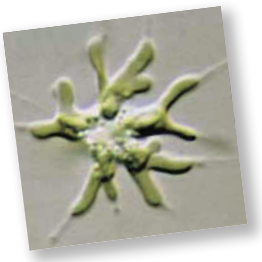
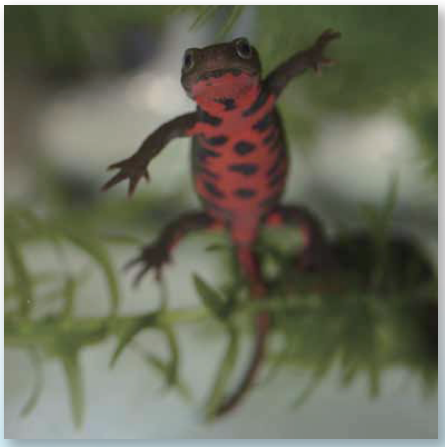
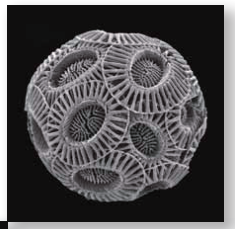
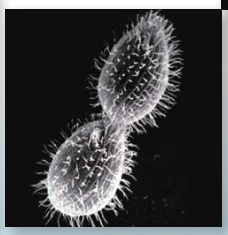
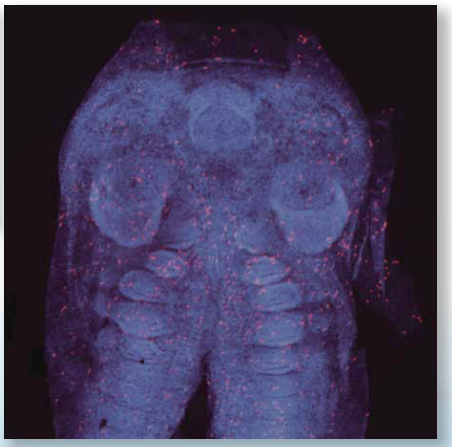
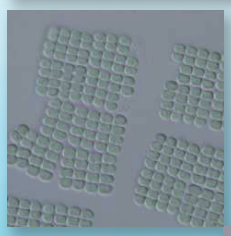
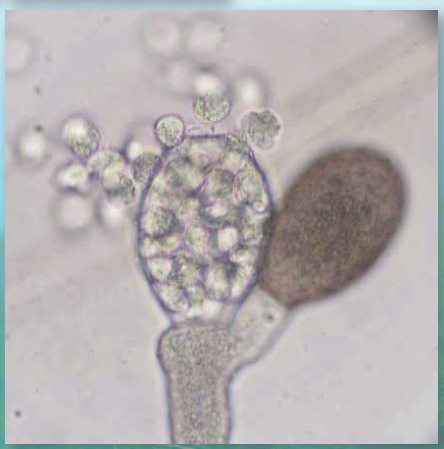
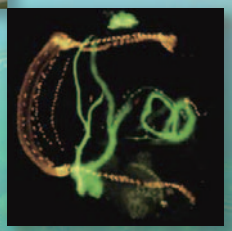
筑波大学大学院

生命環境科学研究科
生物科学専攻



Graduate School of Life and Environmental Sciences
Master's and Doctoral Programs in Biological Sciences



Sylvain Agostini

Ecophysiology of hermatypic corals

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Hermatypic corals are on the fore front of climate change. Rising temperature has resulted in increased mass bleaching and disease occurrence in the tropics, but it has also favor a poleward shift/expansion of corals in Japan and other parts of the world. In order to understand the future extent of this expansion and the possibility that high latitudes provides a future refuge for corals, a better understanding of the effect of environmental parameters on coral ecology and physiology is required.

Monitoring and diverse surveys including citizen surveys of coral communities around Izu and the Izu Islands were established to study the competition with macroalgae, the bleaching occurrence and the growth and diversity of high latitude corals under different pH conditions. The effects of pH on natural coral communities is studied at the recently discovered CO_2 seep in Shikine Island. Laboratory experiments complement the investigation of the stress response of corals. The physiological mechanisms of the effects of high and low temperature stresses and of ocean acidification are studied under controlled conditions in the laboratory.

Porites heronensis is a dominant species of hermatypic corals in high latitude of Japan. It forms dense patchy communities around Shimoda and Izu. It cohabit and compete with a diverse community of macroalgae. Low temperature often cause important bleaching and mortality during winter.

Publications

1. Agostini, S., Fujimura, H., Higuchi, T., Yuyama, I., Casareto, B.E., Suzuki, Y., and Nakano, Y. (2013). The effects of thermal and high-CO2 stresses on the metabolism and surrounding microenvironment of the coral Galaxea fascicularis. Comptes Rendus Biologies *336*, 384–391.
2. Agostini, S., Wada, S., Kon, K., Omori, A., Kohtsuka, H., Fujimura, H., Tsuchiya, Y., Sato, T., Shinagawa, H., Yamada, Y., et al. (2015). Geochemistry of two shallow CO2 seeps in Shikine Island (Japan) and their potential for ocean acidification research. Regional Studies in Marine Science.
3. Agostini, S., Fujimura, H., Hayashi, H., and Fujita, K. (2016). Mitochondrial electron transport activity and metabolism of experimentally bleached hermatypic corals. Journal of Experimental Marine Biology and Ecology *475*, 100–107.
4. Higuchi, T., Agostini, S., Casareto, B.E., Suzuki, Y., and Yuyama, I. (2015). The northern limit of corals of the genus Acropora in temperate zones is determined by their resilience to cold bleaching. Scientific Reports *5*, 18467.

Tomoki Chiba, Ph. D.

Molecular Biology

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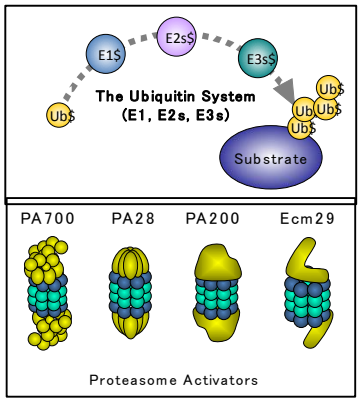
In our body, proteins are in a dynamic state, and the speed of protein synthesis and degradation is tightly regulated. The degradation of protein is individually regulated by the "Ubiquitin and the Proteasome System" which plays critical roles in many biological aspects such as embryogenesis, immune system, and memory.
The major goal of our laboratory is to understand;
(1) The component and regulation of intracellular protein degradation at molecular level.
(2) The physiological roles of selective protein degradation in our body.



The Ubiquitin System.
Ubiquitin acts as a degradation signal and its attachment to the substrate is tightly catalyzed by a cascade reaction composed of E1, E2s and E3s enzymes.
(Keywords; Cullin, NEDD8, signalosome)

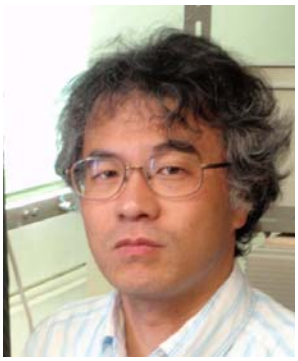
Proteasome Activators
Proteasome is a barrel-shaped multisubunit protease complex that captures and degrades ubiquitinated proteins. The activitiy of the proteasome is regulated by multiple proteasome activators.
(Keywords; Proteasome, PA28, PA200, Ecm29)

My lab is focusing on;
(1) The regulation and function of Cullin-RING-type Ubiquitin ligases.
(2) The regulation and function of proteasome activators using multiple knockout mice.

Publications

1. Huang L, *et al*. Proteasome activators, PA28γ and PA200, play indispensable roles in male fertility. ***Sci. Rep.*** *2016, 6: 23171.*
2. Kigoshi Y, *et al.* CACUL1/CAC1 regulates the antioxidant response by stabilizing Nrf2. ***Sci. Rep.*** *2015, 5: 12857.*
3. Ebina M, *et al.* Myeloma overexpressed 2 (Myeov2) regulates L11 subnuclear localization through Nedd8 modification. ***PLoS ONE*** *2013, 8: e65285.*
4. Qian MX, *et al.* Acetylation-Mediated Proteasomal Degradation of Core Histones during DNA Repair and Spermatogenesis. ***Cell*** *2013, 153: 1012-1024.*
5. Takashima O, *et al.* Brap2 regulates temporal control of NF-kB localization mediated by inflammatory response. ***PLoS ONE*** *2013, 8: e58911.*
6. Kigoshi Y, *et al.* Ubiquitin Ligase Activity of Cul3-KLHL7 Protein Is Attenuated by Autosomal Dominant Retinitis Pigmentosa Causative Mutation. ***J. Biol. Chem.*** *2011 286: 33613-33621.*

Chikafumi Chiba



Trans-regeneration from Newt to Human

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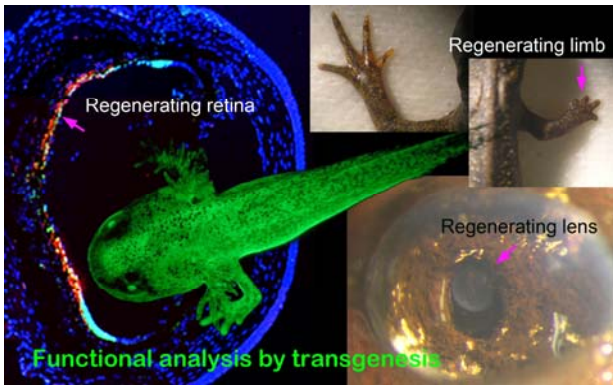
My research aim is to apply the strategy used by newts to regenerate their body parts to medical treatments that will save the lives of people who have suffered traumatic injury. I am currently trying to uncover the cellular and molecular mechanisms of newt body-part regeneration, which has been a biological mystery for more than two centuries. I intend to compare these mechanisms with those of mammalian wound healing and tissue repair, as well as with the pathogenic or oncogenic processes that occur after traumatic injury.

Among vertebrates, the newt is the master of regeneration. No other animal can match its ability to regenerate body parts such as the limbs, the tail and spinal cord, parts of the eye (such as the retina and the lens), and the brain, heart, and jaw. This regeneration is mediated by dedifferentiation or transdifferentiation of somatic cells at the site of injury.



Our current focus is on the retina, lens, and limbs. Recently, we established a highly efficient transgenic system using the newt *Cynops pyrrhogaster*. This is an undoubted breakthrough in our research field and will accelerate the accumulation of knowledge on regeneration of the newt's body parts (*Nature Protocols* 6, 600-608, 2011).

Select Publications

1. Casco-Robles, M.M. et al. (2016). Turning the fate of reprogramming cells from retinal disorder to regeneration by Pax6 in newts. Scientific Reports 6, 33761.
2. Tanaka, H.V. et al. (2016). A developmentally regulated switch from stem cells to dedifferentiation for limb muscle regeneration in newts. Nature Communications *7*, 11069.
3. Islam, M.R., *et al.* (2014). The newt reprograms mature RPE cells into a unique multipotent state for retinal regeneration. Scientific Reports *4*, 6043.
4. Chiba, C. (2014). The retinal pigment epithelium: An important player of retinal disorders and regeneration. Experimental Eye Research *123*:107-114.
5. Casco-Robles, M.M., *et al.* (2011). Expressing exogenous genes in newts by transgenesis. Nature Protocols *6,* 600-608.
6. Tsonis, P.A., *et al.* (2011). Controlling gene loss of function in newts with emphasis on lens regeneration. Nature Protocols *6,* 593-599.

Yousuke Degawa

Natural History of the Kingdom Fungi

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The Kingdom Fungi is one of the most important on Earth. At present there are 100,000 known species, but the total number is estimated to be over 5 million. Our Laboratory of Mycology is situated in the Japan Alps in the Sugadaira Highland, at an elevation of about 1300 m. It has 30 ha of well-preserved natural fields, including grasslands and *Pinus–Quercus* forests. The lab has been managed by the late Emer. Prof. H. Indoh (1908–2003), the late Emer. Prof. K. Tubaki (1924–2005), and Emer. Prof. S Tokumasu (1945–).

The Kingdom Fungi is regarded a sister group of the Kingdom Animalia in the supergroup Opisthokonta. But how did fungi originate and diversify? In our laboratory, we are studying the natural history (taxonomy, phylogeny, and ecology) of a wide range of fungal taxa, by using living natural materials, with the aid of molecular biological approaches. Our focus is 1) the biodiversity of the Chytridiomycota and basal lineages of fungi, in order to elucidate the origin of fungi; 2) the biodiversity of the Zygomycota, to examine the interactions between fungi and other organisms; 3) the biodiversity and life histories (teleomorph–anamorph connections) of the Ascomycota and Basidiomycota.

Biodiversity of the Kingdom Fungi. Top row, left to right: Chytridiomycota (zoospores discharged from zoosporangium of *Chytriomyces*), Zygomycota (sporangiophores of *Pilobolus)*, and Zygomycota (zygospores of *Basidiobolus*). Bottom row, left to right: Ascomycota (conidiophores of the anamorphic hyphomycete *Kumanasamuha*), Ascomycota (apothecium of *Galiella*), Basidiomycota (basidiocarp of *Pluteus*).

Select Publications

1. Degawa, Y., Hosoya, T., Hosaka, K., Hirayama Y., Saito, Y., and Zhao, Y.-J. (2015). Rediscovery of *Roesleria subterranea* from Japan with a discussion of its infraspecific relationships detected using molecular analysis. Mycokeys, *9,* 1-9.
2. Yajima, Y., Inaba, S., Degawa, Y., Hoshino, T., and Kondo, N. (2013). Ultrastructure of cyst-like fungal bodies in myxomycete fruiting bodies. Karstenia *53*, 55-65.
3. Degawa, Y. 2013. *Verrucocephalum*, a new nematophagous genus in the Helicocephalidaceae. Mycoscience, *55,* 144-148.
4. Hirose, D., Degawa, Y., Yamamoto, K., and Yamada, A. (2013). *Sphaerocreas pubescens* is a member of the Mucoromycotina closely related to fungi associated with liverworts and hornworts. Mycoscience *55*, 221-226.
5. An, K.-D., Degawa, Y., Fujihara, E., Mikawa, T., Ohkuma, M., and Okada, G. (2012). Molecular phylogenetic analyses based on the nuclear rRNA genes and the introne exon structures of the nuSSU rRNA gene in *Dictyocatenulata alba* (anamorphic Ascomycota). Myco Res *116*, 1134-1145.

Sumire Fujiwara

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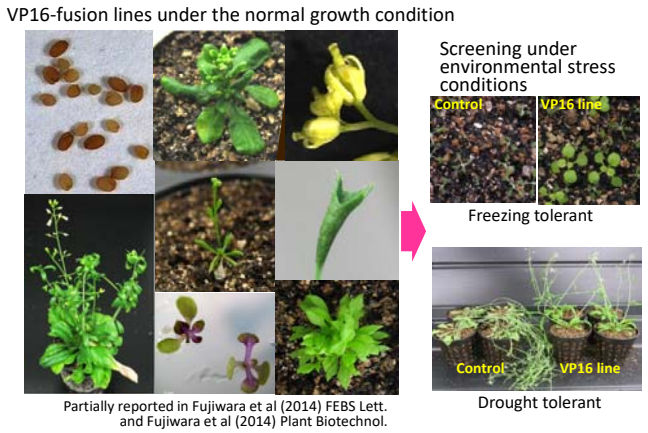
Plant growth and functions are controlled by the dynamic regulation of gene expression by transcription factors. We work on functional analyses and utilization of such transcription factors that are promising to solve many problems we are facing, such as food shortage, energy issues, and global warming. Our current projects include: 1) basic studies of transcriptional regulation mechanisms, 2) identifications and analyses of transcription factors that can be utilized for the development of useful plants, and 3) research and development of useful plants by modifications of transcription factors.



Partially reported in Fujiwara et al (2014) FEBS Lett. and Fujiwara et al (2014) Plant Biotechnol.

To understand the functions of transcriptional repressors and isolate candidates for the targets of super-plant production, we generated approx. 300 Arabidopsis transgenic lines in which a transcriptional repressor fused with an activation domain (VP16) is constitutively expressed. In these lines, the genes whose transcription is usually repressed by the transcriptional repressor are expected to be highly transcribed which could result in causing strong phenotypes. We grew all of them and found many lines showing unique phenotypes or useful traits such as stress tolerance or higher yield.

Select Publications

1. Fujiwara, S., Sakamoto, S., Kigoshi, K., Mitsuda, N., Suzuki, K., and Ohme-Takagi, M. (2014) VP16 fusion induces the multiple-knockout phenotype of redundant transcriptional repressors partly by Med25-independent mechanisms in Arabidopsis. FEBS Lett. *588*, 3665-3672
2. Fujiwara, S., Kigoshi, K., Mitsuda, N., Ohme-Takagi, M., and Suzuki, K. (2014) VP16 fusion efficiently reveals the function of transcriptional repressors in Arabidopsis. Plant Biotechnol. *31*, 123-132
3. Wang, L., Fujiwara, S., and Somers, D.E. (2010) PRR5 regulates nuclear import and subnuclear localization of TOC1 in the Arabidopsis circadian clock. EMBO J., *29*, 1903-1915
4. Fujiwara, S., Oda, A., Yoshida, R., Niinuma, K., Miyata, K., Tomozoe, Y., Tajima, T., Nakagawa, M., Hayashi, K., Coupland, G., and Mizoguchi, T. (2008) Circadian Clock Proteins LHY and CCA1 Regulate SVP Protein Accumulation to Control Flowering in Arabidopsis. Plant Cell *20*, 2960-2971
5. Kim, W.Y.*, Fujiwara, S.*, Suh, S.S., Kim, J., Kim, Y., Han, L., David, K., Putterill, J., Nam, H.G., and Somers, D.E. (2007) ZEITLUPE is a circadian photoreceptor stabilized by GIGANTEA in blue light. Nature *449*, 356-360 (*: equal contribution)

Ben Harvey

Marine Climate Change Ecology

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Ocean acidification (OA), the change in seawater carbonate conditions associated with increasing levels of atmospheric CO_2, has been identified as one of the 21st century's greatest challenges for marine biodiversity. There is now quite an impressive body of scientific literature on how individual species are likely to respond to OA. The variety of responses within and between taxa suggest that OA is likely to drive substantial change in marine ecosystems, and potentially generate novel communities composed of new combinations of species. Hence, the next significant knowledge gap is to understand how OA will affect the structure and functioning of whole communities, with the aim of informing on the implications for the ecosystem services that these communities provide (e.g. food, habitat provisioning, coastal defence, nutrient cycling). My research seeks to address this knowledge gap by using natural *in situ* CO_2 seeps.

