Kumamoto University IRCMS

90th IRCMS Seminar- Symposium on

New Horizons in Developmental Biology

Hosted by IRCMS, Kumamoto University

Date and Time:

9:30 - 17:45 (JST),

20th, February, 2023

Venue: Onsite/Online

Dear Colleagues,

I would like to welcome you to the symposium on “New Horizons in Developmental Biology”, hosted by International Research center for Medical Sciences (IRCMS), Kumamoto University.

Developmental biology is a research field with a long history. It studies basic principles of animal development, from fertilization to functional maturation. Through such studies, we also gain a better, more mechanistic understanding of human diseases. However, conceptual breakthroughs in developmental biology, as in any other field of research, require innovative technologies and fresh perspectives. This symposium sets its focus on such technologies and perspectives which will lead to potential breakthroughs.

I am grateful that speakers of this symposium take time out of their busy schedules to present their most recent findings and participate in this cross-disciplinary discussion. It is my hope that this symposium will serve as a catalyst for future collaborations and discoveries.

Many of you come from other parts of Japan or overseas. You may want to take this opportunity to get to know a bit more about the dynamic biomedical research environment of Kumamoto University and to explore some of many natural and culinary wonders that Kumamoto has to offer.

Thank you again for your participation in this symposium.

With best wishes,

Guojun Sheng, PhD

(On behalf of the organizing committee)

International Research Center for Medical Sciences (IRCMS)

Kumamoto University

Timetable for Symposium

Opening Remarks	**Hitoshi Takizawa**, IRCMS, Kumamoto University	
President Greeting	**Hisao Ogawa**, Kumamoto University	
09:40 - 10:15	**Yingke Wu** Max Planck Institute for Polymer Research, Germany	Nanodiamond quantum sensor for biological application
10:15 - 10:50	**Kenichi Miharada** IRCMS, Kumamoto University,Japan	Maternal 27-hydroxylase activity is essential for fetal organ development
10:50 - 11:00	Break	
11:00 - 11:35	**Li-Kun Phng** RIKEN BDR, Japan	Mechanics of blood vessel lumenization and remodelling
11:35 - 12:10	**Hiroko Sano** Kumure University, Japan	Glucose sensing by the polyol pathway and its significance in developmental biology
12:10 - 13:40	Lunch Break ★Before lunch, we will take a group photo.	
13:40 - 14:15	**Hina Kosakamoto** RIKEN BDR, Japan	Sensing of the non-essential amino acid tyrosine gove rns the response to dietary protein intake in Drosophila
14:15 - 14:50	**Reika Tei** Stanford University, USA	Optogenetic modulation of cellular lipids by a membrane editor
14:50 - 15:00	Break	
15:00 - 15:35	**Daisuke Umeno** Waseda University, Japan	Ditected evolution of Information Processing
15:35 - 16:10	**Jacob Hanna** Weizmann Institute of Science, Israel	Synthetic Ex Utero Embryogenesis: from Naive Pluripotent Stem Cells to Bona Fide Embryo Models
16:10 - 16:25	Break	
16:25 - 17:00	**Hiroaki Okae** IMEG, Kumamoto University, Japan	The microRNA cluster C19MC confers differentiation potential into trophoblast lineages upon human PSCs
17:00 - 17:35	**Julia Marzi** University of Tübingen, Germany	Time and spatially resolved readouts to monitor cell and tissue dynamics
Closing Remarks	**Ryuichi Nishinakamura**, IMEG, Kumamoto University	

