2023 - 2024
Graduate School of Biostudies, Kyoto University
Master's Program in "Global Frontier in Life Science"

Guidelines for International Student Admissions

Philosophy and Admission Policy of the Graduate School of Biostudies

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 document screening to evaluate 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; document screening to assess the applicant's general knowledge of molecular biology, cell biology, biochemistry, and other life science fields; document screening to assess the applicant's fundamental knowledge as required to pursue his or her intended field of study; and an interview (oral exam) to assess the applicant's judgement, thinking ability, communication skills, initiative, and ethical perspective. Admissions decisions will be made based on the applicant's overall performance on these screenings. **Please note that applicants are NOT required to be physically present in Japan for the examination.**

The academic year starts on October 1, 2023 or April 1, 2024.

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. 11-33 of these guidelines and the Graduate School of Biostudies website (http://www.lif.kyoto-u.ac.jp/). Applicants can apply for up to two laboratories. **Thus, applicants must contact the lab heads and fully discuss potential research activities and availability before filing the application.**

III. AAO Process

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

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

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

Available labs are listed in pp. 11-33.

IV-1. Eligibility Requirements for Applicants expecting to start from October 1, 2023

Applicants must match one of the following requirements by September 30, 2023:

1. Individuals with any nationality who have completed (or are expected to complete by September 30, 2023) 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, 2023) from a Japanese university.
3. Individuals who have received (or are expected to receive by September 30, 2023), 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, 2023).

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, 2023).
6. Individuals, other than Japanese nationals, who will be enrolled at least 3 years in a Japanese university by September 30, 2023 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, 2024

Applicants must match one of the following requirements by March 31, 2024:

1. Individuals with any nationality who have completed (or are expected to complete by March 31, 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 March 31, 2024) from a Japanese university.
3. Individuals who have received (or are expected to receive by March 31, 2023) 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, 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 March 31, 2024.
6. Individuals, other than Japanese nationals, who will be enrolled at least 3 years in a Japanese university by March 31, 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.

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 9 (Wed), 2022 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 17 (Thu), 2022 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 8 (Thu), 2022**.

Documents for the Eligibility Screening

When filing under eligibility requirement 4 or 5

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

When filing under the eligibility requirement 6

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

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

Note:

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

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

2) Successful applicants filing under the eligibility requirement 6, expecting to matriculate in April, 2024, 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 22 (Thu), 2024. 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 (Fri), 2024; 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 19 (Mon), 2022 to January 10 (Tue), 2023 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/bio/

2. Payment with Convenience Store (only for applicants residing inside Japan).
Applicants residing inside Japan should pay the application fee (10,000 yen) and Service Fee

(650 yen). Please access the URL below titled “Examination Settlement Service (EXSS)” and complete the payment process following the instructions provided during the designated payment period. For details, please refer to a separate sheet titled “Payment Methods for Application Fees with Convenience Store or Credit Card”. 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/bio/

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

Applicants residing inside Japan should pay the application fee (10,000 yen) with a designated payment request form by bank transfer with the following procedures.
To obtain the form, please contact the GSB Student Affairs Section (*kyomu gakari*).

Payment at a bank window in Japan

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

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

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

Payment via ATM

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

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

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

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

VII. Application Documents

(1) Admission application form, photograph card, examination card	**Use the provided form.** Fill in the blanks and paste a photo to each of the two indicated places. Make sure the photos present your full-face and frontal view, without a hat or cap, and are taken within the past three months.
(2) Research achievement (Questions for application screening)	**Use the provided form.** Fill in the boxes in the designated form. Do not exceed to write expanding the original size of the boxes. The sizes are fixed. Please write in Times New Roman 12 point.
(3) Academic transcript **(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 **(Original Copy)**	Submit a printed original certificate prepared by the university you are currently attending or from which you have graduated.
(5) Recommendation letters (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	**A General Test score is required.** Any scores of the Subject Test are optional. Acceptable test includes: Biology/Biochemistry, Cell and Molecular/Biology/Chemistry/Physics
(7) A valid official score report for IELTS or TOEFL	Unnecessary for English-native speakers (Please contact the Student Affairs Section in advance.)
(8) Evidence of application fee payment form	**Applicants residing outside Japan:** After paying your application fees via internet, the Application Completed page must be printed out

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 Biostudeis.