Volcanic vents releasing CO_2 gas were recently discovered in the shallow bay of Mikama on Shikine Island. This release of gas causes a local acidification of the waters around the vent resulting in similar chemical conditions to the future conditions under OA. My research uses a combination of field surveys at the CO_2 seep in Mikama and *in situ* experiments to investigate the effects of OA on the marine organisms and the ecosystem. From species interaction to alteration in the organism's physiology, my research provides important knowledge for the predictions of the effects that OA will have on marine ecosystems.

[Left] CO_2 bubbling from the natural CO_2 seeps, causing local ocean acidification at the study site.

[Right] Typical communities located on Shikine Island outside of the CO_2 seep system.

Publications

1. **Harvey, B.P.** *et al.* (2016) Linking individual and population-level responses to climate change. *Scientific Reports*, 6, 20194
2. **Harvey, B.P.** *et al.* (2014) Evolution of marine organisms under climate change at different levels of biological organisation, *Water*, 6 (11), 3545-3574
3. Brodie, J. *et al.* (2014) The future of the NE Atlantic benthic flora in a high CO_2 world, *Ecology and Evolution*, 4 (13), 2787-2798
4. **Harvey, B.P**, Gwynn-Jones, D. and Moore, P.J. (2013) Meta-analysis reveals complex biological responses to the combined effects of ocean acidification and warming, *Ecology and Evolution*, 3 (4), 1016-1030

Tetsuo Hashimoto

Molecular Evolution of Microbes

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The central focus of our research is to gain insight into the origin and early evolution of eukaryotes. This is currently the most important open problem in evolutionary biology. We are using molecular and cellular biological methods, including comparative 'omics' analyses and molecular phylogeny, to approach the evolutionarily interesting issues presented by diverse eukaryotic microorganisms.

One of the goals of our research is to reconstruct a reliable eukaryotic tree. We are continuing to perform phylogenomic analyses using high-performance computing to elucidate the early phase of eukaryotic evolution. By using a refined tree of the organisms of interest, we compare genomic, transcriptomic, and proteomic data so as to trace the evolutionary history of the divergence of cellular functions and molecular mechanisms. Our recent focus is elucidation of the reductive evolution of mitochondria in a diverse anaerobic organismal group, the Fornicata, all of which contain no typical mitochondria but have mitochondrion-related, reduced organelles.

Giardia intestinalis is a flagellated organism belonging to a diverse anaerobic group, the Fornicata. It is a mammalian parasite that colonizes and reproduces in the small intestine, causing giardiasis. Tiny double membrane–bound organelles called mitosomes are present in the cell; these are considered to be reduced mitochondria.

(Photo by N. Yubuki)

Select Publications

1. Arisue, N., Hashimoto, T., Mitsui, H., Palacpac, N.M.Q., Kaneko, A., Kawai, S., Hasegawa, M., Tanabe, K., and Horii, T. (2012). The *Plasmodium* apicoplast genome: conserved structure and close relationship of *P. ovale* to rodent malaria parasites. Mol Biol Evol, in press.
2. Takishita, K., Kolisko, M., Komatsuzaki, H., Yabuki, A., Inagaki, Y., Cepicka, I., Smejkalová, P., Silberman, J.D., Hashimoto, T., Roger, A.J., and Simpson, A.G.B. (2012). Multigene phylogenies of diverse Carpediemonas-like organisms identify the closest relatives of 'amitochondriate' diplomonads and retortamonads. Protist *163*, 344-355.
3. Kamikawa, R., Inagaki, Y., Tokoro, M., Roger, A.J., and Hashimoto, T. (2011). Split introns in the genome of a divergent eukaryote *Giardia intestinalis* are excised by spliceosome-mediated trans-splicing. Curr Biol *21*, 311-315.

Yoshihisa Hirakawa

Molecular biology and evolution of algae

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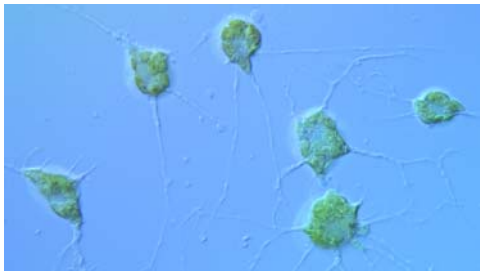
My main research interest is to understand how plastids (chloroplasts) have evolved in diverse organisms. Many species of plants and algae possess plastids as photosynthetic organelles, which were originated by endosymbiotic uptakes that a photosynthetic organism was fully integrated into a phagotrophic eukaryote. Plastids of plants and several algae (red and green algae) were derived from a cyanobacterial endosymbiont. In contrast, many other algal groups acquired complex plastids through secondary endosymbioses of red and green algae. These multiple endosymbiotic events are a significant driving force in evolution of diverse photosynthetic eukaryotes on the earth.

How was an endosymbiont integrated into a host cell as a plastid? To answer the question, I'm currently studying on several topics using a marine unicellular algae, chlorarachniophytes. Research topics: 1) Reductive genome evolution of integrated endosymbionts 2) Endosymbiotic gene transfer 3) Protein targeting into complex plastids 4) Plastid division mechanism 5) Organelle DNA replication.



Picture of the chlorarachniophyte *Amorphochlora amoebiformis*. Each cell contain several green plastids. Chlorarachniophytes evolved by a secondary endosymbiosis between a green algal endosymbiont and a phagotrophic cercozoan protist.

Publications

1. Hirakawa, Y. and Ishida, K. (2015). Prospective function of FtsZ proteins in the secondary plastid of chlorarachniophyte algae. BMC Plant Biol *15*, 276.
2. Hirakawa, Y. (2014). Complex plastids of chlorarachniophyte algae. Perspectives in Phycology *1*, 87-92.
3. Hirakawa, Y., Suzuki, S., Archibald, J. M., Keeling, P. J., and Ishida, K. (2014). Overexpression of molecular chaperone genes in nucleomorph genomes. Mol Biol Evol *31*, 1437-1443.
4. Hirakawa, Y., Burki, F., and Keeling, P. J. (2012). Dual targeting of aminoacyl-tRNA synthetases to the mitochondrion and plastid in chlorarachniophytes. J Cell Sci *125*, 6176-6184.
5. Hirakawa, Y., Burki, F., and Keeling P. J. (2012). Genome-based reconstruction of the protein import machinery in the secondary plastid of a chlorarachniophyte alga. Eukaryot Cell *11*, 324-333.

Mitsuru Hirota

Terrestrial Ecosystem Ecology

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We are seeking to improve process-based understanding of carbon dynamics in terrestrial ecosystems by investigating carbon fluxes and pools. By demonstrating such parameters and their relationships with various environmental factors, we will be able not only to estimate carbon sink capacity with high accuracy, but also to demonstrate the features of individual ecosystems. Current projects include

- ✓ Responses of alpine grassland carbon dynamics to recent environmental changes
- ✓ Relationship between biodiversity and ecosystem functioning in a highly diverse Tibetan grassland ecosystem
- ✓ Island ecosystem restoration focused on decomposition processes after the 2000 eruption on Miyake Island, Japan
- ✓ Reevaluation of the carbon sink capacity of old-growth forest ecosystems.

Select publications

1. Hirota M., Zhang P., Gu S., Shen H., Kuriyama T., Li Y., and Tang, Y. (2010). Small-scale variation in ecosystem CO_2 flux in an alpine meadow depends on plant biomass and species richness. Journal of Plant Research *123*, 531-541.
2. Hirota M., Zhang P., Gu S., Du M., Shimono A., Shen H., Li Y., and Tang. Y. (2009). Altitudinal variation of ecosystem CO_2 fluxes in an alpine grassland from 3600 to 4200 m. Journal Plant Ecology *2*, 197-205.
3. Hirota, M., Senga, Y., Seike, Y., Nohara, S., and Kunii, H. (2007). Fluxes of carbon dioxide, methane and nitrous oxide in two contrastive fringing zones of coastal lagoon, Lake Nakaumi, Japan. Chemosphere *68*, 597-603.
4. Hirota, M., Tang, Y., Hu, Q., Kato, T., Hirata, S., Mo, W., Cao, G., and Mariko, S. (2006). Carbon dioxide dynamics and controls in a deep-water wetland on the Qinghai-Tibetan Plateau. Ecosystems *9*, 673-688.
5. Hirota, M., Tang, Y., Hu, Q., Kato, T., Hirata, S., Mo, W., Cao, G., and Mariko, S. (2005). The potential importance of grazing to the fluxes of carbon dioxide and methane in an alpine wetland on the Qinghai-Tibetan Plateau. Atmospheric Environment *39*, 5255-5259.
6. Hirota, M., Tang, Y., Hu, Q., Hirata, S., Kato, T., Mo, W., Cao, G., and Mariko, S. (2004). Methane emissions from different vegetation zones in a Qinghai-Tibetan Plateau wetland. Soil Biology and Biochemistry *36*, 737-748.

Takeo Horie

Neural Circuits and Behavior in Ascidian Larvae

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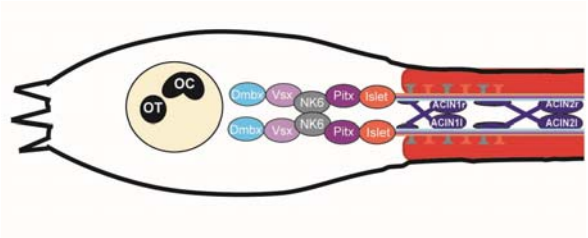
Animal behavior results fundamentally from the coordinated activity of neural circuits. Our laboratory is studying the relationships among neurons, neural circuits, and behavior in ascidian larvae. These larvae have a very simple central nervous system (CNS) consisting of only about 100 neurons. Despite its simplicity, the CNS of ascidian larvae shares several properties with those of vertebrates. The small number of neurons in these larvae enables us to describe neural circuits at the single-cell level. Our ability to manipulate the activity of individual neurons makes it possible to elucidate how neural circuits function. We are using a combination of optogenetics, in vivo Ca^{2+} imaging, proteomics, and behavioral genetics in the ascidian *Ciona intestinalis* to gain an understanding of the operating principles of the neural circuits underlying animal behavior.

Cilia are microtubule-based organelles that extend from basal bodies and form on the apical surfaces of cells. We are also studying the developmental role and physiological functions of the cilia present in the nervous system of ascidian larvae.



Neural circuit that generates swimming behavior in ascidian larvae. This neural circuit is composed of only 14 neurons.

Select Publications

1. Sasakura, Y., Mita, K., Ogura, Y., and Horie, T. (2012). Ascidians as excellent chordate models for studying the development of the nervous system during embryogenesis and metamorphosis. Development, Growth & Differentiation *54*, 420-437.
2. Horie, T., Shinki, R., Ogura, Y., Kusakabe, T.G., Satoh, N., and Sasakura, Y. (2011). Ependymal cells of chordate larvae are stem-like cells that form the adult nervous system. Nature *469*, 525-528.
3. Horie, T., Nakagawa, M., Sasakura, Y., Kusakabe, T., and Tsuda, M. (2010). Simple motor system of the ascidian larva: Neuronal complex comprising putative cholinergic and GABAergic/glycinergic neurons. Zoological Science *27*, 181-190.
4. Horie, T., Nakagawa, M., Sasakura, Y., and Kusakabe T.G. (2009). Cell type and function of neurons in the ascidian nervous system. Development Growth & Differentiation *51*, 207-220..
5. Horie, T., Kusakabe, T., and Tsuda, M. (2008). Glutamatergic networks in the *Ciona intestinalis* larva. Jounal of Comparative Neurology *508*, 249-263.

Tsuyoshi Hosoya

Biodiversity of Fungi

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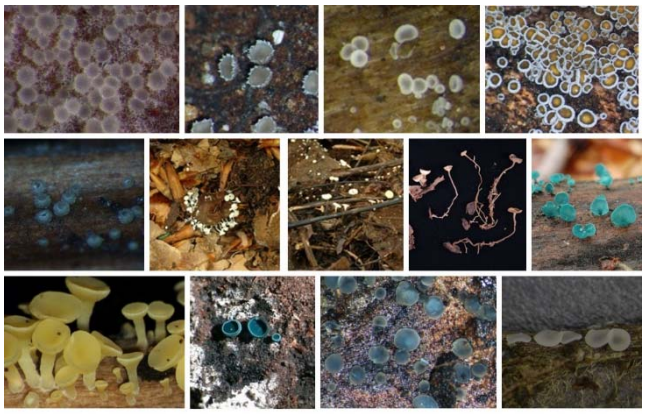
My research is focused on the biodiversity of the order Helotiales, phylum Ascomycota, Kingdom of Fungi. Fungi is one of the largest group of organisms in the world, estimated to consisted of more than 1.5 millions of species. Ascomycota is the largest group of fungi, and Helotiales is one of the most diverse group in Ascomycota. The members of Helotiales produces small saucer to nail-shaped mushroom, called apothecia. The majority of the members of Helotiales were thought to be weak saprophytes occurring on decaying plant substrates. Recently, however, the majority of plant root endophytes (fungi that live in plant symbiotically or without showing any symptoms) turned out to be Helotiales. Helotiales were more versatile than we imagined! Then which species are there? Actually, we cannot tell which species by names, because the taxonomy of Helotiales is so poor, and we are not sure how many species exactly are there in Japan, either.



We use molecular barcoding technique and conventional taxonomic technique (morphology and isolation) to evaluate the biodiversity of species. Enumeration of all the Helotiales in Japan is one of the goal. Another issue is the comparisons with previously known European species. Our predecessors have identified Japanese species based on European literature. However, the present knowledge suggests that Japanese species may be different from that in Europe. We have to critically examine the identity using molecular technique. Finally, we also use isolates to help understanding the lifecycles.

[Selected Publications]

1. Zhao YJ, Hosaka K, Hosoya T (2016) Taxonomic re-evaluation of the genus Lambertella Rutstroemiaceae, Helotiales) and allied stroma-forming fungi. Mycological Progress 15:1215-1228.
2. Hosoya T, Jinbo U, Tanney J (2015) "MolliBase", a new sequence database including unidentified Mollisia and its allied genera. Ascomycete.org 7:311-314.
3. Gross A, Hosoya T, Zhao, Y.-J., Baral, H.-O. (2015) Hymenoscyphus linearis sp. nov.: another close relative of the ash dieback pathogen H. fraxineus. Mycological Progress 14:1-15.
4. Han JG, Hosoya T, Sung GH, Shin HD (2014) Phylogenetic reassessment of Hyaloscyphaceae sensu lato (Helotiales, Leotiomycetes) based on multigene analysses. Fungal Biology 118:150-167.
5. Hosoya T, Hosaka K, Saito Y, Degawa Y, Suzuki R (2013) Naemacyclus culmigenus, a newly reported potential pathogen to Miscanthus sinensis, new to Japan. Mycoscience 54:433-443.

Kazuo Inaba

Cell Biology of Sperm, Cilia and Flagella

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Our research goal is to explore the biological significance of sperm and eukaryotic cilia and flagella by using several marine organisms, including tunicates, sea urchins, sea snails, comb jellies, spiny lobsters, flounder and marine algae. The main projects in my lab are as follows:
Biology of sperm: Molecular characterization of sperm flagella; molecular mechanism and regulation of flagellar motility; sperm activation and chemotaxis by egg-derived substances; genomics and proteomics analyses of testis-expressed genes and proteins; ocean acidification and sperm function; molecular mechanisms of spermatogenesis; the structure and function of gastropod parasperm; and the molecular diversity of sperm protein.
Biology of cilia and flagella: Structure and function of dynein motors; regulation of flagellar motility by protein kinases and protein phosphatases; molecular architecture of the axoneme and comb plate; cDNA and proteomics analysis of axonemal proteins; novel Ca^{2+}-binding protein and photoreceptor protein; in vitro assembly of the axoneme; phylogenetic analysis of ciliary and flagellar proteins; and eukaryotic evolution and diversity of cilia and flagella.

Select Publications

1. Miyata H et al. (2015). Sperm calcineurin inhibition prevents mouse fertility with implications for male contraceptive. Science *350* 442-445.
2. Inaba K. (2015). Calcium sensors of ciliary outer arm dynein: functions and phylogenetic considerations for eukaryotic evolution. Cilia. *4*:6.
3. Mizuno K et al. (2012). Calaxin drives sperm chemotaxis by Ca^{2+}-mediated direct modulation of a dynein motor. Proc Natl Acad Sci U S A. *109*:20497-20502.
4. Inaba K. (2011). Sperm flagella: comparative and phylogenetic perspectives of protein components. Mol Hum Reprod. *17*, 524-538.
5. Konno A et al. (2010). Distribution and structural diversity of cilia in tadpole larvae of the ascidian Ciona intestinalis. Dev Biol. *337*, 42-62.
6. Satouh Y et al. (2005). Molecular characterization of radial spoke subcomplex containing radial spoke protein 3 and heat shock protein 40 in sperm flagella of the ascidian Ciona intestinalis. Mol Biol Cell *16*, 626-636.
7. Murata Y et al. (2005) Phosphoinositide phosphatase activity coupled to an intrinsic voltage sensor. Nature *435*, 1239-1243.

Ken-ichiro Ishida

Plant taxonomy and phylogeny

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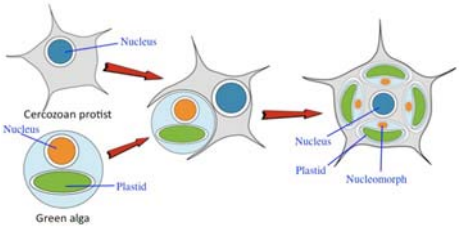
Research interest in my lab is to elucidate the diversity and evolution of photosynthetic protists (algae) and their non-photosynthetic relatives. Following three major subjects are the current focuses in my research.

1. **Cellular evolution in the endosymbiotic acquisition of plastids:** Plastids were born by a primary endosymbiosis and transferred to the different eukaryotic lineages by several secondary endosymbises. We are interested in how a photosynthetic endosymbiont was integrated into a host cell as an organelle. This mystery is being uncovered by various approaches, such as genomics, cell biology, electron microscopy and molecular phylogenetics.

2. **Taxonomy and phylogeny of protists:** We look for new protist species, especially the ones that can connect missing links in the tree of life. We collect protists from the nature, establish clonal cultures if possible, observe them under light and electron microscopes and perform molecular phylogenetic analyses. We are the protist hunters.

3. **Search for useful protists for bio-fuel production:** We are studying how to look for oil-producing algae and protists in the nature and establish cultures of high-performance strains.



