she belongs.
(6) A valid score for GRE General Test and Subject Test	General Test score is required. Any scores of the Subject Test are optional. Acceptable test includes: Biology/Biochemistry, Cell and Molecular/Biology/Chemistry/Physics
(7) A valid score for IELTS or TOEFL	Unnecessary for English-native speakers (Please contact the Student Affairs Section in advance.)
(8) Evidence of application fee payment form	**Applicants residing outside Japan:** After paying your application fees via internet, the Application Completed page must be printed out and submitted. Applications will not be accepted if payment could not be confirmed. Applicants residing inside Japan: After paying your application fees at a convenience store or a bank window or by an ATM, paste the Evidence of Application Fee Payment with the bank's receipt seal stamped or the receipt issued by the ATM. Applications will not be accepted if no receipt seal is stamped on the Evidence of Application Fee Payment form.
(9) Address for further communication	**Use the designated forms.** For further communication on the examination results and the enrollment procedures, clearly write your name, address and post code on the designated form. *If you change your address after applying, you must promptly inform the new address to the Student Affairs Section (Kyomu gakari) of the Graduate School of Biostudeis.

VII. Application Procedures

Applicants must prepare a packet of all necessary admission application documents in print and submit it to the postal address indicated on p.9. When sending the packet by post, use registered mail and write clearly "Admission Application Form for the Graduate School of Biostudies Master's program of Global Frontier in Life Science" on the front of the envelope.

VIII. Application Period

The application period is from May 10 (Fri) to May 17 (Fri), 2019 JST.

When submitting in person: office hours are 9:00 a.m. – 12:00 p.m. and 1:00 p.m. – 5:00 p.m. When sending the application documents by post, ensure that the application documents are delivered by JST 5:00 p.m. on May 17 (Fri), 2019.

Note that the admission application form will not be accepted if the application completed page or the Evidence of Payment for Application Fees with the bank's receipt seal stamped or the receipt issued by the ATM is not pasted on the Form for Affixing Evidence of Payment for Application Fees.

IX. Examination Schedule

May 20 (Mon) ~ June 7 (Fri)	**Documentation Screening** Only successful applicants who pass the screening of the admission documents will be able to take the interview (Oral Examination).
June 17 (Mon) ~ July 12 (Fri)	**Interview** (Oral Examination) The interview date and method* will be arranged individually after the decision is made. ***e.g. Skype or other protocols**

X. Announcement of Successful Applicants

The list of successful applicants is scheduled to be posted on a bulletin board on the 1st floor of the South Campus Research Bldg. (Faculty of Medicine Bldg. G) at approximately 5p.m., July 24 (Wed), 2019. Simultaneously, the same list will be posted on the web site of the Graduate School of Biostudies (http://www.lif.kyoto-u.ac.jp/e/). Telephone inquiries about the selection results shall not be accepted.

XI. Admission Fee and Tuition

Admission Fee: 282, 000 yen (tentative)
(The admission fee amount may be revised at the time of enrollment.)

Tuition for the first semester: 267,900 yen (annual tuition: 535,800 yen, tentative)
(The tuition fee amount may be revised at the time of enrollment or later.)

Notes:

(1) "Master's Program" at Kyoto University refers to the first two-year program in a doctoral program specified in the Standards for the Establishment of Graduate Schools, and is a term used at Kyoto University.

(2) Students who have completed the Master's degree in the Graduate School of Biostudies and wish to continue on for the Doctoral Program must nevertheless submit a formal application for the Doctoral Program.

(3) Others

1) After the application is accepted, no changes are allowed in any of the application items. Furthermore, once received, application fees will not be refundable under any circumstances.
2) **For applicants residing inside Japan:** To request **the Application Fee Payment Request Form**, write your post code, address, and name on a self-addressed 240 mm x 332 mm-sized envelope, and affix 80-yen postage to the self-addressed envelope. Write **"Request for Application Fee Payment Request Form"** on the front of the envelope, place the self-addressed envelope inside, and send it to the address below).
3) The instructions of enrollment procedures will be e-mailed to each successful applicant in late July, 2019 for those who would like to enroll in October, 2019. For those who will enroll in April, 2020, it will be informed in early February, 2020.
4) Applicants with physical disabilities (degree of physical disability as stipulated in the enforcement ordinance of the School Education Law) who require special arrangements for taking examinations or attending courses should immediately contact the Student Affairs Section (Kyomu gakari).

[Handling of Personal Information]
Personal information provided in application documents will be handled in accordance with "Kyoto University's Rules regarding the Protection of Personal Information."

< Where to send your application, and Inquiries >

Student Affairs Section (Kyomu gakari) of the Graduate School of Biostudies,
Kyoto University
Yoshida-Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan
Phone: +81-75-753-9424 Fax: +81-75-753-9229 E-mail: 150kyomu@adm.lif.kyoto-u.ac.jp

December, 2018

Graduate School of Biostudies, Kyoto University
http://www.lif.kyoto-u.ac.jp/e/

Division of Integrated Life Science

1) Laboratory of Chromosome Transmission

PI: NAKASEKO, Yukinobu (Associate Prof.) <nakaseko@lif.kyoto-u.ac.jp>

Outline of the research

Our research is focused on the cell cycle regulation of eukaryotic cells. Using fission yeast as a model system, regulation of chromosome segregation and separation during mitosis has been studied. We are trying to identify individual genes involved in these steps and to elucidate the functional networks of these genes.

Publications

Nakamura, T., Pluskal, T., Nakaseko, Y., and Yanagida, M. Impaired coenzyme A synthesis in fission yeast causes defective mitosis, quiescence-exit failure, histone hypoacetylation and fragile DNA. ***Open Biol.*** 2, 120117 (2012). doi: 10.1098/rsob.120117.

Irvine, D. V., Goto, D. B., Vaughn, M. W., Nakaseko, Y., McCombie, W. R., Yanagida, M., and Martienssen, R. Mapping epigenetic mutations in fission yeast using whole-genome next-generation sequencing. ***Genome Res.*** 19, 1077-1083 (2009). doi: 10.1101/gr.089318.108.

Hanyu, Y., Imai, K. K., Kawasaki, Y., Nakamura, T., Nakaseko, Y., Nagao, K., Kokubu, A., Ebe, M., Fujisawa, A., Hayashi, T., Obuse, C., and Yanagida, M. *Schizosaccharomyces pombe* cell division cycle under limited glucose requires Ssp1 kinase, the putative CaMKK, and Sds23, a PP2A-related phosphatase inhibitor. ***Genes Cells.*** 14, 539-554 (2009). doi: 10.1111/j.1365-2443.2009.01290.x.

Website of the lab: http://www.lif.kyoto-u.ac.jp/e/?post_type=labos&p=135

Key words: chromosome, cell cycle, genetic analysis

2) Laboratory of Gene Biodynamics

PI: SHIRAISHI, Hideaki (Associate Prof.) <siraisi@kuchem.kyoto-u.ac.jp>

Outline of the research

We investigate the growth, morphogenesis, and evolution of photosynthetic microorganisms. We currently focus on developing molecular genetic tools for the analysis and genetic manipulation of the edible alkalophilic cyanobacterium *Arthrospira* (*Spirulina*).

Publications

Shiraishi, H. Cryopreservation of the edible alkalophilic cyanobacterium *Arthrospira platensis*. ***Biosci. Biotechnol. Biochem.*** 80, 2051-2057 (2016). PMID: 27240586

Shiraishi, H. Association of heterotrophic bacteria with aggregated *Arthrospira platensis* exopolysaccharides: implications in the induction of axenic cultures. ***Biosci. Biotechnol. Biochem.*** 79, 331-341 (2015). PMID: 25333502

Shiraishi, H. and Tabuse, Y. The *Apl* I restriction-modification system in an edible cyanobacterium, *Arthrospira* (*Spirulina*) *platensis* NIES-39, recognizes the nucleotide sequence 5'-CTGCAG-3'. ***Biosci. Biotechnol. Biochem.*** 77, 782-788 (2013). PMID: 23563565

Website of the lab: http://kuchem.kyoto-u.ac.jp/seika/

Key words: microbiology, cyanobacteria, spirulina, *Arthrospira platensis*

3) Laboratory of Cell Cycle Regulation

PI: ISHIKAWA, Fuyuki (Prof.) < fishikaw@lif.kyoto-u.ac.jp>

Outline of the research

This laboratory is interested in understanding the mutual interactions between the genome and the surrounding environment. For example, how do organisms preserve their internal resources until their surrounding conditions are suitable for reproduction? How do they prevent mortal pathologies such as cancers until they complete growth and reproduction? Is aging a consequence of damage accumulation caused by fluctuating harsh environments? Does the ever changing microenvironments in the wild in contrast to those persistently cultivated in laboratories, play a significant role, if any, in the life history of an organism in nature? To address these questions, our team branches into three distinct research teams: telomere group, low-dose stress group, and retrotransposon group.

Publications

Takikawa, M., Tarumoto, Y., Ishikawa, F. Fission yeast Stn1 is crucial for semi-conservative replication at telomeres and subtelomeres. Nucleic Acids Res, 45: 1255-1269 (2017). doi: 10.1093/nar/gkw1176

Chujo, M., Tarumoto, Y., Miyatake, K., Nishida, E. and Ishikawa, F. HIRA, a conserved histone chaperone plays an essential role in low-dose stress response via transcriptional stimulation in fission yeast. ***J. Biol. Chem.*** 287: 23440-23450 (2012). doi: 10.1074/jbc.M112.349944

Miyake, Y., Nakamura, M., Nabetani, A., Shimamura, S., Tamura, M., Yonehara, S., Saito, M. and Ishikawa, F. RPA-like mammalian Ctc1-Stn1-Ten1 complex binds to single-stranded DNA and protects telomeres independently of the Pot1 pathway. ***Mol. Cell*** 36: 193-206 (2009). doi: 10.1016/j.molcel.2009.08.009

Website of the lab: http://www.lif.kyoto-u.ac.jp/e/?post_type=labos&p=144

Key words: telomere, stress response, retrotransposon

4) Laboratory of Cell Recognition and Pattern Formation

PI: UEMURA, Tadashi (Prof.) <tauemura@lif.kyoto-u.ac.jp>

Outline of the research

1. Nutri-developmental biology: deciphering regulatory systems that govern nutritional adaptability to ensure animal growth, reproduction, and aging
2. Neuroscience: operating principles of neuronal circuits that evoke selective behavioral outputs in response to nociceptive stimuli
3. Morphogenesis: common principles of epithelial morphogenesis beyond hierarchies of genome, cells and tissues

We are interested in mechanisms that control animal development and behaviors in response to two categories of environmental inputs: nutrition and sensory stimuli. We are trying to unravel underlying mechanisms of adaptations to nutrient balances in Drosophila species. We are also taking prey-predator interspecies approaches to understand contributions of commensal microorganisms. By using Drosophila somatosensory neurons, we are dissecting operating principles of neuronal circuits that evoke selective behavioral outputs in response to thermal or mechanical nociceptive stimuli. As a separate project, we are interested in how genomic information and cells cooperatively build up the entire body of an organism, and trying to understand common principles of epithelial morphogenesis beyond hierarchies of genome, cells and tissues. To conduct these studies, we make full use of molecular, cellular, genomic, imaging, optogenetic, multi-omics, and physiological approaches.

