

2017- 2018
Graduate School of Biostudies, Kyoto University
Master's Program in "Global Frontier in Life Science"

Guidelines for International Student Admissions

Revised as of April 20, 2017

Philosophy and Admission Policy of the Graduate School of Biostudies

The field of life sciences is transforming and evolving into an advanced branch of science that will build a future for humans. With this global trend as a backdrop, the Graduate School of Biostudies was established in 1999 as Japan's first independent graduate school of biostudies with the aim of creating one of the world's top research institutions and developing bioscientists who will lead the next generation in the biostudies field. With a set of such basic units of life as "cells," "molecules," and "genes" as a common language, the Graduate School of Biostudies is home to innovative research and education activities where concepts about diverse organisms and the environments that sustain them are integrated to create new values concerning the future and respect for life.

In response to diverse social demands that call for an increasingly sophisticated and complex life sciences field, the Graduate School of Biostudies strives to develop the following human resources:

- 1) Researchers who explore and discover the basics of life, pursuing the cutting-edge field of biostudies at the highest level in the world;
- 2) Researchers and highly skilled engineers who contribute to society at public and private research institutions, endeavoring to protect the global environment and maintain human health, well-being, and fulfillment;
- 3) Educators and highly skilled practitioners who possess broad knowledge of diverse vital phenomena of living organisms and contribute to society through education, industry, mass media, and the public sector.

In April 2011, the Graduate School of Biostudies launched "Global Frontier in Life Science", a new educational program as a part of K.U. PROFILE (Kyoto University Programs for Future International Leaders: <http://www.opir.kyoto-u.ac.jp/kuprofile/e/index.html>). This program, "Global Frontier in Life Science", is held entirely in English, including the entrance examinations, lectures, experiments and discussions.

The Graduate School of Biostudies seeks international as well as domestic students who hope to join this program. In particular, the School welcomes those who show a respect for life and a desire to create a comprehensive and cutting-edge area within the life sciences field beyond existing disciplinary boundaries.

Admission examinations for the Master's program in "Global Frontier in Life Science" consist of: 1) a documentation screening and 2) an oral examination (interview). **Please note that applicants are NOT required to be physically present in Japan for the examination.**

The academic year starts on October 1, 2017 or April 1, 2018.

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, as part of K.U. PROFILE (Kyoto University Programs for Future International Leaders: <http://www.opir.kyoto-u.ac.jp/kuprofile/e/index.html>). This program, “Global Frontier in Life Science”, is held entirely in English, including the entrance examinations, lectures, experiments, and discussions. Up to ten applicants will be accepted.

II. Division/Laboratories and Enrollment

The Graduate School of Biostudies consists of two divisions, which are made up of 40 laboratories. Details of each laboratory are described on pp. 9 - 16 (to be publicized soon) 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-1. Eligibility Requirements for Applicants expecting to start from October 1, 2017

Applicants must match one of the following requirements by September 30, 2017:

1. Individuals with any nationality who have completed (or are expected to complete by September 30, 2017) 16 years of education in foreign countries.
2. Individuals, other than Japanese nationals, who graduated (or are expected to graduate by September 30, 2017) from a Japanese university.
3. Individuals who have received (or are expected to receive by September 30, 2017) 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 September 30, 2017.
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, 2017.

[Note 1] Regarding requirement 1, this includes individuals who have completed an equivalent of 16 years of education but have less than 16 years due to skipped (advanced) grades.

[Note 2] **Those who are applying under requirement 4 or 5 must undergo a preliminary eligibility screening process before applying.**

III-2. Eligibility Requirements for Applicants expecting to start from April 1, 2018

Applicants must match one of the following requirements by March 31, 2018:

1. Individuals with any nationality who have completed (or are expected to complete by March 31, 2018) 16 years of education in foreign countries.
2. Individuals, other than Japanese nationals, who graduated (or are expected to graduate by March 31, 2018) from a Japanese university.
3. Individuals who have received (or are expected to receive by March 31, 2018) 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, 2018.
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, 2018.
6. Individuals, other than Japanese nationals, who will be enrolled at least 3 years in a Japanese university by March 31, 2018 and are recognized by the Graduate School of Biostudies as having acquired sufficient credits with excellent academic records.

[Note 1] Regarding requirement 1, this includes individuals who have completed an equivalent of 16 years of education but have less than 16 years due to skipped (advanced) grades.

[Note 2] **Those who are applying under requirement 4, 5, or 6 must undergo a preliminary eligibility screening process before applying.**

IV. 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 April 13 (Thu), 2017. Submit the following preliminary eligibility screening documents by 5:00 p.m., April 20 (Thu), 2017 at latest. (When mailing the documents, write "Eligibility Screening Application for International Applicants to the Master's Program of the Graduate School of Biostudies" on the front of the envelope, and use "registered mail" or "simplified registered mail", ensuring that the mail is delivered by 5:00 p.m., April 20 (Thu), 2017 at latest.) When filing the admission application, applicants cannot in principle apply for any laboratory other than the one specified in the documents being submitted for the eligibility screening.

1. 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	This form is provided upon request. (designated form)
(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 E-mail 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)	Any scores of the Subject Test are optional. Acceptable test includes: Biology/ Biochemistry, Cell and Molecular/Biology/Chemistry/Physics.

Note: 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. Screening procedure and Schedule

- (1) Applicants filing an application for preliminary eligibility screening under eligibility requirement 4, 5, or 6 are subject to the preliminary eligibility screening.
- (2) The screening results will be sent by e-mail to the applicants as soon as the decision is made, at latest on May 10 (Wed), 2017.

Note: Successful applicants filing under the eligibility requirement 6, expecting to matriculate in April, 2018, must submit an academic transcript for the 2017 academic year to the Student Affairs Section (Kyomu gakari) of the Graduate School of Biostudies by February 23 (Thu), 2018. 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 30 (Thu), 2018; thus, they cannot obtain a bachelor's degree at the university currently attended.

V. Application Fee

Application fee: 10,000 yen

Payment period: From May 1 (Mon) to May 18 (Thu), 2017 **JST**

Only payments marked as made within this period will be valid; those made outside this period will be invalid.

Note: In the event that the principal household supporter of applicant was afflicted by the east Japan great earthquake in the Disaster-Relief-Law application area in March, 2011 and can receive the “certificate of victim”, etc., the applicant may be exempted from the admission fee. Contact the Student Affairs Section (Kyomu gakari) by May 8 (Mon), 2017, if it is applicable.

[Payment methods] Revised as of April 20, 2017

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 (500 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”.

EXSS: <https://www3.univ-jp.com/kyoto-u/en/bio/>

Note: The Application Completed page must be printed out and submitted along with the other application documents (see section VI below).

Once received, application fees will not be refundable under any circumstances.

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 (500 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”.

EXSS: <https://www3.univ-jp.com/kyoto-u/en/bio/>

Note: The Application Completed page must be printed out and submitted along with the other application documents (see section VI below).

Once received, application fees will not be refundable under any circumstances.

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

Applicants residing inside Japan should pay the application fee (10,000 yen) by bank transfer with the following procedures.

Payment at a bank window in Japan

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

Note: Once received, application fees will not be refundable under any circumstances.

VI. Application Documents

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| (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. |
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| (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. |
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| (3) Academic transcript | Submit an academic transcript prepared and sealed by the university you are currently attending or from which you have graduated. |
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| (4) Graduation certificate (or certificate of expected graduation) | Submit a certificate prepared by the university you are currently attending or from which you have graduated. |
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| (5) Recommendation letters | <u>At least two</u> letters are requested.
(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. |
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(6) A valid score for GRE General Test and Subject Test	General Test score is essential. Any scores of the Subject Test are optional. Acceptable test includes: Biology/Biochemistry, Cell and Molecular Biology/Chemistry/Physics.
(7) A valid score for IELTS or TOEFL	Unnecessary for English-native speakers (Please contact the Student Affairs Section in advance.)
(8) Evidence of Application Fee Payment Form	<p>Applicants residing outside Japan: After paying your application fees via internet, <u>the Application Completed page must be printed out and submitted.</u> Applications will not be accepted if payment could not be confirmed.</p> <p>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.</p>
(9) Address for further communication	<p>Use the designated forms.</p> <p>For further communication on the examination results and the enrollment procedures, clearly write your name, address and post code on the designated form.</p> <p>*If you change your address after applying, you must promptly inform the new address to the Student Affairs Section (Kyomugakari) of the Graduate School of Biostudies.</p>

VII. Application Procedures

Applicants must prepare a packet of all necessary admission application documents and submit it to the address indicated on p. 9. When mailing the packet, 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.