The establishment of the chlorarachniophytes which is a photosynthetic protist group with green secondary plastids. A cercozoan protist engulfed a green alga and kept it as a plastid. The plastid os chlorarachniophytes still have a vestigial nucleus (nucleomorph) of the endosymbiotic green alga.

Publications

1. Shiratori T., Ishida K. (2016) Trachyrhizium urniformis n. g., n. sp., a Novel Marine Filose Thecate Amoeba Related to a Cercozoan Environmental Clade (Novel Clade 4). Journal of Eukaryotic Microbiology 63(6):722-731.
2. Suzuki S., Ishida K., Hirakawa Y. (2016) Diurnal Transcriptional Regulation of Endosymbiotically Derived Genes in the chlorarachniophyte Bigelowiella natans. Genome Biology and Evolution 8(9):2672-2682.
3. Nomura M., Ishida K. (2016) Fine-structural observations on siliceous scale production and shell assembly in the testate amoeba Paulinella chromatophora. Protist 167 (4):303-318.
4. Suzuki S., Shirato S., Hirakawa Y., Ishida K (2015) Nucleomorph genome sequences of two chlorarachniophytes, Amorphochlora amoebiformis and Lotharella vacuolata. Genome Biology and Evolution 7(6):15336-1545.
5. Hirakawa Y., Nagamune K. and Ishida K. (2009). Protein targeting into secondary plastids of chlorarachniophytes. Proc Natl Acad Sci USA 106:12820-12825.

Kaori Ishikawa

Mitochondrial Biology

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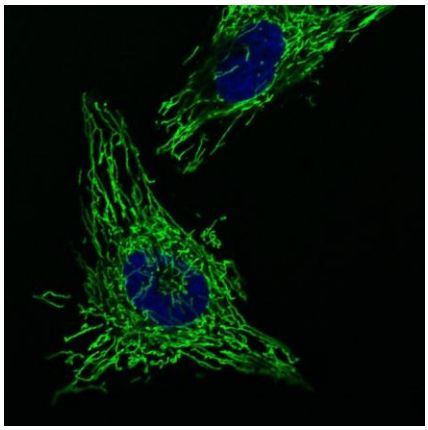
Mitochondria are dynamic organelles which fuse and divide continuously, and they have evolved with eukaryotic cells, developing a symbiotic relationship and complementing each other. Understanding "normal" and "abnormal" mitochondrial functions is very important to uncover the mechanisms of human diseases.

We are studying the impact of mitochondrial DNA (mtDNA) mutations on cellular or tissue functions using *in vitro* and *in vivo* models.

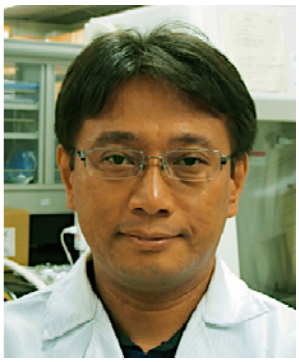


Mitochondria in human cells are visualized by green dye. Blue dye indicates nuclei. Mitochondria construct dynamic networks in cytosols.

Publications

1. Ishikawa K, Takenaga K, Akimoto M, Koshikawa N, Yamaguchi A, Imanishi H, Nakada K, Honma Y, Hayashi J. (2008). ROS-generating mitochondrial DNA mutations can regulate tumor cell metastasis. Science *320*, 661-664.
2. Ishikawa K, Hashizume O, Koshikawa N, Fukuda S, Nakada K, Takenaga K, Hayashi J. (2008). Enhanced glycolysis induced by mtDNA mutations does not regulate metastasis. FEBS Lett *582*, 3525-3530.
3. Ishikawa K, Toyama-Sorimachi N, Nakada K, Morimoto M, Imanishi H, Yoshizaki M, Sasawatari S, Niikura M, Takenaga K, Yonekawa H, Hayashi J. (2010). The innate immune system in host mice targets cells with allogenic mitochondrial DNA. J Exp Med. *207*, 2297-2305.

Yuzuru Ito



Stem Cell Engineering for Regenerative Medicine

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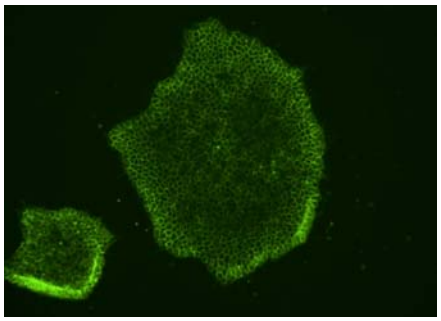
Human pluripotent stem cells (ES/iPS cells) and mesenchymal stem cell are expected as powerful tool for regenerative medicine in the world. However, those cells are likely to lose the useful ability for cell therapy during preparation (establishment, culture, cryopreservation etc.) Moreover, method for preparation of some organ cells is insufficient so safe and effective method of treatment isn't realized yet.

To establish the facile, economical and safe regenerative medicine, we should develop several supporting technology for quality control, safety administration and so on. We will promote the development of technology for supporting regenerative medicine.



Fluoresceinated rBC2LCN directly stains human iPS cell colonies. This new probe that we developed can detect good iPS/ES cells accurately, nondestructively and quickly. We can use this probe as "high-sensitive" and "low-toxic" technology for human ES/iPS cells to facilitate of quality control.

Publications

1. Lin-Gibson, S., Sarkar, S., and Ito, Y. (2016). Defining quality attributes to enable measurement assurance for cell therapy products. Cytotherapy *18*, 1241-1244.
2. Onuma, Y., Higuchi, K., Aiki, Y., Shu, Y., Asada, M., Asashima, M., Suzuki, M., Imamura, T., and Ito, Y. (2015). A Stable Chimeric Fibroblast Growth Factor (FGF) Can Successfully Replace Basic FGF in Human Pluripotent Stem Cell Culture. PLoS One *10*, e0118931.
3. Ogawa-Otomo, A., Kurisaki, A., and Ito, Y. (2015). Aminolevulinate synthase 2 mediates erythrocyte differentiation by regulating larval globin expression during Xenopus primary hematopoiesis. Biochem Biopys Res Commun *456*, 476-481.
4. Haramoto, Y., Oshima, T., Takahashi, S., and Ito, Y. (2014). Characterization of the insulin-like growth factor binding protein family in Xenopus tropicalis. Int J Dev Biol *58*, 705-711.
5. Onuma, Y., Tateno, T., Hirabayashi, J., Ito, Y., and Asashima, M. (2013). rBC2LCN, a new probe for live cell imaging of human pluripotent stem cells. Biochem Biopys Res Commun *431*, 524-529.

Akira Kikuchi
Stress Physiology in Higher Plants

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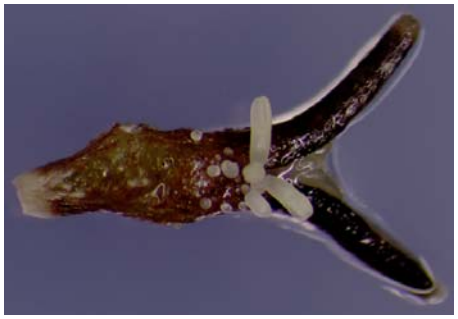
Stress tolerance in higher plants is an interesting phenomenon. Plants are immobile and must evolve defense systems that are uniquely suited to their ambient environmental stresses. Several genes associated with these defense systems have been identified. Our aim here is to generate genetic lines conferring abiotic stress tolerance and to verify their performance. We are also studying the impacts of transgenic plants on biological diversity so as to establish an environmental biosafety risk-assessment system for transgenic plants. In addition, we are trying to elucidate the mechanisms of abiotic stress tolerance in higher plants by using GM (genetically modified) techniques, and we are studying the induction of somatic embryogenesis by abiotic stress. In this way, while elucidating the mechanism of abiotic stress in higher plants, we are also working on the development of abiotic stress–tolerant GM plants that can be used for crop production.



Somatic embryogenesis induced in carrots by abiotic stress
In carrots, somatic embryo production can be induced from apical tip segments by application and removal of stress treatment. The somatic cells are converted to embryogenic cells by the stress treatment. After removal of the stress, the embryogenic cell begins to develop into a somatic embryo.

Select Publications

1. Kikuchi A., Huynh D., Endo T., Watanabe K. (2015) Review of recent transgenic studies on abiotic stress tolerance and future molecular breeding in potato. Breeding science. 65:85-102.
2. Oguchi T., Kashimura Y., Mimura M., Yu X., Matsunaga E., Nanto K., Shimada T., Kikuchi A., Watanabe K. (2014) A Multi-year assesment of the emvironmental impact of transgenic Eucalyptus trees harboring a bacterial choline oxidase gene on biomass, precinct vegettion and the microbal community. Transgenic Research. 23:767-77.
3. Kikuchi A., Asahina M., Tanaka M., Satoh S., Kamada H. (2013) Acquisition of embryogenic competency does not require cell division in carrot somatic cell. J Plant Res, 126:243-250.
4. *Yu X., *Kikuchi A., Matsunaga E., Morishita Y., Nanto K., et al. (2013) The choline oxidase gene *codA* confers salt tolerance to transgenic *Eucalyptus globulus* in a semi-confined condition. Mol Biotech, 54:320-330 (*: equally contributed).
5. Shibukawa T., Yazawa K., Kikuchi A., Kamada H. (2009) Possible involvement of DNA methylation on expression regulation of Carrot *LEC1* gene in its 5'-upstream region. Gene *437*, 22-31.
6. Tanaka M., Kikuchi A., Kamada H. (2008) The *Arabidopsis* histone deacetylases HDA6 and HDA19 contribute to the repression of embryonic properties after germination. Plant Physiol *146*, 149-161.

Satoru Kobayashi

Molecular Mechanisms Regulating Germline Development

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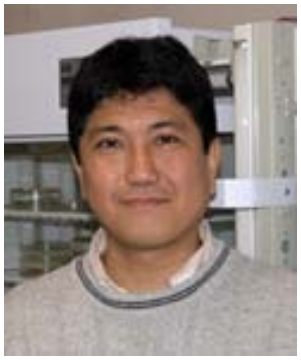
Germ cells are specialized cells that can transmit genetic materials from one generation to the next through sexual reproduction. All other cells of the body are somatic cells. This separation of germ and somatic cells is one of the oldest problems in developmental biology. In many animal groups, a specialized portion of egg cytoplasm, or germ plasm, is inherited by the cell lineage which gives rise to germ cells. This cell lineage is called germline. The germline progenitors eventually migrate into the gonads, where they differentiate as germline stem cells (GSC) to form eggs and sperm when the organisms are physically matured. Our laboratory aims to find the molecular mechanisms regulating germline segregation, germline sex determination, and GSC niche function in *Drosophila*.

Publications

1. Ohhara, Y., Shimada-Niwa, Y., Niwa, R., Kayashima, Y., Hayashi, Y., Akagi, K., Ueda, H., Yamakawa-Kobayashi, K. and Kobayashi, S. (2015) Autocrine regulation of ecdysone synthesis by β3-octopamine receptor in the prothoracic gland is essential for *Drosophila* metamorphosis. Proc. Natl. Acad. Sci., USA., *112*, 1452-1457.
2. Hashiyama, K., Hayashi, Y. and Kobayashi, S. (2011). *Drosophila Sex lethal* gene initiates female development in germline progenitors. Science *333*, 885-888.
3. Kitadate, Y. and Kobayashi, S. (2010). Notch and Egfr signaling act antagonistically to regulate germline stem cell niche formation in *Drosophila* male embryonic gonads. Proc. Natl. Acad. Sci. USA *107*, 14241-14246.
4. Kitadate, Y., Shigenobu, S., Arita, K. and Kobayashi, S. (2007). Boss/Sev signaling from germline to soma restricts germlinestem-cell-niche formation in the anterior region of *Drosophila* male gonad. Dev. Cell *13*, 151-159.
5. Hayashi, Y., Hayashi, M. and Kobayashi, S. (2004). Nanos suppresses somatic cell fate in *Drosophila* germline. Proc. Natl. Acad. Sci. USA. *101*, 10338-10342.
6. Asaoka-Taguchi, M., Yamada, M., Nakamura, A., Hanyu, K. and Kobayashi, S. (1999) Maternal Pumilio acts together with Nanos in germline development in *Drosophila* embryos. Nature Cell Biol. *1*, 431-437.
7. Kobayashi, S., Yamada, M., Asaoka, M., and Kitamura, T. (1996). Essential role of the posterior morphogen nanos for germline development in *Drosophila*. Nature *380*, 708-711.

Hidekazu Kuwayama



Molecular Mechanisms and Dynamics of Biological Self-organization

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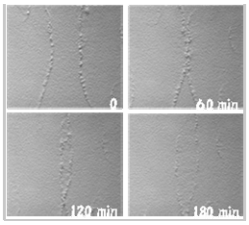
[English page is under construction]

Self-reproduction or Self-organization is a characteristic observed in all biological organisms. In my Lab, we research self-organization using a cellular slime mold, *Dictyostelium discoideum*, as a model system, by a combination of experimental and theoretical methods. Our aim is to clarify the molecular systems that regulate cell orientation and to simulate its dynamics.

Dictyostelium discoideum is a solitary amoeboid microorganism that grows as a single cell, but during starvation it initiates chemotaxis towards a cAMP signal secreted by neighboring cells and constructs a multicellular "slug". This feature is simple but very useful for investigating how cells interact to construct multi-cellular organisms. At present, we are focusing on biological soliton phenomenon which was firstly discovered in my Lab, and chemotaxis which involves questions about how cells recognize their environment using molecular techniques. We are also interested in disease-causing genes related to biological self-organization.



Biological soliton phenomena in multi-cellular movement observed in *Dictyostelium* mutant.

Selected Publications

1. Yuya Kida, Kai Pan, Hidekazu Kuwayama. (2019) Some chemotactic mutants can be progress through development in chimeric populations. Differentiation., 105, 71-79, 2019
2. Kuwayama, H., Kikuchi, H., Oshima, Y. and Kubohara, Y. (2016) Glutathione S-transferase 4 is a putative DIF-binding protein that regulates the size of fruiting bodies in *Dictyostelium discoideum*. Bioch., and Biophy., Reports, 8, 219-226.
3. Kuwayama, H. and Kubohara, Y. (2016) Differentiation-inducing factor 2 modulates chemotaxis via the histidine kinase DhkC-dependent pathway in *Dictyostelium discoideum*. FEBS Lett. *590*,760-768.
4. Kuwayama, H. et al. (2014) Cross-species functional complementation of cellulose synthase during the development of cellular slime molds. Dev. Growth and Diff., *56*, 526–533.
5. Kuwayama, H. et al. (2013) A RabGAP Regulates Life-Cycle Duration via Trimeric G-protein Cascades in *Dictyostelium discoideum*. PLoS One *8,* e81811.
6. Kuwayama, H. and Ishida, S. (2013) Biological soliton in multicellular movement. Scientific Reports, *3*, Article number: 2272.
7. Kuwayama, H. (2012). Arachidonic Acid Enhances Caffeine-Induced Cell Death via Caspase-Independent Cell Death. Scientfic Reports *2*, Article number: 577.
8. Kuwayama, H., Kikuchi, H., Oshima, Y. and Kubohara, Y. (2011). Artificial compounds differentially control *Dictyostelium* chemotaxis and cell differentiation. Cell Struct Funct *36*, 21-26.
9. Kuwayama, H., and Kubohara, Y. (2009). Differentiation-Inducing Factor-1 and -2 Function also as Modulators for *Dictyostelium* Chemotaxis. PLoS One *4,* e6658.
10. Kuwayama, H., Yanagida, T. and Ueda, M. (2008). DNA oligonucleotide-assisted genetic manipulation increases transformation and homologous recombination efficiencies; evidence from gene targeting of *Dictyostelium discoideum*. Journal of Biotech *133*, 418-423.

Fumiaki Maruo

Developmental Biology of Stem Cells

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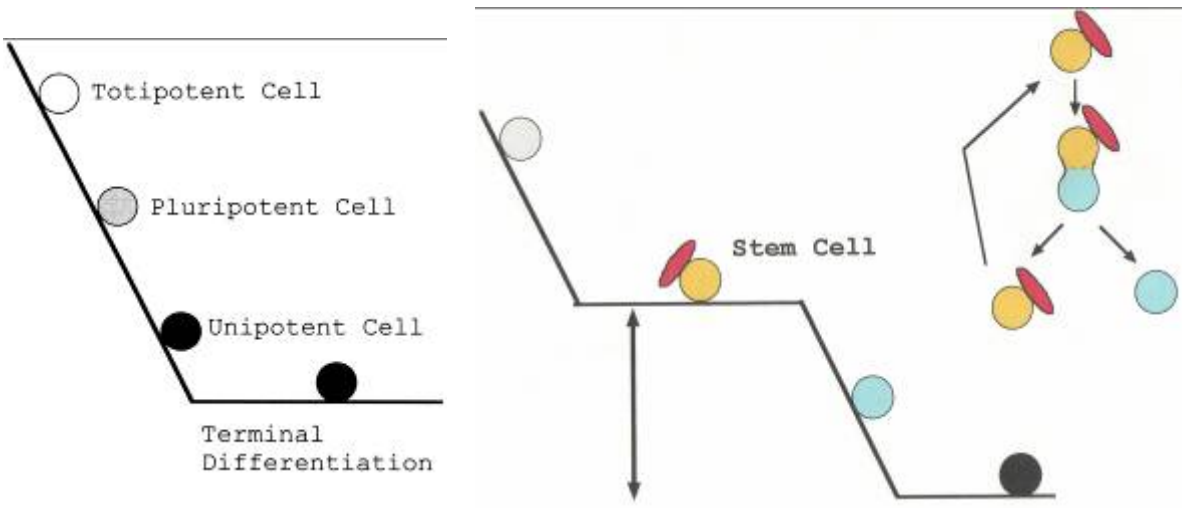
Stem cells and regeneration are currently hot research subjects in the life sciences and provide many possibilities for future treatments for major diseases, including organ damage and degenerative conditions. We are studying the mechanisms regulating stem cell maintenance, proliferation, and differentiation. Our experimental system uses the germline stem cells in *Drosophila* oogenesis. We also use neuronal stem cells in the regenerating newt retina and undifferentiated germline cells in developing newt gonads. Our approaches involve genetic, immunological, and molecular biological techniques.

Keywords on our research are “cell differentiation”, “regeneration”, “*Drosophila*”, “newt”, “germ cell”, and “stem cell”.

