Revised as of April 8, 2020 (SEE p.8)

2020-2021

Graduate School of Biostudies, Kyoto University

Doctoral Program in "Global Frontier in Life Science"

Guidelines for International Student Admissions

Philosophy and Admission Policy of the Graduate School of Biostudies

As an advanced discipline that holds the key to the future of humankind, the life sciences today are undergoing a major evolutionary change. In response to this global trend, the Graduate School of Biostudies was founded in 1999 as Japan's first independent graduate school focused on life sciences with the objective of building a world-class center for research and developing individuals who can lead the life sciences field into the next generation. Our school has engineered a true fusion of cutting-edge areas in several existing fields. By harnessing the common language of "cells, molecules, and genes" that together form the fundamental principles of life, we have developed an integrated understanding of diverse life forms and the environments they help shape, and have launched innovative efforts in research and education that will produce a new set of values for the future and dignity of life.

To meet the diverse expectations of society for advances in the life sciences, which are becoming increasingly sophisticated and complex, our school seeks students from a broad spectrum of backgrounds who share these ideals of our school, who possess broad academic knowledge and advanced expertise gained through their master's education, who possess strong research ability, and who demonstrate an even stronger sense of ethics and responsibility in their academic research. We especially welcome students who possess a pioneering spirit to help propel the comprehensive and advanced branches of the life sciences, free from preconceptions, while fully appreciating the dignity of life. Accordingly, the Graduate School of Biostudies endeavors to cultivate individuals with the following attributes:

1. Researchers ready to discover, or shed fresh light on, fundamental principles of life, who will produce world-class research results in new areas of the life sciences;
2. Researchers and advanced engineers committed to global environmental conservation and gains in human health, welfare, and well-being, who are ready to assume a leading role in public and private research institutions;
3. Educational leaders and high-level working professionals with a broad-based understanding of the varied phenomena of life, who are ready to assume a leading role in education, industry, the news media, and government;
4. Researchers, educational leaders, advanced engineers, and high-level working professionals equipped with strong logical explanation and communication skills, who can convey their ideas broadly to others in Japan and around the world and assume a leading role in a variety of fields.

The entrance exam will comprise achievement tests that include a written exam to evaluate the applicant's ability to think logically in English, which is required for international communication; a presentation of the applicant's research findings during their master's program or elsewhere; and an oral exam to assess the applicant's judgement, thinking ability, communication skills, initiative, and ethical perspective. Admissions decisions will be made based on the applicant's overall performance on these exams.

Please note that applicants are NOT required to be physically present in Japan for the examination.

The academic year starts on October 1, 2020 or April 1, 2021.

I. “Global Frontier in Life Science”

The Graduate School of Biostudies offers “Global Frontier in Life Science”, a joint educational program for Doctoral and Master’s students as 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.

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. 10 - 31 of these guidelines and the Graduate School of Biostudies’ website (http://www.lif.kyoto-u.ac.jp/). Applicants can apply for only one laboratory. **Thus, applicants must contact the lab head and fully discuss potential research activities and availability before filing the application.**

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

Only persons currently falling into one of the following categories, or anticipated to do so as of September 30, 2020, will be eligible to apply:

1. Those who have a master's degree, a master's-level professional degree, or a juris doctor (JD) degree
2. Those who have completed a program equivalent to the Graduate School's master's program or professional degree program in a foreign country
3. Those who, by taking relevant courses via a correspondence program offered by a school in a foreign country, have completed a program equivalent to the University's master's program or professional degree program
4. Those who have completed a graduate school program (i.e., one that is equivalent to the University’s master's program or professional degree program) of a foreign university that is accredited under the educational system of the respective foreign country as offering graduate school programs and which is designated by the Minister of Education, Culture, Sports, Science and Technology (hereinafter referred to as the "Minister")
5. Completion of a curriculum at the United Nations University (under the provisions of Paragraph 2 of Article 1 of the Act on Special Measures Incidental to Enforcement of the Agreement between the United Nations and Japan regarding the Headquarters of the United Nations University, Act No. 72 of 1976), and receipt of a degree equivalent to a Master’s Degree.
6. Applicants who have passed a Qualifying Examination (QE) or equivalent assessment at an institution in another country, and are recognized by Kyoto University as having academic ability on a par with or higher than that of a person with a master's degree.
7. Those who have been designated by the Minister (Notification No.118 [1988] of the Ministry of Education)
   i) Those who have graduated from a university and who have subsequently spent at least two years conducting research at a university, research institute, or other such institution, and are recognized by the Graduate School as having a scholastic ability on par with or higher than that of those with a master’s degree for achievement of said research.
   ii) Those who have completed sixteen years of school education by attending classes in a foreign country or by taking correspondence courses of a school in a foreign country, and who have subsequently spent at least two years conducting research at a university, research institute, or other such institution, and are recognized by the Graduate School as having a scholastic ability on par with or higher than that of those with a master’s degree for achievement of said research.

8. Those who are recognized by the Graduate School as having a scholastic ability on par with or higher than that of those falling into (1) above as a result of the individual eligibility screening, and who have reached 24 years of age, including those who have graduated from a six-year university.

III-2. Eligibility Requirements for Applicants expecting to start from April 1, 2021

Only persons currently falling into one of the following categories, or anticipated to do so as of March 31, 2021, will be eligible to apply:

1. Those who have a master's degree, a master's-level professional degree, or a juris doctor (JD) degree
2. Those who have completed a program equivalent to the Graduate School's master's program or professional degree program in a foreign country
3. Those who, by taking relevant courses via a correspondence program offered by a school in a foreign country, have completed a program equivalent to the University's master's program or professional degree program
4. Those who have completed a graduate school program (i.e., one that is equivalent to the University's master's program or professional degree program) of a foreign university that is accredited under the educational system of the respective foreign country as offering graduate school programs and which is designated by the Minister of Education, Culture, Sports, Science and Technology (hereinafter referred to as the "Minister")
5. Completion of a curriculum at the United Nations University (under the provisions of Paragraph 2 of Article 1 of the Act on Special Measures Incidental to Enforcement of the Agreement between the United Nations and Japan regarding the Headquarters of the United Nations University, Act No. 72 of 1976), and receipt of a degree equivalent to a Master's Degree.
6. Applicants who have passed a Qualifying Examination (QE) or equivalent assessment at an institution in another country, and are recognized by Kyoto University as having academic ability on a par with or higher than that of a person with a master's degree.
7. Those who have been designated by the Minister (Notification No.118 [1988] of the Ministry of Education)
   i) Those who have graduated from a university and who have subsequently spent at least two years conducting research at a university, research institute, or other such institution, and are recognized by the Graduate School as having a scholastic ability on par with or higher than that of those with a master's degree for achievement of said research.
   ii) Those who have completed sixteen years of school education by attending classes in a foreign country or by taking correspondence courses of a school in a foreign country, and who have subsequently spent at least two years conducting research at a university, research institute, or other such institution, and are recognized by the Graduate School as having a scholastic ability on par with or higher than that of those with a master's degree for achievement of said research.
8. Those who are recognized by the Graduate School as having a scholastic ability on par with or higher than that of those falling into 1 above as a result of the individual eligibility screening, and who have reached 24 years of age, including those who have graduated from a six-year university.

IV. Eligibility Screening

Those who intend to apply under requirement 6, 7 or 8 above are subject to screening prior to acceptance of their applications. Please 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 JST April 9 (Thu), 2020. The documents below must be submitted to the Student Affairs Section (Kyomu gakari) of the Graduate School of Biostudies via email to the Student

Affairs Section of the Graduate School of Biostudies (150kyomu@adm.lif.kyoto-u.ac.jp) by JST 5:00 pm, April 16 (Thu), 2020.
When filing the admission application, applicants cannot in principle apply for any laboratory other than the one specified in the documents being submitted for the eligibility screening. The eligibility screening results will be sent to the applicant by e-mail as soon as the decision is made, at the latest on May 14 (Thu), 2020.

