2022 - 2023
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 document screening 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 interview (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, 2022 or April 1, 2023.

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. 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 42 laboratories. Details of each available 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. AAO Process

Once you have familiarized yourself with the publications of a particular laboratory, and have made a well-considered decision to apply, please contact the Kyoto University Admissions Assistance Office (AAO) and complete the AAO process.

AAO: https://u.kyoto-u.jp/graduate-admissions-for-overseas-graduates

Through the AAO process, you may contact the professor in charge of that laboratory to inquire if there is currently space available for you to pursue graduate research in that laboratory.

Available labs are listed in pp. 10-31.

IV-1. Eligibility Requirements for Applicants expecting to start from October 1, 2022

Only persons currently falling into one of the following categories, or anticipated to do so as of September 30, 2022, 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-2. Eligibility Requirements for Applicants expecting to start from April 1, 2023

Only persons currently falling into one of the following categories, or anticipated to do so as of March 31, 2023, 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.

V. 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 November 10 (Wed), 2021. 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, November 18 (Thu), 2021.

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 December 9 (Thu), 2021.

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.

VI. Application Fee

Application fee: 10,000 yen

Payment period: From December 1 (Wed), 2021 to January 11 (Tue), 2022 JST

Only payments 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 VII 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 VII 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) with a designated payment request form by bank transfer with the following procedures. To obtain the form, please contact the GSB Student Affairs Section (*kyomu gakari*).

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.

VII. 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 (Original Copy)	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 (Original Copy)	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 (Original Copy)	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.

VIII. 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.

IX. Application Period

The application period is from December 20 (Mon), 2021 to January 11 (Tue), 2022 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 January 11 (Tue), 2022 JST.
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.

--- Attention ----------

1) If you are unable to submit a GRE General Test score or a TOEFL/IELTS score by January 11 (Tue), 2022 due to your local test schedule change concerning the COVID-19 coronavirus epidemic, later submissions will be accepted until January 28 (Fri), 2022.
In this case, please notify the Student Affairs Section of the Graduate School of Biostudies of your situation, no later than January 11 (Tue), 2022.

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 by January 11 (Tue), 2022 so that the copy can be substituted if your documents sent by post did not arrive in our office by the designated deadline.

X. Examination Schedules

January 17 (Mon), 2022 ~ January 21 (Fri), 2022	**Document Screening** Only successful applicants who pass the screening of the admission documents will be able to take the interview (Oral Examination).
January 26 (Wed), 2022	**Announcement of successful applicants in document screening**
February 3 (Thu), 2022 ~ February 14 (Mon), 2022	**Interview** (Oral Examination) The interview date and method* will be arranged individually after the decision is made. ***e.g. Skype or ZOOM or other protocols**

XI. Announcement of Final 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., February 24 (Thu), 2022. 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.

XII. 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 84 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 of enrollment procedures will be e-mailed to each successful applicant in late July, 2022 for those who would like to enroll in October, 2022. For those who will enroll in April, 2023, it will be informed in late January, 2023.
(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.

<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

September, 2021

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. and Toyoda, A. The use of a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide-based colorimetric assay in the viability analysis of the filamentous cyanobacterium *Arthrospira platensis*. ***Biosci. Biotechnol. Biochem.*** 85, 739-742 (2021). doi: 10.1093/bbb/zbaa050

Tadama, S. and Shiraishi, H. Growth of the edible microalga *Arthrospira platensis* in relation to boron supply. ***Int. J. GEOMATE***, 12, 90-95 (2017). doi: 10.21660/2017.30.2580

Shiraishi, H. Cryopreservation of the edible alkalophilic cyanobacterium *Arthrospira platensis*. ***Biosci. Biotechnol. Biochem*.** 80, 2051-2057 (2016). doi: 10.1080/09168451.2016.1189320

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). doi: 10.1080/09168451.2014.972333

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: MIYOSHI, Tomoichiro (Associate Prof.) <miyoshi.tomoichiro.5e@kyoto-u.ac.jp>

Outline of the research

Our laboratory is interested in understanding the dynamic interactions between transposable elements (TEs) and cellular host factors or environmental stress. In the human genome, Long Interspersed Element-1 (LINE-1 or L1) retrotransposons comprise ~17% of the genome and still mobilize autonomously, generating inter- or intra-genetic diversity, which contributes to genome evolution. However, LINE-1 insertion poses a threat to the genome integrity due to gene disruption associated with disease-causing mutations. Although LINE-1 and other TEs are known to be expressed in various cellular processes including early embryogenesis, tumor progression, and environmental stress responses, it remains unclear how the host factors restrict LINE-1 activity to minimize the risks, and how LINE-1s have evolved to evade the host defense system. Moreover, recent reports link aberrant LINE-1 expression with chronic activation of the innate immune response that contributes to inflammation, tumorigenesis, and aging with unknown mechanisms. To address these questions, we try to provide mechanistic insights into interactions between LINE-1 and the hosts by combining biochemical, genetic, and cytological approaches.