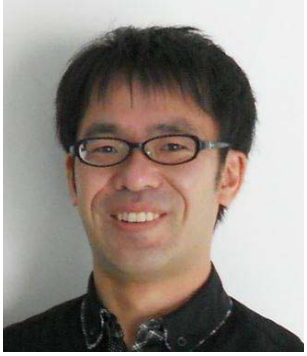


Steps in developmental potency (left), and a model mechanism of stem cell maintenance (right).

Select Publications

1. Chiba, C., Hoshino, A., Nakamura, K., Susaki, K., Yamano, Y., Kaneko, Y., Kuwata, O., Maruo, F., and Saito, T. (2006). Visual cycle protein RPE65 persists in new retinal cells during retinal regeneration of adult newt. The Journal of Comparative Neurology *495*, 391-407.
2. Maruo, F. (1996). Developmental genetics of oogenesis. In *Developmental Genetics* (ed. Okada, M.), pp. 35-68. SHOKABO, Tokyo. (in Japanese)

Hisanori Matsui



Translational Science in Drug Discovery

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Functional analysis of orphan GPCR was my first research area as a biologist in drug discovery research. Kisspeptin was one of the most impactful research topics for me, starting from the discovery of its physiological functions in relation to reproductive neuroendocrinology and its therapeutic application for prostate cancer. Through this program I gained experience and knowledge ranging from the drug target discovery to drug development as clinical studies. I then changed my research field from oncology to drug repurposing, expanded my research therapeutic areas and strengthened translational science. I am now leading External Neuroscience Research to deliver breakthrough medicine through innovative partnership. My experience of therapeutic area includes oncology, reproductive neuroendocrinology, inflammation, and neuroscience.

Drug discovery and development is a teamwork-oriented process where very diverse multi-functional professionals are working together. In addition, drug discovery and development cannot be achieved without external professional partners as well. I really like this multidisciplinary research approach because we can overcome hurdle after hurdle to eventually achieve our goals. Let's work together to make innovation happen.

Selected Publications

1. Ishikawa, K., Tanaka, A., Kogame, A., Watanabe, T., Tagawa, Y., and Matsui, H. (2018). Usefulness of pharmacokinetic/efficacy analysis of an investigational kisspeptin analog, TAK-448, in quantitatively evaluating anti-tumor growth effect in the rat VCaP androgen-sensitive prostate cancer model. Eur. J. Pharmacol. *828*, 126-134.
2. Tanaka, A., Nakata, D., Masaki, T., Kusaka, M., Watanabe, T., and Matsui, H. (2018). Evaluation of pharmacokinetics/pharmacodynamics and efficacy of one-month depots of TAK-448 and TAK-683, investigational kisspeptin analogs, in male rats and an androgen-dependent prostate cancer model. Eur. J. Pharmacol. *822*, 138-146.
3. Suzuki, N., Ito, T., Matsui, H., and Takizawa, M. (2016). Anti-inflammatory and cytoprotective effects of a squalene synthase inhibitor, TAK-475 active metabolite-I, in immune cells simulating mevalonate kinase deficiency (MKD)-like condition. Springerplus *5*, 1429.
4. MacLean, D.B., Matsui, H., Suri, A., Neuwirth, R., and Colombel, M. (2014). Sustained exposure to the investigational Kisspeptin analog, TAK-448, down-regulates testosterone into the castration range in healthy males and in patients with prostate cancer: results from two phase 1 studies. J Clin Endocrinol Metab *99*, E1445-1453.
5. Matsui, H., and Asami, T. (2014). Effects and therapeutic potentials of kisspeptin analogs: regulation of the hypothalamic-pituitary-gonadal axis. Neuroendocrinology *99*, 49-60.
6. Matsui, H., Masaki, T., Akinaga, Y., Kiba, A., Takatsu, Y., Nakata, D., Tanaka, A., Ban, J., Matsumoto, S., Kumano, S., et al. (2014). Pharmacologic profiles of investigational kisspeptin/metastin analogues, TAK-448 and TAK-683, in adult male rats in comparison to the GnRH analogue leuprolide. Eur. J. Pharmacol. *735*, 77-85.
7. Matsui, H., Tanaka, A., Yokoyama, K., Takatsu, Y., Ishikawa, K., Asami, T., Nishizawa, N., Suzuki, A., Kumano, S., Terada, M., et al. (2012). Chronic administration of the metastin/kisspeptin analog KISS1-305 or the investigational agent TAK-448 suppresses hypothalamic pituitary gonadal function and depletes plasma testosterone in adult male rats. Endocrinology *153*, 5297-5308.
8. Matsui, H., Takatsu, Y., Kumano, S., Matsumoto, H., and Ohtaki, T. (2004). Peripheral administration of metastin induces marked gonadotropin release and ovulation in the rat. Biochem. Biophys. Res. Commun. *320*, 383-388.

Kenji Miura

Plant Molecular Biology

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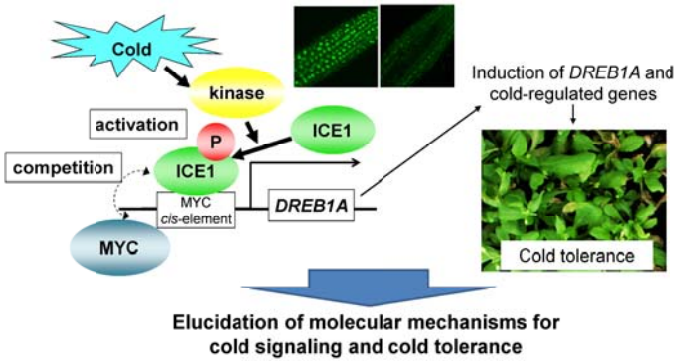
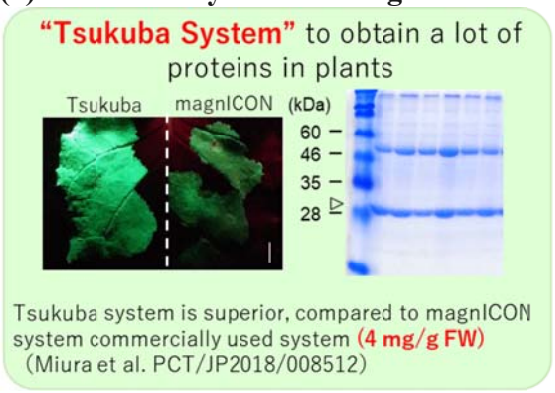
(1) Cold signaling and cold tolerance, how are they regulated? (Figure)



ICE is a transcription factor to control cold-regulated genes and cold tolerance. However, how ICE1 is regulated have not been elucidated. To elucidate molecular mechanism, we isolated several interacting proteins of ICE1, including MYC transcription factors, kinases, and calcium-binding proteins. Characterization of these proteins for cold signaling and how these proteins regulate ICE1 are studied.

(2) "Tsukuba System" for high amount of protein production in plants



We established high amount of protein production system in plants, termed "Tsukuba System". Several applications can be expected. Now, we are establishing following application methodology by using this system.

1. High amount of pharmaceutical protein production in plants for cost effectiveness.
2. High amount of production of plant secondary metabolites by expression of enzymes
3. Genome editing in plants without transformation.

Publications

1. Hoshikawa et al (2019). Efficient transient protein expression in tomato cultivars and wild species using agroinfiltration-mediated high expression system. Plant Cell Rep *38*, 75-84.
2. Ohta et al. (2018). MYC-type transcription factors, MYC67 and MYC70, interact with ICE1 and negatively regulate cold tolerance in Arabidopsis. Sci Rep *8*, 11622.
3. Mori et al. (2018) Ca^{2+}-permeable mechanosensitive channels MCA1 and MCA2 mediate cold-induced cytosolic Ca^{2+} increase and cold tolerance in Arabidopsis. Sci Rep *8*, 550
4. Yamamoto et al. (2018). Improvement of the transient expression system for production of recombinant proteins in plants. Sci Rep *8*, 4755.
5. Yamamoto et al. (2018). Application and development of genome editing technologies to the Solanaceae plants. Plant Physiol Biochem *131*, 37-46.
6. Shimatani et al. (2017) Targeted base editing in rice and tomato using CRISPR-Cas9 cytidine deaminase fusion. Nat Biotechnol *35*, 441-443.

Shinichi Miyamura

Cell Biology of Sexual Dimorphism in Green Plants

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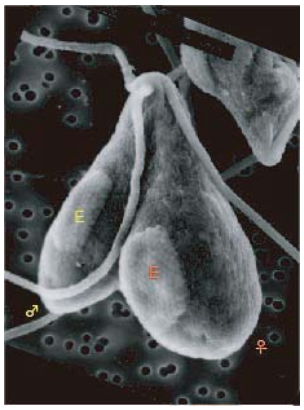
My lab is working on two projects: 1) the cellular and molecular mechanisms of sexual dimorphism of gametes in isogamous, anisogamous, and oogamous green algae; and 2) sexual reproduction in green algae, mosses, ferns, and gymnosperms. Marine green algae belonging to the Ulvophyceae, as well as the unicellular green alga *Chlamydomonas* and land plant sperm, are used mainly as our experimental systems.



Sexual dimorphism of green algal gametes

We have been focusing on asymmetric placement of the mating structure (cell-fusion apparatus) in gametes as a feature of sexual dimorphism in green algae. The gamete of green algae belonging to the Chlorophyta has two flagella elongated from the cell apex and a mating structure that is a specialized plasma membrane near the flagellar apparatus. The spatial position of the mating structure differs between the sexes. In the male gamete, the mating structure is located on the opposite side to the eyespot (E), whereas it is located on the same side as the eyespot in the female gamete. As a result of this difference, the two eyespots align on the same side of the planozygote after fertilization. Our lab is trying to elucidate the cellular and molecular mechanisms of mating structure development and placement in green algal gametes. We also aim to elucidate the machanisms of gamete-type differentiation according to mating-type locus by using *Chlamydomonas* and ulvophycean green algae.

Select Publications

1. Miyamura, S. (2010). Cytoplasmic inheritance in green algae: patterns, mechanisms and relation to sex type. J Plant Res *123*, 171-184.
2. Miyamura, S., Sakaushi, S., Hori, T., and Nagumo, T. (2010). Behavior of flagella and flagellar root systems in the planozygotes and settled zygotes of the green alga *Bryopsis maxima* Okamura (Ulvophyceae, Chlorophyta) with reference to spatial arrangement of eyespot and cell fusion site. Phycol Res *58*, 258-269.
3. Miyamura, S., Mogi, Y., Mitsuhashi, F., Kawano, S., and Nagumo, T. (2009). Visualizing the spatial arrangement of flagella-eyespot-cell fusion sites in gametes and planozygotes of *Chlamydomonas reinhardtii* (Chlorophyceae, Chlorophyta) with high-resolution FE-SEM. Cytologia *74*, 409-415.
4. Mogi, Y., Kagami, Y., Kuwano, K., Miyamura, S., Nagumo, T., and Kawano, S. (2008). Asymmetry of eyespot and mating structure positiobs in *Ulva compressa* (Ulvales, Chlorophyta) revealed by a new field emission scanning electron microscopy method. J Phycol *44*, 1290-1299.
5. Miyamura, S. (2007). Inheritance pattern of chloroplast DNA is correlated with gamete types based on sex-specific arrangement of the cell fusion site in *Caulerpa* (Ullvophyceae, Chlorophyta). Phycol Res *55*, 47-57.

Kisaburo Nagamune

How to Become a Parasite and Survive as One

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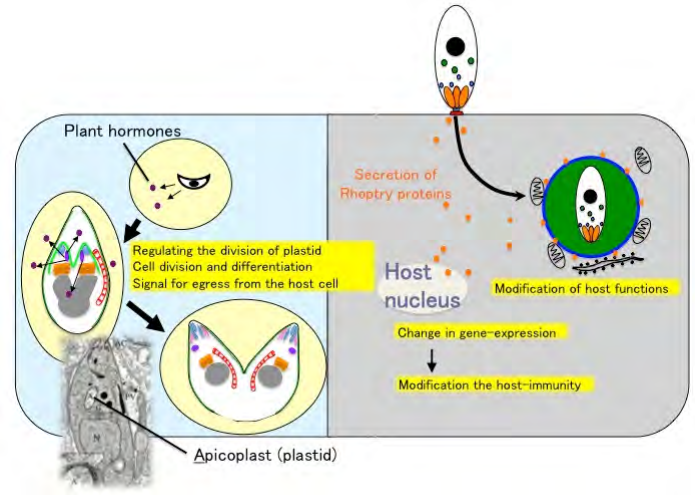
Apicomplexan parasites, including *Toxoplasma gondii* and malarial parasites, have an organelle called the apicoplast, which a kind of plastid and developed from a secondary symbiont of the ancestor of red algae. Apicomplexan parasites have lost their photosynthetic activity because they gained a new, parasitic ability during evolution. However, they still possess the apicoplast, which is essential for their survival. The biology of *T. gondii* and malarial parasites is therefore similar in some ways to that of plant systems because they still have a plant inside the cell. We are investigating the plant-like nature of apicomplexan parasites as a target for the development of anti-parasitic drugs. We are also focusing on the parasitic ability that replaced their photosynthetic ability, and studying how they highjack host functions for their survival.



Toxoplasma gondii produces plant hormones and regulates the progression of the cell cycle and division of plastids. It also secretes rhoptry proteins and highjacks gene expression and organelles in the host cell. Through this highjacking, *T. gondii* can escape the host immune response and take up essential molecules.

Select Publications

1. Toyama, T. *et al.* (2011). Gibberellin Biosynthetic Inhibitors Make Human Malaria Parasite *Plasmodium falciparum* Cells Swell and Rupture to Death. PLoS ONE *7*, e32246.
2. Nakatani, F. *et al.* (2011). Identification of a second catalytically active trans-sialidase in *Trypanosoma brucei*. Biochem Biophysic Res Comm *415*, 421-425.
3. Yamamoto, M. *et al.* (2011). ATF6β is a host cellular target of the *Toxoplasma* virulence factor ROP18. J Exp Med *208*, 1533-1546.
4. Hirakawa, Y. *et al.* (2009). Protein targeting into secondary plastids of chlorarachniophytes. PNAS *106*, 12820-12825.
5. Nagamune, K. *et al.* (2008). Abscisic acid controls calcium-dependent egress and development in *Toxoplasma gondii*. Nature *451*, 207-210.

Kazuto Nakada

Mitochondrial Biology in Mammals

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Mitochondrial genome (mtDNA) mutations and the resultant mitochondrial respiratory abnormalities are associated with a wide variety of disorders, such as mitochondrial diseases, neurodegenerative diseases, diabetes, and cancer, as well as aging. By using model cells and mice carrying mutant mtDNAs, we are studying the pathophysiological mechanisms of mtDNA-based disorders; our goal is to develop effective treatment strategies for these conditions.

Select Publications

1. Inami, Y., Waguri, S., Sakamoto, A., Kouno, T., Nakada, K., Hino, O., Watanabe, S., Ando., J., Iwadate., M., Yamamoto, M., Lee, M.S., Tanaka, K., and Komatsu, M. (2011). Persistent activation of Nrf2 through p62 in hepatocellular carcinoma cells. J Cell Biol, *193*, 275-284.
2. Ogasawara, E., Nakada, K., and Hayashi, J.-I. (2010) Lactic acidemia in the pathogenesis of mice carrying mitochondrial DNA with a deletion. Hum Mol Genet, *19*, 3179-3189.
3. Ishikawa, K., Takenaga, K., Akimoto, M., Koshikawa, N., Yamaguchi, A., Imanishi, H., Nakada, K., Honma, Y., and Hayashi, J.-I. (2008). ROS-generating mitochondrial DNA mutations can regulate tumor cell metastasis. Science, *320*, 661-664.
4. Nakada, K., Sato, A., Yoshida, K., Morita, T., Tanaka, H., Inoue, S.-I., Yonekawa, H., and Hayashi, J.-I. (2006). Mitochondria-related male infertility. Proc Natl Acad Sci USA, *103*, 15148-15153.
5. Sato, A., Nakada, K., Akimoto, M., Ishikawa, K., Ono, T., Shitara, H., Yonekawa, H., and Hayashi, J.-I. (2005). Rare creation of recombinant mtDNA haplotypes in mammalian tissues. Proc Natl Acad Sci USA, 102, 6057-6062.
6. Ono, T., Isobe, K., Nakada, K., and Hayashi, J.-I. (2001). Human cells are protected from mitochondrial dysfunction by complementation of DNA products in fused mitochondria. Nat Genet, *28*, 272-275.
7. Nakada, K., Inoue K., Ono, T., Isobe, K., Ogura, A., Goto, Y.-i., Nonaka, I., and Hayashi. J.-I. (2001). *Inter*-mitochondrial complementation: mitochondria-specific system preventing mice from expression of disease phenotypes by mutant mtDNA. Nat Med, *7*, 934-939.
8. Inoue, K., Nakada, K., Ogura, A., Isobe, K., Goto, Y.-i., Nonaka, I., and Hayashi, J.-I. (2000). Generation of mice with mitochondrial dysfunction by introducing mouse mtDNA carrying a deletion into zygotes. Nat Genet, *26*, 176-181.

Kouji Nakamura

It’s a Small RNA World

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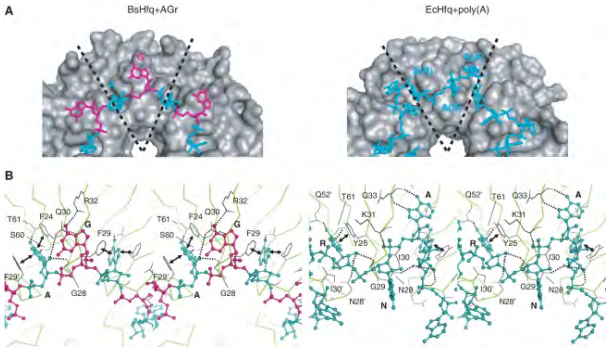
Until recently, gene expression was thought to be controlled mainly at the level of transcription initiation by repressor or activator proteins. It has now been revealed that other mechanisms can regulate gene expression and involve RNAs that might act as antisense RNAs, sequestering molecules, or thermosensors. Bacterial pathogens sense their environments, and in response, virulence genes are induced or repressed through spatial and temporal regulation. These pathogens are also subjected to stress conditions, which require appropriate responses. Recent research has revealed that RNAs are key regulators in pathogens. Small RNAs regulate the translation or stability of mRNAs that encode virulence proteins, namely proteins that are triggered by environmental cues and stresses. In most cases, these small RNAs act directly on target RNAs by an antisense mechanism.