VIII. Application Period

The application period is from May 11 (Thu) to May 19 (Fri), 2017.

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 mailing the application documents, ensure that the application documents are delivered by 5:00 p.m. on May 19 (Fri), 2017.

Note that the admission application form will not be accepted if 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.

IX. Examination Schedule

May 29 (Mon) ~ June 9 (Fri)	<p>Documentation Screening</p> <p>Only successful applicants who pass the screening of the admission documents will be able to take the interview (Oral Examination).</p>
June 19 (Mon) ~ July 14 (Fri)	<p>Interview (Oral Examination)</p> <p>The interview date and method* will be arranged individually after the decision is made.</p> <p>*e.g. Skype or other protocols</p>

X. Announcement of Successful Applicants

The list of successful applicants is scheduled to be posted on a bulletin board on the 1st floor of the South Campus Research Bldg. (Faculty of Medicine Bldg. G) at approximately 5p.m., July 26 (Wed), 2017. Simultaneously, the same list will be posted on the web site of the Graduate School of Biostudies (<http://www.lif.kyoto-u.ac.jp/e/>). Telephone inquiries about the selection results shall not be accepted.

XI. Admission Fee and Tuition

Admission Fee : 282,000 yen (tentative)

The admission fee amount may be revised at the time of enrollment.

Tuition for the first semester : 267,900 yen (annual tuition: 535,800 yen, tentative)

The tuition amount may be revised at the time of enrollment or later.

Notes:

- (1) “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 80-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 and sent by an international courier to each successful applicant in late July, 2017 for those who would like to enroll in October, 2017. For those who will enroll in April, 2018, it will be informed in early February, 2018.
 - 4) Applicants with physical disabilities (degree of physical disability as stipulated in the enforcement ordinance of the School Education Law) who require special arrangements for taking examinations or attending courses should immediately contact the Student Affairs Section (Kyomu gakari).

[Handling of Personal Information]

Personal information provided in application documents will be handled in accordance with “Kyoto University’s Rules regarding the Protection of Personal Information.”

< Where to send your application, and Inquiries >

Student Affairs Section (Kyomu gakari) of the Graduate School of Biostudies, Kyoto University
Yoshida-Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan

Phone: +81-75-753-9424

Fax: +81-75-753-9229

E-mail: 150kyomu@adm.lif.kyoto-u.ac.jp

April, 2017

Graduate School of Biostudies, Kyoto University

<http://www.lif.kyoto-u.ac.jp/e/>

Global Frontier in Life Science
Graduate School of Biostudies (GSB), Kyoto University
Research Fields and Contents of Research – December, 2016

Division of Integrated Life Science

1) Laboratory of Chromosome Transmission

PI: NAKASEKO, Yukinobu (Associate Prof.) <nakaseko@lif.kyoto-u.ac.jp>

Outline of the research

Our research is focused on the cell cycle regulation of eukaryotic cells. Using fission yeast as a model system, regulation of chromosome segregation and separation during mitosis has been studied. We are trying to identify individual genes involved in these steps and to elucidate the functional networks of these genes.

Publications

Nakamura, T., Pluskal, T., Nakaseko, Y., and Yanagida, M. Impaired coenzyme A synthesis in fission yeast causes defective mitosis, quiescence-exit failure, histone hypoacetylation and fragile DNA. *Open Biol.* **2**, 120117 (2012). doi: 10.1098/rsob.120117.

Irvine, D. V., Goto, D. B., Vaughn, M. W., Nakaseko, Y., McCombie, W. R., Yanagida, M., and Martienssen, R. Mapping epigenetic mutations in fission yeast using whole-genome next-generation sequencing. *Genome Res.* **19**, 1077-1083 (2009). doi: 10.1101/gr.089318.108.

Hanyu, Y., Imai, K. K., Kawasaki, Y., Nakamura, T., Nakaseko, Y., Nagao, K., Kokubu, A., Ebe, M., Fujisawa, A., Hayashi, T., Obuse, C., and Yanagida, M. *Schizosaccharomyces pombe* cell division cycle under limited glucose requires Ssp1 kinase, the putative CaMKK, and Sds23, a PP2A-related phosphatase inhibitor. *Genes Cells.* **14**, 539-554 (2009). doi: 10.1111/j.1365-2443.2009.01290.x.

Website of the lab: http://www.lif.kyoto-u.ac.jp/e/?post_type=labos&p=135

Key words: chromosome, cell cycle, genetic analysis

2) Laboratory of Gene Biodynamics

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

Outline of the research

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

Publications

Shiraishi, H. Cryopreservation of the edible alkalophilic cyanobacterium *Arthrospira platensis*. *Biosci. Biotechnol. Biochem.* **80**, 2051-2057 (2016). PMID: 27240586

Shiraishi, H. Association of heterotrophic bacteria with aggregated *Arthrospira platensis* exopolysaccharides: implications in the induction of axenic cultures. *Biosci. Biotechnol. Biochem.* **79**, 331-341 (2015). PMID: 25333502

Shiraishi, H. and Tabuse, Y. The *Apl* I restriction-modification system in an edible cyanobacterium, *Arthrospira (Spirulina) platensis* NIES-39, recognizes the nucleotide sequence 5'-CTGCAG-3'. *Biosci. Biotechnol. Biochem.*, **77**, 782-788 (2013). PMID: 23563565

Fukada, K., Inoue, T. and Shiraishi, H. A post-translationally regulated protease, VheA, is involved in the liberation of juveniles from parental spheroids in *Volvox carteri*. *Plant Cell*, **18**, 2554-2566 (2006). PMID: 17028206

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

Global Frontier in Life Science
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Research Fields and Contents of Research – December, 2016

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

3) Laboratory of Cell Cycle Regulation

PI: ISHIKAWA, Fuyuki (Prof.) <fishikaw@lif.kyoto-u.ac.jp>

Outline of the research

This laboratory is interested in understanding the mutual interactions between the genome and the surrounding environment. For example, how do organisms preserve their internal resources until their surrounding conditions are suitable for reproduction? How do they prevent mortal pathologies such as cancers until they complete growth and reproduction? Is aging a consequence of damage accumulation caused by fluctuating harsh environments? Does the ever changing microenvironments in the wild in contrast to those persistently cultivated in laboratories, play a significant role, if any, in the life history of an organism in nature? To address these questions, our team branches into three distinct research teams: telomere group, low-dose stress group, and retrotransposon group.

Publications

Chujo, M., Tatumoto, Y., Miyatake, K., Nishida, E. and Ishikawa, F. HIRA, a conserved histone chaperone plays an essential role in low-dose stress response via transcriptional stimulation in fission yeast. *J. Biol. Chem.* 287: 23440-23450 (2012). doi: 10.1074/jbc.M112.349944

Miyake, Y., Nakamura, M., Nabetani, A., Shimamura, S., Tamura, M., Yonehara, S., Saito, M. and Ishikawa, F. RPA-like mammalian Ctc1-Stn1-Ten1 complex binds to single-stranded DNA and protects telomeres independently of the Pot1 pathway. *Mol. Cell* 36: 193-206 (2009). doi: 10.1016/j.molcel.2009.08.009

Ishikawa, F. and Naito, T. Why do we have linear chromosomes? A matter of Adam and Eve. *Mut. Res.* 434: 99-107 (1999). doi: 10.1016/S0921-8777(99)00017-8

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

Key words: telomere, stress response, retrotransposon

4) Laboratory of Cell Recognition and Pattern Formation

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

Outline of the research

1. Nutri-developmental biology: Deciphering nutrient balance-dependent animal growth by comparative multi-omics
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

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 by using ecologically distinct *Drosophila* species that have different dietary preferences. We are also taking a prey-predator interspecies genetic approach to understand compositions of nutrients that are optimal to animal growth. 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 separate 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 introduce a variety of molecular, cellular, genomic, imaging, multi-omics, and physiological approaches.