Publications

Arata, M., Sugimura, S. and Uemura, T. Difference in Dachsous levels between migrating cells coordinates the direction of collective cell migration. ***Dev. Cell***, 42: 479-498 (2017).

Tsuyama, T., Tsubouch, A., Usui, U., Imamura, H. and Uemura., T. Mitochondrial dysfunction induces dendritic loss via eIF2α phosphorylation. ***Journal of Cell Biology***, 216: 815-834 (2017).

Onodera K., Baba, S., Murakami, A., Uemura, T., and Usui., T Small conductance Ca^{2+}-activated K^{+} channels induce the firing pause periods during the activation of *Drosophila* nociceptive neurons. ***eLife***, 6:e29754 (2017).

Terada, S., Matsubara, D., Onodera, K., Matsuzaki, M., Uemura, T. and Usui, T. Neuronal processing of noxious thermal stimuli mediated by dendritic Ca^{2+} influx in Drosophila somatosensory neurons. ***eLife*** 5: e12959 (2016).

Shimono, K., Fujishima, K., Nomura, T., Ohashi, M., Usui, T., Kengaku, M., Toyoda, A. and Uemura, T. An evolutionarily conserved protein CHORD regulates scaling of dendritic arbors with body size. ***Sci. Rep.*** 4: 4415 (2014). doi: 10.1038/srep04415

Kondo, T. and Hayashi, S. Mitotic cell rounding accelerates epithelial invagination. ***Nature*** 494: 125-129 (2013). doi:10.1038/nature11792

Website of the lab: http://www.cellpattern.lif.kyoto-u.ac.jp/

Key words: development, nutrition, neuroscience, morphogenesis

5) Laboratory of Plant Molecular Biology

PI: KOHCHI, Takayuki (Prof.) <tkohchi@lif.kyoto-u.ac.jp>

Outline of the research

1. Photomorphogenesis and environmental regulation of plant development
2. Comparative genomics and molecular genetics with the liverwort, *Marchantia polymorpha*
3. Genomic and post-genomic analyses of *Marchantia polymorpha*

Publications

Yamaoka, S., Nishihama, R., Yoshitake, Y., Ishida, S., Okahashi, K., Bao, H., Nishida, H., Yamaguchi, K., Shigenobu, S., Ishizaki, K., Yamato, K. T., and Kohchi, T. Generative cell specification requires transcription factors evolutionarily conserved in land pants. ***Curr. Biol.***, 28: 479–486 (2018). doi: 10.1016/j.cub.2017.12.053

Bowman, J.L., Kohchi, T., Yamato, K.T., *et al*. Insights into land plant evolution garnered from the *Marchantia polymorpha* genome. ***Cell***, 171: 287-304 (2017). dx.doi.org/10.1016/j.cell.2017.09.030

Inoue, K., Nishihama, R., Kataoka, H., Hosaka, M., Manabe, R., Nomoto, M., Tada, Y., Ishizaki, K. and Kohchi, T. Phytochrome signaling is mediated by PHYTOCHROME INTERACTING FACTOR in the liverwort *Marchantia polymorpha*. ***Plant Cell*** 28: 1406-1421 (2016). doi: 10.1105/tpc.15.01063

Kato, H., Ishizaki, K., Kouno, M., Shirakawa, M., Bowman, J. L., Nishihama, R. and Kohchi, T. Auxin-mediated transcriptional system with a minimal set of components is critical for morphogenesis through the life cycle in *Marchantia polymorpha*, ***PLOS Genet.*** 11: e1005084 (2015). doi: 10.1371/journal.pgen.1005084

Komatsu, A., Terai, M., Ishizaki, K., Suetsugu, N., Tsuboi, H., Nishihama, R., Yamato, K. T., Wada, M. and Kohchi, T. Phototropin encoded by a single-copy gene mediates chloroplast photorelocation movements in the liverwort *Marchantia polymorpha* L., ***Plant Physiol.*** 166: 411-427 (2014). doi: 10.1104/pp.114.245100

Kubota, A., Kita, S., Ishizaki, K., Nishihama, R., Yamato, K. T. and Kohchi, T. Co-option of a photoperiodic growth-phase transition system during land plant evolution, ***Nature Comm.*** 5, 3668 (2014). doi: 10.1038/ncomms4668

Website of the lab: http://www.plantmb.lif.kyoto-u.ac.jp/

Key words: land plant evolution, light signaling, plant development, *Marchantia polymorpha*

6) Laboratory of Molecular and Cellular Biology of Totipotency ーー From April 1, 2019 ~

PI: NAKANO, Takeshi (Prof.) < tnakano@riken.jp>

Outline of the research

1. Plant chemical biology for molecular mechanism of plant growth based on cell regulation and photosynthesis.
2. Signaling network of brassinosteroid that cross talks with the other phytohomones and environmental condition.
3. Application of novel genes to regulate plant growth for useful crop production.

Publications

Nosaki, S., Miyakawa, T., Xu, Y., Nakamura, A., Hirabayashi, K., Asami, T., Nakano, T., Tanokura, M. Structural basis for brassinosteroid response by BIL1/BZR1. ***Nature Plants***, 4, 771-776 (2018). doi: 10.1038/s41477-018-0255-1.

Yamagami, A., Saito, C., Nakazawa, M., Fujioka, S., Uemura, T., Matsui, M., Sakuta, M., Osada, H., Nakano, A., Asami, T., Nakano, T. Evolutionarily conserved BIL4 interacts with the brassinosteroid receptor BRI1 and regulates cell elongation. ***Scientific Reports*** 7(1) Article number 5739 (2017). doi: 10.1038/s41598-017-06016-2.

Taishi Nishimura , Ryo Nagao , Takumi Noguchi , Jon Nield , Fumihiko Sato, Kentaro Ifuku (2016) The N-terminal sequence of the extrinsic PsbP protein modulates the redox potential of Cyt b559 in photosystem II. ***Scientific Reports*** 6, Article number: 21490 doi:10.1038/srep21490

Shimada, S., Komatsu, T., Yamagami, A., Nakazawa, M., Matsui, M., Kawaide, H., Natsume, M., Osada, H., Asami, T., Nakano, T. Formation and dissociation of BSS1 protein complex regulates plant development via brassinosteroid signaling. ***Plant Cell***. 27: 375-90. (2015). doi: 10.1105/tpc.114.131508.

Website of the lab:
http://www.callus.lif.kyoto-u.ac.jp/

Key words:
plant chemical biology, plant growth, phytohormone, brassinosteroid, photosynthesis.

7) Laboratory of Biosignals and Response

PI: NAGAO, Masaya (Prof.) <mnagao@kais.kyoto-u.ac.jp>

Outline of the research

1. Screening for discovery of bioactive natural products.
2. Elucidation of the cellular functions of zinc transporters, ZIPs, and ZnTs

Publications

Fujimoto, S., Tsuji, T., Fujiwara, T., Takeda, T.A., Merriman, C., Fukunaka, A., Nishito, Y., Fu, D., Hoch, E., Sekler, I., Fukue, K., Miyamae, Y., Masuda, S., Nagao, M., Kambe, T. The PP-motif in luminal loop 2 of ZnT transporters plays a pivotal role in TNAP activation. ***Biochem J***. 473 (17) 2611-2621 (2016). doi: 10.1042/BCJ20160324

Miyamae, Y., Nishito, Y., Nakai, N., Nagumo, Y., Usui, T., Masuda, S., Kambe, T., Nagao, M. Tetrandrine induces lipid accumulation through blockade of autophagy in a hepatic stellate cell line. ***Biochem Biophys Res Commun***. 477, 40-46 (2016). doi: 10.1016/j.bbrc.2016.06.018

Ohtera, A., Miyamae, Y., Yoshida, K., Maejima, K., Akita, T., Kakizuka, A., Irie, K., Masuda, S., Kambe, T., Nagao, M. Identification of a New Type of Covalent PPARγ Agonist using a Ligand-Linking Strategy. ***ACS Chem Biol.*** 10, 2794-2804 (2015). doi: 10.1021/acschembio.5b00628

Hashimoto, A., Ohkura, K., Takahashi, M., Kizu, K., Narita, H., Enomoto, S., Miyamae, Y., Masuda, S., Nagao, M, Irie, K., Ohigashi, H., Andrews, G.K., Kambe, T. Soybean extracts increase cell surface ZIP4 abundance and cellular zinc levels: a potential novel strategy to enhance zinc absorption by ZIP4 targeting. ***Biochem J.*** 472, 183193 (2015). doi: 10.1042/BJ20150862

Ohtera, A., Miyamae, Y., Nakai, N., Kawachi, A., Kawada, K., Han, J., Isoda, H., Neffati, M., Akita, T., Maejima, K., Masuda, S., Kambe, T., Mori, N., Irie, K., Nagao, M. Identification of 6-octadecynoic acid from a methanol extract of Marrubium vulgare L. as a peroxisome proliferator-activated receptor γ agonist. ***Biochem Biophys Res Commun***. 440, 204-209 (2013). doi: 10.1016/j.bbrc.2013.09.003

Website of the lab: http://www.seitaijoho.lif.kyoto-u.ac.jp/

Key words: bioactive compounds, screening, zinc, transporter

8) Laboratory of Applied Molecular Microbiology

PI: FUKUZAWA, Hideya (Prof.) < fukuzawa@lif.kyoto-u.ac.jp>

Outline of the research

We are focusing on the molecular bases of biological functions of photosynthetic microorganisms contributing to production of food, carbon-neutral renewable bio-energy and industrial materials, and also to environmental remediation by photosynthesis. Especially we employ a green alga, *Chlamydomonas reinhardtii*, as a model eukaryotic microorganism using its genome information, mutants, and molecular or biochemical techniques. In addition, we are applying the scientific findings from this model alga to an industrially important diatom, Chaetoceros gracilis, which is used as a feedstock for shellfish and oysters. The current projects are (1) Molecular characterization and modification of the carbon-concentrating mechanism supporting photosynthetic carbon fixation, bioenergy production, and cell proliferation, (2) Elucidation of regulatory network systems controlling photosynthesis by sensing environmental factors including changes of levels in CO_2 concentration and light, (3) Elucidation and engineering of metabolic pathways for production of neutral lipids, hydrocarbons, and carbohydrates under specific culture conditions, (4) Molecular control and signaling of sexual reproduction by nutrient starvation.