Yingke Wu
Max Planck Institute for Polymer Research, Germany

Nanodiamond quantum sensor for biological application

Living biological systems are challenging to understand due to their high structural complexity and dynamics. They are characterized by the existence of nanoenvironments, molecular gradients, the formation of transient structures and highly dynamic interactions, among others. Many different species, such as biomolecules, ions, and radicals, coexist in the highly crowded and dynamic nanoenvironments within cells. Various biochemical reactions are constantly occuring, resulting in an inhomogeneous distribution of different molecular species, temperatures, and forces. Local and quantitative detection of these environmental parameters and molecules, including transient reactive structures with limited lifetimes, will improve our understanding of living systems. Measurement of certain quantities at the nanoscale is often limited to strict conditions such as low temperature or vacuum, making it challenging to investigate the “warm, wet and noisy” conditions within living cells. Recently developed nanodiamond (ND) quantum sensing technology holds great promise for studying important parameters at ambient conditions within the living cell. Atomic defects (i.e., nitrogen vacancy (NV) center) in the ND lattice provide stable emission and spin-dependent photoluminescence. These unique properties endow ND quantum sensors with the capacity to detect local rotation, temperature, magnetic fields, electric fields, or strain under living “warm, wet and noisy” conditions. Specifically, in combination with the photothermal agents, we have achieved the nanoscale temperature manipulation and sensing inside a single living cell, and further explored the influence of intracellular temperature inhomogeneity on cell apoptosis and intracellular transportation. In the future, we aim to detect and manipulate more intracellular parameters such as rotation, pH, and radical species in living systems to establish communications between NDs and cells, and solve current challenges in biology and medicine.

- **Wu, Y.**; Balasubramanian, P.; Wang, Z.; Coelho, J. A. S.; Prslja, M.; Siebert, R.; Plenio, M. B.; Jelezko, F.; Weil, T.: Detection of Few Hydrogen Peroxide Molecules Using Self-Reporting Fluorescent Nanodiamond Quantum Sensors. **Journal of the American Chemical Society** 144 (28), pp. 12642 - 12651 (2022)
- **Wu, Y.**; Weil, T.: Recent Developments of Nanodiamond Quantum Sensors for Biological Applications. **Advanced Science** 9 (19), 2200059 (2022)
- **Wu, Y.**; Alam, M. N. A.; Balasubramanian, P.; Ermakova, A.; Fischer, S.; Barth, H.; Wagner, M.; Raabe, M.; Jelezko, F.; Weil, T.: Nanodiamond Theranostic for Light-Controlled Intracellular Heating and Nanoscale Temperature Sensing. **Nano Letters** 21 (9), pp. 3780 - 3788 (2021)

Kenichi Miharada
IRCMS, Kumamoto University,Japan

Maternal 27-hydroxylase activity is essential for fetal organ development

During pregnancy, maternal circulation provides essential factors for developing fetuses. In addition, the maternal body degrades toxic metabolites instead of the fetal body. However, what types of factors contribute to fetal-maternal crosstalk is still unclear. We previously reported that bile acids supplied from maternal circulation support the expansion of murine hematopoietic stem cells in the fetal liver (Sigurdsson et al., Cell Stem Cell, 2016). Here, we newly demonstrate that maternal 27-hydroxylase (Cyp27a1) activity is essential for fetal organ formation. Cyp27a1 is involved in various reactions, particularly in bile acid synthesis. Depletion of Cyp27a1 in the mother resulted in abnormalities in many organs, and all newborn mice died right after birth due to respiratory distress syndrome (RDS) regardless of the newborn's genotype. Alveolar structures were poorly developed in the lung of newborn mice delivered from Cyp27a1-/- mothers (mKO fetuses). scRNA-seq of E14.5 embryos found rather increased transcription levels of AE differentiation-related genes and many ribosomal genes. Cyp27a1-/- mice are known for reduced bile acid pool and highly elevated levels of bile acid precursor, oxysterols. Notably, injection of 7α-hydroxycholesterol (7α-HC) into wild-type pregnant mice led to the birth of newborn mice with RDS symptoms. An advanced proteomics technology discovered that 7α-HC destabilizes a protein Fau, which regulates the assembly of ribosomal proteins. Both knockdown of Fau using shRNA and the addition of 7α-HC resulted in lower protein synthesis and slow cycling. Our findings suggest that the abnormal 27-hydroxylase activity may correlate with some types of recurrent pregnancy loss.

Li-Kun Phng
RIKEN BDR, Japan

Mechanics of blood vessel lumenization and remodelling

The optimal distribution of blood to tissues requires the generation of well-patterned, hierarchically organized blood vessels of optimal diameter. How endothelial cells (ECs) behave and respond to haemodynamic forces to control lumenization, vessel morphology and vessel diameter are incompletely understood. By investigating the intersegmental vessels of the zebrafish embryo, we discovered that ECs utilize actomyosin cytoskeleton to control different cellular behaviours at different stages of blood vessel morphogenesis.

Initially, during the process of lumenization, ECs adapt to elevating blood pressure by fortifying the cell cortex with increased assembly of actomyosin cytoskeleton and by generating a balance network of linear and branched actin bundles. The failure of ECs to resist the deforming forces of blood pressure results in ectopic membrane blebbing, cell shape changes and vessel malformation in the zebrafish embryo.