Publications

Global Frontier in Life Science
Graduate School of Biostudies (GSB), Kyoto University
Research Fields and Contents of Research – December, 2016

Terada, S., Matsubara, D., Onodera, K., Matsuzaki, M., *Uemura, T. and *Usui, T. (*Corresponding authors). Neuronal processing of noxious thermal stimuli mediated by dendritic Ca²⁺ influx in *Drosophila* somatosensory neurons. *eLife* 5: e12959 (2016). doi: 10.7554/eLife.12959

Shi, D., Arata M., Usui, T., Fujimori T. and Uemura, T. Seven-pass transmembrane cadherin CELSRs, and Fat4 and Dchs1 cadherins: from planar cell polarity to three-dimensional organ architecture. Chapter 10 (p251-275) in “The Cadherin Superfamily: Key Regulators of Animal Development and Physiology” (S. Suzuki and S. Hirano eds, Springer) (2016).

Shimono, K., Fujishima, K., Nomura, T., Ohashi, M., Usui, T., Kengaku, M., Toyoda, A. and Uemura, T. An evolutionarily conserved protein CHORD regulates scaling of dendritic arbors with body size. *Sci. Rep.* 4: 4415 (2014). doi: 10.1038/srep04415

Hattori, Y., Usui, T., Satoh, D., Moriyama, S., Shimono, K., Itoh, T., Shirahige, K. and Uemura, T. Sensory-neuron subtype-specific transcriptional programs controlling dendrite morphogenesis: genome-wide analysis of *Abrupt* and *Knot/Collier*. *Dev. Cell* 27: 530-544 (2013). doi: 10.1016/j.devcel.2013.10.024

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

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

Key words: development, nutrition, neuroscience, morphogenesis

5) Laboratory of Plant Molecular Biology

PI: KOHCHI, Takayuki (Prof.) <tkohchi@lif.kyoto-u.ac.jp>

Outline of the research

1. Photomorphogenesis and environmental regulation of plant development
2. Comparative genomics and molecular genetics with the liverwort, *Marchantia polymorpha*
3. Genomic and post-genomic analyses of *Marchantia polymorpha*

Publications

Inoue, K., Nishihama, R., Kataoka, H., Hosaka, M., Manabe, R., Nomoto, M., Tada, Y., Ishizaki, K. and Kohchi, T. Phytochrome signaling is mediated by PHYTOCHROME INTERACTING FACTOR in the liverwort *Marchantia polymorpha*. *Plant Cell* 28: 1406-1421 (2016). doi: 10.1105/tpc.15.01063

Kato, H., Ishizaki, K., Kouno, M., Shirakawa, M., Bowman, J. L., Nishihama, R. and Kohchi, T. Auxin-mediated transcriptional system with a minimal set of components is critical for morphogenesis through the life cycle in *Marchantia polymorpha*. *PLOS Genet.* 11: e1005084 (2015). doi: 10.1371/journal.pgen.1005084

Komatsu, A., Terai, M., Ishizaki, K., Suetsugu, N., Tsuboi, H., Nishihama, R., Yamato, K. T., Wada, M. and Kohchi, T. Phototropin encoded by a single-copy gene mediates chloroplast photorelocation movements in the liverwort *Marchantia polymorpha* L. *Plant Physiol.* 166: 411-427 (2014). doi: 10.1104/pp.114.245100

Kubota, A., Kita, S., Ishizaki, K., Nishihama, R., Yamato, K. T. and Kohchi, T. Co-option of a photoperiodic growth-phase transition system during land plant evolution, *Nature Comm.* 5, 3668 (2014). doi: 10.1038/ncomms4668

Website of the lab: <http://www.plantmb.lif.kyoto-u.ac.jp/>

Key words: land plant evolution, light signaling, plant development, *Marchantia polymorpha*

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6) Laboratory of Biosignals and Response

PI: NAGAO, Masaya (Prof.) <mnagao@kais.kyoto-u.ac.jp>

Outline of the research

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

Publications

Fujimoto, S., Tsuji, T., Fujiwara, T., Takeda, T.A., Merriman, C., Fukunaka, A., Nishito, Y., Fu, D., Hoch, E., Sekler, I., Fukue, K., Miyamae, Y., Masuda, S., Nagao, M., Kambe, T. The PP-motif in luminal loop 2 of ZnT transporters plays a pivotal role in TNAP activation. *Biochem J.* 473 (17) 2611-2621 (2016), doi: 10.1042/BCJ20160324

Miyamae, Y., Nishito, Y., Nakai, N., Nagumo, Y., Usui, T., Masuda, S., Kambe, T., Nagao, M. Tetrandrine induces lipid accumulation through blockade of autophagy in a hepatic stellate cell line. *Biochem Biophys Res Commun.* 477, 40-46 (2016), doi: 10.1016/j.bbrc.2016.06.018

Ohtera, A., Miyamae, Y., Yoshida, K., Maejima, K., Akita, T., Kakizuka, A., Irie, K., Masuda, S., Kambe, T., Nagao, M. Identification of a New Type of Covalent PPAR γ Agonist using a Ligand-Linking Strategy. *ACS Chem Biol.* 10, 2794-2804 (2015), doi: 10.1021/acschembio.5b00628

Hashimoto, A., Ohkura, K., Takahashi, M., Kizu, K., Narita, H., Enomoto, S., Miyamae, Y., Masuda, S., Nagao, M., Irie, K., Ohigashi, H., Andrews, G.K., Kambe, T. Soybean extracts increase cell surface ZIP4 abundance and cellular zinc levels: a potential novel strategy to enhance zinc absorption by ZIP4 targeting. *Biochem J.* 472, 183-193 (2015), doi: 10.1042/BJ20150862

Ohtera, A., Miyamae, Y., Nakai, N., Kawachi, A., Kawada, K., Han, J., Isoda, H., Neffati, M., Akita, T., Maejima, K., Masuda, S., Kambe, T., Mori, N., Irie, K., Nagao, M. Identification of 6-octadecynoic acid from a methanol extract of *Marrubium vulgare* L. as a peroxisome proliferator-activated receptor γ agonist. *Biochem Biophys Res Commun.* 440, 204-209 (2013), doi: 10.1016/j.bbrc.2013.09.003

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

Key words: bioactive compounds, screening, zinc, transporter

7) Laboratory of Applied Molecular Microbiology

PI: FUKUZAWA, Hideya (Prof.) <fukuzawa@lif.kyoto-u.ac.jp>

Outline of the research

We are focusing on the molecular bases of biological functions of photosynthetic microorganisms contributing to production of food, carbon-neutral renewable bio-energy and industrial materials, and also to environmental remediation by photosynthesis. Especially we employ a green alga, *Chlamydomonas reinhardtii*, as a model eukaryotic microorganism using its genome information, mutants, and molecular or biochemical techniques. The current projects are (1) Molecular characterization and modification of the carbon-concentrating mechanism supporting photosynthetic carbon fixation, energy production, and cell proliferation, (2) Elucidation of regulatory network systems controlling photosynthesis by sensing environmental factors including changes of levels in CO₂ concentration and light, (3) Elucidation and engineering of metabolic pathways for production of neutral lipids, hydrocarbons, and carbohydrates under specific culture conditions, (4) Molecular control and signaling of sexual reproduction by nutrient starvation.

