2024 – 2025
Graduate School of Biostudies, Kyoto University
Master's Program in "Global Frontier in Life Science"
Guidelines for International Student Admissions

Revised on November 1, 2023

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 the 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 basic academic skills and research aptitudes in the life sciences, and who demonstrate a strong 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 to shed fresh light on, fundamental principles of life, who will pioneer new areas of the life sciences;

2. Researchers and engineers committed to global environmental conservation and gains in human health, welfare, and well-being, who are ready to make social contributions through roles in public and private research institutions;

3. Educators and working professionals with a broad-based understanding of the varied phenomena of life in general, who are ready to make social contributions through roles in education, industry, the news media, and government;

4. Researchers, educators, engineers, and working professionals who possess strong communication skills that enable them to hold discussions with researchers and others from Japan and around the world in life science–related fields.

The entrance exam will comprise achievement tests that include an assessment of the applicant's ability to think logically in English, a skill that is required to read and analyze an article published in an international journal; an assessment of the applicant's general knowledge of molecular biology cell biology , biochemistry, and other life science fields; an assessment of the applicant's fundamental knowledge as required to pursue his or her intended field of study; an assessment of 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, 2024** or **April 1, 2025**.

I. "Global Frontier in Life Science"

The Graduate School of Biostudies launched "Global Frontier in Life Science", an educational program for Doctoral and Master's students. 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. 11-31 of these guidelines and the Graduate School of Biostudies website (http://www.lif.kyoto-u.ac.jp/). Applicants can apply for up to two laboratories. **Thus, applicants must contact the lab heads and fully discuss potential research activities and availability 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.

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

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. 11-31.

IV-1. Eligibility Requirements for Applicants expecting to start from October 1, 2024

Applicants must match one of the following requirements by September 30, 2024:

1. Individuals with any nationality who have completed (or are expected to complete by September 30, 2024) 16 years of education in foreign countries. This includes individuals who have completed an equivalent of 16 years of education but have less than 16 years due to skipped (advanced) grades.
2. Individuals, other than Japanese nationals, who graduated (or are expected to graduate by September 30, 2024) from a Japanese university.
3. Individuals who have received (or are expected to receive by September 30, 2024), a degree equivalent to a bachelor's degree by completing a curriculum with a term of enrollment of at least three years (including completion of such a curriculum by studying relevant subjects in Japan via a correspondence course provided by a school in a foreign countryand completion of a curriculum at an educational facility that has been accredited as having an approved curriculum under the educational system of said country and is designated by the Minister of Education, Culture, Sports, Science and Technology) at a university or other school in a country other than Japan (only those universities or schools for which the overall conditions of education and research activities have been assessed by a party authorized by the government of said country or an organization concerned, or those corresponding to such entities as designated by the Minister of Education, Culture, Sports, Science and Technology).
4. Individuals, other than Japanese nationals, who are recognized by the Graduate School of Biostudies to have completed an education equivalent to a university degree of Japan and are

at least 22 years old by September 30, 2024).

5. Individuals with Japanese nationality who are determined by the Graduate School of Biostudies to have completed an education in foreign countries equivalent to a university degree of Japan or had school education that were mainly given in English, and are at least 22 years old by September 30, 2024).
6. Individuals, other than Japanese nationals, who will be enrolled at least 3 years in a Japanese university by September 30, 2024 and are recognized by the Graduate School of Biostudies as having acquired sufficient credits with excellent academic records.

Those who are applying under requirement 4, 5 or 6 must undergo a preliminary eligibility screening process before applying.

IV-2. Eligibility Requirements for Applicants expecting to start from April 1, 2025

Applicants must match one of the following requirements by March 31, 2025:

1. Individuals with any nationality who have completed (or are expected to complete by March 31, 2025) 16 years of education in foreign countries. This includes individuals who have completed an equivalent of 16 years of education but have less than 16 years due to skipped (advanced) grades.
2. Individuals, other than Japanese nationals, who graduated (or are expected to graduate by March 31, 2025) from a Japanese university.
3. Individuals who have received (or are expected to receive by March 31, 2025) a degree equivalent to a bachelor's degree by completing a curriculum with a term of enrollment of at least three years (including completion of such a curriculum by studying relevant subjects in Japan via a correspondence course provided by a school in a foreign country and completion of a curriculum at an educational facility that has been accredited as having an approved curriculum under the educational system of said country and is designated by the Minister of Education, Culture, Sports, Science and Technology) at a university or other school in a country other than Japan (only those universities or schools for which the overall conditions of education and research activities have been assessed by a party authorized by the government of said country or an organization concerned, or those corresponding to such entities as designated by the Minister of Education, Culture, Sports, Science and Technology).
4. Individuals, other than Japanese nationals, who are recognized by the Graduate School of Biostudies to have completed an education equivalent to a university degree of Japan and are at least 22 years old by March 31, 2025.
5. Individuals with Japanese nationality who are determined by the Graduate School of Biostudies to have completed an education in foreign countries equivalent to a university degree of Japan or had school education that were mainly given in English, and are at least 22 years old by March 31, 2025.
6. Individuals, other than Japanese nationals, who will be enrolled at least 3 years in a Japanese university by March 31, 2025 and are recognized by the Graduate School of Biostudies as having acquired sufficient credits with excellent academic records.

Those who are applying under requirement 4, 5 or 6 must undergo a preliminary eligibility screening process before applying.

V. Eligibility Screening

Applicants filing under eligibility requirement 4, 5 or 6 above are required to contact the Student Affairs Section (*kyomu gakari*) of the Graduate School of Biostudies to request that the designated application form for preliminary eligibility screening to be sent at any time, but no later than **November 8 (Wed), 2023 JST**. Submit the following preliminary eligibility screening documents via email to the Student Affairs Section of the Graduate School of Biostudies (150kyomu@adm.lif.kyoto-u.ac.jp) by **JST 5:00 pm, November 16 (Thu), 2023 at the latest**. When filing the admission application, applicants cannot in principle apply for any laboratory other than the one or two specified in the documents being submitted for the eligibility screening. The screening results will be sent by e-mail to the applicants as soon as the decision is made, at latest on **December 14 (Thu), 2023**.

Required Documents for the Eligibility Screening

When filing under eligibility requirement 4 or 5

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

When filing under the eligibility requirement 6

(1) Application form for the eligibility screening **(designated form)**	This form is provided upon request.
(2) A letter of recommendation	Submit a letter of recommendation prepared and sealed by the university in which you are/were enrolled. Note that recommendation letters must be written on the letterhead of the institution to which the recommender belongs and are valid only when the recommender's handwritten signature and full contact addresses (including Email address) are provided.

(3) Academic transcript (s)	Submit an academic transcript prepared and sealed by the university in which you are/were enrolled. (The transcript does not need to be sealed if it is made of a material that prevents photocopying.)
(4) Statement of personal objectives **(designated form)**	This form is provided upon request.
(5) A valid score for GRE General Test or Subject Test See **Note** below)	**A General Test score is optional.** Any scores of the Subject Test are also optional. Acceptable test includes: Chemistry/Physics.

Note:

1) For applicants who hold a GRE* General Test or Subject Test score for Chemistry/Physics, those scores can be provided as supplemental supporting information.
***GRE (**Graduate Record Examination): http://www.ets.org/gre
Designated Institution (DI) Code: 3814 Kyoto U

2) Successful applicants filing under the eligibility requirement 6, expecting to matriculate in April, 2025, must submit an academic transcript for the 2023 academic year to the Student Affairs Section (*kyomu gakari*) of the Graduate School of Biostudies by February 20 (Thu), 2025. Otherwise, successful applicants whose transcripts demonstrate a failure to meet the admissions standards of the Graduate School of Biostudies may be refused admission. Successful applicants filing under eligibility requirement 6 must also submit a certificate of withdrawal by March 31 (Mon), 2025; thus, they cannot obtain a bachelor's degree at the university currently attended.

VI. Application Fee

Application fee: 10,000 yen
Payment period: **From December 18 (Mon), 2023 to January 10 (Wed), 2024 JST**
Only payments made within this period will be valid; those made outside this period will be invalid. Once received, application fees will not be refundable under any circumstances.

