大学共同利用機関法人 自然科学研究機構
生命創成探究センター

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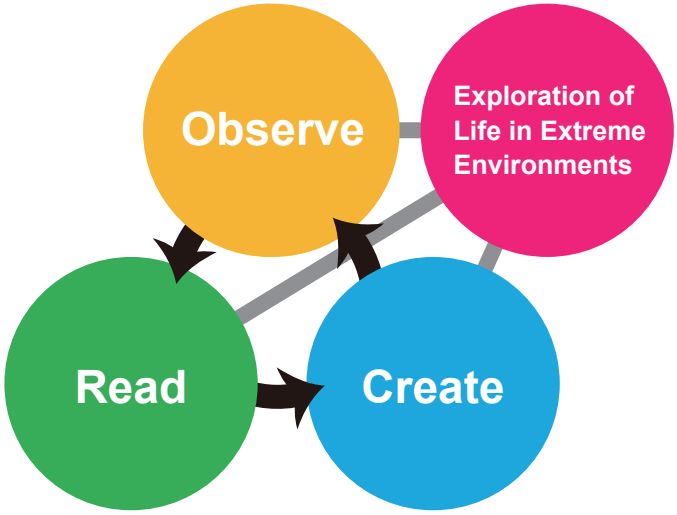
Exploratory Research Center on Life and Living Systems

ExCELLS

KATO, Koichi Ph.D.

The Director of ExCELLS
Koichi KATO

What is life? The Exploratory Research Center on Life and Living Systems (ExCELLS) was established in April 2018 to address this fundamental question. The essence of living systems has long been explored by physicists, including Erwin Schrödinger and Ilya Prigogine, and has been characterized as open systems in disequilibrium. Omics-based approaches that have been developed in recent decades have provided comprehensive knowledge on biomolecules as parts of living systems. However, the fundamental question of how these biomolecules are integrated into living systems remains unanswered. ExCELLS aims to achieve a comprehensive understanding of living systems beyond reductionism by utilizing large-scale data analyses and synthetic biology approaches. For this purpose, ExCELLS develops novel approaches for observing biological entities, deciphering hidden information, and creating living systems to improve understanding of their nature. Moreover, ExCELLS promotes collaborative, interdisciplinary research involving investigators who explore organisms living in extreme environments and provides a unique platform for cross-disciplinary research in an interuniversity, collaborative environment, using the “Observe, Read, and Create” approach. Furthermore, for developing a strong research and innovation base, ExCELLS enlightens young people to become the next generation scientists. To achieve our aims, we would like to expand our international collaborative network. Therefore, your cooperation would be greatly appreciated!



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- Biomolecular Organization Research Group
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- Dynamic Molecular Neurobiology Group
- Metallobiology Group
- Neuronal Networks Research Group
- Protein Design Group
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Collaborative Research Group

- Biomolecular Dynamics Observation Group

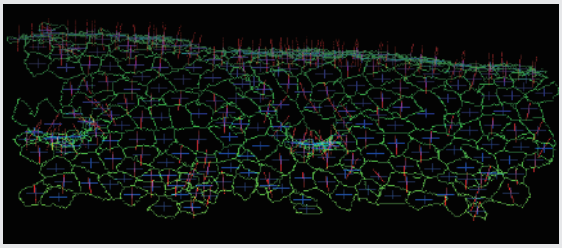
Section for Exploration of Life in Extreme Environments

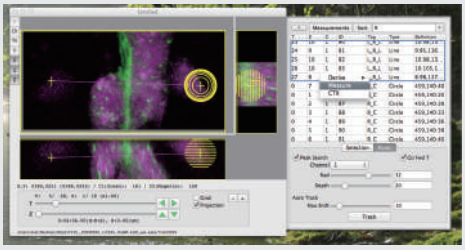
- Deep-Sea and Deep Subsurface Life Research Group
- Extreme Environmental Biomolecular Research Group

Bioimage Informatics Group

TAKADA, Shinji / KATO, Kagayaki / OHTA, Yusaku

Modern microscopic techniques used in the biological field yield large amounts of imaging data that generally include multiple dimensions, such as depth and temporal axes. Thus, they can be difficult to interpret with the naked eye. In addition, these biological specimens take various shapes and are often changing.
To overcome this and extract biological descriptions from them, we are developing specialized algorithms for extracting image features out of multi-dimensional biological images. We will also apply these to processing large amounts of imaging data for further analysis by building an image processing pipeline.