Publications

Wang L. et al., "Chloroplast-mediated regulation of CO₂-concentrating mechanism by Ca²⁺-binding protein CAS in the green alga *Chlamydomonas reinhardtii*." *Proc. Natl. Acad. Sci. USA* 113:12586-12591 (2016). doi: 10.1073/pnas.1606519113, PMID: 27791081

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Kajikawa M. et al. "Production of ricinoleic acid-containing monoester diacylglycerides in an oleaginous diatom, *Chaetoceros gracilis*." *Scientific Reports* 6, 36809 (2016) doi:10.1038/srep36809, PMID: 27830762

Yamano T. et al., "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, PMID: 26015566

Kajikawa M. et al. "Algal dual-specificity tyrosine phosphorylation-regulated kinase, triacylglycerol accumulation regulator 1, regulates accumulation of triacylglycerol in nitrogen or sulfur deficiency." *Plant Physiol.* 168: 7752-764 (2015). doi: 10.1104/pp.15.00319, PMID: 25922058

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

Key words: algal biofuel, CO₂-sensing mechanism, photosynthetic acclimation, calcium signaling

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 relationship between gut microbes and host, and to develop food-and health-oriented application research. We are also focused on the elucidation of mechanisms of mRNA processing, export, and quality control in the nucleus in human and its industrial applications.

Publications

Katoh, T., Katayama, T., Tomabechei, Y., Nishikawa, Y., Kumada, J., Matsuzaki, Y., and Yamamoto, K. Generation of a mutant *Mucor hiemalis* endoglycosidase that acts on core-fucosylated *N*-glycans. *J. Biol. Chem.* in press.

Sugiyama, Y., Gotoh, A., Katoh, T., Honda, Y., Yoshida, E., Kurihara, S., Ashida, H., Kumagai, H., Yamamoto, K., Kitaoka, M. and Katayama, T. Introduction of H-antigens into oligosaccharides and sugar chains of glycoproteins using highly efficient 1,2- α -L-fucosyltransferase. *Glycobiol.* in press. (2016). doi: 10.1093/glycob/cww085

Yamazaki, T., Fujiwara, N., Yukinaga, H., Ebisuya, M., Shiki, T., Kurihara, T., Kioka, N., Kambe, K., Nagao, M., Nishida, E., and Masuda S. The closely related RNA helicases, UAP56 and URH49, preferentially form distinct mRNA export machineries and coordinately regulate mitotic progression. *Mol. Biol. Cell.* 21:2953-2965 (2010).

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

Key words: gut microbes, symbiosis, mRNA, export

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) tissue-specific roles of circadian clock for optimal environmental responses, (4) sexual reproduction processes, and (5)

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origin and evolution of regulatory systems for plastic development.

Publications

Higo, A., Niwa, M., Yamato, K. T., Yamada, L., Sawada, H., Sakamoto, T., Kurata, T., Shirakawa, M., Endo, M., Shigenobu, S., Ishizaki, K., Nishihama, R., Kohchi, T. and Araki, T. Transcriptional framework of male gametogenesis in the liverwort *Marchantia polymorpha* L. *Plant Cell Physiol.* 57: 325-338 (2016). doi: 10.1093/pcp/pcw005

Kawamoto, N., Sasabe, M., Endo, M., Machida, Y. and Araki, T. Calcium-dependent protein kinases responsible for the phosphorylation of a bZIP transcription factor FD crucial for the florigen complex formation. *Sci. Rep.* 5: 8341, 1-9 (2015). doi: 10.1038/srep08341

Shimizu, H., Katayama, K., Koto, T., Torii, K., Araki, T. and Endo, M. Decentralized circadian clocks process thermal and photoperiodic cues in specific tissues. *Nature Plants* 1: 15163, 1-6 (2015). doi: 10.1038/nplants.2015.163

Endo, M., Shimizu, H., Nohales, M.A., Araki, T. and Kay, S.A. Tissue-specific clocks in Arabidopsis show asymmetric coupling. *Nature* 515: 419-422 (2014). doi: 10.1038/nature13919

Niwa, M., Daimon, Y., Kurotani, K., Higo, A., Pruneda-Paz, J.L., Breton, G., Mitsuda, N., Kay, S.A., Ohme-Takagi, M., Endo, M., and Araki, T. BRANCHED1 interacts with FLOWERING LOCUS T to repress the floral transition of the axillary meristems in Arabidopsis. *Plant Cell* 25: 1228-1242 (2013). doi: 10.1105/tpc.112.109090

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

Key words: flowering, florigen, circadian clock, sexual reproduction, 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 dynamic properties of proteins and large protein complexes in cellular environments by using a variety of techniques in biochemistry, molecular biology and cellular biology, in combination with nano-imaging techniques and computational simulation. Specific research topics include: (1) how dynamic assembly-disassembly of intracellular architectures (nuclear envelope, chromosome, etc) proceed in mitosis, (2) how structural dynamics of actin network is regulated by related proteins and mechanical stresses, (3) how endocytotic process is coordinated by membrane-bound proteins, cytoskeletal network and lipid membrane.

Publications

Lolodi, O., Yamazaki, H., Otsuka, S., Kumeta, M. and Yoshimura S.H. Dissecting in vivo steady-state dynamics of karyopherin-dependent nuclear transport. *Mol. Biol. Cell.* 27: 167-176 (2016). doi: 10.1091/mbc.E15-08-0601

Yoshimura, S.H., Kumeta, M. and Takeyasu, K. Structural mechanism of nuclear transport mediated by importin β and flexible amphiphilic proteins. *Structure* 22: 1699-1710 (2014). doi: 10.1016/j.str.2014.10.009

Yoshimura, S.H., Otsuka, S., Kumeta, M., Taga, M., Takeyasu, K. Intermolecular disulfide bonds between nucleoporins regulate karyopherin-dependent nuclear transport. *J. Cell Sci.* 126: 3141-3150 (2013). doi: 10.1242/jcs.124172

Otsuka, S., Iwasaka, S., Yoneda, Y., Takeyasu, K., Yoshimura, S.H. Individual binding pockets of importin-beta for FG-nucleoporins have different binding properties and different sensitivities to RanGTP. *Proc. Natl. Acad. Sci. U S A.* 105: 16101-16116 (2008). doi: 10.1073/pnas.0802647105

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

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Key words: atomic force microscopy, molecular crowding, cytoskeletal dynamics, membrane dynamics, mechano-biology, molecular dynamics simulation

11) Laboratory of Genome Maintenance

PI: MATSUMOTO, Tomohiro (Prof.) <tmatsumo@house.rbc.kyoto-u.ac.jp>

Outline of the research

The spindle checkpoint is a unique negative feedback that converts/amplifies a physical signal sensed by kinetochores (attachment of the spindle and/or tension), and regulates the timing of sister chromatid separation for equal chromosome segregation. Mad2, a signal carrier of this feedback, plays a vital role in the spindle checkpoint. It is specifically localized at unattached kinetochores that are the origin of the checkpoint signal. Mad2 targets CDC20 and inhibits its activity to promote sister chromatid separation. We study Mad2, a central player of the spindle checkpoint, to reveal mechanisms which regulate the activity of Mad2.

Publications

Kitagawa T., Ishii K., Takeda K. and Matsumoto T. (2014) The 19S proteasome subunit Rpt3 regulates distribution of CENP-A by associating with centromeric chromatin. *Nat Commun.* doi: 10.1038/ncomms4597.

Horikoshi Y, Habu T and Matsumoto T. (2013) An E2 enzyme Ubc11 is required for ubiquitination of Slp1/Cdc20 and spindle checkpoint silencing in fission yeast. *Cell Cycle.* 12:961-71.

Ito D, Saito Y and Matsumoto T. (2012) Centromere-tethered Mps1 pombe homolog (Mph1) kinase is a sufficient marker for recruitment of the spindle checkpoint protein Bub1, but not Mad1. *Proc Natl Acad Sci U S A.* 109:209-14.