After blood vessels become perfused, they undergo remodelling where vessels constrict to generate narrower tubes. This is mediated by a decrease in EC size and shortening of the EC. High-resolution image analysis revealed a transition in cortical actin cytoskeleton during the period of constriction, suggesting that actin remodelling may drive cell shape changes underlying vessel constriction. In addition, we observed dynamic oscillations in non-muscle myosin II in the cell cortex as indicated by fluctuations in the intensity if myosin light chain 9b (myl9b). Interestingly, a local increase in myl9b intensity correlates with a decrease in vessel diameter. When myosin II activity is decreased, the extent of vessel constriction is reduced.

Collectively, our studies demonstrate the diverse functions of actin cytoskeleton and myosin II activity in controlling EC mechanics and vessel morphogenesis.

- Kondrychyn I, Kelly DJ, Taberner Carretero N, Nomori A, Kato K, Chong J, Nakajima H, Okuda S, Mochizuki N and **Phng LK**. Marcksl1 modulates endothelial cell mechanoresponse to haemodynamic forces to control blood vessel shape and size. **NATURE COMMUNICATIONS** 11:5476 (2020)

- Gebala V, Collins R, Geudens I, **Phng LK*** and Gerhardt H*. Blood flow drives lumen formation by inverse membrane blebbing during angiogenesis in vivo. **NATURE CELL BIOLOGY** 18 (4), 443 – 451 (2016). *equal contribution

- **Phng LK**, Gebala V, Bentley K, Philippides A, Wacker A, Mathivet T, Sauteur L, Stanchi S, HG Belting, Affolter M, Gerhardt H. Formin-mediated actin polymerization at endothelial junctions is required for vessel lumen formation and stabilization. **DEVELOPMENTAL CELL** 32, 123 -132 (2015).

Hiroko Sano
Kumure University, Japan

Glucose sensing by the polyol pathway and its significance in developmental biology

Cells must modulate the expression levels of metabolic enzymes in response to fluctuating nutrient supply. For glucose, such metabolic remodeling is highly dependent on the master transcription factor ChREBP/Mondo. However, the mechanism by which glucose fluctuations are sensed by ChREBP/Mondo has remained controversial. We have shown that in both flies and mice, a glucose-metabolizing pathway, called the polyol pathway, is involved in the activation of ChREBP/Mondo in the presence of glucose. It has long been believed that the polyol pathway does not function under normal physiological conditions and that its activation under hyperglycemic conditions adversely affects human health. We have now identified the physiological functions of the polyol pathway in the sensing glucose uptake. Furthermore, we have demonstrated that the polyol pathway is required for mating-induced increase in germline stem cells that occurs only in glucose-fed females. The polyol pathway converts dietary glucose to fructose, and the fructose secreted into the hemolymph stimulates the release of germline stem cell-augmenting hormones from enteroendocrine cells. Thus, we propose that the polyol pathway acts as both an intracellular and systemic glucose sensor, influencing physiology and development.

- Hoshino, R., **Sano, H.**, Yoshinari, Y., Nishimura, T., and *Niwa, R. Circulating fructose regulates a germline stem cell increase via gustatory receptor-mediated gut hormone secretion in mated Drosophila. **Science Advances**, in press.

- ***Sano, H.**, Nakamura, A., Yamane, M., Niwa, H., Nishimura, T., Takemoto, K., Ishiguro, K., Aoki, H., and Kojima, M. The polyol pathway is an evolutionarily conserved system for sensing glucose uptake. **PLOS Biology** 20, e3001678 (2022).

- ***Sano, H.**, Nakamura, A., Texada, M.J., Truman, J.W., Ishimoto, H., Kamikouchi, A., Nibu, Y., Kume, K., Ida, T., and Kojima, M. The nutrient-responsive hormone CCHamide-2 controls growth by regulating insulin-like peptides in the brain of Drosophila melanogaster. **PLOS Genetics** 11, e1005209 (2015).