Publications

*Miyoshi T., Makino T., and *Moran J.V. Poly (ADP-ribose) polymerase 2 recruits replication protein A to sites of LINE-1 integration to facilitate retrotransposition. ***Mol. Cell*** 75: 1286-1298 (2019).

Kopera H.C., Flasch D.A., Nakamura M., Miyoshi T., Doucet A.J., and *Moran J.V. LEAP: L1 Element Amplification Protocol. ***Methods Mol. Biol.*** 1400: 339-355 (2016).

Doucet A.J., Wilusz J.E., Miyoshi T., Liu Y., and *Moran J.V. A 3' poly(A) tract is required for LINE-1 retrotransposition. ***Mol. Cell*** 60: 728-741 (2015).

Miyoshi T., Ito M., Kugou K., Yamada S., Furuichi M., Oda A., Yamada T., Hirota K., Masai H., and *Ohta K. A central coupler for recombination initiation linking chromosome architecture to S-phase checkpoint. ***Mol. Cell*** 47: 722-733 (2012). These authors equally contributed to this study.

Hirota K., Miyoshi T., Kugou K., Hoffman C.S., Shibata T., and *Ohta K. Stepwise chromatin remodelling by a cascade of transcription initiation of non-coding RNAs. ***Nature*** 456, 130-134 (2009).

Miyoshi T., Kanoh J., Saito M., and *Ishikawa F. Fission yeast Pot1-Tpp1 protects telomeres and regulates telomere length. ***Science*** 320: 1341-1344 (2008).

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

Key words: genome evolution, transposable elements, LINE-1, DNA repair, immune response

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 of host animals and symbiotic microorganisms 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
4. Learning from reproductive parasites: a comprehensive study of "male killing" caused by insect symbionts

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 using *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, single-cell analysis and multi-omics.

Publications (*: Faculties of the lab)

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*. and 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, optogenetics

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. Sex-determining gene and sex differentiation in haploids

Publications

Kohchi, T., Yamato, K.T., Ishizaki, K., Yamaoka, S., and Nishihama, R. Development and molecular genetics of Marchantia polymorpha. ***Annu. Rev. Plant Biol.*** 72: 19.1–19.26 (2021) doi: 10.1146/annurev-arplant-082520-094256.

Kato, H., Mutte, S. K., Suzuki, H., Crespo, I., Das, S., Radoeva, T., Fontana, M., Yoshitake, Y., Hainiwa, E., Berg, W., Lindhoud, S., Ishizaki, K., Hohlbein, J., Borst, J. W., Boer, D. R., Nishihama, R., Kohchi, T., and Weijers, D. Design principles of a minimal auxin response system. ***Nature Plants*** 6: 473-482 (2020). doi: 10.1038/s41477-020-0662-y

Hisanaga, T., Okahashi, K., Yamaoka, S., Kajiwara, T., Nishihama, R., Shimamura, M., Yamato, K. T., Bowman, J. L., Kohchi, T.,* and Nakajima, K.* A cis-acting bidirectional transcription switch controls sexual dimorphism in the liverwort. ***EMBO J.,*** 38: e100240 (2019). doi: 10.15252/embj.2018100240 *Co-corresponding authors

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

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, sex determination, *Marchantia polymorpha*

6) Laboratory of Molecular and Cellular Biology of Totipotency

PI: NAKANO, Takeshi (Prof.) <nakano.takeshi.6x@kyoto-u.ac.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.) <nagao.masaya.7e@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: YAMANO, Takashi (Associate Prof.) <tyamano@lif.kyoto-u.ac.jp>

Outline of the research
1. Molecular mechanisms of the environmental response of photosynthetic organisms.
2. Molecular mechanisms of the emergence and inheritance of phase-separated organelles.
3. Engineering of the phase-separated organelles for breaking through the limit of photosynthetic carbon fixation.

Photosynthetic carbon fixation is the starting point of the material cycle of the global ecosystem and also the turning point for the conversion of inorganic to organic materials. Therefore, it is crucial to understand the mechanisms that maintain the flexibility and robustness of photosynthetic activities in a fluctuating environment. Using the photosynthetic organism with phase-separated organelle as a model, we aim to understand the survival strategies of photosynthetic organisms in molecular terms with the help of molecular genetics, high-resolution real-time imaging, and multi-omics analyses. Our research will contribute to providing the genetic and molecular foundation for solving various problems that human beings face, such as environmental destruction and food shortage.

