2025 - 2026
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 an assessment of the applicant's ability to think logically in English, which is required for international communication; a presentation of the applicant's research findings during their master's program or elsewhere; and an oral exam to assess the applicant's judgement, thinking ability, communication skills, initiative, and ethical perspective. Admissions decisions will be made based on the applicant's overall performance on these exams.

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

The academic year starts on **October 1, 2025** or **April 1, 2026**.

I. "Global Frontier in Life Science"

The Graduate School of Biostudies offers "Global Frontier in Life Science", an educational program for Doctoral and Master's students. 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 40 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 after completing the AAO process (see below).**

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.

Through the AAO process, you may contact the professor(s) 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.

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

IV-1. Eligibility Requirements for Applicants expecting to start from October 1, 2025

Only persons currently falling into one of the following categories, or anticipated to do so as of September 30, 2025, 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 Kyoto University 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 Kyoto 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 Kyoto 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 of Biostudies 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 of Biostudies 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 of Biostudies 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, 2026

Only persons currently falling into one of the following categories, or anticipated to do so as of March 31, 2026, 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 Kyoto University 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 Kyoto 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 of Biostudies 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 of Biostudies 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 of Biostudies 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 6 (Wed), 2024**. The documents below must be submitted to the Student Affairs Section (*kyomu gakari*) of the Graduate School of Biostudies (150kyomu@adm.lif.kyoto-u.ac.jp) via email by **JST 5:00 pm, November 14 (Thu), 2024 at the latest**. 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 12 (Thu), 2024**.

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(s) of a program equivalent to a master's program which the applicant has Completed	Please submit the original of the documents

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(s)	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, 2023, 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 JST December 16 (Mon), 2024 to January 8 (Wed), 2025**

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/

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/

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. (In the event that the applicant's name is not found in the payment record, his/her application shall not be accepted.)
(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 and make the form with PC. (Please provide your original handwritten signature in black ink on the printed sheet.)**. 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 and make the form with PC. 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(s) (Required: Printed 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 expected completion for Master's degree (Required: Printed 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 for Bachelor's degree (Required: Printed Original Copy)	Submit a printer original copy of your graduation certificate (e.g., diploma) prepared by the university or faculty you have graduated from.
(7) Recommendation letters (Required: Printed Original Copy) **Note:** If the letter is confidentially enclosed in an envelope, please send it to GSB by one of the following methods: 1) By post directly sending from the referee 2) By post sending with your application documents	**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 official score report for IELTS or TOEFL*	Unnecessary for English-native speakers (Please contact the Student Affairs Section in advance. English-native speakers are required to submit its certificate or official documents.) *IELTS: Kyoto University does not have a code. Please request ETS to send your valid score to the GSB Student Affairs Section directly or send it along with the set of your application documents to us. *TOEFL DI Code: 9501 *If you are not an English-native speaker but graduated from a university in an English-speaking country (USA, Canada, UK, Australia, and New Zealand), you are still required to submit an official test score of IELTS or TOEFL.
(9) Evidence of Application Fee Payment **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 of Biostudies while taking administrative leave from their organization need to submit the form provided indicating approval for applying 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 entrance examinations. The application approval form will be provided upon request. Use the designated forms.
(11) Address for further communication	For further communication on the examination results and the enrollment procedures, clearly write your name, address, and postcode 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 Documents 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 JST December 16 (Mon), 2024 to January 8 (Wed), 2025**.
When submitting in person: office hours are 9:00 a.m. – 12:00 p.m. and 1:00 p.m. – 5:00 p.m.
When sending the application documents by post, ensure that the application documents are delivered by **JST January 8 (Wed), 2025**.

Note that the admission application form will not be accepted if the payment 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 ----------

Before enclosing your application documents, please make a scanned copy (pdf) of them and send it to the Student Affairs Section (150kyomu@adm.lif.kyoto-u.ac.jp) via email by JST 5:00 p.m. January 8 (Wed), 2025 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 20 (Mon), 2025 ~ January 24 (Fri), 2025	**Document Screening** Only successful applicants who pass the screening of the admission documents will be able to take the interview (Oral Examination).
January 29 (Wed), 2025	**Announcement of successful applicants in document screening**
February 10 (Mon), 2025 ~ March 4 (Tue), 2025	**Interview** (Oral Examination) The interview date and method* will be arranged individually after the decision is made. ***e.g., 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 JST 5:00 p.m., **March 28 (Fri), 2025**. 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 110-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, 2025 for those who would like to enroll in October, 2025. For those who will enroll in April, 2026, it will be informed in late January, 2026.
(4) Applicants with physical disabilities (degree of physical disability as stipulated in the enforcement ordinance of the School Education Law) who require special arrangements for taking examinations or attending courses should immediately contact the Student Affairs Section (*kyomu gakari*).

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

<Where to send your application, and Inquiries>

Student Affairs Section (*kyomu gakari*) of the Graduate School of Biostudies, Kyoto University
Yoshida-Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan
E-mail: 150kyomu@adm.lif.kyoto-u.ac.jp

September, 2024

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

Global Frontier in Life Science Doctoral Degree Program
Research Fields and Contents of Research
(As of September 1, 2024)

Division of Integrated Life Science

1) Laboratory of Cell Cycle Regulation

PI: AOKI, Kazuhiro (Professor) <aoki.kazuhiro.6v@kyoto-u.ac.jp>

Outline of the research

We are interested in the mechanisms underlying cellular fate decisions; how cells maintain homeostasis by sensing external stimuli and processing information, ultimately leading to distinct phenotypes. The past few decades have illuminated the genes and pathways that constitute intracellular signal transduction, providing us with a comprehensive network overview. Yet, many questions remain elusive. We seek to unravel the mechanisms of how cells acquire information from a noisy environment, to what extent the cells recognize various ligand information (types, concentrations, combinations, physical constrains, etc.), and when and how cell fate such as cell division, differentiation, and apoptosis is determined. We employ cultured cells, fission yeast, and nematodes as our tools, and we're dedicated to pioneering new technologies, such as fluorescence imaging and optogenetics, to advance our understanding. Our research revolves around three core themes:

1. Understanding the Encoding Mechanisms in Cell Signaling: We explore how and to what extent cells sense and process external cues, digging into the mechanisms of information processing within the cell.
2. Understanding the Decoding Mechanisms in Cell Fate Decision-Makings: We investigate when and how cells make cell fate decisions such as cell proliferation, differentiation, and apoptosis by the information encoded from the intracellular signal transduction.
3. Building a whole cell model of eukaryotic cells: Our goal is to integrate all available experimental and computational data - cell signaling, metabolism, DNA replication, gene expression, etc. - into one model, building a whole-cell model of eukaryotic cells.

Publications

Sugiyama H, Goto Y, Kondo Y, Coudreuse D, Aoki K. Live-cell imaging defines a threshold in CDK activity at the G2/M transition. ***Developmental Cell***, 59, 545-557 (2024). doi: 10.1016/j.devcel.2023.12.014

Sakai K, Kondo Y, Goto Y, Aoki K. Cytoplasmic fluidization contributes breaking spore dormancy in fission yeast. ***Proc Natl Acad Sci U S A.***, 121, e2405553121 (2024). doi: https://doi.org/10.1073/pnas.2405553121

Yamamoto K, Miura H, Ishida M, Mii Y, Kinoshita N, Takada S, Ueno N, Sawai S, Kondo Y, and Aoki K. Optogenetic relaxation of actomyosin contractility uncovers mechanistic roles of cortical tension during cytokinesis. ***Nature Communications***, 12, 1–13 (2021). doi:10. 1038/s41467-021-27458-3

Miura H, Kondo Y, Matsuda M, and Aoki K. Cell-to-cell heterogeneity in p38-mediated cross-inhibition of JNK causes stochastic cell death. ***Cell Reports***, 24, 2658-2668 (2018). doi: 10.1016/j.celrep.2018.08.020

Aoki K, Kondo Y, Naoki H, Hiratsuka T, Itoh RE, and Matsuda M. Propagating Wave of ERK Activation Orients Collective Cell Migration. ***Developmental Cell***, 43, 305–317 (2017). doi: 10.1016/j.devcel.2017.10.016

Website of the lab: https://sites.google.com/nibb.ac.jp/qbio/home

Key words: Live cell imaging; cell fate decision-making; optogenetics; whole cell modeling

2) Laboratory of Cell Recognition and Pattern Formation
PI: USUI, Tadao (Senior Lecturer) <usui.tadao.3c@kyoto-u.ac.jp>

Outline of the research

1. Behavioral neurobiology: elucidating the neuromodulation mechanisms of predation avoidance behaviors in the external and internal state-dependent manner
2. Nutri-developmental biology: uncovering the adaptive systems to nutritional environments and the role of microbes supporting animal growth

We are interested in mechanisms that control animal development and behaviors in response to two categories of environmental inputs: nutrition and sensory stimuli. Using *Drosophila* somatosensory neurons, we are dissecting the modulation mechanisms of predation avoidance behaviors in an environment-dependent manner. We aim to unravel adaptive mechanisms to nutritional environments using *Drosophila* species, as well as *Drosophila*-associated yeasts and bacteria. To conduct these studies, we make full use of molecular, optogenetic, and electrophysiological approaches, functional imaging, and multi-omics techniques.

Publications

Kurio M., Tsukasa Y., Uemura T., Usui T. Refinement of a technique for collecting and evaluating the osmolality of haemolymph from *Drosophila* larvae, ***Journal of Experimental Biology***, 227(9):1-6. (2024)

Li, K., Tsukasa, Y., Kurio, M., Maeta, K., Tsumadori, A., Baba, S., Nishimura, R., Murakami, A., Onodera, K., Morimoto, K., Uemura, T., and Usui, T. Belly roll, a GPI-anchored Ly6 protein, regulates *Drosophila melanogaster* escape behaviors by modulating the excitability of nociceptive peptidergic interneurons. ***eLife***, 12:e83856 (2023).

Mure, A., Sugiura, Y., Maeda, R., Honda, K., Sakurai, N., Takahashi, Y., Watada, M., Katoh, T., Gotoh, A., Gotoh, Y., Taniguchi, I., Nakamura, K., Hayashi, T., Katayama, T., Uemura, T., Hattori, Y. Identification of key yeast species and microbe–microbe interactions impacting larval growth of *Drosophila* in the wild. ***eLife***, 12, RP90148 (2023).

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

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

Key words: animal development, nutrition, behavioral neurobiology, symbiotic microorganisms, morphogenesis, multi-omics, optogenetics, functional imaging

3) 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

Suzuki, H., Kato, H., Iwano, M., Nishihama, R., and Kohchi, T. Auxin signaling is essential for organogenesis but not for cell survival in the liverwort *Marchantia polymorpha*. ***Plant Cell* 35**, 1058-1075 (2023). doi: 10.1093/plcell/koac367.