Documents to be submitted for eligibility screening under requirement 6

(1) Eligibility Screening Application Form	Use the designated form. In the application form, write down the e-mail address for receiving screening results.
(2) Documents which detail the examination procedure and qualifying criteria of the Qualifying Examination (QE) or equivalent assessment	Any format is acceptable. Please submit the notarized copy of original document endorsed by the president registrar of the examining institution. a) Certificate that the Applicant has passed the examination b) The curriculum details of a program equivalent to a master's program which the applicant has completed
(3) Academic transcript of a program equivalent to a master's program which the applicant has completed	Please submit the original of the document

Documents to be submitted for eligibility screening under requirement 7 or 8

(1)Eligibility Screening Application Form	Use the designated form. In the application form, make sure to write down the e-mail address for receiving screening results.
(2)Academic transcript	Submit an academic transcript prepared and sealed by the university that you last attended. (The transcript does not need to be sealed if it is made of a material that prevents photocopying.)
(3)Research progress report	Use the designated form. Present a brief, objective statement on the progress of your research in your field of specialization.
(4)Details of previous studies or letter of recommendation	Submit details of previous studies in the designated format and sealed by the institution to which you belong. Those who cannot receive said certificate of details, such as graduates from a six-year university or those who are expected to graduate from a six-year university by September 30, 2020, can submit a letter of recommendation prepared in the designated format and sealed by a research supervisor. 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 hand-written signature and full contact addresses (including E-mail address) are provided.

V. Application Fee

Application fee: 10,000 yen

Payment period: From May 1 (Fri) to May 15 (Fri), 2020 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 (650 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". 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 (650 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". 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 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) Title of research project and its outline	Provide the title and a summary of the research project that you have conducted on one or two sheets of A4-or letter-size paper. The writing must be written horizontally (in English).
(3) 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.
(4) Academic transcript	Submit an academic transcript prepared and sealed by the graduate school that you are currently attending or have graduated from. Those who have been recognized as being eligible to apply by the eligibility screening process do not have to submit the transcript. (The transcript does not need to be sealed if it is made of a material that prevents photocopying.)
(5) Certificate of completion (or certificate of expected completion)	Submit a certificate of (expected) completion prepared by the graduate school that you belong to or have graduated from. Those who have graduated from a six-year university need to submit a graduation certificate (or certificate of expected graduation) prepared by the university.
(6) Graduation certificate	Submit a copy of your graduation certificate (e.g., diploma) prepared by the university or faculty you have graduated from.
(7) Recommendation letters	At least two letters are required. (Mandatory) Letter of recommendation 1: 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. (Choose at least one, as appropriate) Letter of recommendation 2: Written by a faculty member of your current educational institution, who can evaluate your academic performance and potential for success in the doctoral 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. 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.
(8) A valid score for IELTS or TOEFL	Unnecessary for English-native speakers (Please contact the Student Affairs Section in advance.)
(9) Evidence of Application Fee Payment Form **Note:** Those who are expected to complete a master's program in a graduate school of Kyoto University do not need to submit this 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.
(10) Application approval	Applicants belonging to a governmental or private organization who wish to be admitted to the Graduate School while taking administrative leave from their organization need to submit the form provided indicating approval for submitting an application and prepared by the department director or the organization's representative. Applicants belonging to a governmental or private organization who do not submit the approval will not be admitted until after they quit the organization, even if they have passed the enrollment examinations. *The application approval form will be provided upon request.
(11) 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 Biostudies.

VII. Application Procedures

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

VIII. Application Period

The application period is from May 18 (Mon) to May 22 (Fri), 2020 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 22 (Fri), 2020.
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.