Publications
Toyokawa, C., Yamano, T., Fukuzawa, H. Pyrenoid starch sheath is required for LCIB localization and the CO_2-concentrating mechanism in green algae. ***Plant Physiol.*** 182: 1883–1893 (2020) doi: 10.1104/pp.19.01587.

Wang, L., Yamano, T., Takane, T., Niikawa, Y., Toyokawa, C., Ozawa, S., Tokutsu, R., Takahashi, Y., Minagawa, J., Kanesaki, Y., Yoshikawa, H., 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). doi: 10.1073/pnas.1606519113.

Yamano, T., Sato, E., Iguchi, H., Fukuda, Y., Fukuzawa, H. Characterization of cooperative bicarbonate uptake into chloroplast stroma in the green alga *Chlamydomonas reinhardtii*. ***Proc. Natl. Acad. Sci. USA*** 112: 7315–7320 (2015). doi: 10.1073/pnas.1501659112.

Yamano, T., Iguchi, H., Fukuzawa, H. Rapid transformation of *Chlamydomonas reinhardtii* without cell-wall removal. ***J Biosci Bioeng.*** 115: 691–694 (2013) doi: 10.1016/j.jbiosc.2012.12.020.

Yamano, T., Tsujikawa, T., Hatano, K., Ozawa, S., Takahashi, Y., Fukuzawa H. Light and low-CO_2 dependent LCIB/LCIC complex localization in the chloroplast supports the carbon-concentrating mechanism in *Chlamydomonas reinhardtii*. ***Plant Cell Physiol***. 51: 1453–1468 (2010). doi: 10.1093/pcp/pcq105.

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

Keywords: bioinformatics, multi-omics of photosynthetic organisms, photosynthesis, phase separation, pyrenoid, single cell observation, *Chlamydomonas reinhardtii*

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

Outline of the research
Outline of the research
Our aim is to decipher the molecular mechanism underlying the symbiotic evolutionary relationship between gut microbes and host, and to develop food-and health-oriented application research.

Publications

Yoshida K, Hirano R, Sakai Y, Choi MH, Sakanaka M, Kurihara S, Iino H, Xiao JZ, Katayama T, and and Odamaki T. Bifidobacterium response to lactulose ingestion in the gut relies on a solute-binding protein-dependent ABC transporter. ***Commun Biol.*** 4: 541 (2021).

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).

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, coevolution, enzyme

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

Yamaoka, S., Inoue, K., and Araki, T. Regulation of gametangia and gametangiophore initiation in the liverwort *Marchantia polymorpha*. ***Plant Reprod***. 34, published online, (2021). doi: 10.1007/s00497-021-00419-y

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

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

Key words: daylength response, 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 how various cellular processes are governed by nano-scale structures and interactions of biomolecules, as well as their macroscopic bulk behavior in cellular environments. We try to integrate such different hierarchies of biomolecular dynamics by using techniques in single-molecule live-cell imaging, biochemistry, biophysics and bioinformatics. Specific research topics include: (1) how endocytic process is orchestrated by membrane-bound proteins, cytoskeletal network and lipid bilayer, (2) how intracellular membrane-less organelle (nuclear pore complex, mitotic chromosome, nucleolus, etc.) are assembled/disassembled by post-translational modifications, and (3) how viral genome and proteins are assembled in a vast host cell-plasm.

Publications

W. Zhang, R. Watanabe, H.A. Konishi, T. Fujiwara, S.H. Yoshimura, and M. Kumeta “Redox-sensitive cysteines confer proximal control of the molecular crowding barrier in the nuclear pore.” ***Cell Rep.*** 33(11):108484 (2020) doi: 10.1016/j.celrep.2020.108484.

H. Yamazaki, H. Kosako and S.H. Yoshimura “Quantitative proteomics indicate a strong correlation of mitotic phospho-/dephosphorylation with non-structured regions of substrates.” ***Biochim. Biophys. Acta. Proteins Proteom.***,1868(1): 140295 (2020). doi: 10.1016/j.bbapap.2019.140295.

H.A. Konishi and S.H. Yoshimura “Interactions between non-structured domains of FG- and non FG-nucleoporins coordinate the ordered assembly of the nuclear pore complex in mitosis. ***FASEB J.***, 34(1): 1532-1545 (2020). doi: 10.1096/fj.201901669R.

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

M. Kumeta, H.A. Konishi, W. Zhang, S. Sakagami and S.H. Yoshimura “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.

H.A. Konishi, S. Asai, T. Watanabe and S.H. Yoshimura "*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.