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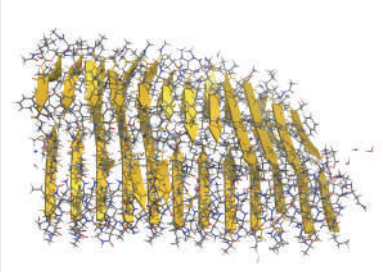
Biomolecular Dynamics Simulation Group

OKUMURA, Hisashi

Biomolecules such as proteins and peptides have complicated free-energy landscape with many local minima. The conventional canonical-ensemble molecular dynamics (MD) simulations tend to get trapped in a few of the local-minimum states. To overcome these difficulties, we have proposed new generalized-ensemble algorithms, such as replica-permutation method. We apply these methods to proteins and peptides and try to predict the native structures of proteins.
We are also interested in protein aggregates such as oligomers and amyloid fibrils, which are associated with more than 20 human neurodegenerative diseases. To understand formation and disruption of these protein aggregates, we perform MD simulations of these systems.



Amyloid fibril of amyloid-β peptides.

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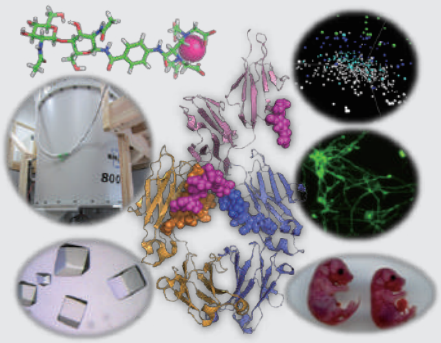
Biomolecular Organization Research Group

KATO, Koichi

Living systems are characterized by the dynamic assembly and disassembly of various self-organized biomolecules in response to external environmental changes. Omics-based approaches developed in recent decades have provided a comprehensive understanding of biomolecules as parts of living organisms. However, fundamental questions concerning how these biomolecules are ordered autonomously to form flexible and robust systems remain unanswered. To acquire an integrative understanding of the principles underlying biomolecular organization, we employ multidisciplinary approaches based on detailed analyses of dynamic structures and interactions of biomolecules using molecular and cellular biology techniques accompanied by synthetic and computational techniques.



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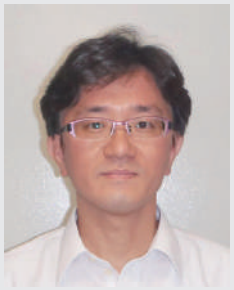
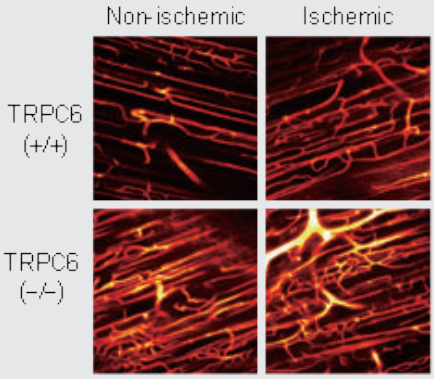
Cardiocirculatory Dynamism Research Group

NISHIDA, Motohiro



Cardiocirculatory system is precisely maintained by the multilevel interactions among muscular organs including heart, blood vessels, and skeletal muscles. We aim to elucidate the mechanisms of stress resilience (i.e., recovery from ischemic and mechanical stress) in cardiocirculatory systems. We aim to elucidate molecular mechanisms underlying regulation of cardiovascular risks by sulfur-based electrophilic/nucleophilic modifications of proteins. We also aim to elucidate the mechanism how exercise promotes vasculogenesis after ischemic stress, and establish an exercise-mimetic therapeutic strategy.