Website of the lab: http://house.rbc.kyoto-u.ac.jp/radiation_system/

Key words: chromosome, mitosis, centromere

12) Laboratory of Developmental Neurobiology

PI: KENGAKU, Mineko (Prof.) <kengaku@icems.kyoto-u.ac.jp>

Outline of the research

We study the dynamics and mechanisms of the formation of neural networks in the brain. We also aim to develop live-imaging techniques for observation of molecular signals controlling cell motility in the developing brain.

Publications

Fukumitsu, K., Hatsukano, T., Yoshimura, A., Heuser, J., Fujishima, K. and Kengaku, M. Mitochondrial fission protein Drp1 regulates mitochondrial transport and dendritic arborization in cerebellar Purkinje cells. *Mol Cell Neurosci.* 71:56-65 (2016). doi: 10.1016/j.mcn.2015.12.006.

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

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

Umeshima, H., Hirano, T. and Kengaku, M. Microtubule-based nuclear movement occurs independently of centrosome positioning in migrating neurons. *Proc. Natl. Acad. Sci. U S A.* 104:16182-16187 (2007). PMID:

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Website of the lab: <http://www.kengaku.icems.kyoto-u.ac.jp/index.html>

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

13) Laboratory of Molecular and Cellular Immunology

PI: FUJITA, Takashi (Prof.) <tfujita@virus.kyoto-u.ac.jp>

Outline of the research

Virus infections such as influenza A epidemic and Chronic Hepatitis B virus infection are still important diseases, and outbreaks of newly emerging viruses are serious problems for modern society. Higher animals, including humans, are genetically equipped with mechanisms, collectively known as innate immunity, to counteract viral infections.

The purpose of our project is to clarify the molecular mechanism underlying antiviral innate immunity regulated by RIG-I, a cytoplasmic sensor for viral RNA, and to develop new diagnostic and therapeutic tools for viral infections.

Publications

Onomoto, K., Yoneyama, M., Fung, G., Kato, H. and Fujita, T: Antiviral innate immunity and stress granule responses. *Trends Immunol.* 35, 420-8 (2014).

Yoneyama, M., Onomoto, K., Jogi, M., Akaboshi, T. and Fujita, T. Viral RNA detection by RIG-I-like receptors. *Curr. Opin. Immunol.* 32: 48-53 (2015). doi: 10.1016/j.coi.2014.12.012

Kato, H. and Fujita, T. RIG-I-like receptors and autoimmune diseases. *Curr. Opin. Immunol.* 37: 40-45 (2015). doi: 10.1016/j.coi.2015.10.002

Website of the lab: <http://www.virus.kyoto-u.ac.jp/Lab/bunshiiden2012/English/index.html>

Key words: virus infection, interferon, innate immunity, non-self nucleic acid recognition, autoimmunity

14) Laboratory of Developmental Dynamics

PI: KAGEYAMA, Ryoichiro (Ptof.) <rkageyam@virus.kyoto-u.ac.jp>

Outline of the research

We analyze the molecular mechanism of embryonic development by using imaging, optogenetics and transgenic mouse technologies. We evaluate mathematical modeling to understand the principles of developmental dynamics.

Publications

Shimojo, H., Isomura, A., Ohtsuka, T., Kori, H., Miyachi, H. and Kageyama, R. Oscillatory control of Delta-like1 in cell interactions regulates dynamic gene expression and tissue morphogenesis. *Genes Dev.* 30: 102-116 (2016). doi: 10.1101/gad.270785.11

Imayoshi, I., and Kageyama, R. bHLH factors in self-renewal, multipotency, and fate choice of neural progenitor cells. *Neuron* 82: 9-23 (2014). doi: 10.1016/j.neuron.2014.03.018

Imayoshi, I., Isomura, A., Harima, Y., Kawaguchi, K., Kori, H., Miyachi, H., Fujiwara, T.K., Ishidate, F., and Kageyama, R. (2013) Oscillatory control of factors determining multipotency and fate in mouse neural progenitors. *Science* 342, 1203-1208. doi: 10.1126/science.1242366

Website of the lab: http://www.virus.kyoto-u.ac.jp/Lab/Kageyama/index_English.html

Key words: live imaging, Notch signaling, optogenetics, oscillatory expression, segmentation clock

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15) Laboratory of Ultrastructural Virology

PI: NODA, Takeshi (Prof.) <t-noda@virus.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 replication mechanism of influenza and Ebola viruses mainly from the ultrastructural point of view, by using 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

Nakatsu, S., Sagara, H., Sakai, Y. T., Sugaya, N., Noda, T. and Kawaoka, Y. Complete and incomplete genome packaging of influenza A and B viruses. *mBio* 7: e01248-16 (2016).

Sugita, Y., Sagara, H., Noda, T., and Kawaoka, Y. The configuration of viral ribonucleoprotein complexes within the influenza A virion. *J Virol.* 87: 12879-12884 (2013).

Goto, H., Muramoto, Y., Noda, T. and Kawaoka, Y. The genome-packaging signal of the influenza A virus genome comprises a genome incorporation signal and a genome-bundling signal. *J. Virol.* 87: 11316-11322 (2013).

Takahashi, K., Halfmann, P., Oyama, M., Kozuka-Hata, H., Noda, T. and Kawaoka, Y. DNA topoisomerase 1 facilitates the transcription and replication of the Ebola virus genome. *J. Virol.* 87: 8862-8869 (2013).

Muramoto, Y., Noda, T., Kawakami, E., Akkina, R., and Kawaoka, Y. Identification of novel influenza A virus proteins translated from PA mRNA. *J. Virol.* 87: 2455-2462 (2013).

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

Key words: influenza virus, reverse genetics, transmission electron microscopy

Division of Systemic Life Science

1) Laboratory of Single-Molecule Cell Biology

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

Outline of the research

By using high-resolution live-cell fluorescence Single-Molecule Speckle (SiMS) microscopy and our new multi-target high-density labeling super resolution microscopy IRIS, we are trying to bridge the gap between molecular behavior and cell/body functions including mechanotransduction, cancer invasion, tissue remodeling and drug response.

Publications

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

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

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

Key words: single-molecule imaging, super-resolution microscopy, cancer therapy

2) Laboratory of Bioimaging and Cell Signaling

PI: MATSUDA, Michiyuki (Prof.) <matsudam@lif.kyoto-u.ac.jp>

Outline of the research

We are visualizing the growth signal transduction cascades in living cells by using probes based on the principle of Foerster resonance energy transfer (FRET). The FRET biosensors are extremely powerful to visualize the spatio-temporal regulation of signal transduction networks within cells and to analyze the activities of individual cells within tissues. These FRET videos are also processed to extract parameters that characterize the property of each signaling molecule. We use these parameters obtained in living cells to build kinetic simulation models of growth signal transduction cascades.

Publications

Yamauchi, F., Kamioka, Y., Yano, T. and Matsuda, M. In Vivo FRET imaging of tumor endothelial cells highlights a role of low PKA activity in vascular hyperpermeability. *Cancer Res.* 76:5266-5276 (2016). doi: 10.1158/0008-5472.CAN-15-3534. PMID: 27488524

Hiratsuka, T., Fujita, Y., Naoki, H., Aoki, K., Kamioka, Y., and Matsuda, M. Intercellular propagation of extracellular signal-regulated kinase activation revealed by in vivo imaging of mouse skin. *eLife* 4:e05178 (2015). doi: 10.7554/eLife.05178. PMID: 25668746

Aoki, K., Kumagai, Y., Sakurai, A., Komatsu, N., Fujita, Y., Shionyu, C. and Matsuda, M. Stochastic ERK activation induced by noise and cell-to-cell propagation regulates cell density-dependent proliferation. *Mol. Cell* 52:529-540 (2013). doi: 10.1016/j.molcel.2013.09.015. PMID: 24140422

Kitano, M., Nakaya, M., Nakamura, T., Nagata, S., and Matsuda, M. Imaging of Rab5 activity identifies essential regulators for phagosome maturation. *Nature* 453:241-245 (2008). doi: 10.1038/nature06857. PMID: 18385674

Website of the lab: <http://www.fret.lif.kyoto-u.ac.jp/e-phogemon/index.htm>

Key words: multiphoton fluorescence microscopy, biosensors, optogenetics, transgenic mouse

3) Laboratory of Molecular and Cellular Biology

PI: SAKAMAKI, Kazuhiro (Associate Prof.) <sakamaki.kazuhiro.7u@kyoto-u.ac.jp>

Outline of the research

We are interested in the signal transduction mechanisms underlying apoptotic cell death and the biological significance and physiological roles of cell death in organisms. To understand these issues, our main research focuses on the apoptosis executors, caspases, and is to visualize the functional processes of these molecules in cells using live cell imaging and computer simulation. We are also trying to generate appropriate model animals such as mouse, *Xenopus*, and medaka to control the phenomenon of apoptosis in organisms.