O. Lolodi, H. Yamazaki, S. Otsuka, M. Kumeta and S.H. Yoshimura "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.

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

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

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

Fujishima, K., Kurisu, J., Yamada, M. and Kengaku, M. βIII spectrin controls the planarity of Purkinje cell dendrites by modulating perpendicular axon-dendrite interactions. ***Development*** 147(24):dev194530. (2020). doi: 10.1242/dev.194530. PMID: 33234719

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.*** 145(5): 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 (18): 3442-3455 (2012). doi: 10.1242/dev. 081315.

Website of the lab: https://kengaku.icems.kyoto-u.ac.jp/

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

Unwanted cells such as dead cells and senescent cells are normally eliminated from our body. Defects in removal during aging result in accumulation of unwanted cells, causing variety of diseases such as autoimmune diseases, cancer and

tissue dysfunction. For their clearance, dead cells expose phosphatidylserine (PS) as an "eat-me signal" to be engulfed by phagocytes. Previously, we identified the PS-exposing proteins called scramblase by cDNA library screening for the first time in the world. Recently, we also discovered their regulators by CRISPR screening. Because compartments (such as synapses) of living neurons are also eliminated by a PS-dependent manner, its molecular mechanism is currently one of our interests. Based on development of unbiased screening systems, *in vivo* screening using living mouse has been performed. Through understanding removal of unwanted cells, we will try to understand how human diseases occur and contribute to their treatment by providing the strategy for diagnosis and treatment.

Publications:

Maruoka M, Zhang P, Mori H, Imanishi E, Packwood DM, Harada H, Kosako H, and Suzuki J. Caspase cleavage releases a nuclear protein fragment that stimulates phospholipid scrambling at the plasma membrane. ***Mol Cell.*** 81(7):1397-1410.e9 (2021). doi: 10.1016/j.molcel.2021.02.025.

Gyobu S, Ishihara K, Suzuki J, Segawa K, Nagata S. Characterization of the scrambling domain of the TMEM16 family. ***Proc Natl Acad Sci U S A.*** 114(24):6274-6279. (2017) doi: 10.1073/pnas.1703391114.

Suzuki J, Imanishi E, Nagata S. Xkr8 phospholipid scrambling complex in apoptotic phosphatidylserine exposure. ***Proc Natl Acad Sci U S A.*** 113(34):9509-14. (2016) doi: 10.1073/pnas.1610403113.

Suzuki J, Denning DP, Imanishi E, Horvitz HR, Nagata S. Xk-related protein 8 and CED-8 promote phosphatidylserine exposure in apoptotic cells. ***Science.*** 341(6144):403-6. (2013) doi: 10.1126/science.1236758.

Suzuki J, Umeda M, Sims PJ, Nagata S. Calcium-dependent phospholipid scrambling by TMEM16F. ***Nature.*** 468(7325):834-8. (2010) doi: 10.1038/nature09583.

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

Key words: Removal, Lipid dynamics, Organelles, Compartments, Unbiased screening, Diseases

14) Laboratory of Multidisciplinary Biology

PI: TANIGUCHI, Yuichi (Prof.) <taniguchi.yuichi.8s@kyoto-u.ac.jp>

Outline of the research

We study on the working principle of the cell as a system comprised of vast numbers of species of bio-molecules such as genome, transcriptome and proteome. We aim at developing technologies with new concepts by integrating knowledge from multiple academic fields including genetics, cell biology, microscopic imaging, chemistry, physics, informatics, large-scale computing and artificial intelligence.

Publications

Ohno, M., Ando, T., Priest, D. G., Taniguchi, Y. "Hi-CO: 3D genome structure analysis with nucleosome resolution", ***Nature Protocols***, published online (2021). doi: 10.1038/s41596-021-00543-z

Kumar, V., Leclerc, S., Taniguchi, Y. "BHi-Cect: A top-down algorithm for identifying the multi-scale hierarchical structure of chromosomes", ***Nucleic Acids Research***, 48, e26 (2020). doi: 10.1093/nar/gkaa004

Ohno, M., Ando, T., Priest, D. G., Kumar, V., Yoshida, Y., Taniguchi, Y. "Sub-nucleosomal genome structure reveals distinct nucleosome folding motifs", ***Cell*** 176, 520-534 (2019). doi: 10.1016/j.cell.2018.12.014

Leclerc, S., Arntz, Y., Taniguchi, Y. "Extending single molecule imaging to proteome analysis by quantitation of fluorescent labeling homogeneity in complex protein samples", ***Bioconjugate Chemistry*** 29, 2541-2549 (2018). doi: 10.1021/acs.bioconjchem.8b00226