Iwasaki, M., Kajiwara, T., Yasui, Y., Yoshitake, Y., Miyazaki, M., Kawamura, S., Suetsugu, N., Nishihama, R., Yamaoka,

S., Wanke, D., Hashimoto, K., Kuchitsu, K., Montgomery, S. A., Singh, S., Tanizawa, Y., Yagura, M., Mochizuki, T., Sakamoto. M., Nakamura, Y., Liu, C., Berger, F., Yamato, K. T., Bowman, J. L., and Kohchi T. Identification of the sex-determining factor in the liverwort Marchantia polymorpha reveals unique evolution of sex chromosomes in a haploid system. ***Curr. Biol.*** 31:5522-5532.e7. (2021) doi: 10.1016/j.cub.2021.10.023.

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.

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

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*

4) Laboratory of Plant Chemical Biology

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

Tachibana, R., Abe, S., Marugami, M., Yamagami, A., Akema, R., Ohashi, T., Nishida, K., Nosaki, S., Miyakawa, T., Tanokura, M., Kim, J., Seki, M., Inaba, T., Matsui, M., Ifuku, K., Kushiro, T., Asami, T., Nakano, T. BPG4 regulates chloroplast development and homeostasis by suppressing GLK transcription factors and involving light and brassinosteroid signaling. ***Nature Communications.*** 15, Article number:370 (2024)

Nosaki, S., Mitsuda, N., Sakamoto, S., Kusubayashi, K., Yamagami, A., Xu, Y., Bao, T., Bui, C., Terada, T., Miura, K., Nakano, T., Tanokura, M., Miyakawa, T. Brassinosteroid-induced gene repression requires specific and tight promoter binding of BIL1/BZR1 via DNA shape readout. ***Nature Plants***, 8(12), 1440–1452. (2022). DOI: 10.1038/s41477-022-01289-6

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.

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: https://plantchembio.lif.kyoto-u.ac.jp/

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

5) Laboratory of Biosignals and Response
PI: KAMBE, Taiho (Associate Prof.) kambe.taiho.7z@kyoto-u.ac.jp

Outline of the research
1. Understanding the regulatory mechanisms of zinc homeostasis
2. Elucidation of the metalation process in metalloenzyme activation
3. Improving zinc nutrition by focusing on zinc absorption mechanism

Publications
Yuasa, H., Morino, N., Wagatsuma, T., Munekane, M., Ueda, S., Matsunaga, M., Uchida, Y., Katayama, T., Katoh, T., Kambe, T. ZNT5-6 and ZNT7 have an integral role in protein N-glycosylation through supplying Zn^{2+} to Golgi α-mannosidase II. ***J Biol Chem***, 300, 107378, (2024). doi: 10.1016/j.jbc.2024.107378

Nishito, Y., Kamimura, Y., Nagamatsu, S., Yamamoto, N., Yasui, H., Kambe, T. Zinc and manganese homeostasis closely interact in mammalian cells. ***FASEB J***, 38, e23605 (2024). doi: 10.1096/fj.202400181R

Wagatsuma, T., Suzuki, E., Shiotsu, M., Sogo, A., Nishito, Y., Ando, H., Hashimoto, H., Petris, MJ., Kinoshita, M., Kambe, T. Pigmentation and TYRP1 expression are mediated by zinc through the early secretory pathway-resident ZNT proteins. ***Commun Biol***, 6, 403 (2023). doi: 10.1038/s42003-023-04640-5

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

Key words: Trace element, Transporter, Enzyme, Homeostasis, Zinc nutrition

6) Laboratory of Molecular Biology of Bioresponse
PI: KATAYAMA, Takane (Prof.) <takane@lif.kyoto-u.ac.jp>
Outline of the research Our aim is to decipher the molecular mechanism underlying the symbiotic evolutionary relationship between gut microbes and host from a viewpoint of microbial enzymology, and to develop food-and health-oriented application research.

Publications
Katoh T, Yamada C, Wallace MD, Yoshida A, Gotoh A, Arai M, Maeshibu T, Kashima T, Hagenbeek A, Ojima MN, Takada H, Sakanaka M, Shimizu H, Nishiyama K, Ashida H, Hirose J, Suarez-Diez M, Nishiyama M, Kimura I, Stubbs KA, Fushinobu S, and Katayama T. A bacterial sulfoglycosidase highlights mucin *O*-glycan breakdown in the gut ecosystem. ***Nat. Chem. Biol.*** 19:778-789 (2023). PMID: 36864192.

Ojima MN, Jiang L, Arzamasov AA, Yoshida K, Odamaki T, Xiao J-Z, Nakajima A, Kitaoka M, Hirose J, Urashima T, Katoh T, Gotoh A, van Sinderen D, Rodionov DA, Osterman AL, Sakanaka M, and Katayama T. Priority effects shape the structure of infant-type *Bifidobacterium* communities on human milk oligosaccharides. ***ISME J***. 16:2265-2279 (2022). PMID: 35768643.

Arzamasov A, Nakajima A, Sakanaka M, Ojima M, Katayama T, Rodionov D, and Osterman A. Human milk oligosaccharide utilization in intestinal bifidobacteria is governed by a global transcriptional regulator NagR.

mSystems 7:e0034322 (2022). PMID: 36094076.

Ojima MN, Yoshida K, Sakanaka M, Jiang L, Odamaki T, and Katayama T. Ecological and molecular perspectives on responders and non-responders to probiotics and prebiotics. ***Curr. Opin. Biotechnol.*** 73:108-120 (2022). PMID: 34375845.

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). PMID: 31489370.

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

Key words: gut microbes, symbiosis, coevolution, enzyme

7) 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

8) Laboratory of Ecosystems and Coevolution

PI: TOJU, Hirokazu (Prof.) <toju.hirokazu.4c@kyoto-u.ac.jp>

Outline of the research

Throughout its four-billion-year evolution, life has expanded into diverse environments. In the history of life, symbiosis has brought about innovations, resulting in explosive evolution and species diversification in new environments. We aim to understand how interactions between species have organized ecosystems on the Earth. Combining fieldwork in natural ecosystems with genomics and information science, we will decipher the driving principles of life systems at the population, community, and ecosystem levels from phenomena at the molecular and cellular levels.