Publications

Nitta N. et al. "Intelligent image-activated cell sorting." ***Cell*** 175: 266-276 (2018) PMID: 30166209

Kajikawa K. et al. "Isolation and characterization of *Chlamydomonas* autophagy-related mutants in nutrient-deficient conditions." ***Plant Cell Physiol.*** (2018) in press. PMID: 30295899

Wang L. et al., "Chloroplast-mediated regulation of CO_2-concentrating mechanism by Ca^{2+}-binding protein CAS in the green alga *Chlamydomonas reinhardtii*." ***Proc. Natl. Acad. Sci. USA*** 113: 12586-12591 (2016). PMID: 27791081

Yamano T. et al., "Characterization of cooperative bicarbonate uptake into chloroplast stroma in the green alga *Chlamydomonas reinhardtii*." ***Proc. Natl. Acad. Sci. USA*** 112: 7315-7320 (2015). PMID: 26015566

Kajikawa M. et al. "Algal dual-specificity tyrosine phosphorylation-regulated kinase, triacylglycerol accumulation regulator 1, regulates accumulation of triacylglycerol in nitrogen or sulfur deficiency." ***Plant Physiol.*** 168: 752-764 (2015). PMID: 25922058

Website of the lab: http://www.molecule.lif.kyoto-u.ac.jp/

Key words: algal biofuel, CO_2-sensing mechanism, photosynthetic acclimation, calcium signaling

9) Laboratory of Molecular Biology of Bioresponse
PI: KATAYAMA, Takane (Prof.) <takane@lif.kyoto-u.ac.jp>

Outline of the research
Our aim is to decipher the molecular mechanism underlying the symbiotic relationship between gut microbes and host, and to develop food-and health-oriented application research. We are also focused on the elucidation of mechanisms of mRNA processing, export, and quality control in the nucleus in human and its industrial applications.

Publications
Gotoh A, Katoh T, Sakanaka M, Ling Y, Yamada C, Asakuma S, Urashima T, Tomabechi Y, Katayama-Ikegami A, Kurihara S, Yamamoto K, Harata G, He F, Hirose J, Kitaoka M, Okuda S. and Katayama T. Sharing of human milk oligosaccharides degradants within bifidobacterial communities in faecal cultures supplemented with *Bifidobacterium bifidum*. ***Sci. Rep.*** 8:13958. (2018).

Okamura M, Yamanaka Y, Shigemoto M, Kitadani Y, Kobayashi Y, Kambe T, Nagao M, Kobayashi I, Okumura K, Masuda S. Depletion of mRNA export regulator DBP5/DDX19, GLE1 or IPPK that is a key enzyme for the production of IP6, resulting in differentially altered cytoplasmic mRNA expression and specific cell defect. ***PLoS One***, **13**, e0197165, (2018)

Yamada C, Gotoh A, Sakanaka M, Hattie M, Stubbs KA, Katayama-Ikegami A, Hirose J, Kurihara S, Arakawa T, Kitaoka M, Okuda S, Katayama T, and Fushinobu S. Molecular insight into evolution of symbiosis between breastfed infants and a member of the human gut microbiome *Bifidobacterium longum*. ***Cell Chem. Biol.*** 24:515-524. (2017).

Katoh, T., Katayama, T., Tomabechi, Y., Nishikawa, Y., Kumada, J., Matsuzaki, Y., and Yamamoto, K. Generation of a mutant *Mucor hiemalis* endoglycosidase that acts on core-fucosylated *N*-glycans. ***J. Biol. Chem.*** 291:2330523317. (2016).

Website of the lab: http://www.bunshioutou.lif.kyoto-u.ac.jp/index.html

Key words: gut microbes, symbiosis, mRNA, export

10) Laboratory of Plant Developmental Biology
PI: ARAKI, Takashi (Prof.) <taraqui@lif.kyoto-u.ac.jp>

Outline of the research

We are interested in molecular mechanisms underlying plant's responses to environment. Plants have evolved plastic developmental programs with both genetic and epigenetic basis to adapt their sessile mode of life to changing environment. Using an angiosperm, *Arabidopsis thaliana* and a liverwort, *Marchantia polymorpha* as model systems, we have been investigating (1) regulation of growth phase transition (especially, flowering) in response to environmental signals, (2) long-distance systemic signaling in the control of development, (3) sexual reproduction processes (especially, male gametogenesis and fertilization), and (4) origin and evolution of regulatory systems for plastic development.

Publications

Higo, A., Kawashima, T., Borg, M., Zhao, M., López-Vidriero, I., Sakayama, H., Montgomery, S. A., Sekimoto, H., Hackenberg, D., Shimamura, M., Nishiyama, T., Sakakibara, K., Tomita, Y., Togawa, T., Kunimoto, K., Osakabe, A., Suzuki, Y., Yamato, K. T., Ishizaki, K., Nishihama, R., Kohchi, T., Franco-Zorrilla, J. M., Twell, D., Berger, F., and Araki, T. Transcription factor DUO1 generated by neo-functionalization is associated with evolution of sperm differentiation in plants. ***Nature Commun.*** 9(5283): 1-13 (2018). doi: 10.1038/s41467-018-07228-3

Endo, M., Yoshida, M., Sasaki, Y., Negishi, K., Horikawa, K., Daimon, Y., Kurotani, K.-i., Notaguchi, M., Abe, M., and Araki, T. Reevaluation of florigen transport kinetics with separation of function by mutations that uncouple flowering initiation and long-distance transport. ***Plant Cell Physiol.*** 59: 1621-1629 (2018). doi: 10.1093/pcp/pcy063

Bowman, J.L., Kohchi, T., Yamato, K.T., Jenkins, J., Shu, S., Ishizaki, K., Yamaoka, S., Nishihama, R., Nakamura, Y., Berger, F., Adam, C., Aki, S.S., Althoff, F., Araki, T., [33名省略] Inoue, K., [64名省略] and Schmutz, J. Insights into land plant evolution garnered from the *Marchantia polymorpha* genome. ***Cell*** 171: 287-304 (2017). doi: 10.1016/j.cell.2017.09.030

Higo, A., Niwa, M., Yamato, K. T., Yamada, L., Sawada, H., Sakamoto, T., Kurata, T., Shirakawa, M., Endo, M., Shigenobu, S., Ishizaki, K., Nishihama, R., Kohchi, T. and Araki, T. Transcriptional framework of male gametogenesis in the liverwort *Marchantia polymorpha* L. ***Plant Cell Physiol.*** 57: 325-338 (2016). doi: 10.1093/pcp/pcw005

Kawamoto, N., Sasabe, M., Endo, M., Machida, Y. and Araki, T. Calcium-dependent protein kinases responsible for the phosphorylation of a bZIP transcription factor FD crucial for the florigen complex formation. ***Sci. Rep.*** 5: 8341, 1-9 (2015). doi: 10.1038/srep08341

Niwa, M., Daimon, Y., Kurotani, K., Higo, A., Pruneda-Paz, J.L., Breton, G., Mitsuda, N., Kay, S.A., Ohme-Takagi, M., Endo, M., and Araki, T. BRANCHED1 interacts with FLOWERING LOCUS T to repress the floral transition of the axillary meristems in Arabidopsis. *Plant Cell* 25: 1228-1242 (2013). doi: 10.1105/tpc.112.109090

Website of the lab: http://www.plantdevbio.lif.kyoto-u.ac.jp/index.html

Key words: flowering, florigen, circadian clock, sexual reproduction, gametogenesis

11) Laboratory of Plasma Membrane and Nuclear Signaling

PI: YOSHIMURA, Shigehiro (Associate Prof.) <yoshimura@lif.kyoto-u.ac.jp>

Outline of the research

Our laboratory studies dynamics of plasma membrane and cytoskeletal architectures by using a variety of techniques in live-cell imaging, molecular and cellular biology, and bioinformatics. Our research interest covers a wide range of biological problems from molecular to cellular levels. We try to elucidate the molecular mechanism underlying structural dynamics of cellular architectures, as well as how a defect in such dynamics causes a disease. Specific

research topics include: (1) how structural dynamics of actin network is regulated by related proteins and how a functional defect of these proteins causes a disease, (2) how virus infection and endocytic process proceed by membrane-bound proteins, cytoskeletal network and lipid membrane, and (3) how dynamic assemblydisassembly of intracellular architectures (nuclear envelope, chromosome, etc) is regulated by mitotic phosphorylation.

Publications

Yoshida, A., Sakai, N., Uekusa, Y., Imaoka, Y., Itagaki, Y., Suzuki, Y., and Yoshimura, S.H. "Morphological changes of plasma membrane and protein assembly during clathrin-mediated endocytosis" ***PLOS Biol.*** 16(5): e2004786 (2018). doi: 10.1371/journal.pbio.2004786.

Kumeta, M., Konishi, H.A., Zhang, W., Sakagami, S. and Yoshimura, S.H. "Prolines in the α-helix confer the structural flexibility and functional integrity of importin β." ***J. Cell Sci.***, 131(1): e0188764 (2018). doi: 10.1242/jcs.206326.