Publications

Sakamaki, K., Ishii, T.M., Sakata, T., Takemoto, K., Takagi, C., Takeuchi, A., Morishita, R., Takahashi, H., Nozawa,

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A., Shinoda, H., Chiba, K., Sugimoto, H., Saito, A., Tamate, S., Satou, Y., Jung, S.-K., Matsuoka, S., Koyamada, K., Sawasaki, T., Nagai, T. and Ueno, N. Dysregulation of a potassium channel, THIK-1, targeted by caspase-8 accelerates cell shrinkage. *Biochim. Biophys. Acta* 1863: 2766-2783 (2016). doi: 10.1016/j.bbamcr.2016.08.010.

Sakamaki, K., Imai, K., Tomii, K. and Miller, D.J. Evolutionary analyses of caspase-8 and its paralogs: Deep origins of the apoptotic signaling pathways. *BioEssays* 37: 767-776 (2015). doi: 10.1002/bies.201500010.

Kominami, K., Nakabayashi, J., Nagai, T., Tsujimura, Y., Chiba, K., Kimura, H., Miyawaki, A., Sawasaki, T., Yokota, H., Manabe, N. and Sakamaki, K. The molecular mechanism of apoptosis upon caspase-8 activation: quantitative experimental validation of a mathematical model. *Biochim. Biophys. Acta* 1823: 1825–1840 (2012). doi: 10.1016/j.bbamcr.2012.07.003.

Kominami, K., Nagai, T., Sawasaki, T., Tsujimura, Y., Yashima, K., Sunaga, Y., Tsuchimochi, M., Nishimura, J., Chiba, K., Nakabayashi, J., Koyamada, K., Endo, Y., Yokota, H., Miyawaki, A., Manabe, N. and Sakamaki, K. *In vivo* imaging of hierarchical spatiotemporal activation of caspase-8 during apoptosis. *PLoS One* 7: e50218 (2012). doi: 10.1371/journal.pone.0050218.

Website of the lab: <http://www.fas.lif.kyoto-u.ac.jp/>

Key words: apoptosis, caspase, computer simulation, live imaging, optogenetics

4) Laboratory of Molecular Cell Biology and Development (Collaboration lab in RIKEN, Kobe)

PI (1): MATSUZAKI, Fumio (Prof.) <fumio@cdb.riken.jp>

Outline of the research

1. Mechanisms by which cell polarity and asymmetric division generate cellular diversity.
2. Genetic and epigenetic programs, which neural stem cells undertake for brain development and maturation, using mouse and *Drosophila* as model organisms.

Publications

Suzuki, K.,[#] Tsunekawa, Y.,[#] Hernandez-Benitez, R.,[#] Wu, J.,[#] Zhu, J.,[#] et al. Matsuzaki, F., (28th/34 authors), Belmonte, JC. In vivo genome editing via CRISPR-Cas9 mediated homology-independent targeted integration. *Nature* 540,144–149 (2016). doi:10.1038/nature20565 [#]equal contribution

Tsunekawa, Y.,[#] Terhune, RK.,[#] Fujita, I., Shitamukai, A., Suetsugu, T., and Matsuzaki F. Developing a de novo targeted knock-in method based on in utero electroporation into the mammalian brain. *Development* 143, 3216-22 (2016). doi: 10.1242/dev.136325 [#]equal contribution

Matsuzaki, F., and Shitamukai, A. Cell division modes and cleavage planes of neural progenitors during mammalian cortical development. *Cold Spring Harb. Perspect. Biol.* 7, (2015) a015719. doi: 10.1101/cshperspect.a015719.

Yoshiura, S., Ohta, N., and Matsuzaki, F. Tre1 GPCR signaling orients stem cell divisions in the *Drosophila* central nervous system. *Dev. Cell* 22, 1-13 (2012). doi.org/10.1016/j.devcel.2011.10.027

Konno, D., Shioi, G., Shitamukai, A., Mori, A., Kiyonari, H., Miyata, T., Matsuzaki, F. Neuroepithelial progenitors undergo LGN-dependent planar divisions to maintain self-renewability during mammalian neurogenesis. *Nat. Cell Biol.* 100, 93-101 (2008). doi:10.1038/ncb1673

Website of the lab: <http://www.cdb.riken.jp/en/research/laboratory/matsuzaki.html>

Key words: neural stem cells, brain development, mouse, ferret, *Drosophila*

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PI (2): KITAJIMA, Tomoya (Associate Prof.) <tkitajima@cdb.riken.jp>

Outline of the research

We are interested in how chromosomes behave in time and space to archive correct chromosome segregation during meiosis and mitosis in mammalian oocytes and zygotes. Taking advantage of our live imaging technology, we conduct comprehensive quantitative analysis of the chromosome dynamics.

Publications

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://www.cdb.riken.jp/lcs>

Key words: chromosome, meiosis, oocyte, zygote

PI (3): TAKASATO, Minoru (Associate Prof.) <minoru.takasato@riken.jp>

Outline of the research

Utilizing our unique technology that generates kidney organoids from human pluripotent stem cells, we are focusing particularly on uncovering the developmental mechanisms of human mesoderm and the kidney. By precisely recapitulating the developmental processes of human kidney in the directed differentiation of human pluripotent stem cells, we are also aiming for the ultimate goal of generating a three-dimensional kidney that is functional and can be transplanted into patients.

Publications

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 self-organizing kidney. *Nat. Cell Biol.* 16, 118–26 (2014). doi: 10.1038/ncb2894

Website of the lab: <http://www.cdb.riken.jp/en/research/laboratory/takasato.html>

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

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,

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and cancer. We take advantage of the powerful genetics of *Drosophila*.

Research subjects:

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

Publications

Yamamoto, M., Ohsawa, S., Kunimasa, K., and Igaki, T. The ligand Sas and its receptor PTP10D drive tumor-suppressive cell competition. *Nature* in press.

Vaughen, J. and Igaki, T. Slit-Robo repulsive signaling excludes tumorigenic cells from epithelia. *Dev Cell* in press.

Nakamura, M., Ohsawa, S. and Igaki, T. Mitochondrial defects trigger proliferation of neighbouring cells via a senescence-associated secretory phenotype in *Drosophila*. *Nature Commun.* 5: 5264 (2014). doi: 10.1038/ncomms6264

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

Ohsawa, S., Sugimura, K., Takino, K., Xu, T., Miyawaki, A., and Igaki, T. Elimination of oncogenic neighbors by JNK-mediated engulfment in *Drosophila*. *Dev. Cell* 20: 315-328 (2011). doi: 10.1016/j.devcel.2011.02.007

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

Key words: cell-cell communication, cancer, development, cell competition, *Drosophila*

6) Laboratory of Functional Biology

PI: KAKIZUKA, Akira (Prof.) <kakizuka@lif.kyoto-u.ac.jp>

Outline of the research

Using animal models of human diseases, such as neurodegenerations, cancers, and obesity-related diseases, and using metabolic imaging techniques, we aim to elucidate molecular bases of such diseases and develop new strategies to cure or prevent them.