Capillary arterialization after hindlimb ischemia in TRPC6-deficient gastrocnemii.

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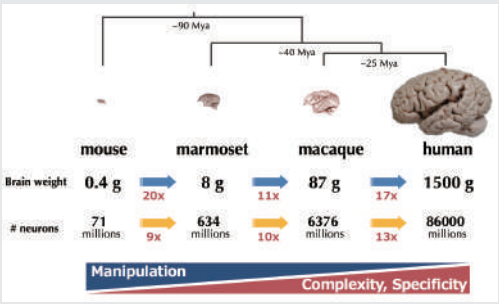
Cognitive Genomics Research Group

GO, Yasuhiro

Spatiotemporal transcriptome gene regulations are essential for the construction of brain structure and for proper function. Comprehensive analyses of the dynamics and the architecture of transcriptome in the both wild and diseased animal models also lead to understanding the molecular causality of the human neuropsychiatric disease. Currently we examine the spatiotemporal transcriptome dynamics using the primate brain to identify the spatiotemporal-specific modulating genes from macro-scale to single-cell level. Through this study, we aim to identify the molecular dynamics and trajectories between proper and atypical brain gene expressional networks. Additionally, we perform massive population genetic analysis for the neuropsychiatric related genes in primates to identify an individual that has a spontaneous loss-of-functional (LoF) mutation in the neuropsychiatric genes and aim to make disease primate models for the neuropsychiatric disease.



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Developmental Signaling Research Group

TAKADA, Shinji

The most popular model to explain the patterning process is the “morphogen gradient and threshold” theory. Many genetic results indicate that secreted signal proteins, including Wnt, FGF, BMP, and Hh, function as morphogens. In spite of the accumulation of genetic evidence, however, the mechanism of morphogen transport, as well as the characteristics of morphogen molecules themselves, remain to be elucidated. One of our major goals is to reveal the real image of morphogens and the molecular mechanism underlying the formation of morphogen gradients, including the secretion and extracellular transport of these morphoge.

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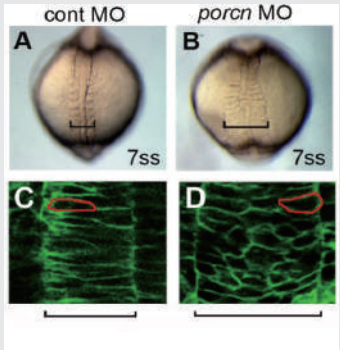
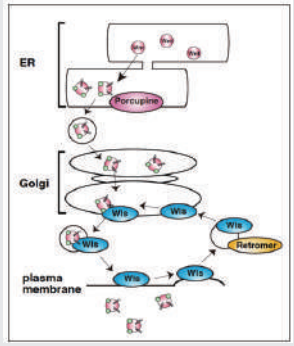


Deficiency in Wnt secretion causes abnormal development



Wnt proteins require specific apparatus in secretion

Dynamic Molecular Neurobiology Group

SHIINA, Nobuyuki

The transport of specific mRNAs and local control of translation in neuronal dendrites represent an important gene expression system that provides localized protein synthesis in dendrites at just the right time and place. This system controls the location at which neurites will connect to each other, thereby forming neural networks. The specific mRNAs are recruited into “RNA granules” in neuronal dendrites. We are researching RNA granule factors regulating mRNA transport and local translation, their target mRNAs, and the mechanisms of localized protein synthesis using mice in order to better understand its relation to the formation of synapses and neural networks, memory, learning, and behavior.