Hina Kosakamoto
RIKEN BDR, Japan

Sensing of the non-essential amino acid tyrosine governs the response to dietary protein intake in Drosophila

The intake of dietary protein regulates growth, metabolism, fecundity, and lifespan across various species. Therefore, amino acid (AA) sensing is vital for adaptation to the nutritional environment. AA sensing is mediated by general control nonderepressible 2 (GCN2)- activating transcription factor 4 (ATF4) pathway and the mechanistic target of rapamycin complex 1 (mTORC1) pathway. However, it is not fully understood which AAs regulate these two pathways in living animals and how they coordinate responses to protein restriction. Here we show in Drosophila that the non-essential AA tyrosine (Tyr) is a nutritional cue in the fat body necessary and sufficient for promoting adaptive responses to a low-protein diet, which entails reduction of protein synthesis and mTORC1 activity and increased food intake. This adaptation is regulated by dietary Tyr through GCN2-independent induction of ATF4 target genes in the fat body. Conversely with a high-protein diet, Tyr degradation pathway is necessary for larvae to survive. In the presentation, I would like to discuss the impact and the mechanisms of Tyr sensing which regulates the physiological response in accordance with the variable dietary environment.

- **Hina Kosakamoto**, Naoki Okamoto, Hide Aikawa, Yuki Sugiura, Makoto Suematsu, Ryusuke Niwa, Masayuki Miura, Fumiaki Obata, Sensing of the non-essential amino acid tyrosine governs the response to protein restriction in Drosophila. **Nature metabolism** 4(7) 944-959 (2022)

- **Hina Kosakamoto**, Toshitaka Yamauchi, Yoriko Akuzawa-Tokita, Kei Nishimura, Tomoyoshi Soga, Takumi Murakami, Hiroshi Mori, Kyosuke Yamamoto, Ryo Miyazaki, Akiko Koto, Masayuki Miura, Fumiaki Obata, Local Necrotic Cells Trigger Systemic Immune Activation via Gut Microbiome Dysbiosis in Drosophila. **Cell Reports** 32(3) 107938-107938 (2020)

Reika Tei
Stanford University, USA

Optogenetic modulation of cellular lipids by a membrane editor

Cellular membranes contain numerous lipid species, and efforts to understand the biological functions of individual lipids have been stymied by a lack of approaches for controlled modulation of membrane composition in situ. In this talk, I will present a strategy for editing phospholipids, the most abundant lipids in biological membranes, using an optogenetic, engineered membrane editor. Our membrane editor is based upon a bacterial phospholipase D (PLD), which exchanges phospholipid head groups through hydrolysis or transphosphatidylation of phosphatidylcholine with water or exogenous alcohols. CRY2-CIBN light-mediated heterodimerization system was used to create an optogenetic PLD, whose intracellular localization can be controlled by blue light. Exploiting activity-dependent directed enzyme evolution in mammalian cells, we developed and structurally characterized a family of "superPLDs" with up to a 100-fold enhancement in intracellular activity. We demonstrated the utility of superPLDs for both optogenetics-enabled editing of phospholipids within specific organelle membranes in live cells and biocatalytic synthesis of natural and unnatural designer phospholipids in vitro. Beyond the superPLDs, activity-based directed enzyme evolution in mammalian cells is a generalizable approach to engineer additional chemoenzymatic biomolecule editors.

- **Tei R**, Bagde SR, Fromme JC, and Baskin JM. "Activity-based directed evolution of a membrane editor in mammalian cells." **Nat Chem** (2023) in press. Preprint available at bioRxiv; 2022.09.26.509516.

- **Tei R** and Baskin JM. "Click chemistry and optogenetic approaches to visualize and manipulate phosphatidic acid signaling." **J Biol Chem** (2022) 298, 4, 101810.

- **Tei R** and Baskin JM. "Spatiotemporal control of phosphatidic acid signaling with optogenetic, engineered phospholipase Ds." **J Cell Biol** (2020) 219, 3, e201907013.

Daisuke Umeno
Waseda University, Japan

Ditected evolution of Information Processing.

The intracellular information process is driven by the cooperation of nanomachines. The design of allosteric proteins that act as key components along those information processing networks is one of the most difficult challenges in protein engineering. For years, we have adopted directed evolution of information processing pathways, thereby having witnessing that various information processing functions easily emerge from random libraries in surprising frequencies. The investigation of these evolvants revealed that such computational functions rely only on phenomena such as system stabilization and/or binding competition, all of which ubiquitously accompanied to every molecular interactions. Considering the ease of appearance, such non-allosteric switchers may have been evolutionary precursors to the highly sophisticated signaling network observed in cells today.