Konishi H.A., Asai S., Watanabe T. and Yoshimura S.H. "*In vivo* analysis of protein crowding within the nuclear pore complex in interphase and mitosis" ***Sci. Rep.,*** 7(1): 5709 (2017). doi: 10.1038/s41598-017-05959-w

Lolodi, O., Yamazaki, H., Otsuka, S., Kumeta, M. and Yoshimura S.H. "Dissecting *in vivo* steady-state dynamics of karyopherin-dependent nuclear transport." ***Mol. Biol. Cell.*** 27: 167-176 (2016). doi: 10.1091/mbc.E15-08-0601

Yoshimura, S.H., Kumeta, M. and Takeyasu, K. "Structural mechanism of nuclear transport mediated by importin β and flexible amphiphilic proteins." ***Structure*** 22: 1699-1710 (2014). doi: 10.1016/j.str.2014.10.009

Website of the lab: http://www.chrom.lif.kyoto-u.ac.jp

Key words: atomic force microscopy, molecular crowding, cytoskeletal dynamics, membrane dynamics, mechano-biology, virus infection, bioinformatics

12) Laboratory of Developmental Neurobiology

PI: KENGAKU, Mineko (Prof.) < kengaku@icems.kyoto-u.ac.jp>

Outline of the research

We study the dynamics and mechanisms of the formation of neural networks in the brain. We also aim to develop live-imaging techniques for observation of molecular signals controlling cell motility in the developing brain.

Publications

Kawabata-Galbraith, K., Fujishima, K., Mizuno, H., Lee, S.J., Uemura, T., Sakimura, K., Mishina, M., Watanabe, N. and Kengaku, M. MTSS1 regulation of actin-nucleating formin DAAM1 in dendritic filopodia determines final dendritic configuration of Purkinje cells. ***Cell Rep.*** 24(1):95-106. (2018).doi: 10.1016/j.celrep.2018.06.013.

Wu, Y.K., Umeshima, H., Kurisu, J. and Kengaku, M. Nesprins and opposing microtubule motors generate a point force driving directional nuclear motion in migrating neurons. ***Development.*** 2018 Mar 8; 145(5) pii: dev158782. (2018). doi: 10.1242/dev.158782.

Fukumitsu, K., Fujishima, K., Yoshimura, A., Wu, Y.K., Heuser, J. and Kengaku, M. Synergistic action of dendritic mitochondria and creatine kinase maintains ATP homeostasis and actin dynamics in growing neuronal dendrites. ***J. Neurosci.*** 35(14):5707- 5723 (2015). doi: 10.1523/JNEUROSCI.4115-14.2015.

Fujishima, K., Horie, R., Mochizuki, A. and Kengaku, M. Principles of branch dynamics governing shape characteristics of cerebellar Purkinje cell dendrites. ***Development*** 139: 3442-3455 (2012). doi: 10.1242/dev. 081315.

Website of the lab: http://www.kengaku.icems.kyoto-u.ac.jp/index.html

Key words: neuronal differentiation, dendrite, cell migration, cortex formation, neural circuit formation

13) Laboratory of Biochemical Cell Dynamics

PI: SUZUKI, Jun (Prof.) <jsuzuki@icems.kyoto-u.ac.jp>

Outline of the research

We are researching on biological phenomenon of our interests by unbiased screening-based identification of key genes regulating it. Currently, we are interested in the phenomenon called phospholipid scrambling, which are involved in variety of biological systems and human diseases. We can classify our research to 3 stages: to explore new fields by identifying the key genes; to develop primary finding; to think how our finding is applicable to medicine or biotechnology. Through all stages, we will conduct the interesting research and enjoy science.

Publication:

Suzuki, J., Imanishi, E. and Nagata, S. The Xkr8 phospholipid scrambling complex in apoptotic phosphatidylserine exposure. ***Proc. Natl. Acad. Sci. USA*** 113: 9509-9514 (2016). doi: 10.1073/pnas.1610403113.

Suzuki, J., Imanishi, E. and Nagata, S. Exposure of phosphatidylserine by Xk-related protein family members. ***J. Biol. Chem.*** 289: 30257-30267 (2014). doi: 10.1074/jbc.M114.583419.

Suzuki, J., Denning, D.P., Imanishi, E., Horvitz, H.R. and Nagata, S. Xk-related protein 8 and CED-8 promote phosphatidylserine exposure in apoptotic cells. ***Science*** 341: 403-406 (2013). doi: 10.1126/science.1236758.

Suzuki, J., Fujii, T., Imao, T., Ishihara, K., Kuba, H. and Nagata, S. Calcium-dependent phospholipid scramblase activity of TMEM16 protein family members. ***J. Biol. Chem.*** 288: 13305-13316 (2013). doi: 10.1074/jbc.M113.457937.

Suzuki, J., Sims, P.J., Umeda, M. and Nagata, S. Calcium-dependent phospholipid scrambling by TMEM16F. ***Nature,*** 468:834-838 (2010). doi: 10.1038/nature09583.

Website of the lab: http://www.suzuki.icems.kyoto-u.ac.jp

Key words: screening, gene identification, phospholipid scrambling, phagocytosis, medicine

14) Laboratory of Developmental Dynamics

PI: KAGEYAMA, Ryoichiro (Prof.) <rkageyam@infront.kyoto-u.ac.jp>

Outline of the research

We analyze the molecular mechanism of embryonic development by using imaging, optogenetics and transgenic mouse technologies. We evaluate mathematical modeling to understand the principles of developmental dynamics.

Publications

Shimojo, H., Isomura, A., Ohtsuka, T., Kori, H., Miyachi, H. and Kageyama, R. Oscillatory control of Delta-like1 in cell interactions regulates dynamic gene expression and tissue morphogenesis. ***Genes Dev.*** 30: 102-116 (2016). doi: 10.1101/gad.270785.11

Imayoshi, I., and Kageyama, R. bHLH factors in self-renewal, multipotency, and fate choice of neural progenitor cells. ***Neuron*** 82: 9-23 (2014). doi: 10.1016/j.neuron.2014.03.018

Imayoshi, I., Isomura, A., Harima, Y., Kawaguchi, K., Kori, H., Miyachi, H., Fujiwara, T.K., Ishidate, F., and Kageyama, R. Oscillatory control of factors determining multipotency and fate in mouse neural progenitors. ***Science*** 342, 1203-1208. (2013). doi: 10.1126/science.1242366

Website of the lab: http://www.virus.kyoto-u.ac.jp/Lab/Kageyama/index_English.html

Key words: live imaging, Notch signaling, optogenetics, oscillatory expression, segmentation clock

15) Laboratory of Ultrastructural Virology

PI: NODA, Takeshi (Prof.) <t-noda@infront.kyoto-u.ac.jp>

Outline of the research

Virus infections are accompanied by numerous ultrastructural changes in viral and cellular components. Our laboratory has been investigating the intracellular replication mechanism of influenza, Ebola and Lassa viruses by using virological, molecular biological, and biochemical techniques combining with different microscopic methods such as electron microscopy and high-speed atomic force microscopy. Visualization and characterization of the virus life cycle at the nano-mesoscopic level give us unique knowledge and novel paradigms, which will advance our understanding of molecular basis of the replication mechanism.

Publications

Sugita Y, Matsunami H, Kawaoka Y, Noda T, Wolf M. Cryo-EM structure of the Ebola virus nucleoprotein-RNA complex at 3.6 Å resolution. ***Nature*** 563:137-140. (2018)

Noda, T., Murakami, S., Nakatsu, S., Imai, H., Muramoto, Y., Shindo, K., Sagara, H. and Kawaoka, Y. Importance of the 1+7 configuration of the ribonucleoprotein complexes for influenza A virus genome packaging. ***Nature Communications*** 9:54 (2018).

Wan, W., Kolesnikova, L., Clarke, M., Koehler, A., Noda, T., Becker, S., and Briggs, J.A.G. Structure and assembly of the Ebola virus nucleocapsid. ***Nature*** 551: 394-397 (2017).

Martyushev, A., Nakaoka, S., Sato, K., Noda, T. and Iwami, S. Modelling Ebola virus dynamics: Implications for therapy. ***Antiviral Research*** 135: 62-73 (2016).

Nakatsu, S., Sagara, H., Sakai, Y. T., Sugaya, N., Noda, T. and Kawaoka, Y. Complete and incomplete genome packaging of influenza A and B viruses. ***mBio*** 7: e01248-16 (2016).

Website of the lab: https://www.facebook.com/NodaLab/

Key words: Influenza virus, Ebola virus, Lassa virus

Division of Systemic Life Science

1) Laboratory of Single-Molecule Cell Biology

PI: WATANABE, Naoki (Prof.) <watanabe.naoki.4v@kyoto-u.ac.jp>

Outline of the research

By using high-resolution live-cell fluorescence Single-Molecule Speckle (SiMS) microscopy and our new multitarget high-density labeling super resolution microscopy IRIS, we are trying to bridge the gap between molecular behavior and cell/body functions including mechanotransduction, cancer invasion, tissue remodeling and drug response by direct viewing of molecules in action.

Publications

Yamashiro, S., Tanaka, S., McMillen, L.M., Taniguchi, D., Vavylonis, D. and Watanabe, N. Myosin-dependent actin stabilization as revealed by single-molecule imaging of actin turnover. ***Mol. Biol. Cell*** 29: 1941-1947 (2018). doi: 10.1091/mbc.E18-01-0061

Mizuno, H., Tanaka, K., Yamashiro, S., Narita, A. and Watanabe, N. Helical rotation of diaphanous-related formin mDia1 generates actin filaments resistant to cofilin. ***Proc. Natl. Acad. Sci. USA*** 115: E5000-E5007 (2018). doi: 10.1073/pnas.1803415115

Kiuchi, T., Higuchi, M., Takamura, A., Maruoka, M. and Watanabe, N. Multitarget super-resolution microscopy with high-density labeling by exchangeable probes. ***Nat. Methods*** 12: 743-746 (2015). doi: 10.1038/nmeth.3466

Higashida, C., Kiuchi, T., Akiba, Y., Mizuno, H., Maruoka, M., Narumiya, S., Mizuno, K. and Watanabe, N. F- and G-actin homeostasis regulates mechanosensitive actin nucleation by formins. ***Nat. Cell Biol.*** 15: 395-405 (2013). doi: 10.1038/ncb2693

Mizuno, H., Higashida, C., Yuan, Y., Ishizaki, T., Narumiya, S. and Watanabe, N. Rotational movement of the formin mDia1 along the double helical strand of an actin filament. ***Science*** 331: 80-83 (2011). doi: 10.1126/science.1197692

Website of the lab: http://www.pharm2.med.kyoto-u.ac.jp/2_index.html

Key words: single-molecule imaging, super-resolution microscopy, cancer therapy

2) Laboratory of Molecular and Cellular Biology

PI: SAKAMAKI, Kazuhiro (Associate Prof.) <sakamaki.kazuhiro.7u@kyoto-u.ac.jp>

Outline of the research

We are interested in the signal transduction mechanisms underlying apoptotic cell death and the biological significance and physiological roles of cell death in organisms. To understand these issues, our main research focuses on the apoptosis executors, caspases, and is to visualize the functional processes of these molecules in cells using live cell imaging and computer simulation. We are also trying to generate appropriate model animals such as mouse, *Xenopus*, and medaka to control the phenomenon of apoptosis in organisms.