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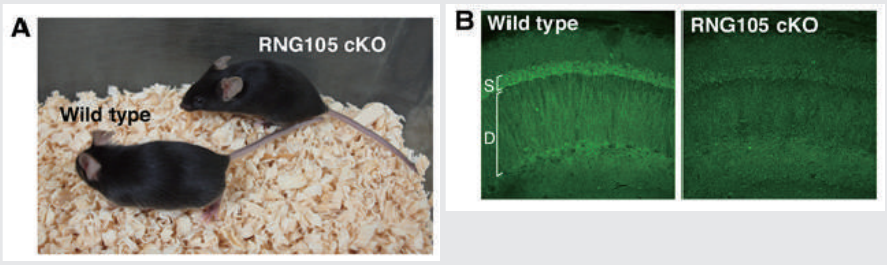
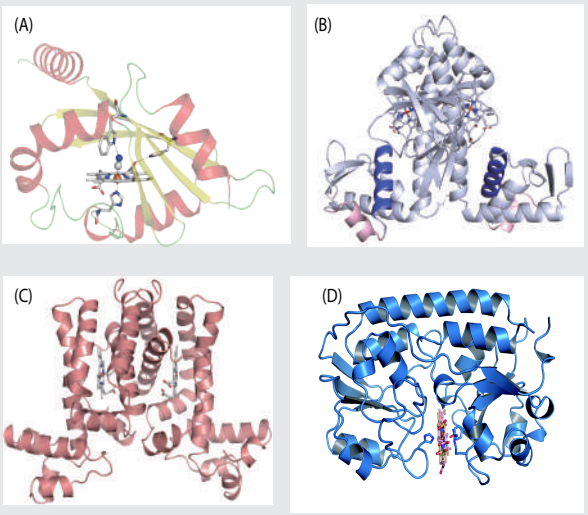


A conditional knockout (cKO) mouse of RNG105, an RNA granule component (A) and brain hippocampal areas stained with an anti-RNG105 antibody (B).

Metallobiology Group

AONO, Shigetoshi

Transition metal ions and metalloproteins play crucial roles in meeting the energy demands of the cell by playing roles in intermediary metabolism and in signal transduction processes. The elucidation of the structure and function of these metalloproteins is central to understanding the regulatory mechanisms associated with biological functioning. We are currently elucidating the structure-function relationships of metalloproteins using experimental methods in the areas of biochemistry, molecular biology, structural biology, inorganic chemistry, and physical chemistry. Our research interest is especially focusing on transition metal ion-containing transcriptional regulators, heme-based gas sensor proteins, and transition metal ions/complexes transport systems.



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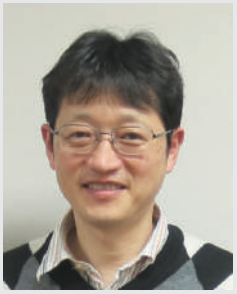
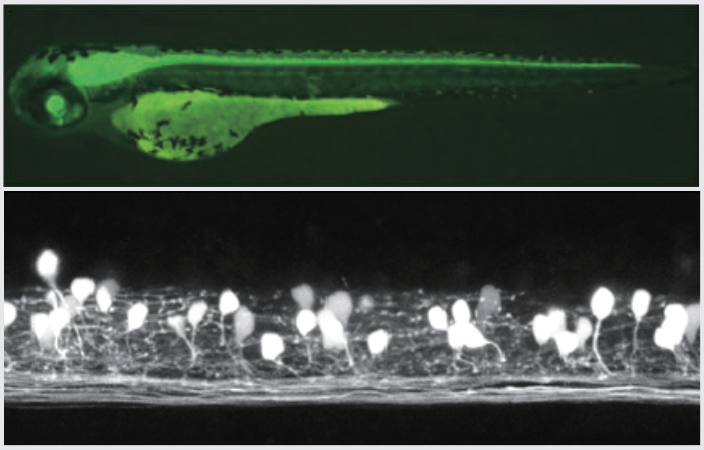
Neuronal Networks Research Group

HIGASHIJIMA, Shin-ichi



Using zebrafish, we are studying the morphology and functional properties of spinal neurons that express a particular transcription factor. Central to our approach is to visualize transcription factor positive cells by making transgenic zebrafish that express fluorescent proteins in these cells. Such transgenic fish allow us to trace development of specific types of neurons, and allow us to perform targeted electrophysiological recordings. We also use optogenetic tools such as ChR2 and halo-rhodopsin to manipulate activity of specific types of neurons.