[Payment methods]

1. Payment by Credit Card (only for applicants residing outside Japan).
Applicants residing outside Japan should pay the application fee (10,000 yen) and Service Fee (650 yen). Please access the URL below titled "Examination Settlement Service (EXSS)" and complete the payment process following the instructions provided during the designated payment period. For details, please refer to a separate sheet titled "Payment Methods for Application Fees with Convenience Store or Credit Card". Note that 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". Note that 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 the Internet is not accepted.**

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

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

Payment via ATM

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

(1) Enter the applicant's name as the payer in the appropriate space in the ATM so that the university will be able to identify by whom the amount was deposited in the university's account. (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) 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.
(3) Academic transcript(s) **(Required: Original Copy)**	Submit an academic transcript prepared and sealed by the university you are currently attending or from which you have graduated.
(4) Graduation certificate or certificate of expected graduation **(Required: Original Copy)**	Submit a printed original certificate prepared by the university you are currently attending or from which you have graduated.
(5) Recommendation letters **(Required: Original Copy)**	At least two letters are required. (Mandatory) Letter of recommendation 1: Written by a faculty member of your current educational institution, who can evaluate your academic performance and potential for success in the Master's program. The letter must be written on the letterhead of the respective institution and must include the recommender's contact information and hand-written signature. (Choose at least one, as appropriate) Letter of recommendation 2: Written by the faculty supervisor of the applicant at the university to which you belong or from which you graduated, who can evaluate your research and your potential to become a productive scientist. The letter must be written on the letterhead of the supervisor's institution and must include the supervisor's contact information and hand-written signature. Letter of recommendation 3: If you are employed at a public agency or company at the time of application, submit a letter of recommendation from your immediate supervisor, with his/her hand-written signature. The letter must include your supervisor's contact information and be written on the letterhead of the agency/company to which he/she belongs.
(6) A valid official score report for GRE General Test and Subject Test * (Please see Note below.)	**A General Test score is optional.** Any scores of the Subject Test are also optional. Acceptable test includes: Chemistry/Physics
(7) A valid official score report for IELTS or TOEFL** (For details, see Note below.)	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.)
(8) Evidence of application fee payment form	**Applicants residing outside Japan:** After paying your application fees via internet, the Application Completed page must be printed out

Note: Those who are expected to graduate from an undergraduate program at Kyoto University do not need to submit this form.	and submitted. Applications will not be accepted if payment could not be confirmed. Applicants residing inside Japan: After paying your application fees at a convenience store or a bank window or by an ATM, paste the Evidence of Application Fee Payment with the bank's receipt seal stamped or the receipt issued by the ATM. Applications will not be accepted if no receipt seal is stamped on the Evidence of Application Fee Payment form.
(9) Address for further communication	**Use the designated forms.** For further communication on the examination results and the enrollment procedures, clearly write your name, address and post code on the designated form. *If you change your address after applying, you must promptly inform the new address to the Student Affairs Section (*kyomu gakari*) of the Graduate School of Biostudies.

Note:

*For applicants who hold a GRE General Test or Subject Test score for Chemistry/Physics, those scores can be provided as supplemental supporting information.
GRE (Graduate Record Examination) http://www.ets.org/gre Designated Institution (DI) Code: 3814
**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

VIII. Application Procedures

Applicants must prepare a packet of all necessary admission application documents in print and submit it to the postal address indicated on p.10. When sending the packet by post, use registered mail and write clearly "Admission Application Documents for the Graduate School of Biostudies Master's program of Global Frontier in Life Science" on the front of the envelope.

IX. Application Period

The application period is **from December 18 (Mon), 2023 to January 10 (Wed), 2024 JST**
When submitting in person: office hours are 9:00 a.m. – 12:00 p.m. and 1:00 p.m. – 5:00 p.m.
When sending the application documents by post, ensure that the application documents are delivered by **January 10 (Wed), 2024 JST**.

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

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

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 January 10 (Wed), 2024 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 Schedule

January 22 (Mon), 2024 ~ January 26 (Fri), 2024	**Document Screening** Only successful applicants who pass the screening of the admission documents will be able to take the interview (Oral Examination).
January 31 (Wed), 2024	**Announcement of successful applicants in document screening**
February 1 (Thu), 2024 ~ March 5 (Tue), 2024	**Interview** (Oral Examination) The interview date and method* will be arranged individually after the decision is made. ***e.g., Skype or ZOOM or other protocols**

XI. Announcement of Final Successful Applicants

The list of successful applicants is scheduled to be posted on a bulletin board on the 1st floor of the South Campus Research Bldg. (Faculty of Medicine Bldg. G) at approximately 5p.m., **March 29 (Fri)**. 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)
(The admission fee amount may be revised at the time of enrollment.)