Publications

Sakamaki, K., Ishii, T.M., Sakata, T., Takemoto, K., Takagi, C., Takeuchi, A., Morishita, R., Takahashi, H., Nozawa, A., Shinoda, H., Chiba, K., Sugimoto, H., Saito, A., Tamate, S., Satou, Y., Jung, S.-K., Matsuoka, S., Koyamada, K., Sawasaki, T., Nagai, T. and Ueno, N. Dysregulation of a potassium channel, THIK-1, targeted by caspase-8 accelerates cell shrinkage. ***Biochim. Biophys. Acta*** 1863: 2766-2783 (2016). doi: 10.1016/j.bbamcr.2016.08.010.

Sakamaki, K., Imai, K., Tomii, K. and Miller, D.J. Evolutionary analyses of caspase-8 and its paralogs: Deep origins of the apoptotic signaling pathways. ***BioEssays*** 37: 767-776 (2015). doi: 10.1002/bies.201500010.

Kominami, K., Nakabayashi, J., Nagai, T., Tsujimura, Y., Chiba, K., Kimura, H., Miyawaki, A., Sawasaki, T., Yokota, H., Manabe, N. and Sakamaki, K. The molecular mechanism of apoptosis upon caspase-8 activation: quantitative experimental validation of a mathematical model. ***Biochim. Biophys. Acta*** 1823: 1825–1840 (2012). doi: 10.1016/j.bbamcr.2012.07.003.

Kominami, K., Nagai, T., Sawasaki, T., Tsujimura, Y., Yashima, K., Sunaga, Y., Tsuchimochi, M., Nishimura, J., Chiba, K., Nakabayashi, J., Koyamada, K., Endo, Y., Yokota, H., Miyawaki, A., Manabe, N. and Sakamaki, K. *In vivo* imaging of hierarchical spatiotemporal activation of caspase-8 during apoptosis. ***PLoS One*** 7: e50218 (2012). doi: 10.1371/journal.pone.0050218.

Website of the lab: http://www.mcb.lif.kyoto-u.ac.jp/

Key words: apoptosis, caspase, computer simulation, live imaging, optogenetics

3) Laboratory of Immunobiology

PI: TAKAHARA, Kazuhiko (Associate Prof.) <ktakahar@zoo.zool.kyoto-u.ac.jp >

Outline of the research

We focus on dendritic cells, macrophages, and their antigen receptor lectins that recognize polysaccharides on pathogens. We are also interested in immunosuppressive mechanisms of pathogens. Based on these studies, we would like to develop new methods to control immune system.

Publications

Ishiguro, T.*, Fukawa, T.*, Akaki, K., Nagaoka, K., Takeda, T., Iwakura, Y., Inaba, K., and Takahara, K. Absence of DCIR1 reduces the mortality rate of endotoxemic hepatitis in mice. ***Eur. J. Immunol.*** 47, 704-712. (*equal contribution) (2017). doi: 10.1002/eji.201646814

Taneo, J., Adachi, T, Yoshida, A., Takeyasu, K., Takahara, K.* and Inaba, K. Amyloid β oligomers induce interleukin-1β production in primary microglia in a cathepsin B- and reactive oxygen species-dependent manner. ***Biochem. Biophys. Res. Commun.*** 458, 561-567. (*corresponding author) (2015). doi: 10.1016/j.bbrc.2015.02.006

Tokieda, S., Komori, M., Ishiguro, Iwakura, Y., Takahara, K.* and Inaba, K. Dendritic cell immunoreceptor 1 alters neutrophil responses in the development of experimental colitis. ***BMC Immunol.*** 16, 64. (*corresponding author) (2015). doi: 10.1186/s12865-015-0129-5

Adachi, T., Takahara, K., Taneo, J., Uchiyama, Y. and Inaba, K. Particle size of latex beads dictates IL-1β production mechanism. ***Plos One*** 8, e68499. (2013). doi: 10.1371/journal.pone.0068499

Takahara, K., Arita, T., Tokieda, S., Shibata, N., Okawa, Y., Tateno, H., Hirabayashi, J. and Inaba, K. Difference in fine specificity to polysaccharides of *C. albicans* mannoprotein between mouse SIGNR1 and human DC-SIGN. ***Infect. Immun.*** 89, 1699-1706. (2012). doi: 10.1128/IAI.06308-11

Website of the lab: http://zoo.zool.kyoto-u.ac.jp/imm/

Key words: lectin, immune modulation, polysaccharide, disease models, dendritic cells

4) Laboratory of Molecular Cell Biology and Development (Collaboration lab in RIKEN, Kobe)
PI (1): MATSUZAKI, Fumio (Prof.) <fumio.matsuzaki@riken.jp >

Outline of the research

1. We investigate physical and molecular mechanisms, by which cell polarity and asymmetric division generate cellular diversity.
2. We investigate genetic and epigenetic programs, by which the brain develops and maturates especially focusing on the roles and behavior of neural stem cells. We use mouse as a simple mammalian brain model, ferret as a complex mammalian brain model, and *Drosophila* as a genetic model system.

Publications

Suzuki, K.,[#], Tsunekawa, Y.,[#] , Hernandez-Benitez, R.,[#], Wu, J.,[#], Zhu, J.,# et al. Matsuzaki, F., (28th/34 authors), Belmonte, JC. In vivo genome editing via CRISPR-Cas9 mediated homology-independent targeted integration. ***Nature*** 540,144–149 (2016). doi:10.1038/nature20565 [#]equal contribution

Tsunekawa, Y.,[#], Terhune, RK.,#, Fujita, I., Shitamukai, A., Suetsugu, T., and Matsuzaki F. Developing a de novo targeted knock-in method based on in utero electroporation into the mammalian brain. ***Development*** 143, 3216-22 (2016). doi: 10.1242/dev.136325 [#]equal contribution

Okamoto M, Miyata T, Konno D, Ueda HR, Kasukawa T, Hashimoto M, Matsuzaki F*, and Kawaguchi A*. Cell cycle–independent transitions in temporal identity of mammalian neural progenitor cells. ***Nat Commun***. 7:11349. doi: 10.1038/ncomms11349. *corresponding authors. (2016).

Matsuzaki, F., and Shitamukai, A. Cell division modes and cleavage planes of neural progenitors during mammalian cortical development. ***Cold Spring Harb. Perspect. Biol.*** 7, (2015) a015719. doi: 10.1101/cshperspect.a015719.

Yoshiura, S., Ohta, N., and Matsuzaki, F. Tre1 GPCR signaling orients stem cell divisions in the Drosophila central nervous system. ***Dev. Cell*** 22, 1-13 (2012). doi.org/10.1016/j.devcel.2011.10.027

Website of the lab: http://www.cdb.riken.jp/en/research/laboratory/matsuzaki.html

Key words: neural stem cells, brain development, mouse, ferret, *Drosophila*

PI (2): KITAJIMA, Tomoya (Associate Prof.) <tomoya.kitajima@riken.jp>

Outline of the research

We are interested in how chromosomes behave in time and space to archive correct chromosome segregation during meiosis and mitosis in mammalian oocytes and zygotes. Taking advantage of our live imaging technology, we conduct comprehensive quantitative analysis of the chromosome dynamics.

Publications

Ding, Y., Kaido, M., Llano, E., Pendas, A.M., and Kitajima, T.S. The post-anaphase SUMO pathway ensures the maintenance of centromeric cohesion through meiosis I-II transition in mammalian oocytes. ***Current Biology*** 28(10), 1661–1669 (2018). doi: 10.1016/j.cub.2018.04.019.

Kyogoku, H., & Kitajima, T. S. Large cytoplasm is linked to the error-prone nature of oocytes. ***Developmental Cell***, 41(3), 287–298 (2017). doi:10.1016/j.devcel.2017.04.009.

Sakakibara, Y., Hashimoto, S., Nakaoka, H., Kouznetsova, A., Höög, C., and Kitajima, T.S. Bivalent separation into univalents precedes age-related meiosis I errors in oocytes.***Nature Communications***, 6, 7550 (2015). doi: 10.1038/ncomms8550

Yoshida, S., Kaido, M., and Kitajima, T.S. Inherent instability of correct kinetochore-microtubule attachments during meiosis I in oocytes. ***Developmental Cell***, 33, 589–602 (2015). doi: 10.1016/j.devcel.2015.04.020

Website of the lab: http://www.cdb.riken.jp/lcs

Key words: chromosome, meiosis, oocyte, zygote

PI (3): TAKASATO, Minoru (Associate Prof.) <minoru.takasato@riken.jp>

Outline of the research
Utilizing our unique technology that generates kidney organoids from human pluripotent stem cells, we are focusing particularly on uncovering the developmental mechanisms of human mesoderm and the kidney. By precisely recapitulating the developmental processes of human kidney in the directed differentiation of human pluripotent stem cells, we are also aiming for the ultimate goal of generating a three-dimensional kidney that is functional and can be transplanted into patients.

Publications
M. Takasato, P. X. Er, H. S. Chiu, M. H. Little, Generation of kidney organoids from human pluripotent stem cells. ***Nat. Protoc***. 11, 1681–1692 (2016). doi: 10.1038/nprot.2016.098

M. Takasato *et al.*, Kidney organoids from human iPS cells contain multiple lineages and model human nephrogenesis. ***Nature***. 526, 564–8 (2015). doi: 10.1038/nature15695

M. Takasato, M. H. Little, The origin of the mammalian kidney: implications for recreating the kidney in vitro. ***Development***. 142, 1937–1947 (2015). doi: 10.1242/dev.104802

M. Takasato *et al.*, Directing human embryonic stem cell differentiation towards a renal lineage generates a selforganizing kidney. ***Nat. Cell Biol***. 16, 118–26 (2014). doi: 10.1038/ncb2894
Website of the lab: http://www.cdb.riken.jp/en/research/laboratory/takasato.html

Key words: kidney organoid, directed differentiation, pluripotent stem cell, human development

5) Laboratory of Molecular Neurobiology
PI: KATOH, Hironori (Associate Prof.) <hirokato@pharm.kyoto-u.ac.jp>

Outline of the research
We study the relationship between the regulation of metabolism and signal transduction in cancer cells, and aim to elucidate the mechanisms underlying cancer development and progression.