A class of inteneurons are easily identified by fluorescence of GFP in live animals

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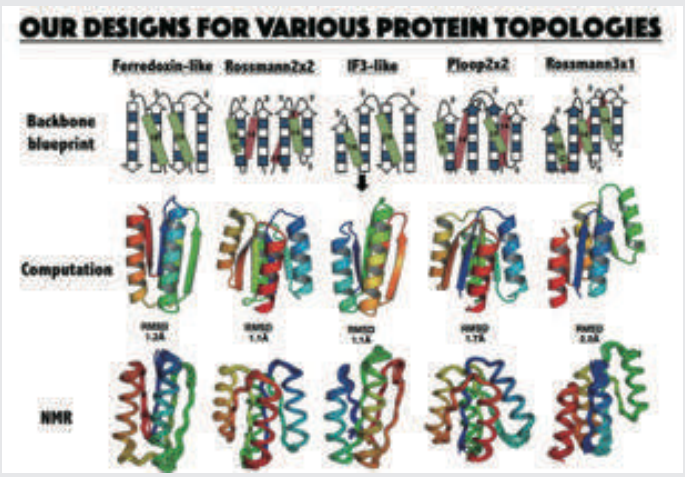
Protein Design Group

KOGA, Nobuyasu

Protein molecules spontaneously fold into unique three-dimensional structures specified by their amino acid sequences from random coils to carry out their functions. Many of protein studies have been performed by analyzing naturally occurring proteins. However, it is difficult to reach fundamental working principles of protein molecules only by analyzing naturally occurring proteins, since they evolved in their particular environments spending billions of years. In our lab, we explore the principles by computationally designing protein molecules completely from scratch and experimentally assessing how they behave.



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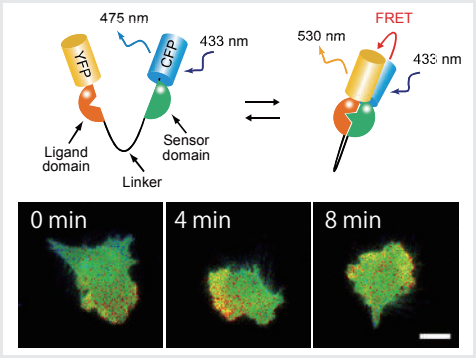
Quantitative Biology Group

AOKI, Kazuhiro

A living cell acts as an input-output (I/O) unit, which senses environment and internal states, processes information, and responds appropriately to adapt the changes. Our laboratory is interested in such a system for the information processing controlled by intracellular signaling devises and networks. Especially, we focus on several signal transduction pathways related to cell proliferation, differentiation, and cell death in mammalian cells, and aim to quantitatively decipher the mechanisms of signaling networks governing cellular decision-making. To this end, we are attempting to visualize, manipulate, and simulate intracellular signaling with fluorescence imaging techniques and computational approaches.



(Upper) Structure of intramolecular FRET biosensor.
(Lower) Spatiotemporal Rac1 activity in a migrating cell.

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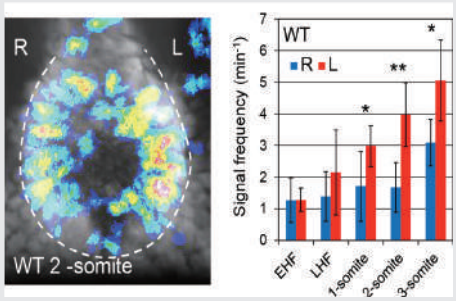
Spatiotemporal Regulations Group

NONAKA, Shigenori

Our main interest is the mechanism how the initial left-right asymmetry is determined in mammalian development. A small patch in a gastrulating mouse embryo called 'the node' generates leftward fluid flow by vortical motion of primary cilia on its ventral surface, and the flow direction is critically important to subsequent asymmetric gene expression and final organ arrangement. We are currently focused on the mechanism how the flow is converted to the asymmetric gene expression, i.e. what kind of information is conveyed by the flow, chemical or mechanical or something else, by combining techniques including whole embryo culture, light-sheet microscopy, etc.