--- Revision (as of April 8, 2020) ----------

1) If you are unable to submit a TOEFL/IELTS score by May 22, 2020 due to your local test schedule change concerning the COVID-19 coronavirus epidemic, later submissions will be accepted until June 30, 2020.
In this case, please notify the Student Affairs Section of the Graduate School of Biostudies of your situation, no later than May 22, 2020.

2) Before enclosing your application documents, please make a scanned copy (pdf) of them and send them to the Student Affairs Section (150kyomu@adm.lif.kyoto-u.ac.jp) via email so that the copy can be substituted if your documents sent by post did not arrive in our office by the designated deadline.

IX. Examination Schedules

June 1 (Mon) ~ June 5 (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 (Wed) ~ July 10 (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 5:00 p.m., July 22 (Wed), 2020. 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)
(Those who are expected to complete a Master's program in a graduate school of Kyoto University do not need to pay this fee. 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 amount may be revised at the time of enrollment or later.)

Notes

(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 an envelope, place the self-addressed envelope inside, and send it to the address where the application is to be sent (see below).
(3) The instructions for enrollment procedures will be emailed to each successful applicant in late July, 2020. For those who will enroll in April, 2021, they will be informed in early February, 2021.
(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".

< Notice >

From 2021, entrance examinations of the Global Frontier in Life Science will be held in winter instead of summer. The application period for enrollment in October, 2021 and April, 2022 will begin in December, 2020, and details will be released in September, 2020. Look for future announcements from the Graduate School of Biostudies.

<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, 2019

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

Ishikawa, S. and Ishikawa, F. Proteostasis failure and cellular senescence in long-term cultured post-mitotic rat neurons. ***Aging Cell***, in press (2019).

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. Learning from reproductive parasites: a comprehensive study of “male killing” caused by insect symbionts
3. Neuroscience: operating principles of neuronal circuits that evoke selective behavioral outputs in response to nociceptive stimuli
4. 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 interspecies approaches to understand contributions of symbiotic microorganisms to animal growth and reproductive manipulation (“male killing”). 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 related 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, optogenetic, and physiological approaches, imaging, and multi-omics.

Publications

Watanabe, K., Kanaoka, Y., Mizutani, S., Uchiyama, H., Yajima, S., Watada, M., Uemura, T. and Hattori, Y. Interspecies comparative analyses reveal distinct carbohydrate-responsive systems among *Drosophila* species. ***Cell Reports***, 28: 2594-2607.e7 (2019).

Kondo, T. and Hayashi, S. Two-step regulation of *trachealess* ensures tight coupling of cell fate with morphogenesis in the *Drosophila* trachea. ***eLife***, 8: e45145 (2019).

Harumoto, T. & Lemaitre, B. Male-killing toxin in a bacterial symbiont of Drosophila. ***Nature***. 557: 252-255 (2018).

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).

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).

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

Key words: animal development, nutrition, neuroscience, symbiotic microorganisms, morphogenesis, multi-omics

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://plantchembio.sun.bindcloud.jp/index.html

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 by revealing the molecular mechanisms of photosynthetic acclimation. Especially we employ a green alga, *Chlamydomonas reinhardtii*, as a model eukaryotic microorganism using its genome information, mutants, and genetic/molecular/biochemical techniques. The current projects are as follows: (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 changes in levels of supplied CO_2 or nitrogen, (3) Molecular mechanisms of controlling of retrograde signal from chloroplast and sexual reproduction by nutrient starvation.