Publications
Hamaoka, Y., Negishi, M., Katoh, H. Tyrosine kinase activity of EphA2 promotes its S897 phosphorylation and glioblastoma cell proliferation. ***Biochem. Biophys. Res. Commun.*** 499, 920-926 (2018) . doi:

10.1016/j.bbrc.2018.04.020.

Goji, T., Takahara, K., Negishi, M., Katoh, H. Cystine uptake through the cystine/glutamate antiporter xCT triggers glioblastoma cell death under glucose deprivation. *J. **Biol. Chem.*** 292, 19721-19732 (2017). doi: 10.1074/jbc.M117.814392.

Hamaoka, Y., Negishi, M., Katoh, H. EphA2 is a key effector of the MEK/ERK/RSK pathway regulating glioblastoma cell proliferation. ***Cell. Signal.*** 28, 937-945 (2016). doi: 10.1016/j.cellsig.2016.04.009.

Okuyama, Y., Umeda, K., Negishi, M., Katoh, H. Tyrosine phosphorylation of SGEF regulates RhoG activity and cell migration. ***PLoS One*** 11, e0159617 (2016). doi: 10.1371/journal.pone.0159617.

Website of the lab: http://www.negishi.lif.kyoto-u.ac.jp/j/toppu.html

Key words: cancer, signal transduction, transporter, receptor

6) Laboratory of Genetics

PI: IGAKI, Tatsushi (Prof.) <igaki@lif.kyoto-u.ac.jp>

Outline of the research

Our research focuses on the molecular basis of cell-cell communication that governs tissue growth, homeostasis, and cancer. We take advantage of the powerful genetics of Drosophila.
Research subjects:

1. Mechanism of cell competition
2. Genetic basis of tissue growth regulation
3. Molecular basis of tumor progression and metastasis

Publications

Katsukawa, M., Ohsawa, S., Zhang, L., Yan, Y., and Igaki, T. Serpin facilitates tumor-suppressive cell competition by blocking Toll-mediated Yki activation in *Drosophila*. ***Curr. Biol.*** 28: 1756-1767 (2018)

Yamamoto, M., Ohsawa, S., Kunimasa, K., and Igaki, T. The ligand Sas and its receptor PTP10D drive tumorsuppressive cell competition. ***Nature*** 542: 246-250 (2017).

Vaughen, J. and Igaki, T. Slit-Robo repulsive signaling excludes tumorigenic cells from epithelia. ***Dev Cell*** 39: 683-695 (2016)
Nakamura, M., Ohsawa, S. and Igaki, T. Mitochondrial defects trigger proliferation of neighbouring cells via a senescence-associated secretory phenotype in *Drosophila*. ***Nature Commun.*** 5: 5264 (2014). doi: 10.1038/ncomms6264

Ohsawa, S., Sato, Y., Enomoto, M., Nakamura, M., Betsumiya, A. and Igaki, T. Mitochondrial defect drives nonautonomous tumor progression through Hippo signaling in *Drosophila*. ***Nature*** 490: 547-551 (2012). doi:10.1038/nature11452

Ohsawa, S., Sugimura, K., Takino, K., Xu, T., Miyawaki, A., and Igaki, T. Elimination of oncogenic neighbors by JNK-mediated engulfment in *Drosophila*. ***Dev. Cell*** 20: 315-328 (2011). doi: 10.1016/j.devcel.2011.02.007

Website of the lab: http://www.lif.kyoto-u.ac.jp/genetics/english/

Key words: cell-cell communication, cancer, development, cell competition, *Drosophila*

7) Laboratory of Functional Biology
PI: KAKIZUKA, Akira (Prof.) <kakizuka@lif.kyoto-u.ac.jp>

Outline of the research
Using animal models of human diseases, such as neurodegenerations, cancers, and obesity-related diseases, and using metabolic imaging techniques, we aim to elucidate molecular bases of such diseases and develop new strategies to cure or prevent them.

Publications
Nakano M, Imamura H, Sasaoka N, Yamamoto M, Uemura N, Shudo T, Fuchigami T, Takahashi R, and Kakizuka A. ATP Maintenance via Two Types of ATP Regulators Mitigates Pathological Phenotypes in Mouse Models of Parkinson's Disease. ***EBioMedicine.*** 22:225-241 **(**2017). doi: 10.1016/j.ebiom.2017.07.024.

Yoshida T, Kakizuka A, Imamura H. BTeam, a novel BRET-based biosensor for the accurate quantification of ATP concentration within living cells. ***Sci Rep***. 7:44873 (2017). doi: 10.1038/srep44873.

Nakano N, Ikeda HO, Hasegawa T, Muraoka Y, Iwai S, Tsuruyama T, Nakano M, Fuchigami T, Shudo T, Kakizuka A, Yoshimura N. Neuroprotective effects of VCP modulators in mouse models of models of glaucoma. ***Heliyon***. 2:e00096 (2016). doi: 10.1016/j.heliyon.2016.e00096.

Ikeda HO, Sasaoka N, Koike M, Nakano N, Muraoka Y, Toda Y, Fuchigami T, Shudo T, Iwata A, Hori S, Yoshimura N, Kakizuka A. Novel VCP modulators mitigate major pathologies of rd10, a mouse model of retinitis pigmentosa. ***Sci Rep***. 4:5970 (2014). doi: 10.1038/srep05970.

Sasaoka N, Sakamoto M, Kanemori S, Kan M, Tsukano C, Takemoto Y, Kakizuka A. Long-term oral administration of hop flower extracts mitigates Alzmeimer phenotypes in mice. ***PLoS One***. 9:e87185. (2014). doi: 10.1371/journal.pone.0087185.

Website of the lab: http://www.funcbiol.lif.kyoto-u.ac.jp/

Key words: drug development, neurodegenerative diseases, cancer, obesity, ATP, FRET biosensor

8) Laboratory of Chromosome Function and Inheritance
PI: CARLTON, Peter (Associate Prof.) <pcarlton@icems.kyoto-u.ac.jp>

Outline of the research
We study how genetic information is correctly maintained and passed on through cell divisions. Combining molecular genetic approaches with advanced microscopy and quantitative imaging, we focus on mechanisms of chromosome pairing, recombination, and segregation and recombination in meiosis in the nematode *C. elegans*.

Publications
Sato-Carlton, A., Nakamura-Tabuchi, C., Chartrand, S.K., Uchino, T., and Carlton, P.M. Phosphorylation of the synaptonemal complex protein SYP-1 promotes meiotic chromosome segregation. ***J. Cell Biol.*** *217*, 555–570. (2017). doi: 10.1083/jcb.201707161

Kafer, G.R., X. Li, T. Horii, I. Suetake, S. Tajima, I. Hatada, and P.M. Carlton. 5-Hydroxymethylcytosine Marks Sites of DNA Damage and Promotes Genome Stability. ***Cell Rep.*** 14:1283–1292. (2016). doi:10.1016/j.celrep.2016.01.035.

Sato-Carlton, A., X. Li, O. Crawley, S. Testori, E. Martinez-Perez, A. Sugimoto, and P.M. Carlton. Protein phosphatase 4 promotes chromosome pairing and synapsis, and contributes to maintaining crossover competence with increasing age. ***PLoS Genet.*** 10:e1004638. (2014). doi:10.1371/journal.pgen.1004638.

Mishima, Y., C.D. Jayasinghe, K. Lu, J. Otani, M. Shirakawa, T. Kawakami, H. Kimura, H. Hojo, P. Carlton, S. Tajima, and I. Suetake. Nucleosome compaction facilitates HP1γ binding to methylated H3K9. ***Nucleic Acids Res.*** 43:10200–10212. (2015). doi:10.1093/nar/gkv841.

Kafer, G.R., P.M. Carlton, and S.A. Lehnert. The histone variant H2A.Z is dynamically expressed in the developing mouse placenta and in differentiating trophoblast stem cells. ***Placenta***. 36:1325–1328. (2015). doi:10.1016/j.placenta.2015.08.018.

Schermelleh, L., P.M. Carlton, S. Haase, L. Shao, L. Winoto, P. Kner, B. Burke, C.M. Cardoso, D.A. Agard, M.G. Gustafsson, H. Leonhardt, and J.W. Sedat. Subdiffraction Multicolor Imaging of the Nuclear Periphery with 3D Structured Illumination Microscopy. ***Science.*** 320:1332–1336. (2008). doi:10.1126/science.1156947.

Website of the lab: https://www.carltonlab.org/

Key words: DNA damage, meiosis, Chromosome segregation, C. elegans, super-resolution microscopy

9) Laboratory of Bioimaging and Cell Signaling

PI: MATSUDA, Michiyuki (Prof.) < matsudam@lif.kyoto-u.ac.jp>

Outline of the research

The current aim of our research is to decipher the mechanism underlying cell-to-cell communication. For this purpose, we are visualizing the activities of signaling molecules by using probes based on the principle of Förster resonance energy transfer (FRET). The FRET biosensors are extremely powerful to visualize the spatiotemporal regulation of signal transduction networks within cells and to analyze the activities of individual cells within tissues. We are also developing a series of optogenetic tools to activate molecules of interest within the tissues of live mice. Our laboratory is in charge of the core facility of fluorescence live imaging of Kyoto University.