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

Note:

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

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

(3) Others

1) After the application is accepted, no changes are allowed in any of the application items. Furthermore, once received, application fees will not be refundable under any circumstances.
2) **For applicants residing inside Japan:** To request **the Application Fee Payment Request Form**, write your post code, address, and name on a self-addressed 240 mm x 332 mm-sized envelope, and affix 84-yen postage to the self-addressed envelope. Write **"Request for Application Fee Payment Request Form"** on the front of the envelope, place the self-addressed envelope inside, and send it to the address below).

3) The instructions of enrollment procedures will be e-mailed to each successful applicant in late July, 2024 for those who would like to enroll in October, 2024. For those who will enroll in April, 2025, it will be informed in late January, 2025.
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, 2023

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

Global Frontier in Life Science Master's Degree Program
Research Fields and Contents of Research
(As of November 1, 2023)

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 cellular fate decisions; how cells maintain homeostasis by perceiving external stimuli, processing information through the intricate system of 'intracellular signal transduction,' and ultimately manifesting 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 mysteries of how cells adeptly acquire information from a constantly changing environment, the extent of their recognition capabilities for various ligand information (types, concentrations, combinations, physical constrains, etc.), and the mechanisms of when and how cell fate – be it cell division, differentiation, or apoptosis – is determined.

Our mission is to quantitatively decipher the fundamental principles underlying intracellular signaling pathways involved in the process of cell fate decision-making. 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 cells perceive 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 the critical moments when and how cells make vital decisions about their fate – whether to divide, differentiate, or meet another cell fate.

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

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

Uda Y, Goto Y, Oda S, Kohchi T, Matsuda M, and Aoki K. Efficient synthesis of phycocyanobilin in mammalian cells for optogenetic control of cell signaling. ***Proc. Natl. Acad. Sci. U.S.A.,*** 114, 11962-11967 (2017). doi: 10.1073/pnas.1707190114

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

Outline of the research

1. Nutri-developmental biology: deciphering regulatory systems of host animals and symbiotic microorganisms that govern nutritional adaptability to ensure animal growth, reproduction, and aging
2. Neuroscience: operating principles of neuronal circuits that evoke selective behavioral outputs in response to nociceptive stimuli
3. Learning from reproductive parasites: a comprehensive study of "male killing" caused by insect symbionts

We are interested in mechanisms that control animal development and behaviors in response to two categories of environmental inputs: nutrition and sensory stimuli. We are trying to unravel underlying mechanisms of adaptations to nutrient balances using *Drosophila* species. We are also taking interspecies approaches to understand contributions of symbiotic microorganisms to animal growth and reproductive manipulation ("male killing"). By using *Drosophila* somatosensory neurons, we are dissecting operating principles of neuronal circuits that evoke selective behavioral outputs in response to thermal or mechanical nociceptive stimuli. To conduct these studies, we make full use of molecular, optogenetic, and physiological approaches, imaging, single-cell analysis and multi-omics.

Publications (*: Faculties of the lab)

Li, K., Tsukasa, Y., Kurio, M., Maeta, K., Tsumadori, A., Baba, S., Nishimura, R., Murakami, A., Onodera, K., Morimoto, K. and Uemura, T,,* 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).

Tsuyama, T., Hayashi, Y., Komai, H., Shimono, K. and Uemura, T.* Dynamic de novo adipose tissue development during metamorphosis in *Drosophila melanogaster*. ***Development***, 150:dev200815 (2023).

Kanaoka, Y., Onodera, K., Watanabe, K., Hayashi, Y., Usui, T., Uemura, T,,* and Hattori, Y.* Inter-organ Wingless/Ror/Akt signaling regulates nutrient-dependent hyperarborization of somatosensory neurons. ***eLife***, 12:e79461 (2023).

Kageyama, D., Harumoto, T.,* Nagamine, K., Fujiwara, A., Sugimoto, T.N., Jouraku, A., Tamura, M., Katoh, T.K., and Watada, M. A male-killing gene encoded by a symbiotic virus of *Drosophila*. ***Nature communications***, 14:1357 (2023).