Self-made light-sheet microscope

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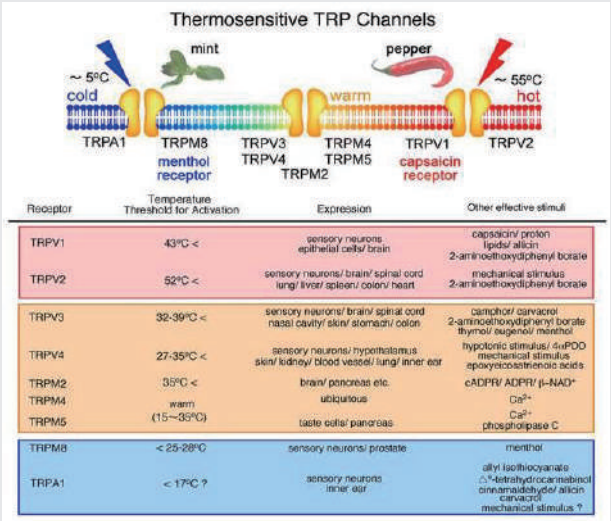
Thermal Biology Group

TOMINAGA, Makoto

We mainly investigate molecular mechanisms of thermosensation and nociception by focusing on TRP ion channels. We are trying to clarify the molecular mechanisms of thermosensation and their physiological significance by focusing on the thermosensitive TRP channels from mammals to insects. We are also trying to clarify the nociceptive mechanisms at peripheral nerve endings by focusing on TRPV1 and TRPA1. We are doing behavioral analyses of mice lacking the thermosensitive TRP channels. Furthermore, we are cloning the thermosensitive TRP channels genes from various species, which would help us to understand the mechanisms of thermosensation in the evolution. We also utilize fruit flies as a model to investigate temperature preference and adaptation, particularly focusing on regulatory roles of lipid components.



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Biomolecular Interaction Research Group

UCHIYAMA, Susumu

We have been studying dynamic protein assembly using native mass spectrometry (native MS) that provides mass of biological complexes such as protein complex formed through non-covalent interactions. With native MS we can obtain the high resolution information on mass of complex molecule, from which stoichiometry of the complex are identified. Assembly of not only biological molecules but also of synthetic molecules has been determined with high accuracy using native MS. Researchers who are highly interested in native MS can potentially ask to perform native MS at this research center under the collaboration scheme.

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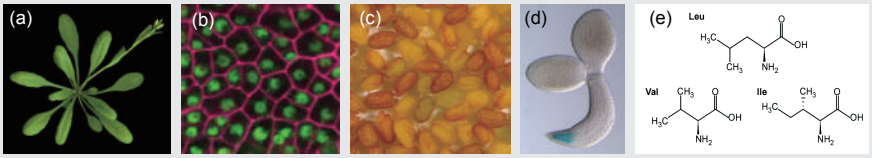
Plant Development and Physiology Research Group

TSUKAYA, Hirokazu / KAWADE, Kensuke

Emerging evidences depict that each developmental process requires specific regulation of metabolism most likely to produce signaling molecules and/or to support the progression itself. Despite an importance, less attention has been paid to this relationship due to an insufficient interaction between development and metabolism research fields. The aim of our laboratory is to understand how metabolic systems are coordinately modulated with developmental progression. To address this, we are carrying out genetic screening using *Arabidopsis thaliana* as a model experimental system to explore as-yet-unknown relationship between development and metabolism. Also, cutting-edge techniques including metabolomics, together with solid biochemistry and molecular biology, are currently working to know the functional significance of specific metabolism in development of multicellular organisms.



(a) A model plant, *Arabidopsis thaliana* (b) AN3 protein (green) is a signaling molecule for proliferation of leaf cells (magenta). (c) The *an3* mutant shows unstable seed pigmentation, suggesting an involvement of this protein also in metabolism. (d) Blue indicates that AN3 is expressed in root tip. (e) Metabolism of branched chain amino acids might be regulated by the AN3 in the root tip.