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 Form 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 19 (Mon), 2022 to January 10 (Tue), 2023 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 (Tue), 2023 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 (Tue), 2023 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 16 (Mon), 2023 ~ January 20 (Fri), 2023	**Document Screening** Only successful applicants who pass the screening of the admission documents will be able to take the interview (Oral Examination).
January 25 (Wed), 2023	**Announcement of successful applicants in document screening**
February 2 (Thu), 2023 ~ February 13 (Mon), 2023	**Interview** (Oral Examination) The interview date and method* will be arranged individually after the decision is made. ***e.g. Skype or ZOOM or other protocols**

XI. Announcement of Final Successful Applicants

The list of successful applicants is scheduled to be posted on a bulletin board on the 1st floor of the South Campus Research Bldg. (Faculty of Medicine Bldg. G) at approximately 5p.m., **February 22 (Wed), 2023**. 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, 2023 for those who would like to enroll in October, 2023. For those who will enroll in April, 2024, it will be informed in late January, 2024.
4) Applicants with physical disabilities (degree of physical disability as stipulated in the enforcement ordinance of the School Education Law) who require special arrangements for taking examinations or attending courses should immediately contact the Student Affairs Section (*kyomu gakari*).

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

< Notice >

From 2021, entrance examinations of the Global Frontier in Life Science will be held in winter instead of summer.

< Where to send your application, and Inquiries >

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

September, 2022

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

Division of Integrated Life Science

1) Laboratory of Gene Biodynamics

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

Outline of the research

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

Publications

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

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

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

Shiraishi, H. Association of heterotrophic bacteria with aggregated *Arthrospira platensis* exopolysaccharides: implications in the induction of axenic cultures. ***Biosci. Biotechnol. Biochem.*** 79, 331-341 (2015). doi: 10.1080/09168451.2014.972333

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

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

2) Laboratory of Cell Cycle Regulation

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

Outline of the research

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

Publications

Yamamoto I., *Nakaoka H., Takikawa M., Tashiro S., Kanoh J., *Miyoshi T., and *Ishikawa F. Fission yeast Stn1 maintains stability of repetitive DNA at subtelomere and ribosomal DNA regions. ***Nucleic. Acids Res.*** 49: 10465-10476 (2021).

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

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

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

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

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

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

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

3) Laboratory of Cell Recognition and Pattern Formation

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

Outline of the research

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

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

Publications (*: Faculties of the lab)

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

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

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

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

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

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

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

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

4) 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

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.

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

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

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

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

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*

5) 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.

6) 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

7) Laboratory of Applied Molecular Microbiology

PI: YAMANO, Takashi (Associate Prof.) <tyamano@lif.kyoto-u.ac.jp>

Outline of the research

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

Photosynthetic carbon fixation is the starting point of the global ecosystem's material cycle and also the turning point for the conversion of inorganic to organic materials. Therefore, it is crucial to understand the molecular mechanisms that maintain the flexibility and robustness of photosynthetic activities in a fluctuating environment. Using the photosynthetic organisms with phase-separated organelles as model, we aim to understand the survival strategies of photosynthetic organisms in molecular terms with the help of genetics, cell biology, high-resolution real-time imaging, and multi-omics analyses. Our research will help build the genetic and molecular foundation of photosynthetic engineering for solving various problems that human beings face, such as environmental destruction, CO_2 reduction, global warming, and food shortage.

Publications

Yamano, T., Toyokawa, C., Shimamura, D., Matsuoka, T., Fukuzawa, H. CO_2-dependent migration and relocation of LCIB, a pyrenoid-peripheral protein in *Chlamydomonas reinhardtii.* ***Plant Physiol.*** 188: 1081–1094 (2022) doi: 10.1093/plphys/kiab528.

Toyokawa, C., Yamano, T., Fukuzawa, H. Pyrenoid starch sheath is required for LCIB localization and the CO_2-

concentrating mechanism in green algae. ***Plant Physiol.*** 182: 1883–1893 (2020) doi: 10.1104/pp.19.01587.

Wang, L., Yamano, T., Takane, T., Niikawa, Y., Toyokawa, C., Ozawa, S., Tokutsu, R., Takahashi, Y., Minagawa, J., Kanesaki, Y., Yoshikawa, H., Fukuzawa, H. Chloroplast-mediated regulation of CO_2-concentrating mechanism by Ca^{2+}-binding protein CAS in the green alga *Chlamydomonas reinhardtii*. ***Proc. Natl. Acad. Sci. USA*** 113: 12586–12591 (2016). doi: 10.1073/pnas.1606519113.

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

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

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

Keywords: bioinformatics, chloroplast, CO_2-concentrating mechanism, multi-omics of photosynthetic organisms, photosynthesis, liquid-liquid phase separation, pyrenoid, single cell observation, *Chlamydomonas reinhardtii*

8) 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, and to develop food-and health-oriented application research.

Publications

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. ***The ISME J***. online (2022).

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).

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. ***Science Adv.*** 5:eaaw7696, (2019).

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

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

Key words: gut microbes, symbiosis, coevolution, enzyme

9) 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

10) 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

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.