Jacob Hanna
Weizmann Institute of Science, Israel

Synthetic *Ex Utero* Embryogenesis: from Naive Pluripotent Stem Cells to *Bona Fide* Embryo Models

The identity of somatic and pluripotent cells can be epigenetically reprogrammed and forced to adapt a new functional cell state by different methods and distinct combinations of exogenous factors. The aspiration to utilize such in vitro reprogrammed pluripotent and somatic cells for therapeutic purposes necessitates understanding of the mechanisms of reprogramming and differentiation and elucidating the extent of equivalence of the in vitro derived cells to their in vivo counterparts. In my presentation, I will present my group's recent advances toward understanding these fundamental questions and further detail our ongoing efforts to generate developmentally unrestricted human naive pluripotent cells with embryonic and extra-embryonic developmental potential. I will expand on new avenues for utilizing custom made electronically controlled ex utero platforms and optimized conditions for growing natural mammalian embryos ex utero for extended periods capturing development from pre-gastrulation until advanced organogenesis, for better studying of stem cell transitions during embryogenesis and organogenesis. I will detail how the latter platforms offered an exclusive technical platform to demonstrate and unleash the self-organizing capacity of mouse naïve PSCs to generate post-gastrulation synthetic Bona Fide and organ-filled, synthetic embryo models with both embryonic and extraembryonic compartment ex utero. Collectively, I will be highlighting prospects for new platforms for advancing human disease and developmental modelling

1) Aguilera-Castrejon A, Oldak B, Shani T, Ghanem N, Itzkovich C, Slomovich S, Tarazi S, Bayerl J, Chugaeva V, Ayyash M, Ashouokhi S, Sheban D, Livnat N, Lasman L, Viukov S, Zerbib M, Addadi Y, Rais Y, Cheng S, Stelzer Y, Keren-Shaul H, Shlomo R, Massarwa R, Novershtern N, Maza I & **Hanna JH**. "Ex utero mouse embryogenesis from pre-gastrulation to late organogenesis". **Nature** (2021) 593(7857):119-124. [URL]

2) Tarazi S, Aguilera-Castrejon A, Joubran C, Ghanem N, Ashouokhi S, Roncato F, Wildschutz E, Haddad M, Oldak B, Gomez-Cesar E, Livnat N, Viukov S, Lokshtanov D, Naveh-Tassa S, Rose M, Hanna S, Raanan C, Brenner O, Kedmi M, Keren-Shaul H, Lapidot T, Maza I, Novershtern N, **Hanna JH**. "Post-gastrulation synthetic embryos generated ex utero from mouse naive ESCs". **Cell** (2022) 185(15):3290-3306. [URL]

Hiroaki Okae

IMEG, Kumamoto University, Japan

The microRNA cluster C19MC confers differentiation potential into trophoblast lineages upon human PSCs

The first cell fate commitment during mammalian development is the specification of the inner cell mass and trophectoderm. This irreversible cell fate commitment should be epigenetically regulated, but the precise mechanism is largely unknown in humans. We recently succeeded in the establishment of human trophoblast stem cells (hTSCs) that can be maintained for a long-time in culture without losing their ability to differentiate into all trophoblast lineages. In this talk, we show that naïve human embryonic stem cells (hESCs) can transdifferentiate into trophoblast stem cells (hTSCs), but primed hESCs cannot. Our transcriptome and methylome analyses revealed that a primate-specific miRNA cluster on chromosome 19 (C19MC) is active in naïve hESCs but epigenetically silenced in primed ones. Moreover, genome and epigenome editing using CRISPR/Cas systems demonstrated that C19MC is essential for hTSC maintenance, and C19MC-reactivated primed hESCs can give rise to hTSCs. These data show that C19MC activation confers differentiation potential into trophoblast lineages on hESCs. Our findings are fundamental to understanding the epigenetic regulation of human early development and pluripotency.