Publications

Sano, T., Kobayashi, T., Ogawa, O. & Matsuda, M. Gliding basal cell migration of the urothelium during wound healing. ***Am. J. Pathol.*** 188, 2564-2573, (2018). doi:10.1016/j.ajpath.2018.07.010

Muta, Y., Fujita, Y., Sumiyama, K., Sakurai, A., Taketo, M. M., Chiba, T., Seno, H., Aoki, K., Matsuda, M. & Imajo, M. Composite regulation of ERK activity dynamics underlying tumour-specific traits in the intestine. ***Nat. Commun.*** 9, 2174, (2018). doi:10.1038/s41467-018-04527-8

Konagaya, Y., Terai, K., Hirao, Y., Takakura, K., Imajo, M., Kamioka, Y., Sasaoka, N., Kakizuka, A., Sumiyama, K., Asano, T. & Matsuda, M. A Highly Sensitive FRET Biosensor for AMPK Exhibits Heterogeneous AMPK Responses among Cells and Organs. ***Cell Rep.*** 21, 2628-2638, (2017). doi:10.1016/j.celrep.2017.10.113

Website of the lab: http://www.fret.lif.kyoto-u.ac.jp/e-phogemon/index.htm

Key words: multiphoton fluorescence microscopy, biosensors, optogenetics, transgenic mouse

10) Laboratory of Theoretical Biology

PI: HONDA, Naoki (Associate Prof.) < honda.naoki.4v@kyoto-u.ac.jp>

Outline of the research

Our laboratory aims to elucidate the theoretical logic of dynamic living systems. By developing and simulating mathematical models, we are trying to understand mechanisms underlying phenomena in a bottom-up manner. We are also utilizing machine learning to extract hidden rules of dynamic, complicated phenomena from experimental quantitative data in a top-down manner. By means of these theoretical approaches, we are studying neuronal wiring in the brain, emotional neural dynamics, noise-resistant embryonic development, mechano-chemical mechanisms of collective cell migration, cytoskeleton-based cellular morphogenesis, identification of intracellular information processing, and animal behavioral strategies.

Publications

Honda N*, Akiyama R, Sari DWK, Ishii S, Bessho Y and Matsui T: Noise-resistant developmental reproducibility in vertebrate somite formation. ***PLoS Computational Biology*** (in press, doi: 10.1371/journal.pcbi.1006579)

Yamaguchi S, Honda N*, Ikeda M, Tsukada Y, Nakano S, Mori I and Ishii S: Identification of animal behavioral strategies by inverse reinforcement learning. ***PLoS Computational Biology*** 14(5): e1006122 (2018)

Honda N*: Revisiting chemoaffinity theory: Chemotactic implementation of topographic axonal projection ***PLoS Computational Biology*** 13(8), e1005702 (2017)

Li Y, Nakae K, Ishii S and Honda N*: Uncertainty-dependent extinction of fear memory in an amygdala-mPFC neural circuit model. ***PLoS Computational Biology*** 12(9), e1005099 (2016)

Yamao M, Honda N (Co-first), Kunida K, Aoki K, Matsuda M and Ishii S Distinct predictive performance of Rac1 and Cdc42 in cell migration. ***Scientific Reports*** 5, 17527 (2015)

Website of the lab: https://sites.google.com/view/theoretical-biology/

Key words: Mathematical model, Computer simulation, Machine learning, Data-driven modeling, Data analysis

11) Laboratory of Brain Development and Regeneration

PI: IMAYOSHI, Itaru (Prof.) <imayoshi.itaru.2n@kyoto-u.ac.jp>

Outline of the research

We aim to understand the cellular and molecular mechanism of the growth and fate-determination of neural stem cells in the developing and adult mammalian brain. We are also interested in the functional significance of postnatal/adult neurogenesis on higher brain functions, such as spatial learning/memory and olfactory-related behaviors. Our lab has expertise in the optical regulation of gene expression and neuronal activity, genetic manipulation of neural development and plasticity, and long-term monitoring of neural circuit plasticity in vivo with the two-photon microscope and brain endoscope.

Publications

Yamada, M., Suzuki, Y., Nagasaki, S., Okuno, H. and Imayoshi, I. Light-inducible Tet-gene expression system in mammalian cells. ***Cell Reports***, 25, 487-500 (2018)

Suzuki, Y. and Imayoshi, I. Network analysis of exploratory behaviors of mice in a spatial learning and memory task. ***PLoS One*** Jul 10;12(7):e0180789 (2017). doi: 10.1371/journal.pone.0180789.

Imayoshi, I. and Kageyama, R. bHLH Factors in Self-Renewal, Multipotency, and Fate Choice of Neural Progenitor Cells. ***Neuron*** 82: 9-23 (2014).

Sakamoto, M., Ieki, N., Miyoshi, G., Mochimaru, D., Miyachi, H., Imura, T., Yamaguchi, M., Fishell, G., Mori, K., Kageyama, R. and Imayoshi, I. Continuous postnatal neurogenesis contributes to formation of the olfactory bulb neural circuits and flexible olfactory associative learning. ***The Journal of Neuroscience*** 34: 5788-5799 (2014).

Imayoshi, I., Isomura, A. (equal contribution), Harima, Y., Kawaguchi, K., Kori, H., Miyachi, H., Fujiwara, T.K., Ishidate, F. and Kageyama, R. Oscillatory control of factors determining multipotency and fate in mouse neural progenitors. ***Science*** 342: 1203-1208 (2013).

Imayoshi, I., Sakamoto, M., Ohtsuka, T., Takao, K., Miyakawa, T., Yamaguchi, M., Mori, K., Ikeda, T., Itohara, S. and Kageyama, R. Roles of continuous neurogenesis in the structural and functional integrity of the adult forebrain. ***Nature Neuroscience*** 11: 1153-1161 (2008).

Website of the lab: https://brainnetworks.jimdofree.com

Key words: Neural stem cells, Neurogenesis, Optogenetics, Hippocampus, Olfactory bulb

12) Laboratory of Genome Maintenance

PI: MATSUMOTO, Tomohiro (Prof.) <tmatsumo@house.rbc.kyoto-u.ac.jp>

Outline of the research

The spindle checkpoint is a unique negative feedback that converts/amplifies a physical signal sensed by kinetochores (attachment of the spindle and/or tension), and regulates the timing of sister chromatid separation for equal chromosome segregation. Mad2, a signal carrier of this feedback, plays a vital role in the spindle checkpoint.
It is specifically localized at unattached kinetochores that are the origin of the checkpoint signal. Mad2 targets CDC20 and inhibits its activity to promote sister chromatid separation. We study Mad2, a central player of the spindle checkpoint, to reveal mechanisms which regulate the activity of Mad2.

Publications

Kitagawa T., Ishii K., Takeda K. and Matsumoto T. The 19S proteasome subunit Rpt3 regulates distribution of CENP-A by associating with centromeric chromatin. ***Nat Commun*****.** (2014). doi: 10.1038/ncomms4597.

Horikoshi Y, Habu T and Matsumoto T. An E2 enzyme Ubc11 is required for ubiquitination of Slp1/Cdc20 and spindle checkpoint silencing in fission yeast. **C*ell Cycle.*** 12:961-71 (2013).

Ito D, Saito Y and Matsumoto T. Centromere-tethered Mps1 pombe homolog (Mph1) kinase is a sufficient marker for recruitment of the spindle checkpoint protein Bub1, but not Mad1. ***Proc Natl Acad Sci U S A.*** 109:209-14 (2012).

Website of the lab: **http://house.rbc.kyoto-u.ac.jp/radiation_system/**

Key words: chromosome, mitosis, centromere

13) Laboratory of Genome Damage Signaling

PI: TAKATA, Minoru (Prof.) < mtakata@house.rbc.kyoto-u.ac.jp>

Outline of the research

DNA damage response (DDR) is the fundamental mechanism that stabilizes our genome. Genome stability underlies all biological processes. We try to identify molecules involved in genome stability/replication stress/DDR by methods

such as screening mutations in human patients, and further analyze their function using genome engineering in various cell lines, iPS cells, and model organisms.

Publications

Inano, S., Sato, K., Katsuki, Y., Kobayashi, W., Tanaka, H., Nakajima, K., Nakada, S., Miyoshi, H., Knies, K., Takaori-Kondo, A., Schindler, D., Ishiai, M., Kurumizaka, H., Takata, M. RFWD3-mediated ubiquitination promotes timely removal of both RPA and RAD51 from DNA damage sites to facilitate homologous recombination. ***Mol Cell***. 66 (5):622-634.e8. (2017). doi: 10.1016/j.molcel.2017.04.022. PMID: 28575658

Knies, K., Inano, S., Ramírez, M. J., Ishiai, M., Surallés, J., Takata, M., and Schindler, D. Biallelic mutations in the ubiquitin ligase *RFWD3* cause Fanconi anemia. ***Journal of Clinical Investigation*** (2017). 127 (8):3013-3027. doi: 10.1172/JCI92069. Epub 2017 Jul 10. PMID: 28691929

Katsuki, Y. and Takata, M. Defects in HR repair behind the human diseases: FA and HBOC. ***Endocr. Relat. Cancer*** (2016). PMID: 27550963

Hira, A., Yoshida, K., Sato, K., Okuno, Y., Shiraishi, Y., Chiba, K., Tanaka, H., Miyano, S., Shimamoto, A., Tahara, H., Ito, E., Kojima, S., Kurumizaka, H., Ogawa, S., Takata, M., Yabe, H. and Yabe, M. Mutations in the gene encoding the E2 conjugating enzyme UBE2T cause fanconi anemia. ***Am. J. Hum. Genet***. 96: 1001-1007 (2015). doi: 10.1016/j.ajhg.2015.04.022. PMID: 26046368

Unno, J., Itaya, A., Taoka, M., Sato, K., Tomida, J., Sakai, W., Sugasawa, K., Ishiai, M., Ikura, T., Isobe, T., Kurumizaka, H. and Takata, M. FANCD2 binds CtIP and regulates DNA-end resection during DNA interstrand crosslink repair. ***Cell Rep.*** 7:1039-47 (2014). doi: 10.1016/j.celrep.2014.04.005

Website of the lab: http://house.rbc.kyoto-u.ac.jp/late-effect

Key words: DNA damage response, DNA repair, genetic disorders, genome editing

14) Laboratory of Cancer Cell Biology

PI: HARADA, Hiroshi (Prof.) < harada.hiroshi.5e@kyoto-u.ac.jp>

Outline of the research

Cells maintain their functions and morphology by exploiting a suitable adaptive response system to diverse and complex tissue microenvironments. Several lines of evidence have suggested that hypoxic, acidic and nutrient-depleted microenvironments exist in solid tumors and induce malignant phenotypes and chemo/radioresistance of cancer cells. We aim to elucidate molecular mechanisms underlying both cellular adaptive responses to the tumor-specific microenvironments and malignant progression of cancer cells.