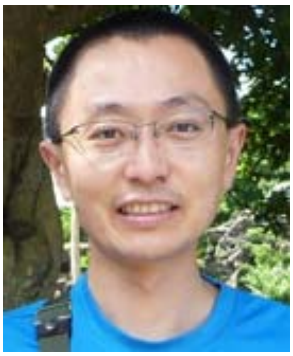


Molecular recognition of RNA by distal site of Hfq. (**A**) Left panel: surface representation of hexameric BsHfq (gray) with stick representation of A (cyan) and G (magenta) residues of AGr. Right panel: surface representation of hexameric EcHfq (gray) with stick representation of poly(A) (cyan). Subunit boundaries are indicated by dashed lines. (**B**) Stereo view of BsHfq–AGr and EcHfq–poly(A) (left and right panel, respectively). R is a purine nucleotide and N is any nucleotide [6].

Select Publications

1. Someya, T., Baba, S., Fujimoto, M., Kawai, G., Kumasaka, T., and Nakamura, K. (2012). Crystal structure of Hfq from *Bacillus subtilis* in complex with SELEX-derived RNA aptamer: insight into RNA-binding properties of bacterial Hfq. Nucleic Acids Research *40*, 1856-1867.
2. Kakeshita, H., Kageyama, Y., Endo, K., Tohata, M., Ara, K., Ozaki, K., and Nakamura,K. (2011b). Secretion of biologically-active interferon-β by *Bacillus subtilis*. Biotechnology letters *33*, 1847-1852.
3. Obana, N., and Nakamura, K. (2011a). A novel regulator, the CPE1446-1447 protein heterodimeric complex, controls toxin genes in *Clostridium perfringens*. J. Bacteriology *193*, 4417-4424.
4. Obana, N., Shirahama, Y., Abe, K., and Nakamura, K. (2010b). Stabilization of *Clostridium perfringens* collagenase mRNA by VR-RNA-dependent cleavage in 5’ leader sequence. Molecular Microbiology *77*, 1416-1428.
5. Abe, K., Obana, N., and Nakamura, K. (2010a). Effects of depletion of RNA-binding protein Tex on the expression of toxin genes in *Clostridium perfringens*. Bioscience, Biotechnology and Biochemistry *74*, 1564-1571.
6. Saito, S., Kakeshita, H., and Nakamura, K. (2009). Novel small RNA-encoding genes in the intergenenic regions of *Bacillus subtilis*. Gene *428*, 2-8.

Hiroaki Nakano



Metazoan and Deuterostome Evolution

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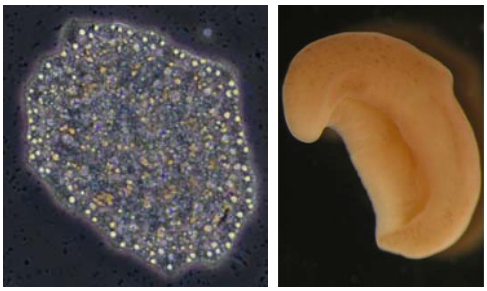
We are studying the development of less studied, non-model animal groups, currently focusing on placozoans, *Xenoturbella*, and sea lilies. Despite their phylogenetic importance, development of these groups are largely unknown, with that of placozoans still remaining a mystery. By revealing their developmental patterns, we aim to gain new information on the evolution of metazoans and deuterostomes.

Placozoans are amoebae-like marine flat animals about 1mm in diameter, lacking tissues or organs, and even neurons or muscle cells. *Xenoturbella* is a marine animal belonging to the Xenacoelomorpha, a phylum suggested to be a sister group to all other bilaterian animals. Sea lilies are regarded as the most basal living echinoderm, and we have uncovered its development in 2003 for the first time since it was discovered in 1864.



Placozoa (left) possesses one of the simplest body plans within the metazoans. The simple body plan may represent the ancestral state of metazoans.

Xenoturbella (right) lacks an anus, gonads, coelomic cavities, and brain. In 2013, we made the first report of its development, 135 years after it was first discovered.

Selected Publications

1. Miyazawa, H., and Nakano, H. (2018). Multiple surverys employing a new sample-processing protocol reveal the genetic diversity of placozoans in Japan. Ecology and Evolution *8*, 2407-2417.
2. Nakano, H., *et al*. (2017). A new species of *Xenoturbella* from the western Pacific Ocean and the evolution of *Xenoturbella*. BMC Evolutionary Biology *17*, 245.
3. Nakano, H. (2015). What is *Xenoturbella*? Zoological Letters *1*, 22.
4. Nakano, H. (2014). Survey of the Japanese coast reveals abundant placozoan populations in the northern Pacific Ocean. Scientific Reports *4*, 5356.
5. Nakano, H., *et al.* (2013). *Xenoturbella bocki* exhibits direct development with similarities to Acoelomorpha. Nature Communications *4*, 1537.
6. Philippe, H., *et al.* (2011). Acoelomorph flatworms are deuterostomes related to *Xenoturbella*. Nature *470*, 255-258.
7. Nakano, H., Nakajima, Y., and Amemiya, S. (2009). Nervous system development of two crinoid species, the sea lily *Metacrinus rotundus* and the feather star *Oxycomanthus japonicus*. Development Genes Evolution *219*, 565-576.
8. Bourlat, S.J., *et al.* (2006). Deuterostome phylogeny reveals monophyletic chordates and the new phylum Xenoturbellida. Nature *444*, 85-88.
9. Nakano, H., *et al*. (2003). Larval stages of a living sea lily (stalked crinoid echinoderm). Nature *421*, 158-160.

Kentaro Nakano

Molecular Dynamics and Cellular Function of the Cytoskeleton

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My goal is to understand the molecular mechanisms regulating cell behavior, including cell division, cell morphogenesis, and intracellular transport, from the perspective of the cytoskeleton. These processes are fundamental to life. In my lab, unicellular organisms are used as a model to this purpose. We are using a combination of several methodologies, including genetics, cell biology and biochemical approaches, to achieve our aims.

Publications

1. Doi, A., Kita, A., Kanda, Y., Uno, T., Asami, K., Satoh, R., Nakano, K., and Sugiura, R. (2015). Geranylgeranyltransferase Cwg2-Rho4/Rho5 module is implicated in the Pmk1 MAP kinase-mediated cell wall integrity pathway in fission yeast. Genes Cells, in press.
2. Kushida, Y., Takaine, M., Nakano, K., Sugai, T., and Numata, O. (2015). Analysis of localization of γ-tubulin during conjugation of ciliate *Tetrahymena thermophila* using confocal lazar-scanning microscope. Zoological Sci., vol. 32, 25-32.
3. Takaine, M., Imada, K., Numata, O., Nakamura, T., and Nakano, K. (2014). The meiosis-specific nuclear passenger protein is required for proper assembly of forespore membrane in fission yeast. J. Cell Sci., vol. 127, 4429-4442.
4. Takaine, M., Numata, O., and Nakano, K. (2014). Fission yeast IQGAP maintains F-actin-independent localization of myosin-II in the contractile ring. Genes Cells, vol. 19, 161-176.
5. Shimizu, Y., Kushida, Y., Kiriyama, S., Nakano, K., and Numata, O. (2013). Formation of division furrow and its ingression can progress under the inhibitory condition of actin polymerization in ciliate *Tetrahymena pyriformis*. Zoological Sci., vol. 30, 1044-1049.
6. Shiozaki, N., Nakano, K., Kushida, Y., Noguchi, T., Uyeda, T., Wloga, D., Dave, D., Vasudevan, K., Gaertig, J., and Numata, O. (2013), ADF/cofilin is not essential but critically important for actin activities during phagocytosis in *Tetrahymena thermophila*. Eukaryot. Cell, vol. 12, 1080-1086.
7. Nakano, K., Toya, M., Yoneda, A., Asami, Y., Yamashita, A., Kamasaki, N., Osumi, M., and Yamamoto, M. (2011). Pob1 ensures cylindrical cell shape by coupling two distinct Rho signaling events during secretory vesicle targeting. Traffic, vol. 12, 726-739.
8. Nakano, K., Kuwayama, H., Kawasaki, M., Numata, O., and Takaine, M. (2010). GMF is an evolutionarily developed ADF/cofilin-super family protein involved in the Arp2/3 complex-mediated organization of the actin cytoskeleton. Cytoskeleton, vol. 67, 373-382.

Ryusuke Niwa

Molecular, Cellular, and Neuro-endocrine Mechanisms of development, germline stem cell and parasitism in insects

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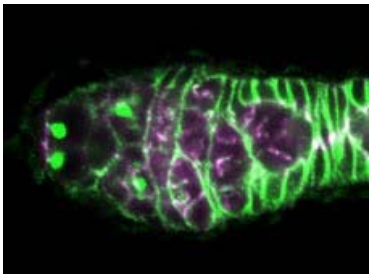

My research interests are in the areas of developmental biology, cell biology, neuroendocrinology, and molecular genetics in insects, particularly the fruit fly *Drosophila melanogaster*. Currently I am interested in understanding how molecular and neuro-endocrine mechanisms are adaptively involved in regulations of nutrient-dependent developmental plasticity, mating-induced female germline stem cell proliferation, and the host-parasitoid wasp interactions.

Recent selected Publications

1. Yoshinari Y, Kurogi Y, Ameku T, **Niwa R** (2019) Endocrine regulation of female germline stem cells in the fruit fly *Drosophila melanogaster*. ***Current Opinion in Insect Science*** 31:14-19.
2. Ameku T, Yoshinari Y, Texada MJ, Kondo S, Amezawa K, Yoshizaki G, Shimada-Niwa Y, **Niwa R** (2018) Midgut-derived neuropeptide F controls germline stem cell proliferation in a mating-dependent manner. ***PLOS Biology*** 16: e2005004.
3. Uryu O, Ou Q, Komura-Kawa T, Kamiyama T, Iga M, Syrzycka M, Hirota K, Kataoka H, Honda BM, King-Jones K, **Niwa R** (2018) Cooperative Control of Ecdysone Biosynthesis in *Drosophila* by Transcription Factors Séance, Ouija board, and Molting Defective. ***Genetics*** 208: 605-622.
4. Enya S, Yamamoto C, Mizuno H, Esaki T, Lin H-K, Iga M, Morohashi K, Hirano T, Kataoka H, Masujima H, Shimada-Niwa Y, **Niwa R** (2017) Dual Roles of Glutathione in Ecdysone Biosynthesis and Antioxidant Function During the Larval Development in *Drosophila*. ***Genetics*** 207: 1519-1532.
5. Ameku T, **Niwa R** (2016) Mating-Induced Increase in Germline Stem Cells via the Neuroendocrine System in Female *Drosophila*. ***PLOS Genetics*** 12: e1006123.
6. Komura-Kawa K, Hirota K, Shimada-Niwa Y, Yamauchi R, Shimell M, Shinoda T, Fukamizu A, O'Connor MB, **Niwa R** (2015) The *Drosophila* Zinc Finger Transcription Factor Ouija Board Controls Ecdysteroid Biosynthesis through Specific Regulation of *spookier*. ***PLOS Genetics*** 11:e1005712.
7. Uryu O, Ameku T, **Niwa R** (2015) Recent progress in understanding the role of ecdysteroids in adult insects: Germline development and circadian clock in the fruit fly *Drosophila melanogaster*. ***Zoological Letters*** 1: 32.
8. Shimada-Niwa Y, **Niwa R** (2014) Serotonergic neurons respond to nutrients and regulate the timing of steroid hormone biosynthesis in *Drosophila*. ***Nature Communications*** 5: 5778
9. Enya S, Ameku T, Igarashi F, Iga M, Kataoka H, Shinoda T, **Niwa R** (2014) A Halloween gene *noppera-bo* encodes a glutathione *S*-transferase essential for ecdysteroid biosynthesis via regulating the behaviour of cholesterol in *Drosophila*. ***Scientific Reports*** 4:6586.
10. **Niwa R**, Niwa YS (2014) Enzymes for ecdysteroid biosynthesis: their biological functions in insects and beyond. ***Bioscience, Biotechnology, and Biochemistry*** 78: 1283-1292.

Kazuharu Ohashi

Floral Adaptation to Pollinator Behavior

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I maintain diverse research interests, with the common theme of plant–animal interactions. My current interest is to understand how plants have evolved their traits to maximize reproductive success, as mediated through interactions with animal pollinators. According to the questions to be addressed, I adopt various approaches in my research: field observations or experiments, mathematical models, computer simulations, and laboratory experiments with bumble bees, which are among the major pollinators in temperate regions.

Some pollinators, such as bees and hummingbirds, learn to visit particular plants in repeatable sequences while collecting nectar or pollen from flowers. My recent studies have focused on the ontogeny and economics of this "traplining" behavior, as well as its possible consequences for floral evolution. I have found that the responses of pollinators to floral traits change significantly as they gain experience, and that this change this could have enhanced the evolution of complex combinations of floral traits. Currently I have been looking closely at floral color change as an evolutionary outcome of such dynamic interactions between plants and learning pollinators.

Left: *B. diversus* with flowers of *Salvia nipponica.* The seesaw-like anther filaments discourage bees from staying on the plant and thus reduce self-pollination rates. See [3]. Right: Floral color change (FCC), i.e., the retention of old, non-reproductive, rewardless, but fully turgid flowers in an altered color, has been suggested to enhance pollination by visually oriented floral visitors. Nevertheless, FCC appears rather infrequent in nature. Why? See [1].

Select Publications

1. Ohashi, K., Makino, T.T., and Arikawa, K. (2015) Floral colour change in the eyes of pollinators: testing possible constraints and correlated evolution. Functional Ecology *DOI*: 10.1111/1365-2435.12420.
2. Ohashi, K., and Thomson, J.D. (2009). Trapline foraging by pollinators: its ontogeny, economics and possible consequences for plants. Annals of Botany *103*, 1365-1378.
3. Ohashi, K. (2002). Consequences of floral complexity for bumble-bee-mediated geitonogamous self pollination in *Salvia nipponica* Miq. (Labiatae). Evolution *56*, 2414-2423.
4. Ohashi, K., and Yahara, T. (2002). Visit larger displays but probe proportionally fewer flowers: counterintuitive behaviour of nectar-collecting bumble bees achieves an ideal free distribution. Functional Ecology *16*, 492-503.

Kazuo Ohnishi, Ph.D.

Immunology and Infection Biology

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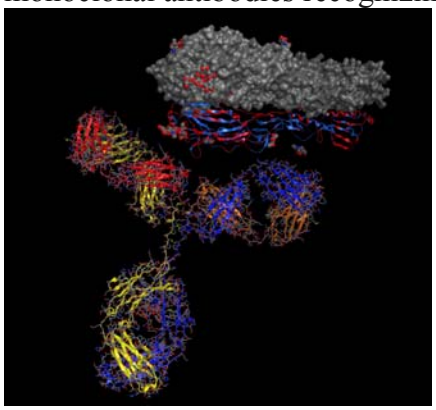
Our body fights against pathogens by using its immune system, which is a vast, systemic network of specialized cells and diversified molecules. Antibodies play a pivotal role in the immune system by discriminating and attacking infectious “non-self” agents. B-lymphocytes produce antibodies by regulating the rearrangement of antibody genes and maintaining the antigen specificities of antibody molecules. After an infection, subpopulations of antigen-specific B-lymphocytes achieve longevity to form immunological memory, which is reactivated upon infectious challenge a second time with the same pathogen.

My research interests include 1) the molecular mechanisms of antibody repertoire formation by pre-B-cell receptors in the early stages of B-lymphocyte differentiation; 2) the search for immunological niches that sustain memory B cells; 3) new in silico methods for optimizing the antigen-recognition sites of antibody molecules; and 4) establishment of monoclonal antibodies recognizing the universal epitopes of viruses.



In silico representation of IgG1 antibody (lower molecule) and antigen (upper molecule, hemagglutinin of H5N1 avian influenza virus). Infection with the newly emerging H5N1 virus is life-threatening, and a virus pandemic would be a serious problem for human health worldwide. Our immune system has not experienced the newly emerging H5N1 virus, but it is able to see the so-called “universal epitope,” in other words the common molecular structure that is conserved among many influenza viruses. We are searching for new universal epitopes in silico and trying to establish new methods for making effective antibodies against them.

Select Publications

1. Knoll, M., Yanagisawa, Y., Simmons, S., Engels, N., Wienands, J., Melchers, F., and Ohnishi, K. (2012). The Non-Ig Parts of the VpreB and λ5 Proteins of the Surrogate Light Chain Play Opposite Roles in the Surface Representation of the Precursor B Cell Receptor. J Immunol *188*, 6010-6017.
2. Ohnishi, K., Takahashi, Y., Kono, N., Nakajima, N., Mizukoshi, F., Misawa, S., Yamamoto, T., Mitsuki, Y., Fu, S., Hirayama, N., et al. (2012). Immunological detection of H5N1 influenza viruses by newly established monoclonal antibodies. Jpn J Infect Dis *65*, 19-27.
3. Ohnishi, K. (2008). Establishment and characterization of monoclonal antibodies against SARS coronavirus. Methods Mol Biol *454*, 191-203.
4. Ohnishi, K., and Melchers, F. (2003). The nonimmunoglobulin portion of λ5 mediates cell-autonomous pre-B cell receptor signaling. Nature Immunol *4*, 849-856.

Michiyuki Ono

Plant Physiology, Biotechnology, and Gene Literacy Education

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Ono Lab's Researches:

We are approaching the universal mechanisms of the photoperiodic regulation of flowering. We are using *Pharbitis nil* (*Ipomoea nil*), an obligate short-day plant, as well as *Arabidopsis thaliana*. We cloned and studied several genes for components of circadian clock, photoreceptors, floral regulators and florigen.

As development researches on genetically modified (GM) plants, we are developing new methods for modifying the shapes and colors of flowers. We are also studying production of edible vaccines *etc.* using transgenic crops in collaboration with medical doctors.

We are investigating ways to deepen the understanding of secondary students on genes "gene literacy" through practice of hands on laboratory activities. For citizens, we are practicing activities, such as holding "Science Cafe" and "Science & Art", to promote science communication and facilitate scientists to fulfill their accountability.

Seedling of *Pharbitis nil* is very sensitive to short-day induction of flowering (Left). Therefore, it has long been used as a model plant for studies on photoperiodic induction of flowering. *P. nil* (Japanese Morning glory) is chosen as one of the National BioResource Project (NBRP, http://www.nbrp.jp).
A genetically modified flower shape in *P. nil*: the sympetalous corolla was disrupted to form choripetalous corolla (Right).