- Kobayashi N, **Okae H***, Hiura H, Kubota N, Kobayashi EH, Shibata S, Oike A, Hori T, Kikutake C, Hamada H, Kaji H, Suyama M, Bortolin-Cavaillé ML, Cavaillé J, Arima T*. The microRNA cluster C19MC confers differentiation potential into trophoblast lineages upon human pluripotent stem cells. **Nature Communications** 2022

- **Okae H***, Toh H, Sato T, Hiura H, Takahashi S, Shirane K, Kabayama Y, Suyama M, Sasaki H, Arima T*. Derivation of Human Trophoblast Stem Cells. **Cell Stem Cell**. 2018

Julia Marzi
University of Tübingen, Germany

Time and spatially resolved readouts to monitor cell and tissue dynamics

Non-invasive imaging techniques such as Raman Microspectroscopy (RMS) and Fluorescence Lifetime Imaging Microscopy (FLIM) are promising tools for marker-independent in situ monitoring and biomarker development. Whereas FLIM is especially sensitive to metabolic changes by targeting the endogenous fluorophores NADH and FAD, RMS can access various cell and tissue structures due to their unique molecular-sensitive spectral fingerprints. Combined with advanced 3D in vitro models, non-destructive investigations of (patho-)physiological cellular processes can be obtained.
We implemented RMS and FLIM for ex vivo tissue analysis and in in vitro models, such as Organ-on-Chip platforms. It was demonstrated, that RMS enables the identification and visualization of major subcellular structures e.g., nuclei, proteins, lipids. In addition to quantitative image-based assessment, analysis of the extracted spectral information can further identify alterations in molecular composition, e.g. changes in lipid composition and oxidation were demonstrated upon culture duration or external stimulation. Moreover, FLIM enabled to investigate the metabolic balance between glycolysis and oxidative phosphorylation in tissue spheroids and was sensitive to detect early signs of apoptosis.
Overall, our results showed that both, RMS and FLIM, provide real-time insights on tissue dynamics and should be further established and developed as complementary tools in tissue diagnostics and 3D in vitro culture systems.

- K Sugiyama*, **J Marzi***, J Alber, EM Brauchle, M Ando, Y Yamashiro, B Ramkhelawon, K Schenke-Layland, H Yanagisawa; Raman Microspectroscopy and Raman Imaging Reveal Biomarkers Specific for Thoracic Aortic Aneurysms, **Cell Reports Medicine**, 2021, https://doi.org/10.1016/j.xcrm.2021.100261

- N Feuerer, **J Marzi**, EM Brauchle, DA Carvajal Berrio, F Billing, M Weiss, M Jakobi, N Schneiderhan-Marra, C Shipp, K Schenke-Layland. Lipidome profiling with Raman microspectroscopy identifies macrophage response to surface topographies of implant materials. **PNAS**, 2021, https://doi.org/10.1073/pnas.2113694118

- L Becker, F Fischer, J L Fleck, N Harland, A Herkommer, A Stenzl, W K Aicher, K Schenke-Layland, **J Marzi**, Data-Driven Identification of Biomarkers for In Situ Monitoring of Drug Treatment in Bladder Cancer Organoids. **IJMS**, 2022, https://doi.org/10.3390/ijms23136956

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Welcome to Kumamoto!

Kumamoto University is located in Kumamoto city, which is at the center of the Kyushu island (Southwest Japan).Kumamoto is is not only a place blessed with natural resources like mountains, rivers, and oceans, but it is also quite rich in history and culture.

Kumamoto Castle is the most symbolic attraction in Kumamoto, which has a history of more than 400 years. Its main feature is its stone walls, known as Musha-gaeshi（武者返し）. These walls are warped to prevent enemy invasion. Unfortunately, in the earthquake of 2016, Kumamoto Castle was severely damaged and is going through a 20-years' restoration.

The damage caused by the Kumamoto earthquake extends through several areas of Kumamoto prefecture. The Aso area, which we will visit on this excursion, was one of the most damaged areas. However, we would like you to see not only the great hurt that Kumamoto people has experienced, but also their resilience and the way these people are overcoming such adversities.

Aso is a place where you can feel the magnificence of nature with your whole being. Despite being a place where you can feel the danger of earthquakes and volcanic eruptions, the area is blessed with rich groundwater and hot springs.

In fact, the groundwater which is nurtured by the Aso mountains, is one of the most valuable resources of Kumamoto City. This groundwater provides for well-being of all the 740,000 habitants of Kumamoto City.

Welcome to Kumamoto!

くまもとへようこそ！

The bountiful waters of Kumamoto also nurture delicious food. All the famous foods in Kumamoto can be summarised by the word ‘red’. Here is where we produce the most amount of tomatoes and watermelons in Japan. Basashi（馬刺し） is a must-try food for visitors of Kumamoto, it is sashimi prepared with horse meat instead of fish. Kumamoto is also famous for its ‘Aka-Ushi’ (red cow) wagyu beef. In Kumamoto, horses and cows live in the grasslands of Aso and grow up drinking clean water and breathing pure air, which make their meat delicious.