Main themes:

- Roles of microbiomes in environmental adaptations of plants
- Coevolutionary history of land plants and mycorrhizal/endophytic symbionts
- Effects of aquatic/gut microbiomes on fish's physiology and ecology
- Coevolution of invertebrates and their symbionts/parasites
- Multistability and temporal dynamics of ecosystems

Publications

Toju H, Suzuki SS, Baba YG. (2024) Dynamics of interaction networks and species' contributions to community-scale flexibility. ***PNAS Nexus*** 3: page047 https://doi.org/10.1038/s41586-024-07658-9

Hayashi, Fujita H, Toju H (2024) Deterministic and stochastic processes generating alternative states of microbiomes. ***ISME Communications*** 4: ycae007 https://www.kyoto-u.ac.jp/ja/research-news/2024-02-29-0

Suzuki SS, Baba YG, Toju H. Dynamics of species-rich predator–prey networks and seasonal alternations of core species. ***Nature Ecology & Evolution*** 7:1432-1443 (2023) https://doi.org/10.1038/s41559-023-02130-9

Fujita H, Ushio M, Suzuki K, Abe MS, Yamamichi Y, Iwayama K, Canarini A, Hayashi I, Fukushima K, Fukuda S, Kiers ET, Toju H. Alternative stable states, nonlinear behavior, and predictability of microbiome dynamics. ***Microbiome*** 11:63 (2023) https://doi.org/10.1186/s40168-023-01474-5

Yajima D, Fujita H, Hayashi I, Shima G, Suzuki K, Toju H. Core species and interactions prominent in fish-associated microbiome dynamics. ***Microbiome*** 11:53 (2023) https://doi.org/10.1186/s40168-023-01498-x

Toju H, Peay KG, Yamamichi M, Narisawa K, Hiruma K, Naito K, Fukuda S, Ushio M, Nakaoka S, Onoda Y, Yoshida K, Schlaeppi K, Bai Y, Sugiura R, Ichihashi Y, Minamisawa K, Kiers ET. Core microbiomes for sustainable agroecosystems. ***Nature Plants*** 4:247-257 (2018) https://doi.org/10.1038/s41477-018-0139-4

Toju H, Yamamichi M, Guimarães PR Jr, Olesen JM, Mougi A, Yoshida T, Thompson JN (2017) Species-rich

networks and eco-evolutionary synthesis at the metacommunity level. ***Nature Ecology & Evolution*** 1:0024. http://www.nature.com/articles/s41559-016-0024

Website of the lab: https://sites.google.com/view/tojulab

Key words: Coevolution, Biodiversity, Ecosystem functions, Informatics, Microbiomes

9) 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 post-translational modifications regulate liquid-liquid phase separation of cellular proteins and dynamics of intracellular membrane-less organelles (nucleolus, nuclear pore complex, mitotic chromosome, etc.), (2) how endomembrane system (endoplasmic reticulum, nuclear envelope and mitochondria) is shaped and deformed by membrane-bound proteins and mechanical forces generated by cytoskeletal filaments, and (3) how viral proteins interact with host proteins to escape from host innate immune system and replicate viral particles.

Publications

Y. Yu and *S.H. Yoshimura “Self-assembly of CIP4 drives actin-mediated asymmetric pit-closing in clathrin-mediated endocytosis” ***Nat. Commun.***, 14, 4602 (2023). doi: 10.1038/s41467-023-40390-y.

H. Yamazaki, M. Takagi, H. Kosako, T. Hirano and *S.H. Yoshimura “Cell cycle-specific phase separation regulated by protein charge blockiness.” ***Nat. Cell Biol.*** 24(5): 625-632 (2022). doi: 10.1038/s41556-022-00903-1.

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.

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.

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, bioinformatics, innate immune system, retroviruses, atomic force microscopy

10) 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 brain development with special focuses on neuronal migration and dendrite patterning. To this end, we use multidisciplinary approach including molecular and cellular biology, high- and super-resolution microscopy, next generation sequencing and mechanobiology. We also aim to develop live-imaging techniques for observation of molecular signals controlling cell motility in the developing brain. Please visit our lab website for details.

Publications

Hatsuda, A., Kurisu, J., Fujishima, K., Kawaguchi, A., Ohno, N. and Kengaku, M. Calcium signals tune AMPK activity and mitochondrial homeostasis in dendrites of developing neurons. ***Development***, 150(21): dev201930. (2023). doi: 10.1242/dev.201930.

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.

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.

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

Key words: brain development, cell migration, dendrites, organelle transport, neural circuit formation

11) Laboratory of Biochemical Cell Dynamics
PI: SUZUKI, Jun (Prof.) <jsuzuki@icems.kyoto-u.ac.jp>

Outline of the research
The fundamental property of cells lies in their ability to establish an asymmetrical distribution of molecules across membranes and swiftly alter this distribution in response to environmental changes. Notably, this asymmetry extends beyond ions to encompass lipids consisting of membranes, undergoing rapid changes to oversee a range of vital biological processes. These processes include the elimination of unwanted cells and synapses, cell fusion, viral infections, hemostasis, autophagy and more. Importantly, defects in lipid scrambling give rise to various human diseases. Despite the acknowledged significance of lipid scrambling, the molecular identities of the proteins responsible for regulating this process, known as scramblases, remained elusive for decades. Our groundbreaking identification of the inaugural scramblase through cDNA library screening marked a pivotal moment. Subsequently, our research has expanded to comprehend the molecular mechanisms underpinning lipid scrambling and its diverse physiological roles. This expansion has involved the development of unbiased screening methodologies, utilizing CRISPR sgRNA libraries, to further uncover insights. As we advance, this realm of research is poised for even greater development and exploration.