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

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

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

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

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

11) 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

12) Laboratory of Biochemical Cell Dynamics

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

Outline of the research

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

Publications:

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

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

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

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

Suzuki J, Umeda M, Sims PJ, Nagata S. Calcium-dependent phospholipid scrambling by TMEM16F. ***Nature.***

468(7325):834-8. (2010) doi: 10.1038/nature09583.

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

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

13) 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

14) Laboratory of Ultrastructural Virology

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

Outline of the research

Virus infections are accompanied by numerous ultrastructural changes in viral and cellular components. Our laboratory

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

Publications

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)

Miyamoto S, Nakano M, Morikawa T, Hirabayashi A, Tamura R, Fujita-Fujiharu Y, Hirose N, Muramoto Y, Noda T*. Migration of influenza virus nucleoprotein into the nucleolus is essential for ribonucleoprotein complex formation. ***mBio*** 13(1):e03315-21. (2022)

Miyamoto S, Muramoto Y, Shindo K, Fujita-Fujiharu Y, Morikawa T, Tamura R, Gilmore JL, Nakano M, Noda T*. Contribution of RNA–RNA interactions mediated by the genome packaging signals for the selective genome packaging of influenza A virus. ***J Virol.*** 96(6):e0164121. (2022)

Takenaga T, Zhang Z, Muramoto Y, Fehling SK, Hirabayashi A, Takamatsu Y, Kajikawa J, Miyamoto S, Nakano M, Urata S, Groseth A, Strecker T, Noda T*. CP100356 Hydrochloride, a P-Glycoprotein Inhibitor, Inhibits Lassa Virus Entry: Implication of a Candidate Pan-Mammarenavirus Entry Inhibitor. ***Viruses*** 13(9):1763. (2021)

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, Lassa virus

Division of Systemic Life Science

1) Laboratory of Single-Molecule Cell Biology

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

Outline of the research

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

Publications:

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

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

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

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

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

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

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

Key words: Single-molecule imaging, actin, formin, mechanotransduction, super-resolution microscopy, cancer, neuron, tissue remodeling, target-based drugs

2) Laboratory of Immunobiology

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

Outline of the research

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

Publications

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

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

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

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

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

M. Takasato *et al.*, Directing human embryonic stem cell differentiation towards a renal lineage generates a selforganizing kidney. ***Nat. Cell Biol***. 16, 118–26 (2014). doi: 10.1038/ncb2894

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

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

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

Outline of the research

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

Publications

Li W, Cheng T, Jiang T, Zhou M, Gong B, Zhao G, Li J, Tan R, Yang X, Joshi K, Peng Y, Cheng M, Li T*, Wang DO*, Zheng J*. Hepatic RNA adduction derived from metabolic activation of retrorsine in vitro and in vivo. ***Chemico-Biological Interactions.*** Sep 365(25), 110047 (2022)

Sukegawa M, Yoshihara T*, Hou S, Asano M, Hannan A, Wang DO*. Behavioral impact of enriched environment, social isolation, and enrichment removal on BALB/c mice. ***Eur J Neurosci***. 2022 Mar; 55(5): 1118-1140

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Outline of the research
Our research focuses on the molecular basis of cell-cell communication that governs tissue growth, homeostasis, and cancer. We take advantage of the powerful genetics of Drosophila.
Research subjects:
1. Mechanism of cell competition
2. Genetic basis of tissue growth regulation
3. Molecular basis of tumor progression and metastasis
4. Cellular senescence and aging

Publications
Enomoto, M., Takemoto, D., and Igaki, T. Interaction between Ras and Src clones causes interdependent tumor malignancy via Notch signaling in *Drosophila*. ***Dev Cell*** in press 56: 2223-2236 (2021)

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

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

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

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

Vaughen, J. and Igaki, T. Slit-Robo repulsive signaling excludes tumorigenic cells from epithelia. ***Dev Cell*** 39: 683-695 (2016)

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

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

6) Laboratory of Chromosome Function and Inheritance

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

Outline of the research

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

Publications

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

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

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

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

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

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

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

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

7) Laboratory of Bioimaging and Cell Signaling

PI: KOBAYASHI, Taeko (Associate Prof.) < kobayashi.taeko.7e@kyoto-u.ac.jp>

Outline of the research

How is brain function maintained throughout life? In this increasingly aging society, it is imperative to keep healthy brain functions even in old age. **Quiescence in adult neural stem cells** might be crucial to addressing this question. Most neural stem cells (more than 90%) in the adult brain are quiescent. It remains unclear why so many neural stem cells (NSCs) persist in the quiescent state in the adult brain. Quiescence is essential in order to avoid precocious exhaustion of neural stem cells, ensuring a sustainable source of available stem cells in a specific niche without senescence throughout the lifespan. Quiescence of adult NSCs is tightly regulated by intrinsic and extrinsic factors, and diverse signaling from local NSC niches are involved in this process. We aim to reveal the mechanism of adult NSC maintenance from novel viewpoints of the '**lysosome**' and '**extracellular stiffness**' and to improve the functional decline of NSCs with age. We will clarify the molecular and physical mechanisms for maintenance of NSCs based on lysosomal control and contribute to developing new therapeutic tools for degenerative brain diseases, such as Alzheimer's disease.