Taniguchi, Y., Choi, P. J., Li, G., Chen, H., Hearn, J., Babu, M., Emili, A. & Xie, X. S. "Quantifying E. coli proteome and transcriptome with single-molecule sensitivity in single cells", ***Science*** 329, 533-538 (2010). doi: 10.1126/science.1188308

Taniguchi, Y., Nishiyama, M., Ishii, Y. & Yanagida, T. "Entropy rectifies the Brownian steps of kinesin", ***Nature Chemical Biology*** 1, 342-347 (2005). doi: 10.1038/nchembio741

Website of the lab: https://www.taniguchi.icems.kyoto-u.ac.jp

Key words: multi-omics, microscopic imaging, biophysics, systems medicine, large-scale computing

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

Nakano M, Sugita Y, Kodera N, Miyamoto S, Muramoto Y, Wolf M, Noda T. Ultrastructure of influenza virus ribonucleoprotein complexes during viral RNA synthesis. ***Commun Biol.*** 9;4(1):858. (2021)

Noda T. Selective genome packaging mechanisms of influenza A viruses. ***Cold Spring Harb Perspect*** 11(7): a038497. (2021)

Takamatsu Y, Kolesnikova L, Schauflinger M, Noda T, Becker S. The integrity of the YxxL motif of Ebola virus VP24 is important for the transport of nucleocapsid-like structures and for the regulation of viral RNA synthesis. ***J Virol.*** 94(9): e02170-19. (2020)

Takamatsu Y, Krahling V, Kolesnikova L, Halwe S, Lier C, Baumeister S, Noda T, Biedenkopf N, Becker S. Serine-arginine protein kinase 1 regulates Ebola virus transcription. ***mBio*** 11(1): e02565-19. (2020)

Kuwahara T, Yamayoshi S, Noda T, Kawaoka Y. G protein pathway suppressor 1 promotes influenza virus polymerase activity by activating the NF-kB signaling pathway. ***mBio*** 10(6): e02867-19. 2019

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).

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)

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

"Why not watch individual protein molecules in action?" By using live-cell Single-Molecule Speckle (SiMS) microscopy and our original multi-target super-resolution microscopy IRIS, we are elucidating the gap between molecular and biological functions in mechanotransduction, cancer invasion, tissue and neural circuit remodeling. We are also visualizing real-time effects of anti-cancer drugs in hope of developing a new type of allosteric kinase activity modulators. "Seeing (or thinking) single-molecules is believing!"

Publications:

Higuchi, M., Ishiyama, K., Maruoka, M., Kanamori, R., Takaori-Kondo, A. and Watanabe, N. Paradoxical activation of c-Src as a drug-resistant mechanism. ***Cell Rep.*** 34: 108876 (2021). doi: 10.1016/j.celrep.2021.108876

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, actin, formin, mechanotransduction, super-resolution microscopy, cancer, neuron, tissue remodeling, target-based drugs

2) 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
Kawakita, M., Oyama, T., Shirai, I., Tanaka, S., Akaki, K., Abe, S., Asahi, T., Cui, G., Itoh, F., Sasaki, M., Shibata, N., Ikuta, K., Hatakeyama, T. and Takahara, K. (2021) Cell wall N-glycan of Candida albicans ameliorates early hyper- and late hypo-immunoreactivity in sepsis. ***Commun. Biol.*** DOI: 10.1038/s42003-021-01870-3

Cui G., Shimba A., Ma G, Takahara K., Tani-ichi S., Zhu Y., Asahi T., Abe A., Miyachi H., Kitano S., Hara T., Yasunaga J., Suwanai H., Yamada H., Matsuoka M., Ueki K., Yoshikai Y, and Ikuta K. IL-7R-dependent Phosphatidylinositol-3 Kinase Competes with STAT5 Signal to Modulate T Cell Development and Homeostasis. ***J. Immunol.*** 204, 844–857. (2020). doi: 10.4049/jimmunol.1900456

Goji, T., Takahara, K., Negishi, M. and 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

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

3) Laboratory of Molecular Cell Biology and Development (Collaboration lab in RIKEN, Kobe)
PI (1): KITAJIMA, Tomoya (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. Findings are exploited to investigate how aging causes egg aneuploidy.