Publications

Noguchi Y, Onodera Y, Miyamoto T, Maruoka M, Kosako H, Suzuki J. In vivo CRISPR screening directly targeting testicular cells. ***Cell Genomics***. 4(3):100510. (2024) doi: 10.1016/j.xgen.2024.100510.

Zhang P, Maruoka M, Suzuki R, Katani H, Dou Y, Packwood DM, Kosako H, Tanaka M, Suzuki J. Extracellular calcium functions as a molecular glue for transmembrane helices to activate the scramblase Xkr4. ***Nature Commun*** 14(1):5592. (2023) doi: 10.1038/s41467-023-40934-2

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.

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

12) 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

13) Laboratory of Ultrastructural Virology

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

Outline of the research

We have been investigating the replication mechanisms of influenza virus, Ebola virus, and SARS-CoV-2 through virological and structural analysis using conventional electron microscopy, cryo-electron microscopy, and high-speed atomic force microscopy. Additionally, we have been studying SARS-CoV-2 replication and host responses in human respiratory organs using human respiratory organoids. Revealing virus structure, intracellular replication mechanisms, and pathogenesis at molecular to individual levels provides us valuable knowledge that advances our understanding of molecular basis of virus replication mechanisms and facilitates the development of novel antiviral drugs.

Publications

Muramoto Y, Takahashi S, Halfmann PJ, Gotoh S, Noda T*, Kawaoka Y*. Replicative capacity of SARS-CoV-2 omicron variants BA.5 and BQ.1.1 at elevated temperatures. ***Lancet Microbe*** S2666-5247(23)00100-3. (2023)

Shangfan H, Fujita-Fujiharu Y, Sugita Y, Wendt L, Muramoto Y, Nakano M, Hoenen T, Noda T*. Cryo-electron microscopic structure of the nucleoprotein-RNA complex of the European filovirus, Lloviu virus. ***PNAS Nexus***, 2(4):pgad120. (2023)

Fujita-Fujiharu Y, Sugita Y, Takamatsu Y, Houri K, Igarashi M, Muramoto Y, Nakano M, Tsunoda Y, Taniguchi I, Becker S, Noda T*. Structural insight into Marburg virus nucleoprotein-RNA complex formation. ***Nat. Commun.*** 13(1):1191. (2022)

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*., 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. ***Nat. Commun.*** 9:54 (2018).

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

Key words: Influenza virus, Ebola virus, SARS-CoV-2, organoid, EM, high-speed AFM

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 watching individual molecules in action?" By using live-cell Single-Molecule Speckle (SiMS) microscopy and our original multi-target super-resolution microscopy IRIS, we study mechanotransduction, cancer invasion, drug effects, tissue and neural circuit remodeling at the molecular level. With innovative antibody engineering, we are developing a new multi-cell marker detection devise. Real-time monitoring of actions of anti-cancer kinase inhibitors enables to develop a new type of allosteric modulators. "Seeing single-molecules is believing!"

Publications

Yamashiro, S., Rutkowski, D.M., Lynch, K.A., Liu, Y., Vavylonis, D. and Watanabe, N. Force transmission by retrograde actin flow-induced dynamic molecular stretching of Talin. ***Nat. Commun***. 14: 8468 (2023). doi: 10.1038/s41467-023-44018-z

Zhang, Q., Miyamoto, A., Watanabe, S., Arimori, T., Sakai, M., Tomisaki, M., Kiuchi, T., Takagi, J. and Watanabe, N. Engineered fast-dissociating antibody fragments for multiplexed super-resolution microscopy. ***Cell Reports Methods*** 2: 100301 (2022). doi: 10.1016/j.crmeth.2022.100301

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

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 (with YouTube video link)

Key words: Single-molecule imaging, actin, formin homology proteins, 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

Tanaka, S.†, Kawakita, M.†, Yasui, H., Sudo, K., Itoh, F., Sasaki, M., Shibata, N., Hara, H., Iwakura, Y., Hashidate-Yoshida, T., Shindou, H., Shimizu, T., Oyama, T., Matsunaga, H. and Takahara, K., An immune-adrenergic pathway induces lethal levels of platelet-activating factor in mice. ***Commun. Biol.*** (2024) (†equal contribution) DOI: 10.1038/s42003-024-06498-7.

Sudo, K., Todoroki, T., Ka Y., and Takahara, K., Vγ5Vδ1 TCR signaling is required to different extents for embryonic versus postnatal development of DETCs. ***Int. Immunol.***, 34, 263–276 (2022). DOI: 10.1093/intimm/dxac001

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. Cell wall N-glycan of Candida albicans ameliorates early hyper- and late hypo-immunoreactivity in sepsis. ***Commun. Biol.*** (2021) 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

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

Uno, W., Ofuji, K., Wymeersch, F. J. & Takasato, M. In vitro induction of prostate buds from murine urogenital epithelium in the absence of mesenchymal cells. ***Dev. Biol.*** 498, 49–60 (2023). doi: 10.1016/j.ydbio.2023.03.006

Banan Sadeghian, R., Ueno, R., Takata, Y., Kawakami, A., Ma, C., Araoka, T., Takasato, M. & Yokokawa, R. Cells sorted off hiPSC-derived kidney organoids coupled with immortalized cells reliably model the proximal tubule. ***Commun. Biol.*** 6, 483 (2023). doi: 10.1038/s42003-023-04862-7

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

Outline of the research
The organismal healthspan is significantly influenced by the quality and quantity of the diet, but our understanding of the detailed molecular mechanisms remains limited. In our laboratory, we study the physiological functions of various nutrients during each life stage, including development, growth, reproduction, and aging. We aim to elucidate the adaptive mechanisms in response to nutritional imbalances, whether transient or chronic, and their impact on molecular mechanisms related to metabolic physiology, tissue homeostasis, feeding behavior, stress response, reproductive capacity, and overall lifespan.