Kumamoto is proud of its “Sake（清酒/日本酒）” and “Shochu（焼酎）”, made from a combination of its nutritious water and locally-produced rice. In fact, Kumamoto is the southernmost area where sake is produced in its natural environment. In the past, it was difficult to produce good sake due to the weather, but people spent years doing research to achieve the current amazing taste. This achievement was only possible because of Kumamoto yeast (No. 9 yeast). Interestingly, Kumamoto yeast is still considered one of the conditions for making good sake, as yeast is an important ingredient in the production of alcohol. A yeast called Kumadai-Yeast was recently discovered at Kumamoto University.

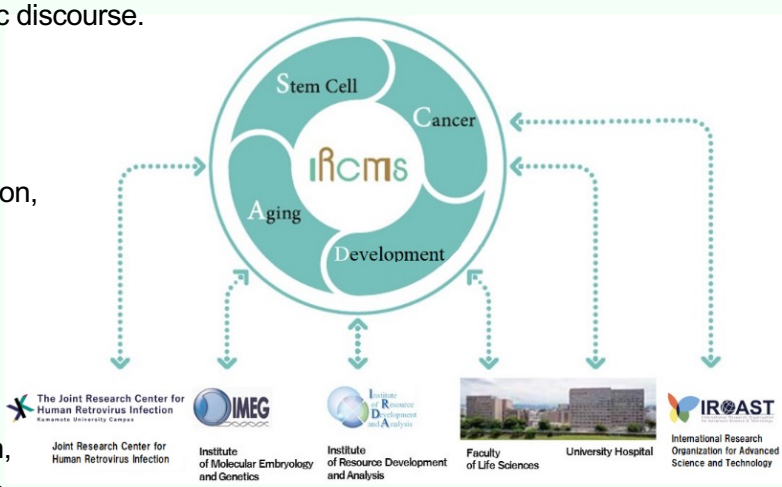
In Hitoyoshi-Kuma area, the most southerly region of Kumamoto Prefecture, spirits alcohol have been produced for more than 500 years. The name Kuma-shochu is an alcoholic beverage for which a specific regional name is used as a brand name, similar to Bordeaux for wine or Cognac for brandy. Kuma-Shochu has a variety of flavours depending on how it is made and how it has aged.Three days is a short time, but please enjoy Kumamoto! (by Hanami)

About IRCMS

The International Research Center for Medical Sciences (IRCMS) was established in 2015 as the center of excellence in Kumamoto University for world-class research in life sciences through the internationalization of its research environment and the establishment of global collaborations.

The Center features an open lab layout with few walls and partitions between labs to facilitate communication among scientists. A meeting lounge and an open café on the 1st floor support active, informal scientific exchange between researchers. English is the official language for all seminars and lab meetings to promote international scientific discourse.