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

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

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

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 Molecular and Cellular Biology of Totipotency
PI: NAKANO, Takeshi (Prof.) <nakano.takeshi.6x@kyoto-u.ac.jp>

Outline of the research

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

Publications

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

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

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

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

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

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

5) Laboratory of Biosignals and Response
PI: NAGAO, Masaya (Prof.) <nagao.masaya.7e@kyoto-u.ac.jp>

Outline of the research

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

Publications

Wagatsuma, T., Shimotsuma, K., Sogo, A., Sato, R., Kubo., N, Ueda, S., Uchida, Y., Kinoshita, M., Kambe, T. Zinc transport via ZNT5-6 and ZNT7 is critical for cell surface glycosylphosphatidylinositol-anchored protein expression. ***J. Biol. Chem***., 298, 102011 (2022). doi: 10.1016/j.jbc.2022.102011

Nagamatsu, S., Nishito, Y., Yuasa, H., Yamamoto, N., Komori, T., Suzuki, T., Yasui, H., Kambe, T. Sophisticated expression responses of ZNT1 and MT in response to changes in the expression of ZIPs. ***Sci. Rep.***, 12, 7334 (2022). doi: 10.1038/s41598-022-10925-2

Ueda, S., Manabe, Y., Kubo, N., Morino, N., Yuasa, H., Shiotsu, M., Tsuji, T., Sugawara, T., Kambe, T. Early secretory pathway-resident Zn transporter proteins contribute to cellular sphingolipid metabolism through activation of sphingomyelin phosphodiesterase 1. ***Am J Physiol Cell Physiol***, 322, C948–C959 (2022). doi: 10.1152/ajpcell.00020.2022

Hasegawa T, Osaka M, Miyamae Y, Nishino K, Isoda H, Kawada K, Neffati M, Irie K and Nagao M. "Two Types of PPARγ Ligands Identified in the Extract of *Artemisia campestris*. ***Chemistry*** 3(2), 647-657 (2021). https://doi.org/10.3390/chemistry3020045

Nishino K, Someya K, Ksouri R, Ishikawa T, Isoda H, Irie K, Nagao M. "Abietane diterpenoids from *Salvia officinalis* leaves as aryl hydrocarbon receptor ligands." ***Phytochem Lett*** 41, 78-82 (2021) https://doi.org/10.1016/j.phytol.2020.11.006

Yanagimichi M, Nishino K, Sakamoto A, Kurodai R, Kojima K, Eto N, Isoda H, Ksouri R, Irie K, Kambe T, Masuda S, Akita T, Maejima K, and Nagao M. "Analyses of putative anti-cancer potential of three STAT3 signaling inhibitory compounds derived from *Salvia officinalis*." ***Biochem Biophys Rep*** 25, 10882 (2021) https://doi.org/10.1016/j.bbrep.2020.100882

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

Key words: bioactive compounds, screening, zinc, transporter

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: Hirokazu Toju (Professor) <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

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, Guimarães PR Jr, Olesen JM, and Thompson JN. Assembly of complex plant–fungus networks. ***Nature Communications*** 5:5273 (2014) https://doi.org/10.1038/ncomms6273

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 innate immune system recognizes and inactivates retroviruses, and (3) how endocytic process is orchestrated by membrane-bound proteins, cytoskeletal network and lipid bilayer.

Publications

Y. Yu and *S.H. Yoshimura "Self-assembly of CIP4 drives actin-mediated asymmetric pit-closing in clathrin-mediated endocytosis" ***Nat. Commun.*** (2023) in press.

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 brain development using multidisciplinary approach including molecular and cellular biology, live-cell imaging 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
Fujishima, K., Kurisu, J., Yamada, M. and Kengaku, M. βIII spectrin controls the planarity of Purkinje cell dendrites by modulating perpendicular axon-dendrite interactions. ***Development*** 147(24):dev194530. (2020). doi: 10.1242/dev.194530. PMID: **33234719**

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

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

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

Fujishima, K., Horie, R., Mochizuki, A. and Kengaku, M. Principles of branch dynamics governing shape characteristics of cerebellar Purkinje cell dendrites. ***Development*** 139 (18): 3442-3455 (2012). doi: 10.1242/dev. 081315.

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

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

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:

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*** (in press)

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

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

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

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

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

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

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

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:

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

Yamashiro, S., Taniguchi, D., Tanaka, S., Kiuchi, T., Vavylonis, D. and Watanabe N. Convection-induced biased distribution of actin probes in live cells. ***Biophys.*** J. 116: 142-150 (2019). doi: 10.1016/j.bpj.2018.11.022

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
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).