Publications

Shinkawa H, et al.: Algal protein kinase, Triacylglycerol Accumulation Regulator 1, modulates cell viability and gametogenesis in carbon/nitrogen imbalanced conditions. ***Plant Cell Physiol.*** 60: 916–930 (2019)

Yamano T, Toyokawa C, Fukuzawa H*: High-resolution suborganellar localization of Ca^{2+}-binding protein CAS, a novel regulator of CO_2-concentrating mechanism. ***Protoplasma*** 255: 1015–1022 (2018) PMID: 29372336

Wang L, Yamano T,,, Fukuzawa H*: 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

Yamaoka Y, *et al*.: The bZIP1 transcription factor regulates lipid remodeling and contributes to ER stress management in *Chlamydomonas reinhardtii*. ***Plant Cell*** 31: 1127–1140 (2019) PMID: 30894460

Nitta N, *et al*.: Intelligent Image-Activated Cell Sorting. ***Cell*** 175: 266–276 (2018) PMID: 30166209

Isozaki A, *et al*.: A practical guide to intelligent image-activated cell sorting. ***Nature Protocol.*** 14: 2370–2415 (2019). PMID: 31278398

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

Key words: CO_2-sensing mechanism, photosynthetic acclimation, retrograde signaling, autophagy, sexual reproduction

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

Sakanaka M, Hansen ME, Gotoh A, Katoh T, Yoshida K, Odamaki T, Yachi H, Sugiyama Y, Kurihara S, Hirose J, Urashima T, Xiao JZ, Kitaoka M, Fukiya S, Yokota A, Lo Leggio L, Abou Hachem M, and Katayama T. Evolutionary adaptation in fucosyllactose uptake systems supports bifidobacteria-infant symbiosis. ***Sci. Adv.*** 5:eaaw7696, (2019).

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).

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

Tuzuki, M., Futagami, K., Shimamura, M., Inoue, C., Kunimoto, K., Oogami, T., Tomita, Y., Inoue, K., Kohchi, T., Yamaoka, S., Araki, T., Hamada, T., and Watanabe, Y. An early arising role of microRNA156/529c-*SPL* module in reproductive development revealed by the liverwort *Marchantia polymorpha*. ***Curr. Biol.*** 29: 3307-3314., e1-e5 (2019). doi: 10.1016/ j.cub.2019.07.084

Hisanaga, T., Yamaoka, S., Kawashima, T., Higo, A., Nakajima, K., Araki, T., Kohchi, T., and Berger, F. Building new insights in plant gametogenesis from an evolutionary perspective. ***Nature Plants*** 5: 663-669 (2019). doi: 10.1038/s41477-019-0466-0

Inoue, K., Nishihama, R., Araki, T., and Kohchi, T. Reproductive induction is far-red high irradiance response mediated by phytochrome and PHYTOCHROME INTERACTING FACTOR in *Marchantia polymorpha*. ***Plant Cell Physiol.*** 60: 1136-1145 (2019). doi: 10.1093/pcp/pcz029

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 authors omitted] Inoue, K., [64 authors omitted] 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

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

Key words: flowering, florigen, sexual reproduction, germ line specification, 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 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., Taniguchi, D., Tanaka, S., Kiuchi, T., Vavylonis, D. and Watanabe N. Convection-induced biased distribution of actin probes in live cells. Biophys. J. 116: 142-150 (2019). doi: 10.1016/j.bpj.2018.11.022

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

Jaspers, C., Fraune, S., Arnold, A.E., Miller, D.J., Bosch, T., Voolstra, C.R., and Consortium of Australian Academy of Science Boden Research Conference Participants. Resolving structure and function of metaorganisms through a holistic framework combining reductionist and integrative approaches. ***Zoology*** 133:81-87 (2019). doi: 10.1016/j.zool.2019.02.007.

Moya, A., Sakamaki, K., Mason, B.M., Huisman, L., Forêt, S., Weiss, Y., Bull, T.A., Tomii, K., Imai, K., Hayward, D.C., Ball, E.E., and Miller, D.J. Functional conservation of the apoptotic machinery from coral to man: the diverse and complex Bcl-2 and caspase repertoires of *Acropora millepora*. ***BMC Genomics*** 17:62 (2016). doi: 10.1186/s12864-015-2355-x.