Publications

1. Ono, M., Kataoka, M., Yokoyama, M., Ifuku, O., Ohta, M., Arai, S., Kamada, H., and Sage-Ono, K. (2013). Effects of 9,10-ketol-octadecadienoic acid (KODA) application on single and marginal short-day induction of flowering in *Pharbitis nil* cv. Violet. Plant Biotech. *30*, 1-8.
2. Sage-Ono, K., Ozeki, Y., Hiyama, S., Higuchi, Y., Kamada, H., Mitsuda, N., Ohme-Takagi, M., and Ono, M. (2011). Induction of double flowers in *Pharbitis nil* using a class-C MADS box transcrition factor with chimeric repressor gene-silencing technology. Plant Biotech. *28*, 153-165.
3. Oto, M., Ono, M., and Kamada, H. (2006). Gene lieteracy education in Japan: Fostering public understanding through practice of hands on laboratory activities in high schools. Plant Biotech. *23*, 339-346.

Kazuichi Sakamoto

Molecular Biology of Health and Nutrition

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We have developed a new bioassay system to find and evaluate natural bioactive compounds (e.g. phytochemicals, plant extracts, fermented foods, and animal tissues) that influence health and aging; this novel bioassay system uses nematodes to characterize the bioactivity of natural substances. Because of its biological characteristics (easy culture, short lifespan, and availability of mutants), the nematode is a suitable and well-characterized model for investigating the physiology and mechanisms of human aging and disease. We are using this animal to screen for biomaterials with potential benefits for human health.

To promote health (prevention and amelioration of lifestyle-related diseases) and youth (anti-aging and vitality), we are searching for natural bioactive compounds. We are scientifically evaluating the bioactivity of these substances and developing novel bioactive materials. We are also conducting applied studies to develop functional foods, functional feeds, cosmetics, and medicines.

Phytochemicals such as catechin from tea, resveratrol from red grapes, and hydroxytyrosol from olives are famous bioactive compounds that can act against aging and help protect against lifestyle-related diseases. We are using these materials in functional foods, cosmetics, medicines, and other materials to promote health and slow aging.

Select Publications

1) Drira, R., Chen, S., and Sakamoto, K. (2011). Oleuropein and hydroxytyrosol inhibited adipocyte differentiation in 3T3-L1 cells. Life Sciences, *89*, 708-716.
2) Kim, H., and Sakamoto, K. (2011). (-)-Epigallocatechin gallate suppresses adipocyte differentiation through the MEK/ERK and PI3K/AKT pathways. Cell Biology International, *36*, 147-153.
3) Shintani, H., Furuhashi, T., Hano, H., Matsunaga, M., Usumi, K., Shudo, N., and Sakamoto, K. (2011). Physiological Effects of Salmon Milt Nucleoprotein on Movement, Stress Tolerance and Lifespan of *C. elegans.* Food and Nutrition Sciences, *3*, 48-54.
4) Nomura, T., Horikawa, M., Shimamura, S., Hashimoto, T., and Sakamoto, K. (2010). Fat accumulation in *Caenorhabditis elegans* is mediated by SREBP homolog SBP-1. Genes and Nutrition, *5*, 17-27.
5) Kamon, M., Zhao, R., and Sakamoto, K. (2010). Green tea polyphenol (-)-epigallocatechin gallate suppressed the differentiation of murine osteoblast MC3T3-E1. Cell Biology International, *34*, 109-116.

Keisuke Sakurai

Molecular Physiology of Photoreception

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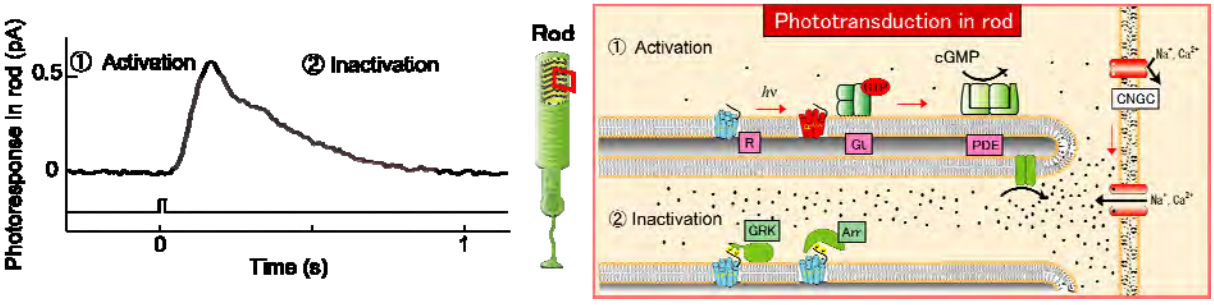
Vertebrate species derive most of ambient information through photoreceptors, where light is absorbed and signaled to the nervous system. Visual perception initiates with the absorption of light by rod and cone photoreceptors in the retina, which mediate dim light vision and bright light vision, respectively. In addition to this classical vision, light reception by inner retinal neurons or extraocular photoreceptors is thought to be of great importance to animal behaviors such as circadian phase shift and magnetoreception. The aim of our research is to elucidate underlying mechanism of the photoperceptions by which absorbed photons are converted into an electrical response and signaled to the brain. To achieve this goal, we mainly use electrophysiological technique, a powerful tool to characterize molecular mechanism in neurons, in combination with genetically manipulated animals.



A rod photoresponse and simplified scheme of phototransduction in outer segment of rod photoreceptor. The pathway for converting light into an electric impulse, known as phototransduction, has been well characterized in rods. Rods and cones employ homologous or sometimes even identical proteins in their phototransduction cascades, indicating that the same principles of phototransduction are likely to exist in cones. Despite these similarities, rods and cones exhibit important functional differences, with still largely unknown origins.

Selected publications

1. Sakurai, K., Chen, J., and Kefalov, V. J. (2011). Role of guanylyl cyclase modulation in mouse cone phototransduction. Journal of Neuroscience *31*, 7991-8000.
2. Sakurai, K., Young, J. E., Kefalov V. J., and Khani S. C. (2011). Variation in rhodopsin kinase expression alters the dim flash response shut off and the light adaptation in rod photoreceptors. Investigative Ophthalmology & Visual Science *52*, 6793-6800.
3. Fan, J.*, Sakurai, K. *, Chen, C. K., Rohrer, B., Wu, B. X., Yau, K. W., Kefalov, V., and Crouch, R. K. (2010). Deletion of GRK1 causes retina degeneration through a transducin-independent mechanism. Journal of Neuroscience *30*, 2496-2503. (*equal contribution)
4. Sakurai, K., Onishi, A., Imai, H., Chisaka, O., Ueda, Y., Usukura, J., Nakatani, K., and Shichida, Y. (2007). Physiological properties of rod photoreceptor cells in green-sensitive cone pigment knock-in mice. Journal of General Physiology *130*, 21-40.

Yasunori Sasakura

Developmental Genetics

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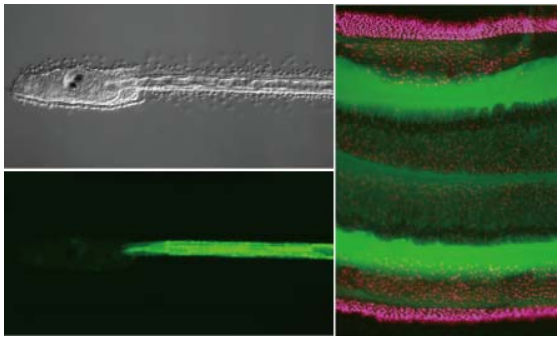
Our group is studying the mechanisms of development of the ascidian *Ciona intestinalis*. This ascidian is an excellent model, because 1) its genome sequence has been determined; 2) it has quick embryogenesis (~18 h from fertilization to the swimming larval stage); 3) it has a simple body plan, with about 2600 cells making up the body in the tadpole stage; 4) its basic body plan is shared with the vertebrates; and 5) technologies for studying its genetic functions have been established; they include transposon-mediated germline transformation and mutagenesis.

In particular, we are focusing on 1) mutagenesis of *Ciona intestinalis* with transposons to uncover novel gene functions; 2) the molecular and cellular mechanisms of metamorphosis; 3) formation and differentiation of the nervous system; 4) maternal gene functions and egg formation; and 5) the evolution of chordates in terms of genetic function.

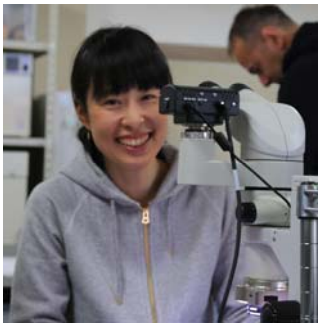


Left: A swimming larva of *Ciona intestinalis*, and green fluorescent protein (GFP) expression in the larva, which was created by transposon-mediated transformation. Right: GFP and RFP (red fluorescent protein) fluorescence in the endostyle of a *C. intestinalis* transgenic line. The endostyle is orthologous to the vertebrate thyroid gland.

Select Publications

1. Sasakura, Y., Kanda, M., Ikeda, T., Horie, T., Kawai, N., Ogura, Y., Yoshida, R., Hozumi, A., Satoh, N., and Fujiwara, S. (2012). Retinoic acid-driven Hox1 is required in the epidermis for forming the otic/atrial placodes during ascidian metamorphosis. Development *139*, 2156-2160.
2. Horie, T., Shinki, R., Ogura, Y., Kusakabe, T.G., Satoh, N., and Sasakura, Y. (2011). Ependymal cells of chordate larvae are stem-like cells that form the adult nervous system. Nature *469*, 525-528.
3. Ogura, Y., Sakaue-Sawano, A., Nakagawa, M., Satoh, N., Miyawaki, A., and Sasakura, Y. (2011). Coordination of mitosis and morphogenesis: role of a prolonged G2 phase during chordate neurulation. Development *138*, 577-587.
4. Sasakura, Y., Suzuki, M.M., Hozumi, A., Inaba, K., and Satoh, N. (2010). Maternal factor-mediated epigenetic gene silencing in the ascidian *Ciona intestinalis*. Mol. Genet. Genomics *283*, 99-110.
5. Nakayama-Ishimura, A., Chambon, J.P., Horie, T., Satoh, N., and Sasakura, Y. (2009). Delineating metamorphosis pathways in the ascidian *Ciona intestinalis*. Dev. Biol. *326*, 357-367.

Yukie Sato



Behavioral Ecology

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The general aim of my research is to reveal the mechanisms of ecological diversification at the level of species and populations, as well as speciation mechanisms. Furthermore, I deal with behavioral variations in different individuals of the same population. In particular, I focus on social behavior and mating behavior in spider mites. Spider mites are small arthropod herbivores less than 1 mm in length. They are good model organisms because they complete their development (egg to adult) in a short period (ca. 5 - 20 days under optimal conditions) and they can be mass-reared in small spaces. These advantages allow investigation of the following projects:

- ✓ Kin selection and kin competition
- ✓ Geographic variation in lethal male-male combat
- ✓ Reproductive isolation among populations showing different male-male aggression
- ✓ Evolution of alternative male mating tactics
- ✓ Reproductive interference between invasive and native spider mites
- ✓ Evolution of social behavior in spider mites

Females of two congeneric spider mites (*Tetranychus evansi* -left, *T. urticae* -right), one endemic to Europe and the other invasive, at least partly due to reproductive interference.

Publications

1. Sato, Y., Tsuda, Y., Sakamoto, H., Egas, M., Gotoh, T., Saito, Y., Zhang, Y.-X., Lin, J.-Z., Chao, J.-T. and Mochizuki, A. (2019). Phylogeography of lethal male fighting in a social spider mite. Ecology and Evolution *9*, 1590-1602.
2. Sato, Y., Sakamoto, H., Gotoh, T., H., Saito, Y., Chao, J.-T., Egas, M. and Mochizuki, A. (2018). Patterns of reproductive isolation in a haplodiploid – strong post-mating, prezygotic barriers among three forms of a social spider mite. Journal of Evolutionary Biology *31*, 866-881.
3. Sato, Y., Rühr P.T., Schmitz, H., Egas, M., and Blanke, A. (2016). Age-dependent male mating tactics in a spider mite - a life history perspective. Ecology and Evolution *6*, 7367-7374.
4. Sato, Y., Alba, J.M., and Sabelis, M.W. (2014). Testing for reproductive interference in the population dynamics of two congeneric species of herbivorous mites. Heredity *113*, 495-502.
5. Sato, Y., Sabelis, M.W., and Egas, M. (2014). Alternative male mating behaviour in the two-spotted spider mite: dependence on age and density. Animal Behaviour *92*, 125-131.

Kyoichi Sawamura

Mechanisms of Speciation in *Drosophila*

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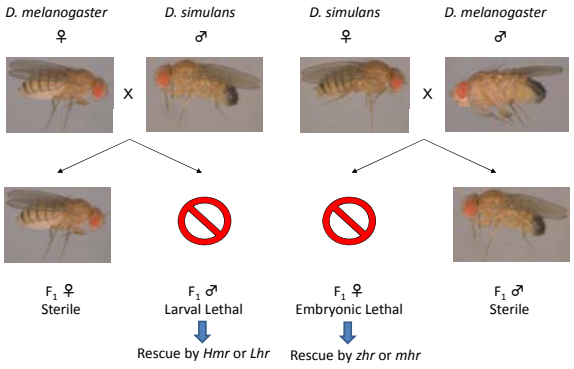
Do you know what an interspecific hybrid is? Mules from mares and donkeys, leopons from lionesses and leopards… Interspecific hybrids are rare in nature; most of them are sterile and therefore cannot produce descendants. If these hybrids were not rare, then biological species would become fused and lost from the world. In other words, species exist because of reproductive isolation: the origin of new species is completed by acquiring reproductive isolation between populations. Therefore, speciation is a major driving force of evolution. The purpose of our research is to elucidate the genetic mechanisms of speciation.

Our model organism is *Drosophila*. Genomic sequencing has been completed in 12 *Drosophila* species. The biodiversity of this genus is spectacular: 3950 extant species (and 12 fossil species) have been described in the Drosophilidae. Furthermore, *Drosophila* has many crossable sibling species pairs and can be used to provide useful experimental systems for investigating the genetic mechanisms of speciation.



A cross between *Drosophila melanogaster* and *Drosophila simulans* produces unisexual sterile hybrids. We have elucidated the genetic bases of postmating isolation by analyzing mutations that rescue the hybrids from lethality or sterility. The genes isolated so far are *Lethal hybrid rescue*, *Hybrid male rescue*, *zygotic hybrid rescue*, *Nucleoporin 96*, *Nucleoporin 160*, and *JYalpha*.

Select Publications

1. Sawamura, K., Maehara, K., Mashino, S., Kagesawa, T., Kajiwara, M., Matsuno, K., Takahashi, A., and Takano-Shimizu, T. (2010). Introgression of *Drosophila simulans Nuclear Pore Protein 160* in *Drosophila melanogaster* alone does not cause inviability but does cause female sterility. Genetics *186*, 669-676.
2. Sawamura, K., Roote, J., Wu, C.I., and Yamamoto, M.T. (2004). Genetic complexity underlying hybrid male sterility in *Drosophila*. Genetics *166*, 789-796.
3. Sawamura, K., Davis, A.W., and Wu, C.I. (2000). Genetic analysis of reproductive isolation by means of introgression into *Drosophila melanogaster*. Proc Natl Acad Sci USA *97*, 2652-2655.
4. Davis, A.W., Roote, J., Morley, T., Sawamura, K., Herrmann, S., and Ashburner, M. (1996). Rescue of hybrid sterility in crosses between *D. melanogaster* and *D. simulans*. Nature *380*, 157-159.

Kogiku Shiba

Cell Biology of Cilia and Flagella

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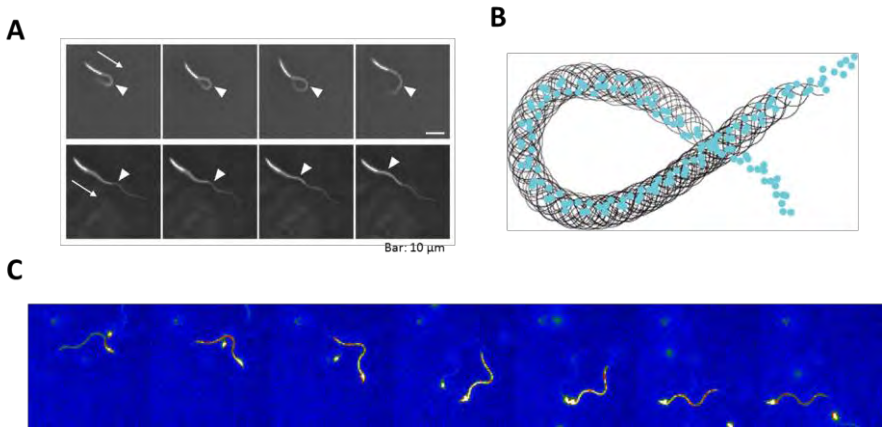
Eukaryotic cilia and flagella are projections on eukaryotic cells. The microtubule-based structure in cilia and flagella is called an axoneme and is composed of molecular motor dynein and several regulatory proteins. The structures of the axonemes have been highly conserved through evolution and play important roles in sperm motility, embryonic locomotion, current generation in epidermal tissues such as the oviduct and trachea, and cell signal reception.

We are using the embryos or sperm of marine invertebrates such as tunicates, sea urchins, fishes and snails to study the regulatory mechanism of ciliary and flagellar movement. Research topics are signaling pathway in sperm motility activation and sperm chemotaxis toward egg-derived substances, and regulation of flagellar and ciliary waveforms. To analyze motility and waveforms in cilia and flagella we are using a high-speed camera, a stroboscopic lighting system, auto-tracking software, and a Ca^{2+}-imaging system.

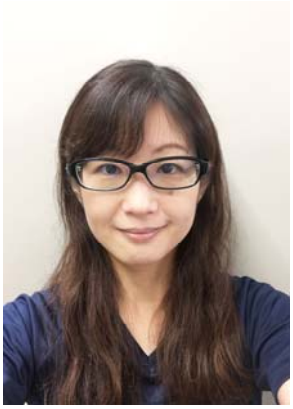


A. Backward swimming of sperm in the gastropod
B. Flagellar waveforms (line) and sperm head trajectory (dot) during sperm chemotaxis in *Ciona* sperm
C. Intraflagellar Ca^{2+} imaging in *Ciona* sperm.