Publications

Yoshida T, Kakizuka A, Imamura H. BTeam, a novel BRET-based biosensor for the accurate quantification of ATP concentration within living cells. *Sci Rep.* (in press)

Nakano N, Ikeda HO, Hasegawa T, Muraoka Y, Iwai S, Tsuruyama T, Nakano M, Fuchigami T, Shudo T, Kakizuka A, Yoshimura N. Neuroprotective effects of VCP modulators in mouse models of models of glaucoma. *Heliyon.* 2016 . 2:e00096. doi: 10.1016/j.heliyon.2016.e00096.

Ikeda HO, Sasaoka N, Koike M, Nakano N, Muraoka Y, Toda Y, Fuchigami T, Shudo T, Iwata A, Hori S, Yoshimura N, Kakizuka A. Novel VCP modulators mitigate major pathologies of rd10, a mouse model of retinitis pigmentosa. *Sci Rep.* 2014. 4:5970. doi: 10.1038/srep05970.

Sasaoka N, Sakamoto M, Kanemori S, Kan M, Tsukano C, Takemoto Y, Kakizuka A. Long-term oral administration of hop flower extracts mitigates Alzheimer phenotypes in mice. *PLoS One.* 2014. 9:e87185. doi: 10.1371/journal.pone.0087185.

Website of the lab: <http://www.funcbiol.lif.kyoto-u.ac.jp/>

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Key words: drug development, neurodegenerative diseases, cancer, obesity, ATP, FRET biosensor

7) Laboratory of Chromosome Function and Inheritance

PI: CARLTON, Peter (Associate Prof.) <pcarlton@icems.kyoto-u.ac.jp>

Outline of the research

We study how genetic information is correctly maintained and passed on through cell divisions. Combining molecular genetic approaches with advanced microscopy and quantitative imaging, we focus on mechanisms of chromosome pairing and recombination in meiosis in the nematode *C. elegans*, as well as epigenetic modification of DNA and chromatin during the mammalian DNA damage response.

Publications

Kafer, G.R., X. Li, T. Horii, I. Suetake, S. Tajima, I. Hatada, and P.M. Carlton. 5-Hydroxymethylcytosine Marks Sites of DNA Damage and Promotes Genome Stability. *Cell Rep.* 14:1283–1292. (2016). doi:10.1016/j.celrep.2016.01.035.

Sato-Carlton, A., X. Li, O. Crawley, S. Testori, E. Martinez-Perez, A. Sugimoto, and P.M. Carlton. Protein phosphatase 4 promotes chromosome pairing and synapsis, and contributes to maintaining crossover competence with increasing age. *PLoS Genet.* 10:e1004638. (2014). doi:10.1371/journal.pgen.1004638.

Mishima, Y., C.D. Jayasinghe, K. Lu, J. Otani, M. Shirakawa, T. Kawakami, H. Kimura, H. Hojo, P. Carlton, S. Tajima, and I. Suetake. Nucleosome compaction facilitates HP1 γ binding to methylated H3K9. *Nucleic Acids Res.* 43:10200–10212. (2015). doi:10.1093/nar/gkv841.

Kafer, G.R., P.M. Carlton, and S.A. Lehnert. The histone variant H2A.Z is dynamically expressed in the developing mouse placenta and in differentiating trophoblast stem cells. *Placenta.* 36:1325–1328. (2015). doi:10.1016/j.placenta.2015.08.018.

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

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

Key words: DNA damage, meiosis, 5-hydroxymethylcytosine, *C. elegans*, super-resolution microscopy

8) Laboratory of Cell Regulation and Molecular Network

PI: SUGITA, Masahiko (Prof.) <msugita@virus.kyoto-u.ac.jp>

Outline of the research

Full attention of this laboratory has been directed to previously unappreciated aspects of the acquired immunity that we call “lipid immunity”. An important extension of this research is a challenge for developing a new type of lipid-based vaccines against cancer and microbial infection.

Publications

Morita, D., Yamamoto, Y., Mizutani, T., Ishikawa, T., Suzuki, J., Igarashi, T., Mori, N., Shiina, T., Inoko, H., Fujita, H., Iwai, K., Tanaka, Y., Mikami, B., Sugita, M. Crystal structure of the N-myristoylated lipopeptide-bound MHC class I complex. *Nature Communications*, 7, 10356 (2016). doi: 10.1038/ncomms10356.

Kim, J.H., Hu, Y., Yongqing, T., Kim, J., Hughes, V.A., Le Nours, J., Marquez, E.A., Purcell, A.W., Wan, Q.,

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Sugita, M., Rossjohn, J., Winau, F. CD1a on Langerhans cells controls inflammatory skin disease. *Nature Immunology*, 17, 1159-1166 (2016). doi: 10.1038/ni.3523.

Yoshioka, Y., Mizutani, T., Mizuta, S., Miyamoto, A., Murata, S., Ano, T., Ichise, H., Morita, D., Yamada, H., Hoshino, Y., Tsuruyama, T., Sugita, M. Neutrophils and the S100A9 protein critically regulate granuloma formation. *Blood Advances*, in press.

Website of the lab: <http://www.virus.kyoto-u.ac.jp/Lab/SugitaLab.html>

Key words: lipid immunity, microbial infection, vaccine development, transgenic mice

9) Laboratory of Viral Oncology

PI: TOMONAGA, Keizo (Prof.) <tomonaga@virus.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

Horie, M., Honda, T., Suzuki, Y., Kobayashi, Y., Daito, T., Oshida, T., Ikuta, K., Jern, P., Gojobori T., Coffin, J. M. and Tomonaga, K. Endogenous non-retroviral RNA virus elements in mammalian genomes. *Nature* 463:84-87 (2010). doi: 10.1038/nature08695

Matsumoto, Y., Hayashi, Y., Omori, H., Honda, T., Daito, T., Horie, M., Ikuta, K., Fujino, K., Nakamura, S., Schneider, U., Chase, J., Yoshimori, T., Schwemmler, M. and Tomonaga, K. Bornavirus closely associates and segregates with host chromosomes to ensure persistent intranuclear infection. *Cell Host Microbe* 11:492-503 (2012). doi: 10.1016/j.chom.2012.04.009

Ikeda, Y., Makino, A., Holditch, S. J., Lu, B., Dietz, A. B. and Tomonaga, K. A novel intranuclear RNA vector system for long-term stem cell modification. *Gene Ther.* 23: 256-262 (2016). doi: 10.1038/gt.2015.108

Website of the lab: <https://t.rnavirus.virus.kyoto-u.ac.jp/>

Key words: bornavirus, endogenous viruses, RNA virus vector

10) Laboratory of Cell Division and Differentiation

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

Outline of the research

Alignment of the cell division axis along the predetermined cortical cues plays an essential role in asymmetric stem cell division, cell differentiation, stem cell self-renewal and embryogenesis. Our group seeks to explore the molecular mechanisms underlying the determination of cell division axis in both culture cells and mammalian tissues. We are interested in how these mechanisms contribute to cell differentiation and tissue homeostasis.

Publications

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

Iwano, S., Satou, A., Matsumura, S., Sugiyama, N., Ishihama, Y., and Toyoshima, F. PCTK1 regulates integrin-dependent spindle orientation via PKA regulatory subunit KAP0 and myosin X. *Mol. Cell. Biol.* 35, 1197-1208

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(2015).