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- Kensuke Kawade*, Hirokazu Tanimoto, Gorou Horiguchi, and Hirokazu Tsukaya. Biophysical Journal, 113; 1109-1120. (2017)

Biofunctional Systems Construction Research Group

SATO, Koji

The senses of olfaction and gustation are essential chemosensory systems to recognize the tens of thousands of chemical compounds in nature. The genes of olfactory receptors (ORs) encode the large a large family of seven-transmembrane-domain G protein coupled receptors (GPCRs). However insect ORs possess the seven transmembrane topology with the intracellular amino terminus, and comprise the odor-gated ion channels (fig. 1). We focus on the molecular mechanism of signal transduction in chemical senses, which enable the complex neuronal coding of multiple of chemical information.

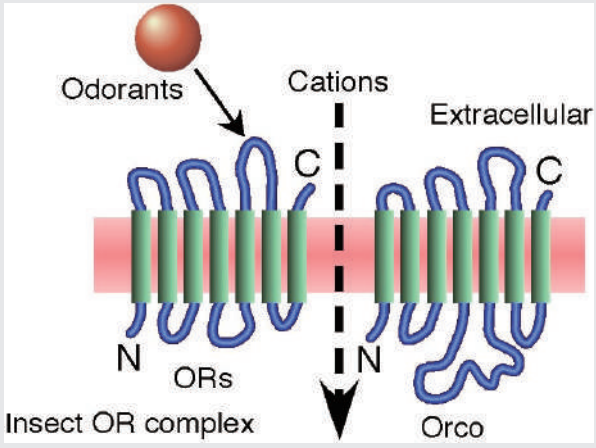

Fig. 1 Schematic model for ligand-gated channel properties of the insect conventional OR + olfactory co-receptor (Orco) complex.

References：

- Sato, K. (correspondence) and Sorensen, P.W. Chemical Senses, 43:249-260. (2018)
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Constructive Biology Group

KURIHARA, Kensuke

Construction of protocells, which are created from simple molecules, has drawn much attention as part of researchers' ongoing exploration of life' s origins and the creation of artificial life. Such protocells are assumed to have replicating systems of information and producing systems of compartments via metabolic systems. As advanced protocell models, vesicles, which are composed of amphiphiles, have been widely used due to similarities in the structure and morphological behavior of biological cell membranes. We aim to construct cell-mimic vesicles from organic chemical and supramolecular approach. In the lecture, I introduce our self-reproducing vesicular system in which the production of the catalyst intertwines with that of the vesicular membrane molecules.

References：

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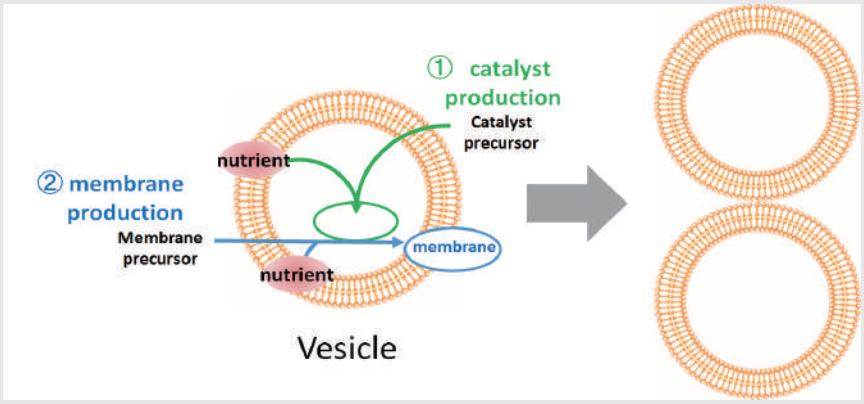
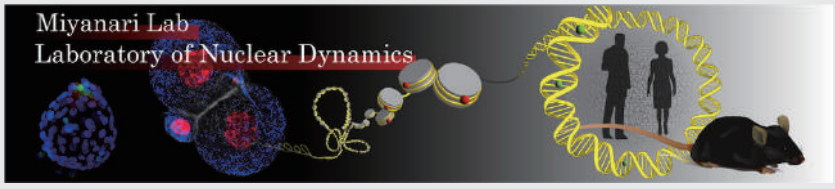