Publications
Yoshida, S., Nishiyama, S., Lister, L., Hashimoto, S., Mishina, T., Courtois, A., Kyogoku, H., Abe, T., Shiraishi, A., Choudhary, M., Nakaoka, Y., Herbert, M. and Kitajima, T.S. Prc1-rich kinetochores are required for error-free acentrosomal spindle bipolarization during meiosis I in mouse oocytes. ***Nature Communications*** 11: 2652 (2020). doi: 10.1038/s41467-020-16488-y

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 kidney and the bladder. By precisely recapitulating the developmental processes of human urinary tract in the directed differentiation of human pluripotent stem cells, we are also aiming for the ultimate goal of generating a three-dimensional whole urinary tract 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

PI (3): WANG, Dan Ohtan (Associate Prof.) <ohtan@riken.jp>

Outline of the research

Building and maintaining neuronal networks and cognitive functions require mRNA localization and regulated protein synthesis in time and space. “RNA” and “Brain” are the two keywords of our research. Using dynamic synapses and their association with intellectual ability, memory, and susceptibility to neurological disorders as the conceptual framework, we are studying a novel RNA neuroepigenetic mechanism in the central nervous system regarding to synapse function. The outcome of this quest will allow us to understand the regulatory mechanisms of gene networks for experience-based behavioral changes and diseases, over our lifespan. Our research is embraced by current revolution in quantitative and omics technology, fluorescence imaging, and genetic animal model systems.

Publications

Tan L‡, Cheng W‡, Liu F, Wang DO, Cao N, Wang J*. Positive natural selection of N6-methylademosine on the RNAs of processed pseudogenes. ***Genome Biol*** 22: 180 (2021)

Joshi K*, Wang DO*. epidecodeR: a functional exploration tool for epigenetic and epitranscriptomic regulation. (2021) ***Bioconductor*** DOI: 10.18129/B9.bioc.epidecodeR

Yang X, Feng Y, Zhang Z, Wang H, Li W, Wang DO, Peng Y, Zheng J*. in vitro and in vivo evidence for RNA adduction resulting from metabolic activation of methyleugenol. (2020) ***J Agric Food Chem.*** 68, 51, 15134-15141

Wang DO*. RNA modifications in the central nervous system. ***Oxford Handbook on Neuronal Protein synthesis.*** (DOI:10.1093/oxfordhb/9780190686307.013.23)

Wang DO*. Mapping m6A and m1A with mutational signatures. (2019) ***Nat Methods.*** DOI:10.1038/s41592-019-0636-z.

Merkurjev D, Hong WT, Iida K, Goldie BJ, Yamaguti H, Oomoto I, Ohara T, Kawaguchi S, Hirano T, Martin KC, Pellegrini M, Wang DO*. Synaptic N6 methyladenosine (m6A) reveals functional partitioning of localized transcripts. (2018) ***Nat Neurosci,*** 21, 1004–1014

Wang DO, Kim SM, Zhao Y, Hwang HG, Miura SK, Sossin WS, and Martin KC*. Synapse- and stimulus-specific local translation during long-term neuronal plasticity. (2009) ***Science.*** 324(5934): 1536-40.

Website of the lab: https://www.bdr.riken.jp/en/research/labs/wang-do/index.html

Key words: RNA, brain, neuron, synapse, microtubule

PI (4): OBATA, Fumiaki (Associate Prof.) <fumiaki.obata@riken.jp>

Outline of the research
Nutrition and gut microbiota are vital players for organismal homeostasis and therefore influence our healthspan. Diet contributes to metabolic and physiological homeostasis by altering nutritional balance and gut microbiota, however our understanding of the molecular mechanism is far from complete. Our laboratory studies the functions of each nutrient and gut bacterial species using a model organism Drosophila melanogaster. We also aim to elucidate mechanistically how early-life diet alters life-long health. Our goal is to reveal evolutionally-conserved "dietological" mechanisms that govern organismal ageing and lifespan.

Publications
Yamauchi T, Oi A, Kosakamoto H, Akuzawa-Tokita Y, Murakami T, Mori H, Miura M and *Obata F. Gut Bacterial Species Distinctively Impact Host Purine Metabolites during Aging in Drosophila. ***iScience*** 23, 101477, (2020)

Kosakamoto H, Yamauchi T, Akuzawa-Tokita Y, Nishimura K, Soga T, Murakami T, Mori H, Yamamoto K, Miyazaki R, Koto A, *Miura M, *Obata F. Local Necrotic Cells Trigger Systemic Immune Activation via Gut Microbiome Dysbiosis in Drosophila. ***Cell Reports*** 32, 107938, (2020)

Obata F, Tsuda-Sakurai K, Yamazaki T, Nishio R, Nishimura K, Kimura M, Funakoshi M, *Miura M. Nutritional control of stem cell division through S-adenosylmethionine in Drosophila intestine. ***Developmental Cell*** 44, 741-751, (2018)

Obata F, Fons CO, *Gould AP. Early-life exposure to low-dose oxidants can increase longevity via microbiome remodelling in Drosophila. ***Nature Communications*** 9, 975, (2018)