Publications
Fumiaki Obata, Masayuki Miura. Regulatory Mechanisms of Aging through the Nutritional-Metabolic Control of Amino Acid Signaling in Model Organisms. ***Annual Review of Genetics***, (2024)

Hina Kosakamoto†, Fumiaki Obata†*, Junpei Kuraishi, Hide Aikawa, Rina Okada, Joshua N. Johnstone, Taro Onuma, Matthew D. W. Piper, Masayuki Miura*. Early-adult methionine restriction reduces methionine sulfoxide and extends lifespan in Drosophila. ***Nature Communications*** 14, 7832, (2023)

Hina Kosakamoto, Naoki Okamoto, Hide Aikawa, Yuki Sugiura, Makoto Suematsu, Ryusuke Niwa, Masayuki Miura, Fumiaki Obata*. Sensing of the non-essential amino acid tyrosine governs the response to protein restriction in Drosophila. ***Nature Metabolism*** 4, 944-959, (2022)

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)

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

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

PI (4): KONDO, Takefumi (Associate Prof.) <takefumi.kondo@riken.jp **>**

Outline of the research
Embryonic development is a dynamic and beautiful phenomenon that proceeds with remarkable precision. Our goal is to elucidate the principles that ensure the accuracy of the entire developmental process. We view development as an information network system consisting of multiple hierarchies of "genome"-"cell"-"tissue", and study its feedback mechanisms between the layers by quantitatively measuring and analyzing the dynamics at each layer using techniques such as *Drosophila* genetics, single-cell genomics, imaging and large-scale data analysis.

Publications
Tsuboi, A., Fujimoto, K., and Kondo, T. Spatio-temporal remodeling of extracellular matrix orients epithelial sheet folding. ***Science Advances***, 9, eadh2154 (2023). doi: 10.1126/sciadv.adh2154

Sakaguchi, S., Mizuno, S., Okochi, Y., Tanegashima, C., Nishimura, O., Uemura, T., Kadota, M., Naoki, H., and Kondo, T. Single-cell transcriptome atlas of *Drosophila* gastrula 2.0. ***Cell Reports***, 42, 112707 (2023). doi: 10.1016/j.celrep.2023.112707

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). doi: 10.7554/eLife.45145

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

Kondo, T., Plaza, S., Zanet, J., Benrabah, E., Valenti, P., Hashimoto, Y., Kobayashi, S., Payre, F., and Kageyama, Y. Small peptides switch the transcriptional activity of Shavenbaby during *Drosophila* embryogenesis. ***Science***, 329, 336-339 (2010). doi: 10.1126/science.1188158

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

Key words: Development, Single-cell Genomics, Imaging, Morphogenetic feedback, Drosophila

PI (5): KONAGAYA, Yumi (Associate Prof.) <yumi.konagaya@riken.jp>

Outline of the research

Adult tissues are constantly undergoing turnover to maintain tissue homeostasis. The intestinal epithelium is one of the most rapidly renewing tissues, with new epithelial cells replacing old ones every 3 to 5 days in mice. Precise control of cell proliferation during intestinal epithelial differentiation is essential for maintaining tissue homeostasis, and its breakdown can lead to tissue atrophy or cancer.

In the intestinal epithelium, Lgr5-positive stem cells divide every 24 hours to produce transit-amplifying cells. These transit-amplifying cells then divide 4 to 6 times at a rate approximately twice as fast as Lgr5-positive stem cells. After that, the transit-amplifying cells slow down the cell cycle as they terminally differentiate into absorptive or secretory cells, and eventually exit the cell cycle. Remarkably, despite descriptions of the cell cycle in the intestinal epithelium as mentioned above being reported more than 25 years ago, the elucidation of the molecular mechanisms by which intestinal epithelial cells regulate cell proliferation rates during differentiation has made little progress, likely due to technical constraints.

Therefore, our laboratory uses mouse intestinal epithelium as a model to clarify the molecular mechanisms that regulate cell proliferation rates as stem cells transit through transit-amplifying cells to terminally differentiated cells. Particularly, we use multiplexed imaging of intestinal organoids and tissues, quantitative analysis, and mathematical modeling. These studies will reveal universal and fundamental therapeutic targets for tissue homeostasis disorders.

Our lab ongoing projects include:

1. Investigation of the coordinated control of cell proliferation and differentiation in mouse intestinal epithelium.
2. Analysis of the role of mechanical sensing in stem cell maintenance in mouse intestinal epithelium.
3. Development of fluorescent reporters using machine learning algorithms for protein structure prediction.