Publications:

Goto, Y., Zeng, L., Yeom, C. J., Zhu, Y., Morinibu, A., Shinomiya, K., Kobayashi, M., Hirota, K., Itasaka, S., Yoshimura, M., Tanimoto, K., Torii, M., Sowa, T., Menju, T., Sonobe, M., Kakeya, H., Toi, M., Date, H., Hammond E. M, Hiraoka, M. and Harada, H. UCHL1 provides diagnostic and antimetastatic strategies due to its deubiquitinating effect on HIF-1α. ***Nature Commun.*** 6: 6153 (2015). doi: 10.1038/ncomms7153

Zeng, L., Morinibu, A., Kobayashi, M., Zhu, Y., Wang, X., Goto, Y., Yeom, C. J., Zhao, T., Hirota, K., Shinomiya, K., Itasaka, S., Yoshimura, M., Guo, G., Hammond, E. M., Hiraoka, M. and Harada, H. Aberrant IDH3alpha expression promotes malignant tumor growth by inducing HIF-1-mediated metabolic reprogramming and angiogenesis. ***Oncogene*** 34: 4758-4766. (2015). doi: 10.1038/onc.2014.411

Harada, H., Inoue, M., Itasaka, S., Hirota, K., Morinibu, A., Shinomiya, K., Zeng, L., Ou, G., Zhu, Y., Yoshimura, M., McKenna, W. G,, Muschel, R. J. and Hiraoka, M. Cancer cells that survive radiation therapy acquire HIF-1 activity and translocate towards tumour blood vessels. ***Nature Commun.*** 3: 783 (2012). doi:10.1038/ncomms3314.

Website of the lab: http://www.rbc.kyoto-u.ac.jp/cancer_biology/

Key words: cancer, tumor microenvironments, hypoxia, chemo/radioresistance

15) Laboratory of Laboratory of Chromatin Regulatory Network

PI: IKURA, Tsuyoshi (Associate Prof.) <ikurat@house.rbc.kyoto-u.ac.jp>

Outline of the research

The eukaryotic genome is tightly packed into the chromatin, a hierarchically organized complex of DNA, histone and nonhistone proteins. This packing represents a common obstacle for the metabolic processes of DNA including transcription, replication, recombination, and DNA repair. Current evidence indicates that chromatin reorganization involving histone modification, histone variant exchange, histone eviction and ATP-dependent chromatin remodeling play an integral role in DNA repair and DNA damage response. However, it remains unclear how such chromatin reorganization is coupled with the initiation of DNA repair process and/or activation of checkpoint machinery after DNA damage. We are now investigating the following issues:

1.The molecular mechanisms by which the TIP60 histone acetylase complex regulates histone H2AX exchange induced by ionizing radiation.

2.The cross-talk between the histone signaling network regulated by histone H2AX exchange and DNA damage response pathways.

Publications

Ikura, M., Furuya, K., Fukuto, A., Matsuda, R., Adachi, J., Matsuda, T., Kakizuka A., Ikura, T. Coordinated regulation of TIP60 and PARP-1 in damaged chromatin dynamics. ***Mol Cell Biol.*** 36:1595-1607 (2016). doi: 10.1128/MCB.01085-15.

Ikura, M., Furuya, K., Matsuda, S., Matsuda, R., Shima, H., Adachi, J., Matsuda, T., Shiraki, T., Ikura, T. Acetylation of histone H2AX at Lys 5 by the TIP60 histone acetyltransferase complex is essential for the dynamic binding of NBS1 to damaged chromatin. ***Mol Cell Biol.*** 35: 4147-4157 (2015). doi: 10.1128/MCB.00757-15.

Ikura T., Tashiro, S., Kakino, A., Shima, H., Jacob, N., Amunugama, R., Yoder, K., Izumi, S., Kuraoka, I., Tanaka, K., Kimura, H., Ikura, M., Nishikubo, S., Ito, T., Muto, A., Miyagawa, K., Takeda, S., Fishel, R., Igarashi, K., *Kamiya, K. DNA damage-dependent acetylation and ubiquitination of H2AX enhances chromatin dynamics. ***Mol Cell Biol.*** 27:7028-7040 (2007). doi:10.1128/MCB.00579-07

Ikura, T., Ogryzko, V V., Grigoriev, M., Groisman, R., Wang, J., Horikoshi, M., Scully, R., Qin, J., Nakatani, Y Involvement of the TIP60 Histone Acetylase Complex in DNA repair and apoptosis. ***Cell***. 102:463-473 (2000). doi.org/10.1016/S0092-8674(00)00051-9

Website of the lab: http://house.rbc.kyoto-u.ac.jp/mutagenesis2/index1

Key words: chromatin dynamics, histone acetyltransferase, histone variant, DNA damage response

16) Laboratory of RNA Viruses

PI: TOMONAGA, Keizo (Prof.) <tomonaga@infront.kyoto-u.ac.jp>

Outline of the research

The main purpose of our research is to investigate the molecular mechanisms underlying the replication and pathogenesis of animal-derived RNA viruses. Analysis of the endogenization of RNA viruses and its role on hostvirus co-evolution is also focused on this laboratory.

Publications

Ikeda, Y., Makino, A., Holditch, S. J., Lu, B., Dietz, A. B. and Tomonaga, K. A novel intranuclear RNA vector system for long-term stem cell modification. ***Gene Ther.*** 23: 256-262 (2016). doi: 10.1038/gt.2015.108

Matsumoto, Y., Hayashi, Y., Omori, H., Honda, T., Daito, T., Horie, M., Ikuta, K., Fujino, K., Nakamura, S., Schneider, U., Chase, J., Yoshimori, T., Schwemmle, M. and Tomonaga, K. Bornavirus closely associates and segregates with host chromosomes to ensure persistent intranuclear infection. ***Cell Host Microbe*** 11:492-503 (2012). doi: 10.1016/j.chom.2012.04.009

Horie, M., Honda, T., Suzuki, Y., Kobayashi, Y., Daito, T., Oshida, T., Ikuta, K., Jern, P., Gojobori T., Coffin, J. M. and Tomonaga, K. Endogenous non-retroviral RNA virus elements in mammalian genomes. ***Nature*** 463:84-87 (2010). doi: 10.1038/nature08695

Website of the lab: https://t.rnavirus.virus.kyoto-u.ac.jp/

Key words: bornavirus, endogenous viruses, RNA virus vector

17) Laboratory of Cell Division and Differentiation

PI: TOYOSHIMA, Fumiko (Prof.) <ftoyoshi@infront.kyoto-u.ac.jp>

Outline of the research

Stem cell self-renew and differentiation is essential for tissue homeostasis. Stem cells divide symmetrically or asymmetrically to self-renew and/or generate differentiation-committed progenitor cells. Our group seeks to explore the mechanisms of the stem cell fate decision, focusing on oriented cell division, gene expression regulation, mechanotransduction, and metabolism during steady state homeostasis and under physiological alteration of the body. We are interested in how the tissue stem cell regulation contributes to our health.

Publications

Ichijo, R., Kobayashi, H., Yoneda, S., Iizuka, Y., Kubo, H., Matsumura, S., Kitano, S., Miyachi, H., Honda, T., and Toyoshima, F. Tbx3-dependent amplifying stem cell progeny drives interfollicular epidermal expansion during pregnancy and regeneration. ***Nat. Commun.*** 8: 508 (2017). doi:10.1038/s41467-017-00433-7

Matsumura, S., Kojidani, T., Kamioka, Y., Uchida, S., Haraguchi, T., Kimura, A., and Toyoshima, F. Interphase adhesion geometry is transmitted to an internal regulator for spindle orientation via caveolin-1. ***Nat. Commun.*** 7:11857 (2016). doi: 10.1038/ncomms11858

Iwano, S., Satou, A., Matsumura, S., Sugiyama, N., Ishihama, Y., and Toyoshima, F. PCTK1 regulates integrindependent spindle orientation via PKA regulatory subunit KAP0 and myosin X. ***Mol. Cell. Biol.*** 35, 1197-1208
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Matsumura S., Hamasaki M., Yamamoto T., Ebisuya M., Sato M., Nishida E. and Toyoshima F. ABL1 regulates spindle orientation in adherent cells and mammalian skin. ***Nat. Commun.*** 3:626 (2012). doi: 10.1038/ncomms 1634

Website of the lab: http://www.virus.kyoto-u.ac.jp/Lab/Toyoshima-HP/Home.html

Key words: oriented cell division, stem cells, tissue homeostasis

18) Laboratory of Cellular and Molecular Biomechanics

PI: ADACHI, Taiji (Prof.) <adachi@infront.kyoto-u.ac.jp>

Outline of the research

We aim to clarify the mechanisms by which cells sense mechanical stimuli and regulate their activities in tissue adaptation, regeneration and stem cell differentiation in morphogenesis. Based on multiscale biomechanics, our group is involved in the integrated biomechanics and mechanobiology researches of modeling and simulation combined with experiments, focusing on mechano-biochemical couplings in the system dynamics.

Publications

Kim, Y. K., Kameo, Y., Tanaka, S. and Adachi, T. Capturing microscopic features of bone remodeling into a macroscopic model based on biological rationales of bone adaptation. ***Biomech. Model Mechanobiol.*** 16-5: 16971708 (2017). doi: 10.1007/s10237-017-0914-6

Inoue, Y., Adachi, T. Mechanosensitive kinetic preference of actin-binding protein to actin filament. ***Phys. Rev. E.*** 93: 042403 (2016). doi: 10.1103/PhysRevE.93.042403

Maki, K., Han, S.-W., Hirano, Y., Yonemura, S., Hakoshima, T. and Adachi, T. Mechano-adaptive sensory mechanism of α-catenin under tension. ***Sci. Rep.*** 6: 24878 (2016). doi: 10.1038/srep24878

Okuda, S., Inoue, Y., Eiraku, M., Sasai, Y., Adachi, T. Reversible network reconnection model for simulating large deformation in dynamic tissue morphogenesis. ***Biomech. Model Mechanobiol.*** 12: 627-644 (2013). doi: 10.1007_s10237-012-0430-7

Kameo, Y., Adachi, T. and Hojo, M. Transient response of fluid pressure in a poroelastic material under uniaxial cyclic loading. ***J. Mech. Phys. Solids*** 56: 1794-1805 (2008). doi: 10.1016/j.jmps.2007.11.008

Website of the lab: https://www2.infront.kyoto-u.ac.jp/bf05/index-e.html

Key words: biomechanics, mechanobiology, adaptation, morphogenesis, modeling and simulation