Obata F, *Miura M. Enhancing S-adenosyl-methionine catabolism extends Drosophila lifespan. ***Nature Communications*** 6, 8332, (2015)

Website of the lab: https://www.bdr.riken.jp/en/research/labs/obata-f/index.html

Key words: Nutrition, Microbiota, Metabolism, Ageing, Drosophila

4) Laboratory of Molecular Neurobiology
PI: KIMURA, Ikuo (Prof.) <ikimura@cc.tuat.ac.jp >

Outline of the research
1. Dietary signaling via nutrient-sensing receptors and metabolic syndrome
2. Non-genomic effects via sex steroid hormone receptors and neurological disorder

Publications
Kimura I*, Miyamoto J, Ohue-Kitano R, Watanabe K, Yamada T, Onuki M, Aoki R, Isobe Y, Kashihara D, Inoue D, Inaba A, Takamura Y, Taira S, Kumaki S, Watanabe M, Ito M, Nakagawa F, Irie J, Kakuta H, Shinohara M, Iwatsuki K, Tsujimoto G, Ohno H, Arita M, Itoh H, Hase K. Maternal gut microbiota in pregnancy influences offspring metabolic phenotype in mice. ***Science.*** 367, eaaw8429 (2020).

Kimura I*, Ichimura A, Ohue-Kitano R, Igarashi M. Free Fatty Acid Receptors in Health and Disease. ***Physiol Rev.*** 100, 171-210 (2020).

Miyamoto J, Ohue-Kitano R, Mukouyama H, Nishida A, Watanabe K, Igarashi M, Irie J, Tsujimoto G, Satoh-Asahara N, Itoh H, Kimura I*. Ketone body receptor GPR43 regulates lipid metabolism under ketogenic condition. ***Proc Natl Acad Sci U S A.*** 116, 23813-23821 (2019).

Miyamoto J, Igarashi M, Watanabe K, Karaki SI, Mukouyama H, Kishino S, Li X, Ichimura A, Irie J, Sugimoto Y, Mizutani T, Sugawara T, Ogawa J, Drucker DJ. Arita M, Itoh H, Kimura I*. Gut microbiota confers host resistance to obesity by metabolizing dietary polyunsaturated fatty acids. ***Nature Commun.*** 10, 4007 (2019).

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

Key words: Endocrinology, GPCR, Fatty Acid, Steroid Hormone, Energy Metabolism

5) 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
4. Cellular senescence and aging

Publications

Enomoto, M., Takemoto, D., and Igaki, T. Interaction between Ras and Src clones causes interdependent tumor malignancy via Notch signaling in *Drosophila*. ***Dev Cell*** in press

Ito, T. and Igaki, T. Yorkie drives Ras-induced tumor progression by microRNA-mediated inhibition of cellular senescence. ***Sci Signal*** 14: eaaz3578 (2021)

Sanaki, Y., Nagata, R., Kizawa, D., Leopold, P., and Igaki, T. Hyperinsulinemia drives epithelial tumorigenesis by abrogating cell competition. ***Dev Cell*** 53: 379-389 (2020)

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

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)

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

Key words: cell-cell communication, cancer, cell competition, cellular senescence, aging, *Drosophila*

6) 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 chromosomes, the carriers of genetic information, are correctly maintained and passed on through generations. Combining molecular genetic approaches with advanced microscopy and quantitative imaging, we focus on elucidating mechanisms of chromosome pairing, recombination, and segregation in meiosis in the nematode *C. elegans*.

Publications
Kafer, G. R., Tanaka, Y., Rillo-Bohn, R., Shimizu, E., Hasegawa, K. & Carlton, P. M. Sequential peripheral enrichment of H2A.Zac and H3K9me2 during trophoblast differentiation in human embryonic stem cells. ***J. Cell Sci.*** **133,** (2020). doi:10.1242/jcs.245282.

Sato-Carlton, A., Nakamura-Tabuchi, C., Li, X., Boog, H., Lehmer, M. K., Rosenberg, S. C., Barroso, C., Martinez-Perez, E., Corbett, K. D. & Carlton, P. M. Phosphoregulation of HORMA domain protein HIM-3 promotes asymmetric synaptonemal complex disassembly in meiotic prophase in Caenorhabditis elegans. ***PLoS Genet.*** **16,** e1008968 (2020). doi:10.1371/journal.pgen.1008968

Nono, M., Kishimoto, S., Sato-Carlton, A., Carlton, P. M., Nishida, E. & Uno, M. Intestine-to-Germline Transmission of Epigenetic Information Intergenerationally Ensures Systemic Stress Resistance in C. elegans. ***Cell Rep.*** **30,** 3207–3217.e4 (2020). doi:10.1016/j.celrep.2020.02.050