Publications

1. Shiba, K., and Inaba, K. (2014). Distinct roles of soluble and transmembrane adenylyl cyclases in the regulation of flagellar motility in *ciona* sperm. Int J Mol Sci *15*, 13192-208.
2. Shiba, K., Shibata, D,, and Inaba, K. (2014) Autonomous changes in the swimming direction of sperm in the gastropod *Strombus luhuanus*. J Exp Biol *217*, 986-96.
3. Mizuno, K., Shiba, K., Okai, M., Takahashi, Y., Shitaka, Y., Oiwa, K., Tanokura, M., and Inaba, K. (2012) Calaxin drives sperm chemotaxis by Ca^{2+}-mediated direct modulation of a dynein motor. Proc Natl Acad Sci U S A *109*, 20497-502.
4. Saito, T., Shiba, K., Inaba, K., Yamada, L. and Sawada, H. (2012). Self-incompatibility response induced by calcium increase in sperm of the ascidian *Ciona intestinalis*. Proc Natl Acad Sci U S A *109*, 4158-4162.

Yuko Shimada



Neuro-endocrine Mechanisms of Maturation in *Drosophila melanogaster*

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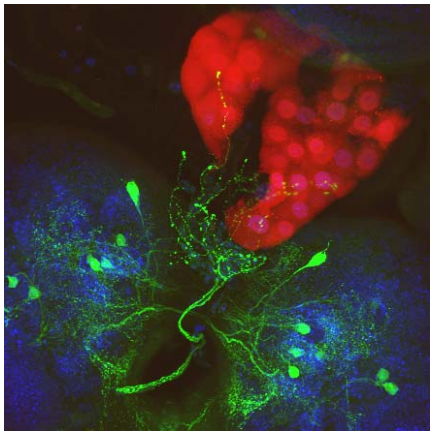

How do the organisms know their appropriate timing of maturation from the juvenile to the adult? One of the key regulatory mechanisms is steroid hormone biosynthesis in response to various environmental conditions. We have been studying the neuronal regulatory mechanism of steroid hormone biosynthesis in the fruit fly *Drosophila melanogaster*. By using molecular genetics, cell biological analysis, and live-imaging system, we are trying to understand how the genetic program of organisms is flexibly coordinated to accomplish the development from eggs to individuals. Anyone and everyone is welcome to share our scientific interests in the lab!

Selected Publications:

1. Enya S, Yamamoto C, Mizuno H, Esaki T, Lin H-K, Iga M, Morohashi K, Hirano T, Kataoka H, Masujima H, **Shimada-Niwa Y**, Niwa R (2017). Dual Roles of Glutathione in Ecdysone Biosynthesis and Antioxidant Function During the Larval Development in *Drosophila*. ***Genetics*** 207: 1519-1532
2. Imura E, Yoshinari Y, **Shimada-Niwa Y**, Niwa R (2017). Protocols for Visualizing Steroidogenic Organs and Their Interactive Organs with Immunostaining in the Fruit Fly *Drosophila melanogaster*. ***Journal of visualized experiments*** : JoVE (122)
3. **Niwa YS**, Niwa R (2016). Transcriptional regulation of insect steroid hormone biosynthesis and its role in controlling timing of molting and metamorphosis. ***Development, growth & differentiation*** 58(1) 105
4. **Niwa YS**, Niwa R (2016). Ouija board: A transcription factor evolved for only one target in steroid hormone biosynthesis in the fruit fly *Drosophila melanogaster*. ***Transcription*** 7(5) 196-202
5. Komura-Kawa K, Hirota K, **Shimada-Niwa Y,** Yamauchi R, Shimell M, Shinoda T, Fukamizu A, O'Connor MB, Niwa R (2015). The *Drosophila* Zinc Finger Transcription Factor Ouija Board Controls Ecdysteroid Biosynthesis through Specific Regulation of *spookier*. ***PLOS Genetics*** 11:e1005712.
6. Ohhara Y, **Shimada-Niwa Y**, Niwa R, Kayashima Y, Hayashi Y, Akagi K, Ueda H, Yamakawa-Kobayashi K, Kobayashi S (2015). Autocrine regulation of ecdysone synthesis by β3-octopamine receptor in the prothoracic gland is essential for *Drosophila* metamorphosis. ***Proceedings of the National Academy of Sciences of the United States of America*** 112(5) 1452-1457
7. **Shimada-Niwa Y**, Niwa R (2014) Serotonergic neurons respond to nutrients and regulate the timing of steroid hormone biosynthesis in *Drosophila*. ***Nature Communications*** 5: 5778

Hiroshi Shitara

Molecular Genetics of Mitochondrial DNA in Mammals

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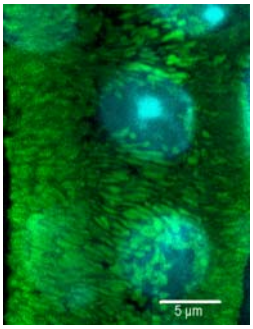
Mitochondria play important roles in cell functions such as ATP production and apoptosis. Mammalian mitochondria contain multiple copies of approximately 16-kbp double-stranded DNA with a closed circular conformation. Two genetic characteristics that are major specific phenomena observed during the inheritance of mitochondrial DNA (mtDNA) are maternal inheritance and rapid segregation. We have been investigating the mode of mtDNA transmission in a mouse model.

Our particular focus is the genetic machinery of rapid segregation. Usually, 1000 to 10,000 copies of mtDNA molecules exist in a single somatic cell, and the mutation rate of mtDNA is higher than that of nuclear DNA. Thus, mtDNA is thought to show heteroplasmy: in other words, more than one type of mtDNA exists in a cell. However, rapid shifts in mtDNA variants between generations have been observed in several species, and mtDNA homoplasmy is maintained in most individuals. Our group previously proposed models for the mitochondrial bottleneck effect, which is a concept for the genetic machinery of rapid segregation. We are currently investigating mtDNA and mitochondrial segregation by using transgenic mouse strains.



Confocal image of mitochondria in kidney from mtGFP-Tg mice. Mitochondria were visualized by using green fluorescent protein. Nuclei are counterstained with DAPI (blue).

Select Publications

1. Yamaguchi, J., Nishiyama, S., Shimanuki, M., Ono, T., Sato, A., Nakada, K., Hayashi, J., Yonekawa, H., and Shitara, H. (2012). Comprehensive application of an mtDsRed2-Tg mouse strain for mitochondrial imaging. Transgenic Res *21*, 439-447.
2. Nishiyama, S., Shitara, H., Nakada, K., Ono, T., Sato, A., Suzuki, H., Ogawa, T., Masaki, H., Hayashi, J., and Yonekawa, H. (2010). Over-expression of Tfam improves the mitochondrial disease phenotypes in a mouse model system. Biochem Biophys Res Commun *401*, 26-31.
3. Cao, L., Shitara, H., Sugimoto, M., Hayashi, J., Abe, K., and Yonekawa, H. (2009). New evidence confirms that the mitochondrial bottleneck is generated without reduction of mitochondrial DNA content in early primordial germ cells of mice. PLoS Genet *5*, e1000756.
4. Cao, L., Shitara, H., Horii, T., Nagao, Y., Imai, H., Abe, K., Hara, T., Hayashi, J., and Yonekawa, H. (2007). The mitochondrial bottleneck occurs without reduction of mtDNA content in female mouse germ cells. Nat Genet *39*, 386-390.

Akiko Shoji

Behavioural Ecology

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My research focuses on many facets of behavioural ecology, dealing with spatial ecology, life-history, individuality, ecotoxicology and population dynamics. I study the interactions between prey and predator as well as individuality and fitness mainly on top avian predators such as colonial seabirds and raptors, addressing a range of questions from understanding the consequences of migratory strategies on individual fitness and population dynamics, to investigating foraging strategies in sympatric species and incubation strategies from an ecophysiology point of view, the mechanism of carry-over effects in migratory species. I recently expanded my research interest to include understanding the mechanism of biotransport through behaviour and the extent of the consequences on trans-ecosystems. I am currently leading projects on seabirds and raptors breeding in the Pacific Ocean. I am collaborating with various researchers and NGOs which lead some of my research results to help making conservation policies in the Atlantic Ocean.

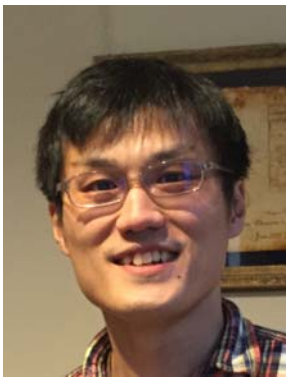
Bio-logging devices
Right: GPS logger
Middle: Time-Depth-Temp logger
Left: Geolocator

Tufted puffins breeding at Middleton Island, Alaska, USA where we are currently studying wintering movements and behaviour with bio-logging techniques. Through collaboration with Dr. Kyle Elliott at McGill University in Montréal, Dr. Stéphane Aris-Brosou at University of Ottawa in Canada, and Dr. Anntte Fayet at Oxford University, and many more cannot be listed all here, we are tagging several seabirds in the Pacific Ocean.

Selected publications

1. Shoji, A.*et al.*(2019) Biotransport of metallic trace elements from marine to terrestrial ecosystems by seabirds. Environmental Toxicology & Chemistry 38: 106-114.
2. Van-Tatenhove, A. *et al.* (2018) Streaked shearwater *Calonectris leucomelas* moonlight avoidance in response to low aerial predation and effects of wind speed and direction on colony attendance. Marine Ornithology 46: 177-185
3. Shoji, A.*et al.*(2016) Physiological constraints scale with body mass during dives in auks: a comparative analysis. Comparative Biochemistry and Physiology 196:54-60
4. Shoji, A.*et al.*(2016) Foraging flexibility and search patterns are unlinked during breeding in a free-ranging seabird. Marine Biology 163: 1-10
5. Shoji, A.*et al.*(2015) Breeding phenology and winter activity predict subsequent breeding success in a trans-global migratory seabird. Biology Letters 11: 20150671

Takuya Suzaki



Plant Developmental Biology

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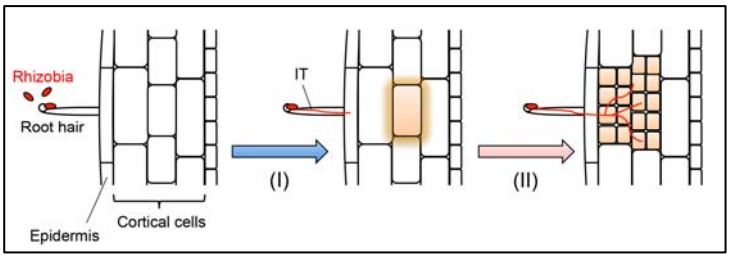
A nodule formed on the root of *Lotus japonicus*

Legumes (Fabaceae) are well-known for their ability to form nodules on their roots through symbiotic interaction with soil bacteria (rhizobia), a relationship termed "root nodule symbiosis". Within the nodules, the rhizobia fix gaseous nitrogen and make it available to the host plants as a nitrogen source; in turn, the plants provide a carbon source for the rhizobia. During nodulation, signaling initiated by rhizobial infection alters the fate of differentiated cortical cells and causes formation of new organs. Two qualitatively different regulatory events, namely bacterial infection and nodule organogenesis, need to be coordinated in the epidermis and cortical cells to establish proper nodule formation. We aim to elucidate molecular mechanisms underlying these processes using a model leguminous plant, *Lotus japonicus*.



Cell fate conversion process in nodule development. In response to rhizobial infection, the dedifferentiation of some cortical cells beneath root hairs with infection thread (IT) is induced (I). The activated cortical cells then undergo a new developmental program to form a nodule primordium (II).

Select Publications

1. Suzaki, T., Yano, K., Ito, M., Umehara, Y., Suganuma, N., and Kawaguchi, M (2012). Positive and negative regulation of cortical cell division during nodule development in *Lotus japonicus* is accompanied by auxin response. Development *139*, 3997-4006.
2. Suzaki, T., Kim, C.S., Takeda, N., Szczyglowski, K., and Kawaguchi, M. (2013). *TRICOT* encodes an AMP1-related carboxypeptidase that regulates root nodule development and shoot apical meristem maintenance in *Lotus japonicus*. Developmnet *140*, 353-361.
3. Suzaki, T., Ito, M., Yoro, E., Sato, S., Hirakawa, H., and Kawaguchi, M. (2014). Endoreduplication-mediated initiation of symbiotic organ development in *Lotus japonicus*. Development *141*, 2441-2445.
4. Sasaki, T., Suzaki, T., Soyano, T., Kojima, M., Sakakibara, H., and Kawaguchi, M. (2014). Shoot-derived cytokinins systemically regulate root nodulation. Nature Communications *5*, 4983.

Iwane Suzuki

Mechanisms of signal perception by sensory kinases in photosynthetic organisms

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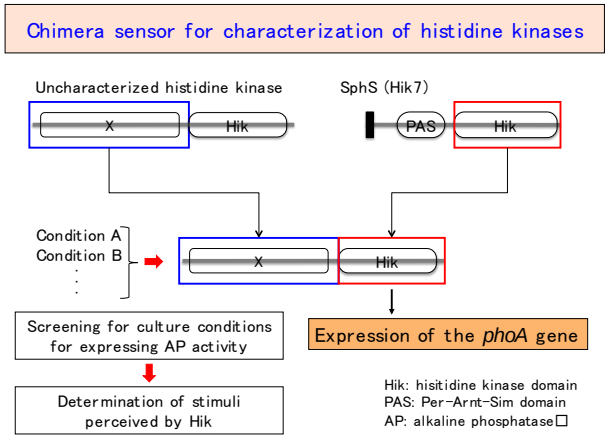
Living organisms recognize changes in their environmental conditions and regulate their gene expression to acclimate to such changes. However, the molecular mechanisms of signal perception by cellular sensors are not yet well characterized. We developed a way to construct chimeric sensors, which contain a signal-recognition domain from an unknown sensory kinase and a kinase domain from the well-studied phosphate-deficient sensor, SphS, from the cyanobacterium *Synechocystis* sp. PCC 6803. This system is a powerful tool for studying the functions of sensory kinases and the molecular mechanisms of signal perception, as well as for developing artificial switches to regulate gene expression in systems biology.



Construction of a chimeric sensory kinase in *Synechocystis*. A phosphate sensor, SphS, regulates expression of the *phoA* gene encoding alkaline phosphatase (AP). The chimeric sensory kinase containing the signal-recognition domain of an uncharacterized kinase and the kinase domain of SphS regulate the expression of the *phoA* gene under the conditions perceived by the uncharacterized sensory kinase.

Select Publications

1. Y. Shimura, Y. Shiraiwa, I. Suzuki (2012) Characterization of the subdomains in the amino-terminal region of histidine kinase Hik33 in the cyanobacterium *Synechocystis* sp. PCC 6803, *Plant Cell Physiol.*, **53**, 1255–1266
2. J.G. Rowland, X. Pang, I. Suzuki, N. Murata, W.J. Simon, A.R. Slabas (2010) Identification of components associated with thermal acclimation of photosystem II in *Synechocystis* sp. PCC6803, *PLoS One* **5**, e10511
3. S. Kimura, Y. Shiraiwa, I. Suzuki (2009) Function of the N-terminal region of the phosphatesensing histidine kinase, SphS, in *Synechocystis* sp. PCC 6803, *Microbiol.* **155**, 2256-2264
4. T. Sakayori, Y. Shiraiwa, I. Suzuki (2009) A *Synechocystis* homolog of SipA protein, Ssl3451, enhances the activity of the histidine kinase Hik33, *Plant Cell Physiol.* **50**, 1439-1448
5. Y. Kanesaki, H. Yamamoto, K. Paithoonrangsarid, M. Shoumskaya, I. Suzuki, H. Hayashi, N. Murata (2007) Histidine kinases play important roles in the perception and signal transduction of H_2O_2 in the cyanobacterium, *Synechocystis*. *Plant J.* **49**, 313-324

Tanaka Kenta

Regeneration and Adaptive Evolution of Wild Plants with Environmental Variation

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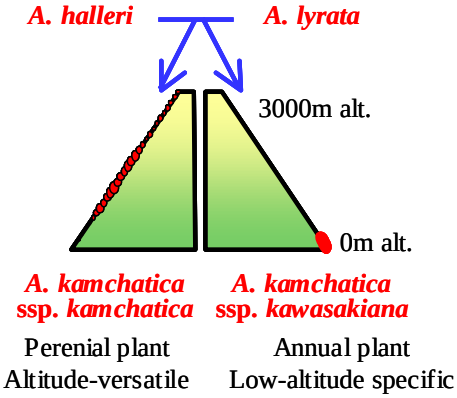
My goal is the integration of population ecology and population genetics to elucidate (1) the effects of natural selection due to ecological factors on genes and allele dynamics; and (2) the ecological and population consequences of genetic change. One of our recent targets has been wild Arabidopsis, which is ecologically diverse and genetically tractable. *Arabidopsis kamchatica* ssp. *kamchatica* and ssp. *kawasakiana* are allopolyploids originating independently from the same parental species (see Figure below). Although these allopolyploids inherited identical genome components, they show surprising differences in their ecology. Subpecies *kamchatica* is a perennial herb with a remarkably wide altitudinal distribution—from 30 to 3000 m—even at a single latitude, whereas ssp. *kawasakiana* is an annual herb limited to low altitudes. We performed a natural demography census, laboratory and field common-garden experiments, and genome-wide microarray and next-generation sequencing. We found that 1) natural selection and population maintenance mechanisms change with altitude; 2) many traits related to life history, defense, and stress tolerance are genetically distinguished with altitude; 3) populations have evolutionarily adapted to their own altitudes; and 4) there is strong diversifying selection of the genes for trichomes and photoreceptors, and the allele frequencies of these genes change with altitude.



Hybridisation between two wild Arabidopsis species has generated contrasting subspecies with marked ecological variation, providing a model system for the evolution of altitudinal adaptation and life history.