Publications

Konagaya, Y., Rosenthal, D., Ratnayeke, N., Fan, Y. and Meyer, T. An intermediate Rb–E2F activity state safeguards proliferation commitment. ***Nature***, 631, 424–431 (2024). doi: 10.1038/s41586-024-07554-2

Konagaya, Y., Takakura, K., Sogabe, M., Bisaria, A., Liu, C., Meyer, T., Sehara-Fujisawa, A., Matsuda, M. and Terai, K. Intravital imaging reveals cell cycle-dependent myogenic cell migration during muscle regeneration. ***Cell Cycle***, 19, 3167-3181 (2020). doi: 10.1080/15384101.2020.1838779

Liu, C., Konagaya, Y., Chung, M., Daigh, L.H., Fan, Y., Yang, H.W., Terai, K., Matsuda, M. and Meyer, T. Altered G1 signaling order and commitment point in cells proliferating without CDK4/6 activity. ***Nature Communications***, 11, 5305 (2020). doi: 10.1038/s41467-020-18966-9

Konagaya, Y., Terai, K., Hirao, Y., Takakura, K., Imajo, M., Kamioka, Y., Sasaoka, N., Kakizuka, A., Sumiyama, K., Asano, T. and Matsuda, M. A highly sensitive FRET biosensor for AMPK exhibits heterogeneous AMPK responses among cells and organs. ***Cell Reports***, 21, 2628-2638 (2017). doi: 10.1016/j.celrep.2017.10.113

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

Key words: intestinal organoids, live cell imaging, cell fate decision, cell signaling, quantitative biology

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*** 56: 2223-2236 (2021) DOI: 10.1016/j.devcel.2021.07.002

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) DOI: 10.1016/j.devcel.2020.04.008

Nagata, R., Nakamura, M., Sanaki, Y., and Igaki, T. Cell competition is driven by autophagy. ***Dev Cell*** 51: 99-112 (2019) DOI: 10.1016/j.devcel.2019.08.018

Yamamoto, M., Ohsawa, S., Kunimasa, K., and Igaki, T. The ligand Sas and its receptor PTP10D drive tumor-suppressive cell competition. ***Nature*** 542: 246-250 (2017). DOI: 10.1038/nature21033

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

Website of the lab: https://igakilab.lif.kyoto-u.ac.jp/

Key words: cell competition, cancer, aging, cell death, cellular senescence

6) Laboratory of Functional Biology

PI: ODA, Yukako (Prof.) oda.yukako.6r@kyoto-u.ac.jp

Outline of the research

We focus on peptides that induce cell–cell adhesion, which we have recently identified. We also aim to control various diseases caused by disruption of intercellular adhesion, such as inflammation, cancer, and aging, and to develop drug discovery.

Research Subjects:

・Induction and regulation of cell–cell adhesion

・Control of malignant cancer by regulating cell–cell adhesion

・Elucidation of stress response mechanism in epithelial cells

・Understanding of the aging based on the intestinal barrier function

Publications:

Kira A, Tatsutomi I, Saito K, Murata M, Hattori I, Haruna K, Muraki N, Oda Y, Satoh S, Tsukamoto Y, Kimura S, Onoue K, Yonemura S, Arakawa S, Kato H, Hirashima T, Kawane K. Apoptotic extracellular vesicle formation mediated by local phosphatidylserine exposure drives efficient cell extrusion. ***Dev. Cell,*** 24, 58(14), 1282-1298, (2023). doi: 10.1016/j.devcel.2023.05.008

Oda Y, Takahashi C, Harada S, Nakamura S, Sun D, Kiso K, Urata Y, Miyachi H, Fujiyoshi Y, Honigmann A, Uchida S, Ishihama Y, Toyoshima F. Discovery of anti-inflammatory physiological peptides that promote tissue repair by reinforcing epithelial barrier formation. ***Science Advances***, 7(47) eabj6895, (2021). doi: 10.1126/sciadv.abj6895

Oda Y, Sugawara T, Fukata Y, Izumi Y, Otani T, Higashi T, Fukata M, Furuse M. The extracellular domain of angulin-1 and palmitoylation of its cytoplasmic region are required for angulin-1 assembly at tricellular contacts. ***J. Biol. Chem.*** 295(13), 4289-4302 (2020). doi: 10.1074/jbc.RA119.010491

Oda Y, Otani T, Ikenouchi J and Furuse M. Tricellulin-Cdc42 GEF Tuba system regulates actomyosin tension underlying epithelial cell–cell junctions at tricellular contacts. ***J. Cell. Sci.,*** **127**, 4201-12 (2014). doi: 10.1242/jcs.150607

Website of the lab: in preparation

Key words: epithelial cell, cell–cell junction, physiologically active peptide, tissue repair, cancer

7) 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*. Our work involves extensive use of computational methods, such as biophysical simulation of diffusion within chromosomes, and we incorporate AI-based structure prediction, phylogenetic analysis, and protein language models into our experimental design process.

Publications
Guo, H., Stamper, E. L., Sato-Carlton A., Shimazoe M. A., Li X., Zhang L., Stevens L., Tam K. C. J., Dernburg A. F., & Carlton, P. M. Phosphoregulation of DSB-1 mediates control of meiotic double-strand break activity. ***eLife*** **11**:e77956 (2022). doi:10.7554/eLife.77956

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

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

GR Kafer, Y Tanaka, R Rillo-Bohn, E Shimizu, K Hasegawa, PM Carlton. 5-Hydroxymethylcytosine marks sites of DNA damage and promotes genome stability Cell ***reports*** (2016) 14 (6), 1283-1292 2016

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

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

8) 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
Yokoyama, T., Manita, S., Uwamori, H., Tajiri, M., Imayoshi, I., Yagishita, S., Murayama, M., Kitamura, K. and

Sakamoto, M. A multicolor suite for deciphering population coding in calcium and cAMP in vivo. ***Nature Methods*** 21:897–907 (2024) doi: 10.1038/s41592-024-02222-9

Tachiki, Y., *Suzuki, Y. II., Kurahashi, M., Ohki, K., Mavuk, O., Nakagawa, T., Ishihara, S., Gyoten, Y., Yamamoto, A. and *Imayoshi, I. (2023) Scale space calibrates present and subsequent spatial learning in Barnes maze in mice. ***eNeuro*** 10(6), doi: 10.1523/ENEURO.0505-22.2023

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., 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

9) Laboratory of Genome Stress Response

PI: YASUHARA, Takaaki (Prof.) <yasuhara.takaaki.7r@kyoto-u.ac.jp>

Outline of the research

Cells have sophisticated mechanisms to respond to cellular stresses from external stressors, thereby maintaining homeostasis. Our laboratory aims to elucidate the molecular mechanisms of cellular stress responses, especially the ones caused by genotoxic stresses, and the fundamental mechanisms underlying many types of diseases caused by inefficient stress responses. We hope to contribute to solving various problems in this age of long-life expectancy, such as cancer and infertility in reproductive medicine.