Takemoto, K., Imai, Y., Saito, K., Kawasaki, T., Carlton, P. M., Ishiguro, K.-I. & Sakai, N. Sycp2 is essential for synaptonemal complex assembly, early meiotic recombination and homologous pairing in zebrafish spermatocytes. ***PLoS Genet.*** **16,** e1008640 (2020). doi:10.1371/journal.pgen.1008640

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

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: Meiosis, Chromosome segregation, C. elegans, super-resolution microscopy

7) 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., Nagasaki, C.S., Suzuki, Y., Hirano, Y. and *Imayoshi, I. (2020) Optimization of light-inducible Gal4/UAS gene expression system in mammalian cells. ***IScience*** 23, 101506, September 25, 2020. https://doi.org/10.1016/j.isci.2020.101506

Imayoshi, I., Tabuchi, S., Matsumoto, M., Kitano, S., Miyachi, H., *Kageyama, R. and Yamanaka, A. (2020) Light-induced silencing of neural activity in Rosa26 knock-in and BAC transgenic mice conditionally expressing the microbial halorhodopsin eNpHR3. ***Sci Rep.***, 10(1):3191. doi: 10.1038/s41598-020-59984-3.

Yamada, M., Nagasaki, C.S., Ozawa, T. and Imayoshi, I. (2020) Light-mediated control of gene expression in mammalian cells. Neurosci Res., 152:66-77. doi: 10.1016/j.neures.2019.12.018.

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).

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

8) 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

9) 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 host-virus co-evolution is also focused on this laboratory.

Publications
Yanai M et al., ADAR2 is involved in self and nonself recognition of Borna disease virus genomic RNA in the nucleus. ***J Virol*** 94(6):e01513-19 (2020) doi: 10.1128/JVI.01513-19

Kojima S et al., Splicing-dependent subcellular targeting of Borna disease virus nucleoprotein isoforms. ***J Virol*** 93(5) e01621-1618 (2019) doi: 10.1128/JVI.01621-18.

Sofuku K et al., Transcription profiling demonstrates epigenetic control of non-retroviral RNA virus-derived elements in the human genome. ***Cell Rep*** 12:1548-1554 (2015) doi: 10.1016/j.celrep.2015.08.007.

Fujino K et al., Inhibition of Borna disease virus replication by an endogenous bornavirus-like element in the ground squirrel genome. ***Proc Natl Acad Sci USA*** 111:13175-13180 (2014). doi: 10.1073/pnas.1407046111

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

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

Publications

Ichijo R, Kabata M, Kidoya H, Muramatsu F, Ishibashi R, Abe K, Tsutsui K, Kubo H, Iizuka Y, Kitano S, Miyachi H, Kubota Y, Fujiwara H, Sada A, Yamamoto T, Toyoshima F. Vasculature-driven stem cell population coordinates tissue scaling in dynamic organs. ***Sci. Adv.*** 7, ea2575 (2021). doi: 10.1126/sciadv.abd2575.

Ishibashi R, Abe K, Ido N, Kitano S, Miyachi H, Toyoshima F. Genome editing with the donor plasmid equipped with synthetic crRNA-target sequence. ***Sci. Rep.*** 10, 14120 (2020) doi: 10.1038/s41598-020-70804-6

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
(2015).

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: https://www2.infront.kyoto-u.ac.jp/Toyoshima-HP/index-En.html

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

11) 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

Kameo, Y., Miya, Y., Hayashi, M., Nakashima, T., Adachi, T. In silico experiments of bone remodelling explores metabolic diseases and their drug treatment. ***Sci. Adv.,*** 6-10: eaax0938 (2020). doi: 10.1126/sciadv.aax0938

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

Ando, Y., Okeyo, K. O., Adachi, T. Modulation of adhesion microenvironment using mesh substrates triggers self-organization and primordial germ cell-like differentiation in mouse ES cells. ***APL Bioeng,*** 3: 016102 (2019). doi: 10.1063/1.5072761

Maki, K., Han, S. W., Hirano, Y., Yonemura, S., Hakoshima, T., Adachi, T. Real-time TIRF observation of vinculin recruitment to stretched α-catenin by AFM. ***Sci Rep,*** 8: 1575 (2018). doi: 10.1038/s41598-018-20115-8

Okuda S., Takata, N., Hasegawa, Y., Kawada, M., Inoue, Y., Adachi, T., Sasai, Y., Eiraku, M. Strain-triggered mechanical feedback in self-organizing optic cup morphogenesis. ***Sci. Adv.*** 4-11: eaau1354 (2018). doi: 10.1126/sciadv.aau1354

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

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