Select Publications

1. Kenta, T., *et al*. (2011). Clinal variation in flowering time and vernalisation requirement across a 3000-m altitudinal range in perennial *Arabidopsis kamchatica* ssp. *kamchatica* and annual lowland subspecies *kawasakiana*. J Ecos Ecog *S6*, 001.
2. Kunin, W.E., Vergeer, P., Kenta, *et al*. (2009). Variation at range margins across multiple spatial scales: environmental temperature, population genetics and metabolomic phenotype. Proc Roy Soc B *276*, 1495-1506.
3. Kenta, T., *et al*. (2008). Multiplex SNP-SCALE: a cost-effective medium-throughput single nucleotide polymorphism genotyping method. Mol Eco Res *8*, 1230-1238.
4. Kenta, T., Inari, N., Nagamitsu, T., Goka K., & Hiura, T. (2007). Commercialized European bumblebee can cause pollination disturbance: an experiment on seven native plant species in Japan. Bio Cons *134*, 298-309.
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Yukihiko Toquenaga

Population Biology

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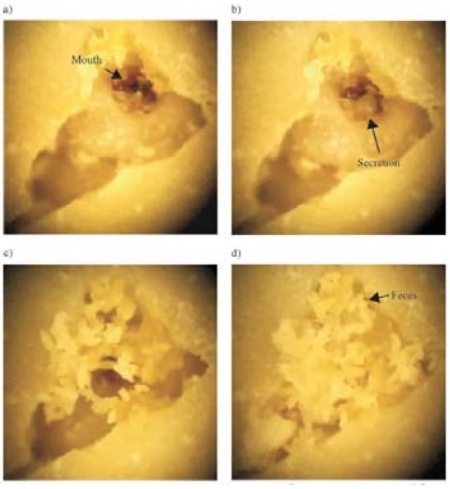
I am an associate professor in the Doctoral Program in Biological Sciences at the University of Tsukuba, where I teach ecology, theoretical biology, biometry, and computer programming. I specialize in population biology using a wide range of materials, including natural communities of egrets and herons in the eastern region of the Kanto Plain; laboratory populations of bean weevils collected from all over the world; natural populations of bumble bees in urban and rural regions, and the *in silico* digital bugs that occupy gigabytes on the hard disks attached to my computers. I am using these materials to question, in an evolutionary sense, why some organisms live in groups but others tend to live solitarily. My speciation philosophy was converted to Wrightian from Fisherian when I studied evolution and ecology under Prof. Michael Wade in 1995–1996. I believe that Wright's shifting balance scheme is realistic. I'm often described as a theoretician, but I consider myself primarily to be an ecological field worker. Somehow I have become good at capturing wild egrets and herons by hand!



The photographs (clockwise from the top left panel) show a larva of *Callosobruchus maculatus*, a notorious bean-weevil pest of legume seeds, constructing a rough wall inside a bean when it happened to break into the cavity of another larva. The larva has used feces and a secreted substance to form the wall. The *C. maculatus* larvae are of the scramble type, so multiple adults can emerge from a bean, but if the wall structure is artificially removed the larva will fight with the other larva in the cavity and one or both of them will die as a result. The rough wall acts as a kind of language that prevents fights between inherently quarrelsome larvae.

Select Publications

1. Mashiko, M., Fujioka, M., Moriya, K., Hagimoto, T., Yamaguchi, M., and Toquenaga, Y. (2012). Natural hybridization between a Little Egret (*Egretta garzetta*) and a Chinese Pond Heron (*Ardeola bacchus*) in Japan. Waterbirds *35*, 160-163.
2. Kondo, N., Tuda, M., Toquenaga, Y., Lan, Y-C., Buranapanichpan, S., Horng, S-B., Shimada, M., and Fukatsu, T. (2011). *Wolbachia* infections in world populations of bean beetles (Coleoptera: Chrysomelidae: Bruchinae) infesting cultivated and wild legumes. Zool Sci *14*, 166-172.
3. Suzuki-Ohno, Y., Kawaguchi, L., Munidasa, D., and Toquenaga, Y. (2010). Do bumble bee queens choose nest sites to maximize foraging rate? -Testing models of nest site selection- Behav. Ecol Sociol *63*, 1353-1362.
4. Toquenaga, Y., and Kokuvo, N. (2010). Full-sib reconstruction in haplodiploid populations. Appl Entomol Zool *45*, 59-64.
5. Otsuka, Y. , and Toquenaga, Y. (2009). The Patch Distribute Producer-Scrounger Game, J Theor Biol, *260*, 261-266.
6. Mano, H., and Toquenaga, Y. (2008). Wall-making Behavior in *Callosobruchus maculatus* (Coleoptera: Bruchidae). Ann Entomol Soc Am *101*, 449-455.

Fuminori Tsuruta

Neuron–Glia Network Mediated by Protein Degradation

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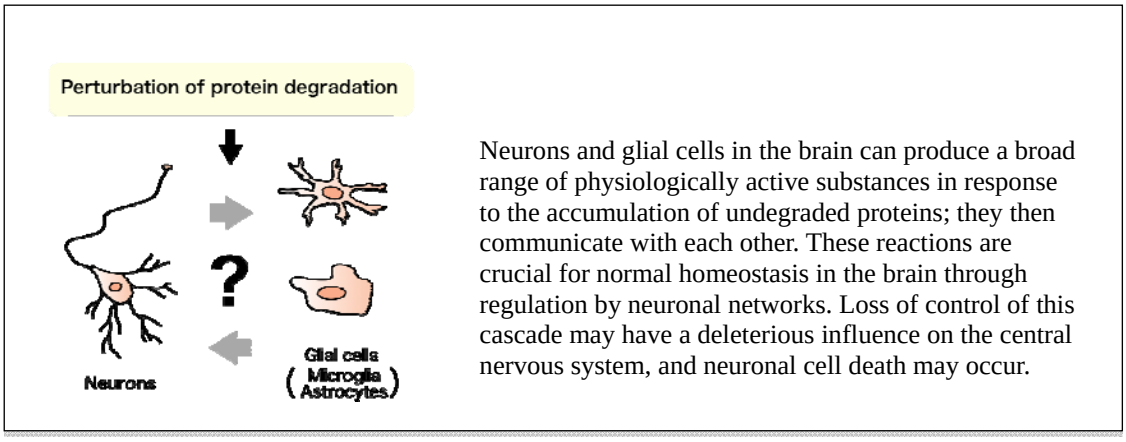
Protein degradation regulated by ubiquitin proteasome and autophagy systems in the central nervous system is critically important to the cellular basis of neuronal networks. Perturbation of this cascade causes various disorders, such as neuronal degeneration and mental retardation. The major goal of our project is to understand the mechanisms that underlie the modification of synaptic connections and neuronal inflammation regulated by both neurons and glial cells. We are focusing on how impairment of protein degradation leads to synaptic dysfunction and inflammation in the brain. We are also interested in developing new tools to screen for small compounds and proteins associated with neuronal disorders caused by aberrant protein degradation.



Neurons and glial cells in the brain can produce a broad range of physiologically active substances in response to the accumulation of undegraded proteins; they then communicate with each other. These reactions are crucial for normal homeostasis in the brain through regulation by neuronal networks. Loss of control of this cascade may have a deleterious influence on the central nervous system, and neuronal cell death may occur.

Select Publications

1. Kigoshi, Y., Tsuruta, F., and Chiba, T. (2011). Ubiquitin ligase activity of Cul3-KLHL7 protein is attenuated by autosomal dominant retinitis pigmentosa causative mutation. J Biol Chem *286*, 33613-33621.
2. Tsuruta, F., Green, E.M., Rousset, M., and Dolmetsch, R.E. (2009). PIKfyve regulates CaV1.2 degradation and prevents excitotoxic cell death. J Cell Biol *187*, 279-294.
3. Gomez-Ospina, N., Tsuruta, F., Barreto-Chang, O., Hu, L., and Dolmetsch, R. (2006). The C terminus of the L-type voltage-gated calcium channel Ca(V)1.2 encodes a transcription factor. Cell *127*, 591-606.
4. Sunayama, J., Tsuruta, F., Masuyama, N., and Gotoh, Y. (2005). JNK antagonizes Akt-mediated survival signals by phosphorylating 14-3-3. J Cell Biol *170*, 295-304.
5. Tsuruta, F., Sunayama, J., Mori, Y., Hattori, S., Shimizu, S., Tsujimoto, Y., Yoshioka, K., Masuyama, N., and Gotoh, Y. (2004). JNK promotes Bax translocation to mitochondria through phosphorylation of 14-3-3 proteins. EMBO J *23*, 1889-1899.

Hiroshi Wada

Evolutionary Developmental Biology

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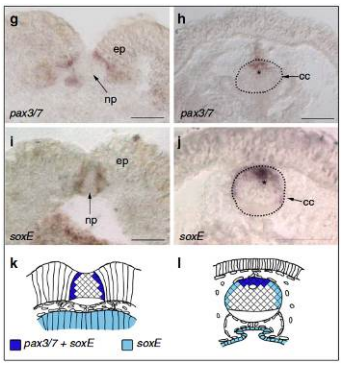
Our interest is in the evolutionary processes of various animal body plans. We are especially interested in the following issues.
1) Establishment and evolution of the chordate body plan. Chordates acquired several novel characters such as notochord, dorsal central nervous system, vertebrae, and pharyngeal arches. We explore how these novel organs evolved by comparing developmental genetics in amphioxus and lampreys.
2) Evolution of echinoderm larval morphology. Echinoderms show two types of larvae, pluteus and auricularia. We asked how these discrete larval morphologies evolved by comparing developmental genetics in sea urchins and starfish.
3) Evolution of bivalve shell plate in bivalve mollusks. Bivalve mollusks acquired bilaterally separated shell plates, and this unique morphology is visible as early as the gastrula stage, showing that the separated shell plates are established by modifying their early embryogenesis.
4) Establishment of the unique body plan of caprellids. The unique body plan of the caprellids was established from a gammarid-like body plan through the loss of some thoracic limbs and abdominal segments. We are seeking the genetic modification response for this loss. We are interested in this phenomenon because some caprellid species re-acquired the limbs.



Expression of *pax3/7* and *soxE*, whose homologues are involved in the differentiation of the dorsal neural tube in vertebrates, mark dorsal part of the acorn worm nerve cord, showing that acorn worms possess similar DV patterning mechanism in their nerve cord. (Miyamoto and Wada, Nature Comm. (2013).

Publications

1. Suzuki, D. G., Murakami, Y., Escriva, H. and Wada. H. (2015) A comparative examination of neural circuit and brain patterning between the lamprey and amphioxus reveals the evolutionary origin of the vertebrate visual center. J. Comp. Neurol. 523, 251-261.
2. Miyamoto, N. and Wada. H. (2013) Hemichordate neurulation and the origin of the neural tube. Nat. Comm. 4, 2713
3. Morino, Y., Koga, H., Tachibana, K., Shoguchi, E., Kiyomoto, M. and Wada. H. (2012). Heterochronic Activation of VEGF Signaling and the Evolution of the Skeleton in Echinoderm Pluteus Larvae. Evol. Dev. 14, 428-436.

Shigeki Wada

Biological Oceanography

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Organisms interact with other organisms and with their ambient environments. Because these processes are components of ecosystems, we need to understand not only biological activities but also environmental factors if we are to understand ecosystem mechanisms.

Although humans receive various ecological services from marine ecosystems, the mechanisms by which this occurs are less well understood than it the case in terrestrial ecosystems. We are trying to figure out the dynamics and flows of organic matter derived from marine organisms (e.g., macroalgae, phytoplankton, and bacteria) by using field investigations and chemical analyses. Recently, we have been focusing on 1) the fate of macroalgal organic matter; 2) ocean acidification and its effect on marine organisms; and 3) biotic and abiotic formation of marine snow particles.

Field sampling by scuba diving and from a research ship. Because our research center fronts onto the Padific Ocean, we can easily go out sampling.

Selected Publications

1. Wada, S., and Hama, T. (2013) Contributioin of macroalgae to coastal dissovled organic matter pool. Estuarine, Coastal and Shelf Science *129*, 77-85.
2. Seto, M., Wada, S., and Suzuki, S. (2013). The effect of zinc on aquatic microbial ecosystems and the degradation of dissolved organic matter. Chemosphere 90, 1091-1102.
3. Wada, S., and Suzuki, S. (2011). Inhibitory effect of zinc on the remineraliastion of dissolved organic matter in the coastal environment. Aquatic Microbial Ecology, 63, 47-59.
4. Hama, T., Kawashima, S., Shimotori, K., Satoh, Y., Omori, U., Wada, S., Adachi, T., Hasegawa, S., Midorikawa, T., Ishii, M., Saito, S., Sasano, D., Endo, H., Nakayama, T., Inoue, I. (2012) Effect of ocean acidification on coastal phytoplankton composition and accompanying organic nitrogen production. Journal of Oceanography *68*, 183-194

Matthew Wood

Science Communication

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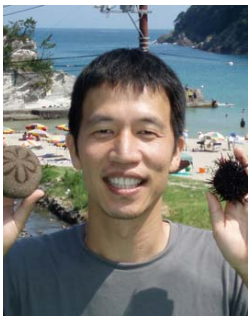
Carefully considered public communication of science and related issues is vital for a healthy relationship between science and the society that both depends on and supports it. It is becoming increasingly apparent that this communication is multifaceted, highly complex, and must be better understood to face the challenges of our progressively science-reliant society.

I have broad academic interests in the areas of public perceptions of science and scientists; the portrayal of science in news and the media; risk perception; and the use of visual media to communicate science concepts and issues in informal education settings.

I develop and conduct undergraduate and postgraduate courses in communication skills and introductory science communication. These courses are designed to equip students to effectively communicate their future research. In a previous life I trained in marine biology and environmental chemistry, and worked on projects searching for potential new drugs from marine invertebrates.

Shunsuke Yaguchi



Developmental Biology of the Sea Urchin

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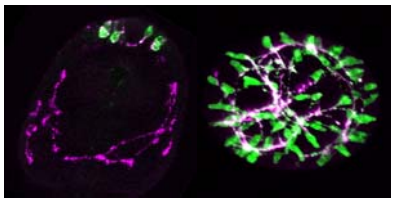
The primary research goal of our lab is to understand the molecular mechanisms of embryonic axis specification and formation in the sea urchin. It has been suggested that this embryo has two independent, maternally specified axes, primary (anterior–posterior) and secondary (dorsal–ventral). My previous work [3] showed that specification of these two axes is linked by a single transcription factor, FoxQ2, during early embryogenesis. The linking pathway involves a double repression mechanism in which Wnt/ß-catenin signaling, which is essential for primary axis specification, represses FoxQ2, which represses both the *nodal* expression required for secondary axis specification, and BMP2/4, a factor downstream of Nodal. My goal is to try to understand how FoxQ2 is related to, or interacts with, those signaling pathways like the Wnt/ß-catenin, Nodal, and BMP2/4, which are responsible for axis specification and formation.

Another research goal is to understand the molecular mechanisms of neurogenesis, including the specification and patterning of the neurogenic ectoderm that develops at the anterior end of the sea urchin embryo.



Blocking Wnt/ß-catenin signaling produces permanent blastulae with an expanded anterior neurogenic ectoderm. Left: Serotonin (green) and synaptotagmin (magenta) in a normal embryo. Right: The number of serotonergic neurons is increased in the Wnt/ß-catenin–blocked embryo.

Select Publications

1. Yaguchi, J., Angerer, L.M., Inaba, K., and Yaguchi, S. (2012). Zinc finger homeobox is required for the differentiation of serotonergic neurons in the sea urchin embryo. Dev Biol *363*, 74-83.
2. Yaguchi, S., Yaguchi, J., Wei, Z., Jin, Y., Angerer, L.M., and Inaba, K. (2011). Fez function is required to maintain the size of the animal plate in the sea urchin embryo. Development *138*, 4233-4243.
3. Yaguchi, S., Yaguchi, J., Angerer, R.C., and Angerer, L.M. (2008). A Wnt-FoxQ2-nodal pathway links primary and secondary axis specification in sea urchin embryos. Dev Cell *14*, 97-107.
4. Yaguchi, S., Yaguchi, J., and Burke, R.D. (2006). Specification of ectoderm restricts the size of the animal plate and patterns neurogenesis in sea urchin embryos. Development *133*, 2337-2346.

Kensuke Yahata

What is the Arthropoda ?
Discover the Unknown Structures and Reveal its Phylogenetic Significance

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[English page is under construction]

Phylum Arthropoda is known to have a huge species diversity. And there is also great diversity in the morphology of various organs and tissues. Although morphological features of many organs and tissues have been investigated in the past centuries, there will be many structures that we do not know well yet. Some of these unknown structures may have important phylogenetic significance. In my laboratory, we are clarifying the phylogenetic significance of the characteristics newly discovered in the arthropods from the viewpoint of comparative morphology. The following are two examples of our research.

In one project, we identified distinctive structure in ovaries of myriapods. Although the Myriapoda has been known to have few new traits that characterize the taxon, this ovarian structure is considered to have important phylogenetic significance as an undoubted synapomorphy of the Myriapoda. In another project, we newly found some structures for appendage autotomy in centipedes. And we clearly suggested that the difference in the degree of development of the autotomic structures is related to the frequency of their autotomic behaviors and that the difference also corresponds to their order level phylogeny. Our researches will not only add new insights to arthropod morphology but also contribute to a better understanding of arthropod phylogeny and evolution.

Selected Publications

1. Yahata, K., Umetani, E., and Chikami, Y. (2018). Morphological study of the ovary in *Hanseniella caldaria* (Myriapoda; Symphyla): The position of oocyte-growth and evolution of ovarian structure in Arthropoda. Arthropod Structure and Development *47*, 655–661.
2. Niikura, M., Honda, M., and Yahata, K. (2015). Phylogeography of semiterrestrial isopod, *Tylos granuliferus*, on East Asian coasts. Zoological Science *32*, 105–113.
3. Suguro, T., and Yahata, K. (2014). Taxonomic notes on Japanese species of the genera *Pseudicius* and *Tasa* (Araneae: Salticidae). Acta Arachnologica *63*, 87–97.
4. Miyachi, Y., and Yahata, K. (2012). Morphological study of ovarian structures in scolopendromorph centipedes (Myriapoda: Chilopoda) with special reference to the position of oocyte growth. Proceedings of the Arthropodan Embryological Society of Japan *47*, 21–28.
5. Matsui, A., and Yahata, K. (2012). Study of autotomic structure in centipedes (Arthropoda: Chilopoda). Proceedings of the Arthropodan Embryological Society of Japan *47*, 11–19.
6. Yahata, K. (2012). Comparative study on ovarian structure of polydesmid diplopods (Diplopoda: Polydesmida). Proceedings of the Arthropodan Embryological Society of Japan *47*, 5–10.
7. Suguro, T., and Yahata, K. (2012). A new species of the Genus *Evarcha* (Araneae: Salticidae) from Japan. Acta Arachnologica *61*, 1–4.
8. Mitsumoto, H., and Yahata, K. (2006). Evidence of cross-fertilization in a gonochoric population of the tadpole shrinp *Triops numidicus* (Crustacea: Branchiopoda: Notostraca). Zoological Science *23*, 1109–1113.
9. Yahata, K. (2005). Ovarian structure of five penicillate diplopods (Diplopoda: Penicillata). Proceedings of Arthropodan Embryological Society of Japan *40*, 23–25.

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