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Publications

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

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

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

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

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

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

5) Laboratory of Genetics

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

Outline of the research

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

Research subjects:

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

Publications

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

PI: CARLTON, Peter (Associate Prof.) <carlton.petermark.3v@kyoto-u.ac.jp>

Outline of the research

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

Publications

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

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

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

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

7) Laboratory of Brain Development and Regeneration

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

Outline of the research

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

development and plasticity, and long-term monitoring of neural circuit plasticity in vivo with the two-photon microscope and brain endoscope.

Publications

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

*Nagasaki, S.C., Fukuda, T.D., Yamada, M., Suzuki, Y.I., Kakutani, R., Guy, A.T. and *Imayoshi, I. (2023) Enhancement of Vivid-based Photo-Activatable Gal4 Transcription Factor in Mammalian Cells. Cell Struct Funct. 48: 31–47. doi: 10.1247/csf.22074., doi: 10.1247/csf.22074.

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

8) 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

9) Laboratory of Cancer Cell Biology

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

Outline of the research

Tumor microenvironment is highly heterogeneous and dynamic. Several lines of evidence have suggested that hypoxic, acidic, and nutrient-depleted microenvironments exist in solid tumors and induce malignant phenotypes and chemo/radioresistance of cancer cells. We aim to elucidate molecular mechanisms underlying malignant progression and therapy resistance of cancer cells by analyzing adaptive responses of cancer cells to the tumor-specific microenvironments.

Publications:

Koyasu S, Horita S, Saito K, Kobayashi M, Ishikita H, Chow CC, Kambe G, Nishikawa S, Menju T, Morinibu A, Okochi Y, Tabuchi Y, Onodera Y, Takeda N, Date H, Semenza GL, Hammond EM, *Harada H. ZBTB2 links p53 deficiency to HIF-1-mediated hypoxia signaling to promote cancer aggressiveness. ***EMBO Rep***. 24:e54042. 2023.

Suwa, T., Kobayashi, M., Shirai, Y., Nam J.M., Tabuchi, Y., Takeda, N., Akamatsu, S., Ogawa, O., Mizowaki, T., Hammond, E.M., *Harada, H. SPINK1 as a plasma marker for tumor hypoxia and a therapeutic target for radiosensitization. ***JCI Insights***. 6:e148135. 2021.

Maruoka, M., Zhang, P., Mori, H., Imanishi, E., Packwood, D.M., Harada, H., Kosako, H., Suzuki, J. Caspase cleavage releases a nuclear protein fragment that stimulates phospholipid scrambling at the plasma membrane. ***Mol Cell***. 81:1397-1410. 2021.

Koyasu S, Kobayashi M, Goto Y, Hiraoka M, *Harada H. Regulatory mechanisms of hypoxia-inducible factor 1 activity: Two decades of knowledge. ***Cancer Science***. 109:560-571. 2018.

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

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

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

Key words: cancer, tumor microenvironments, hypoxia, chemo/radioresistance, hypoxia-related diseases

10) Laboratory of Laboratory of Chromatin Regulatory Network
PI: IKURA, Tsuyoshi (Associate Prof.) <ikurat@house.rbc.kyoto-u.ac.jp>

Outline of the research
The eukaryotic genome is tightly packed into the chromatin, a hierarchically organized complex of DNA, histone and nonhistone proteins. This packing represents a common obstacle for the metabolic processes of DNA including transcription, replication, recombination, and DNA repair. Current evidence indicates that chromatin reorganization involving histone modification, histone variant exchange, histone eviction and ATP-dependent chromatin remodeling play an integral role in DNA repair and DNA damage response. However, it remains unclear how such chromatin reorganization is coupled with the initiation of DNA repair process and/or activation of checkpoint machinery after DNA damage. We are now investigating the following issues:
1. The molecular mechanisms by which the TIP60 histone acetylase complex regulates histone H2AX exchange induced by ionizing radiation.
2. The cross-talk between the histone signaling network regulated by histone H2AX exchange and DNA damage response pathways.

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

Publications

Yokoyama, Y., Kameo, Y., Adachi, T. Development of continuum-based particle models of cell growth and proliferation for simulating tissue morphogenesis. ***J Mech Behav Biomed Mat***, 142: 105828 (2023). doi: 10.1016/j.jmbbm.2023.105828

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

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