Publications:

Zhang, J., Uchiyama, J., Imami, K., Ishihama, Y., Kageyama, R. and ***Kobayashi,T.** (2021) Novel roles of small extracellular vesicles in regulating the quiescence and proliferation of neural stem cells. ***Front. Cell. Dev. Biol.*** 9, 762293

Kobayashi, T. and *Kageyama, R. (2021) Lysosomes and signaling pathways for maintenance of quiescence in adult neural stem cells. ***FEBS J.*** 288, 3082-3093. (Review)

Kobayashi, T., Piao, W., Takamura, T., Kori, H., Miyachi, H., Kitano, S., Iwamoto, Y., Yamada, M., Imayoshi, I., Shioda, S., Ballabio, A., and *Kageyama, R. (2019) Enhanced lysosomal degradation maintains the quiescent state of neural stem cells. ***Nat. Commun.*** 10, 5446.

Kobayashi, T., Iwamoto, Y., Takashima, K, Isomura, A., Kosodo, Y., Kawakami, K., Nishioka, T., Kaibuchi, K., and *Kageyama, R. (2015) Deubiquitinating enzymes regulate Hes1 stability and neuronal differentiation. ***FEBS J.*** 282, 2475-2487.

Kobayashi, T. and *Kageyama, R. (2010) Hes1 regulates embryonic stem cell differentiation by suppressing Notch signaling. ***Genes Cells.*** 15, 689-698.

Kobayashi, T., Mizuno, H., Imayoshi, I., Furusawa, C., Shirahige, K. and *Kageyama, R. (2009) The cyclic gene Hes1 contributes to diverse differentiation responses of embryonic stem cells. ***Genes Dev.*** 23, 1870-1875.

Web site: https://takobayas.wixsite.com/homepage

Key words: Adult neural stem cells, Quiescence, Lysosomes, Extracellular stiffness, Alzheimer's disease

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

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

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

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

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

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

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

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

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

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

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

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

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

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:

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

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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

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

Publications

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: bornavirus, endogenous viruses, RNA virus vector

12) Laboratory of Cell Division and Differentiation

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

Outline of the research

Our laboratory studies on the physiological and pathophysiological organ remodeling during life-stages, such as pregnancy, obesity, and aging. We aim to clarify the mechanism of organ remodeling by which heterologous cell populations of stem cells, stromal cells, vasculature cells, immune cells, and neuronal cells communicate each other in cooperation with mechanofields and humoral factors. Based on the mechanisms, we are developing new technologies and therapeutic agents for regenerative and anti-aging medicine. We also study maternal organ remodeling during pregnancy to reveal molecular basis of developmental origin of health and disease (DOHaD).

Publications

Ichijo R, Maki K, Kabata M, Murata T, Nagasaka A, Ishihara S, Haga H, Honda T, Adachi T, Yamamoto T, Toyoshima F. Vasculature atrophy causes a stiffened microenvironment that augments epidermal stem cell differentiation in aged skin. ***Nat. Aging*** (in press. 2022). doi: 10.1038/s43587-022-00244-6.

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. ***Sci. Adv***. 7; eabj6895, 2021

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

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

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

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

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

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

13) 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., Kamioka, H., Adachi, T. High-resolution image-based simulation reveals membrane strain concentration on osteocyte processes caused by tethering elements. ***Biomech & Model Mechanobiol***., 20-6: 2353-2360 (2021). doi: 10.1007/s10237-021-01511-y

Kim, J., Ishikawa, K., Sunaga, J., Adachi, T. Uniaxially-fixed mechanical boundary condition elicits cellular alignment in collagen matrix with induction of osteogenesis. ***Sci Rep***, 11: #9009 (2021). doi: 10.1038/s41598-021-88505-z

Maki, K., Nava, M. M., Villeneuve, C., Chang, M., Furukawa, K., Ushida, T., Wickstrom, S. Hydrostatic pressure prevents chondrocyte differentiation through heterochromatin remodeling. ***J Cell Sci***, 134-2 (2021). doi: 10.1242/jcs.247643

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

Takeda, H., Kameo, Y., Adachi, T. Continuum modeling for neuronal lamination during cerebral morphogenesis considering cell migration and tissue growth. ***Comp Meth Biomech & Biomed Eng***, 24-7: 799-805 (2020). doi: 10.1080/10255842.2020.1852554

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

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