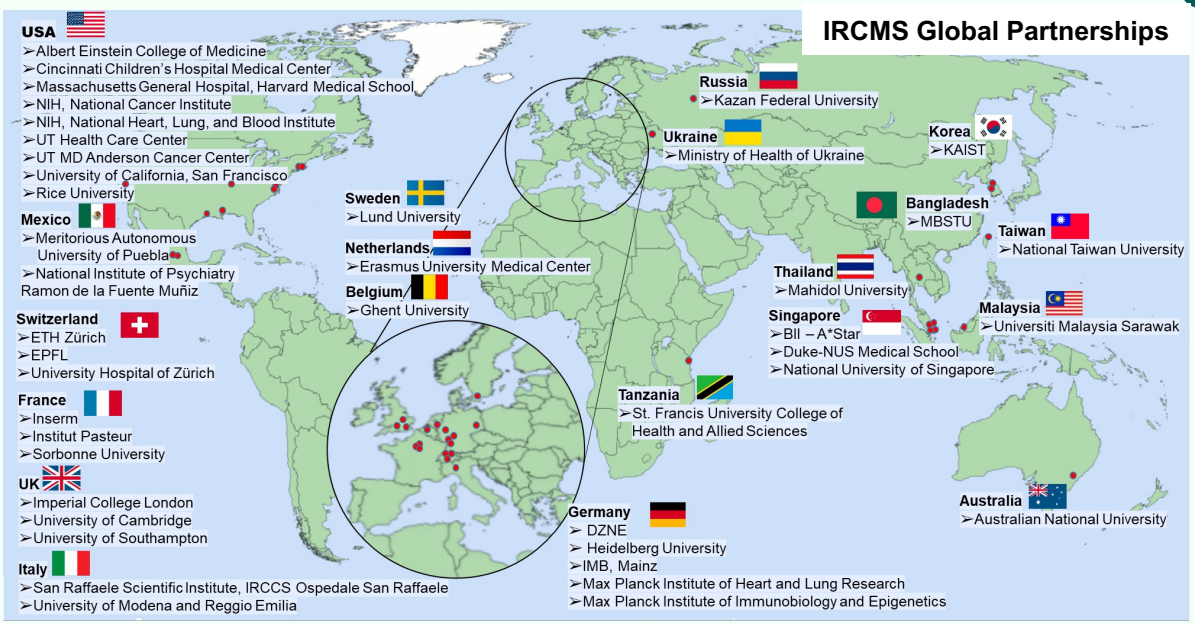
IRCMS is located in the Honjo-Kuhonji area along with Kumamoto University's School of Medicine, the University Hospital, the Joint Research Center for Human Retrovirus Infection, the Institute of Resource Development and Analysis (IRDA) and the Institute of Molecular Embryology and Genetics (IMEG). Through cooperation with these institutes, IRCMS will create a strong collaborative network in the areas of Stem Cell Research, Aging Research, Development Research and Cancer Research.



At present, 12 principal investigators (PIs) and their lab members are conducting research at the Center. IRCMS also aims to establish an international research collaboration network with visiting researchers who hold positions in research institutes abroad. Non-Japanese nationals currently account for 40% of the people working at the Center, excluding visiting researchers, and this number is expected to increase to 50% in the future.

The ultimate goal of IRCMS is to become a successful and innovative role model for the internationalization of academic research. IRCMS is now laying new framework that extends beyond the existing research environment to reach this ultimate goal.

About IRCMS



Open Lab / Core Facility

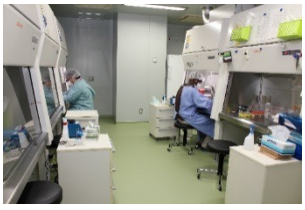
IRCMS has adopted an "Open Lab" System to stimulate scientific interaction among the scientists and cultivate inter-laboratory collaboration across multiple disciplines. Scientists share lab space and equipment. All of the laboratories and office are visible through the window from the hallway.

To make research equipment sharing and time management efficient, we have established an online booking system and started technical support for cutting-edge technology such as single cell analysis. There is an open café space on the 1st floor to facilitate discussion and networking.

Open Lab

Core facility

Café space



Experiment in the lab

Internship

IRCMS has provided research internship opportunities since 2015 for overseas students who have a strong interest toward the advanced medical research, aiming to raise the interest of IRCMS research and recruit the next generation of young researchers internationally.

We have invited more than 35 interns from 19 countries so far, and some of them came back to IRCMS as Ph.D. course students or Postdoc- Researchers.

Internship student conducting experiment

Visiting president of Kumamoto university

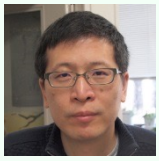
Research instruction

IRCMS Principal investigator

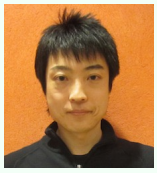
SUDA Toshio
M.D., Ph.D.
Distinguished Professor (Director)
Research Field
Stem Cell Regulation
Double Appointment:
National University of Singapore

TAKIZAWA Hitoshi
Ph.D.
Professor (Vice Director)
Research Field
Stem Cell Stress

SASHIDA Goro
M.D., Ph.D.
Professor
Research Field
Transcriptional Regulation in Leukemogenesis



Guojun Sheng
Ph.D.
Professor
Research Field
Developmental Morphogenesis



MIHARADA Kenichi
Ph.D.
Professor
Research Field
Proteostasis in Stem Cell

BABA Masaya
M.D., Ph.D.
Associate Professor
Research Field
Cancer Metabolism

MIZUNO Hidenobu
Ph.D.
Associate Professor
Research Field
Multi-dimensional Imaging

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