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.

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): 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://chromosegr.riken.jp/index_en.html

Key words: chromosome, meiosis, oocyte, zygote

PI (2): 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
Phipson, B., Er, P.X., Combes, A.N., Forbes, T.A., Howden, S.E., Zappia, L., Yen, H.-J., Lawlor, K.T., Hale, L.J., Sun, J., Wolvetang, E., Takasato, M., Oshlack, A., Little, M.H., Evaluation of variability in human kidney organoids. ***Nat. Methods*** 16, 79–87 (2019). doi: 10.1038/s41592-018-0253-2

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: https://www.bdr.riken.jp/en/research/labs/takasato-m/index.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

Nagata, R., Nakamura, M., Sanaki, Y., and Igaki, T. Cell competition is driven by autophagy. ***Dev Cell*** 51: 99-112 (2019)

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*. ***Nat Commun*** 5: 5264 (2014).

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).

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

Ide Y, Horie T, Saito N, Watanabe S, Otani C, Miyasaka Y, Kuwabara Y, Nishino T, Nakao T, Nishiga M, Nishi H, Nakashima Y, Nakazeki F, Koyama S, Kimura M, Tsuji S, Rodriguez RR, Xu S, Yamasaki T, Watanabe T, Yamamoto M, Yanagita M, Kimura T, Kakizuka A, Ono K. Cardioprotective Effects of VCP Modulator KUS121 in Murine and Porcine Models of Myocardial Infarction. ***JACC Basic Transl Sci.*** 28;4(6):701-714. (2019). doi: 10.1016/j.jacbts.2019.06.001.

Sugiyama Y, Shudo T, Hosokawa S, Watanabe A, Nakano M, Kakizuka A. Emodin, as a mitochondrial uncoupler, induces strong decreases in adenosine triphosphate (ATP) levels and proliferation of B16F10 cells, owing to their poor glycolytic reserve. ***Genes Cells.*** 24(8):569-584. **(**2019**).** doi: 10.1111/gtc.12712.

Alfaqaan S, Yoshida T, Imamura H, Tsukano C, Takemoto Y, Kakizuka A. PPARα-Mediated Positive-Feedback Loop Contributes to Cold Exposure Memory. Sci Rep. 14;9(1):4538. (2019). doi: 10.1038/s41598-019-40633-3.

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.

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.) <carlton.petermark.3v@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

Kinjo, T., Terai, K., Horita, S., Nomura, N., Sumiyama, K., Togashi, K., Iwata, S., and Matsuda, M. FRET-assisted photoactivation of flavoproteins for in vivo two-photon optogenetics. ***Nat Methods.*** 16, 1029-1036, (2019)

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).

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).

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

Sueda, R., *Imayoshi, I. (equal contribution), Harima, Y., and *Kageyama, R. High Hes1 expression and resultant Ascl1 suppression regulate quiescent versus active neural stem cells in the adult mouse brain. Genes Dev, 33, 511-523 (2019).

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).

I*mayoshi, 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 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

14) 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

15) 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

16) Laboratory of Cell Division and Differentiation

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

Outline of the research

Balance between self-renewal and differentiation of stem cells is essential for tissue homeostasis. Biased stem cell self-renewal or differentiation leads to changes in tissue organization. Our group studies on the mechanisms of

symmetric/asymmetric stem cell division, stem cell differentiation, stem cell plasticity, and cell lineage-commitment in tissue homeostasis and regeneration. We are interested in how tissue stem cells adapt to physiological changes of the body throughout life stages, such as pregnancy, obesity and aging.

Publications

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

17) Laboratory of Cellular and Molecular Biomechanics

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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

Takeda, H., Kameo, Y., Inoue, Y., Adachi, T. An energy landscape approach to understanding variety and robustness in tissue morphogenesis. ***Biomech Model Mechanobiol***. (2019). doi: 10.1007/s10237-019-01222-5

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