Publications

Yasuhara, T., Xing, YH., Bauer, NC., Lee, LK., Dong, R., Soberman, RJ., Rivera, MN., and Zou, L. Defective RNAPII elongation mislocalizes active chromatin to nucleoli and promotes gene fusion. ***Molecular Cell*** 82:2738-2753 2022.

Yasuhara, T.*,#, Kato, R.#, Yamauchi, M., Uchihara, Y., Zou, L., Miyagawa, K.*, and Shibata, A.* RAP80 suppresses the vulnerability of R-loops during DNA double-strand break repair. ***Cell Reports*** 38:110335 2022. (*co-corresponding, #co-first)

Yasuhara, T.*,#, Kato, R.#, Hagiwara, Y., Shiotani, B., Yamauchi, M., Nakada, S., Shibata, A., and Miyagawa, K. Human Rad52 promotes XPG-mediated R-loop processing to initiate transcription-associated homologous recombination repair. ***Cell*** 175:558-570 2018. (*Lead contact, #co-first)

Yasuhara, T., Suzuki, T., Katsura, M. and Miyagawa, K. Rad54B serves as a scaffold in the DNA damage response that limits checkpoint strength. ***Nature Communications*** 5:5426 2014.

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

Key words: Cellular stress response, DNA damage repair, Phase separation, Cancer, Aging/Senescence

10) 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

Furuya K, Ikura M, Ikura T*: Machine learning extracts oncogenic-specific γ-H2AX foci formation pattern upon genotoxic stress. ***Genes to Cells*** 28:237-243, 2023.

Ikura M, Furuya K, Matsuda T, Ikura T*: Impact of Nuclear De Novo NAD+ Synthesis via Histone Dynamics on DNA Repair during Cellular Senescence To Prevent Tumorigenesis. ***Mol Cell Biol***. 42: e0037922, 2022.

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

11) Laboratory of RNA Viruses
PI: TOMONAGA, Keizo (Prof.) <tomonaga@infront.kyoto-u.ac.jp>

Outline of the research
The main goal of our research is to investigate the molecular mechanisms underlying the replication and pathogenesis of animal-derived RNA viruses. Endogenization of RNA viruses and its role in host-virus co-evolution is also a focus of this laboratory. In addition, we are actively involved in the development of a groundbreaking RNA viral vector, REVec, generated from bornaviruses. This novel vector would be a promising tool for gene cell therapies.

Publications
Minamiyama S et al., Efficacy of oligodendrocyte precursor cells as delivery vehicles for single-chain variable fragment to misfolded SOD1 in ALS rat model. ***Mol Ther Methods Clin Dev.*** 4:28:312-329 (2023). doi: 10.1016/j.omtm.2023.01.008.

Kawasaki J et al., One hundred million years history of bornavirus infections hidden in vertebrate genomes. ***Proc Natl Acad Sci USA.*** 118(20):e2026235118. (2021). doi: 10.1073/pnas.2026235118

Kojima S et al., Virus-like insertions with sequence signatures similar to those of endogenous non-retroviral RNA viruses in the human genome. ***Proc Natl Acad Sci USA.*** 118(5):e2010758118. (2021). doi: 10.1073/pnas.2010758118

Parrish NF and Tomonaga K. A viral (Arc)hive for metazoan memory. ***Cell*** 172(1-2):8-10 (2018). doi: 10.1016/j.cell.2017.12.029

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 et al., 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 et al., 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: RNA viruses, endogenous viruses, RNA virus vector, gene cell therapy

12) Laboratory of Cellular and Molecular Biomechanics
PI: ADACHI, Taiji (Prof.) <adachi@infront.kyoto-u.ac.jp>

Outline of the research
We aim to understand multiscale dynamics of biological systems from mechanical viewpoints, by combining experiments and modeling. Our research interests are cell fate determination under mechano-biochemical environment, morphogenesis of multicellular tissues, and functional adaptation through remodeling,

Publication:

Yokoyama, Y., Kameo, Y., Sunaga, J., Maki, K., Adachi, T. Chondrocyte hypertrophy in the growth plate promotes stress anisotropy affecting long bone development through chondrocyte column formation. ***Bone***, 182: 117055 (2024). doi: 10.1016/j.bone.2024.117055

Fukute, J., Maki, K., Adachi, T. The nucleolar shell provides anchoring sites for DNA untwisting in the core. ***Communications Biology***, 7: 83 (2024). doi.org/10.1038/s42003-023-05750-w

Kim, Y.K., Kameo, Y., Tanaka, S., Adachi, T. Aging effects on osteoclast progenitor dynamics affect variability in bone turnover via feedback regulation. ***JBMR Plus***, 8-1: ziad003 (2024). doi: 10.1093/jbmrpl/ziad003

Yoshimoto, K., Maki, K., Adachi, T., Kamei, K. Cyclic stretching enhances angiocrine signals at liver bud stage from hPSCs in 2-dimensional culture. ***Tissue Eng Part A***, 30-9: 426-439 (2023). doi: 10.1089/ten.TEA.2023.0148

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

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

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