Matsumura S., Hamasaki M., Yamamoto T., Ebisuya M., Sato M., Nishida E. and Toyoshima F. ABL1 regulates spindle orientation in adherent cells and mammalian skin. *Nat. Commun.* 3:626 (2012). doi: 10.1038/ncomms1634

Website of the lab: <http://www.virus.kyoto-u.ac.jp/Lab/Toyoshima-HP/Home.html>

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

11) Laboratory of Cellular and Molecular Biomechanics

PI: ADACHI, Taiji (Prof.) <adachi@frontier.kyoto-u.ac.jp>

Outline of the research

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

Publications

Inoue, Y., Adachi, T. Mechanosensitive kinetic preference of actin-binding protein to actin filament. *Phys. Rev. E.* 93: 042403 (2016). doi: 10.1103/PhysRevE.93.042403

Maki, K., Han, S.-W., Hirano, Y., Yonemura, S., Hakoshima, T. and Adachi, T. Mechano-adaptive sensory mechanism of α -catenin under tension. *Sci. Rep.* 6: 24878 (2016). doi: 10.1038/srep24878

Okuda, S., Inoue, Y., Eiraku, M., Sasai, Y., Adachi, T. Reversible network reconnection model for simulating large deformation in dynamic tissue morphogenesis. *Biomech. Model Mechanobiol.* 12: 627-644 (2013). doi: 10.1007_s10237-012-0430-7

Matsushita, S., Inoue, Y., Hojo, M., Sokabe, M. and Adachi, T. Effect of tensile force on the mechanical behaviour of actin filaments. *J. Biomech.* 44: 1776-1781 (2011). doi: 10.1016/j.jbiomech.2011.04.01

Kameo, Y., Adachi, T. and Hojo, M. Transient response of fluid pressure in a poroelastic material under uniaxial cyclic loading. *J. Mech. Phys. Solids* 56: 1794-1805 (2008). doi: 10.1016/j.jmps.2007.11.008

Website of the lab: <http://www.frontier.kyoto-u.ac.jp/bf05/index-e.html>

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

12) Laboratory of Genome Damage Signaling

PI: TAKATA, Minoru (Prof.) <mtakata@house.rbc.kyoto-u.ac.jp>

Outline of the research

DNA damage response (DDR) is the fundamental mechanism that stabilizes our genome. Genome stability underlies all biological processes. We try to identify molecules involved in genome stability/replication stress/DDR by methods such as screening mutations in human patients, and further analyze their function using genome engineering in various cell lines, iPS cells, and model organisms.

Publications

Katsuki, Y. and Takata, M. Defects in HR repair behind the human diseases: FA and HBOC. *Endocr. Relat. Cancer* in press (2016). PMID: 27550963

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Hira, A., Yoshida, K., Sato, K., Okuno, Y., Shiraishi, Y., Chiba, K., Tanaka, H., Miyano, S., Shimamoto, A., Tahara, H., Ito, E., Kojima, S., Kurumizaka, H., Ogawa, S., Takata, M., Yabe, H. and Yabe, M. Mutations in the gene encoding the E2 conjugating enzyme UBE2T cause fanconi anemia. *Am. J. Hum. Genet.* 96: 1001-1007 (2015). doi: 10.1016/j.ajhg.2015.04.022. PMID: 26046368

Unno, J., Itaya, A., Taoka, M., Sato, K., Tomida, J., Sakai, W., Sugawara, K., Ishiai, M., Ikura, T., Isobe, T., Kurumizaka, H. and Takata, M. FANCD2 binds CtIP and regulates DNA-end resection during DNA interstrand crosslink repair. *Cell Rep.* 7:1039-47 (2014). doi: 10.1016/j.celrep.2014.04.005

Hira, A., Yabe, H., Yoshida, K., Okuno, Y., Shiraishi, Y., Chiba, K., Tanaka, H., Miyano, S., Nakamura, J., Kojima, S., Ogawa, S., Matsuo, K., Takata, M and Yabe, M. Variant ALDH2 is associated with accelerated progression of bone marrow failure in Japanese Fanconi anemia patients. *Blood* 122: 3206-3209 (2013). doi: 10.1182/blood-2013-06-507962

Website of the lab: <http://house.rbc.kyoto-u.ac.jp/late-effect>

Key words: DNA damage response, DNA repair, genetic disorders, genome editing

13) Laboratory of Cancer Cell Biology

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

Outline of the research

Cells maintain their function and morphology by exploiting a suitable adaptive response system to diverse and complex tissue microenvironments. Several lines of evidence have suggested that hypoxic, acidic and nutrients-depleted microenvironments exist in solid tumors and induce malignant phenotypes and chemo/radioresistance of cancer cells. We aim at elucidating molecular mechanisms responsible for cellular adaptive responses to the tumor-specific microenvironments and malignant progression of cancer cells.

- Cellular adaptive responses to diverse and complex tissue microenvironments
- Molecular mechanisms underlying malignant progression and radioresistance of cancer cells
- Regulatory mechanisms of carbohydrate metabolic pathway

Publications:

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

Zeng, L., Morinibu, A., Kobayashi, M., Zhu, Y., Wang, X., Goto, Y., Yeom, C. J., Zhao, T., Hirota, K., Shinomiya, K., Itasaka, S., Yoshimura, M., Guo, G., Hammond, E. M., Hiraoka, M. and Harada, H. Aberrant IDH3 α expression promotes malignant tumor growth by inducing HIF-1-mediated metabolic reprogramming and angiogenesis. *Oncogene* 34: 4758-4766. (2015). doi: 10.1038/onc.2014.411

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

Website of the lab: <http://radiotherapy.kuhp.kyoto-u.ac.jp/biology/>

Key words: cancer, tumor microenvironments, hypoxia, chemo-/radio/resistance

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14) Laboratory of Laboratory of Chromatin Regulatory Network

PI: IKURA, Tsuyoshi (Associate Prof.) <ikurat@house.rbc.kyoto-u.ac.jp>

Outline of the research

The eukaryotic genome is tightly packed into the chromatin, a hierarchically organized complex of DNA, histone and nonhistone proteins. This packing represents a common obstacle for the metabolic processes of DNA including transcription, replication, recombination, and DNA repair. Current evidence indicates that chromatin reorganization involving histone modification, histone variant exchange, histone eviction and ATP-dependent chromatin remodeling play an integral role in DNA repair and DNA damage response. However, it remains unclear how such chromatin reorganization is coupled with the initiation of DNA repair process and/or activation of checkpoint machinery after DNA damage. We are now investigating the following issues:

1. The molecular mechanisms by which the TIP60 histone acetylase complex regulates histone H2AX exchange induced by ionizing radiation.
2. The cross-talk between the histone signaling network regulated by histone H2AX exchange and DNA damage response pathways.

Publications

Ikura, M., Furuya, K., Fukuto, A., Matsuda, R., Adachi, J., Matsuda, T., Kakizuka A., Ikura, T. Coordinated regulation of TIP60 and PARP-1 in damaged chromatin dynamics. *Mol Cell Biol.* 36:1595-1607 (2016). doi: 10.1128/MCB.01085-15.

Ikura, M., Furuya, K., Matsuda, S., Matsuda, R., Shima, H., Adachi, J., Matsuda, T., Shiraki, T., Ikura, T. Acetylation of histone H2AX at Lys 5 by the TIP60 histone acetyltransferase complex is essential for the dynamic binding of NBS1 to damaged chromatin. *Mol Cell Biol.* 35: 4147-4157 (2015). doi: 10.1128/MCB.00757-15.

Ikura T., Tashiro, S., Kakino, A., Shima, H., Jacob, N., Amunugama, R., Yoder, K., Izumi, S., Kuraoka, I., Tanaka, K., Kimura, H., Ikura M., Nishikubo, S., Ito, T., Muto, A., Miyagawa K., Takeda, S., Fishel, R., Igarashi, K., *Kamiya, K. DNA damage-dependent acetylation and ubiquitination of H2AX enhances chromatin dynamics. *Mol Cell Biol.* 27:7028-7040 (2007). doi:10.1128/MCB.00579-07

Ikura, T., Ogryzko, V V., Grigoriev, M., Groisman, R., Wang, J., Horikoshi, M., Scully, R., Qin, J., Nakatani, Y. Involvement of the TIP60 Histone Acetylase Complex in DNA repair and apoptosis. *Cell.* 102:463-473 (2000). doi.org/10.1016/S0092-8674(00)00051-9

Website of the lab: <http://house.rbc.kyoto-u.ac.jp/mutagenesis2/index1>

Key words: chromatin dynamics, histone acetyltransferase, histone variant, DNA damage response