Nuclear Dynamics Group

MIYANARI, Yusuke

We have just open a new lab in early 2014. A fundamental question in biology for us is to understand the mechanisms underlying cell-fate decision. Genomic reprogramming after mammalian fertilization reverts terminally differentiated gametes into toti- or pluripotent state to start a new developmental program. The cell lineage allocation is accompanied by drastic changes in the pattern of gene expression, epigenetic configurations, and nuclear organization. We are interested in a "microscopic" view of the nuclear architecture, which is subnuclear distribution of chromatin and studying functional roles of nuclear dynamics in cell lineage-allocation by deciphering the molecular mechanisms underlying remodeling of nuclear organization and their effects on developmental gene expression, using mouse embryos and ES cells as model systems.



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Live visualization of chromatin dynamics using fluorescent TALEs, Nature Structural & Molecular Biology. 2013 Nov;20(11):1321-4.
#Corresponding authors. Highlighted by Nature Methods.
4 Li Y#, Miyanari Y#, Shirane K, Nitta H, Kubota T, Ohashi H, Okamoto A, Sasaki H. Sequence-specific microscopic visualization of DNA methylation status at satellite repeats
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Control of ground-state pluripotency by allelic regulation of Nanog. Nature. 2012 Feb 12;483(7390):470-3
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Biomolecular Dynamics Observation Group

UCHIHASHI, Takayuki

Dynamic events on a molecular level are essential for a living system because biological molecules fulfil a wide variety of unique functions through conformational change and molecular interactions triggered by binding of ligand/substrate and changes in the external environment. We aim to elucidate function mechanisms of proteins from the aspect of single-molecule dynamics based on direct visualization using high-speed atomic force microscopy (HS-AFM), which enables real-time imaging of individual molecules in action. Further, we carry out functional extensions of the HS-AFM towards imaging dynamics of morphology and mechanical property of a living cell.

References：

- Mori T, et al, Revealing circadian mechanisms of integration and resilience by visualizing clock proteins working in real time. Nat Commun. 9, 3245 (2018)
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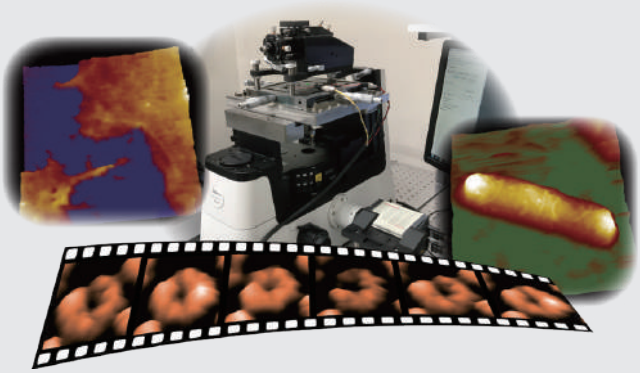

Section for Exploration of Life in Extreme Environments

Deep-Sea and Deep Subsurface Life Research Group

TAKAI, Ken

We look for real limits of life and biosphere and boundary conditions between habitable and uninhabitable in the dark world, namely deep-sea and deep subsurface environments by means of top-rated exploration platforms such as human-occupied submersible vehicle (HOV), remotely operative vehicles (ROV), research vessels including scientific drilling vessels. Naturally observed limits of life and biosphere and fringe functional mechanisms provide significant clues to understanding universal and specific habitability of living forms, finding unique chemical and biological systems established in the long history of evolution and synthesizing novel artificial systems in laboratory and for application.

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- T Nunoura et al, A primordial and reversible TCA cycle in a facultatively chemolithoautotrophic thermophile, Science 359 (6375), 559-563. (2018)
- K Yanagawa et al, Defining boundaries for the distribution of microbial communities beneath the sediment-buried, hydrothermally active seafloor, The ISME journal 11 (2), 529. (2017)
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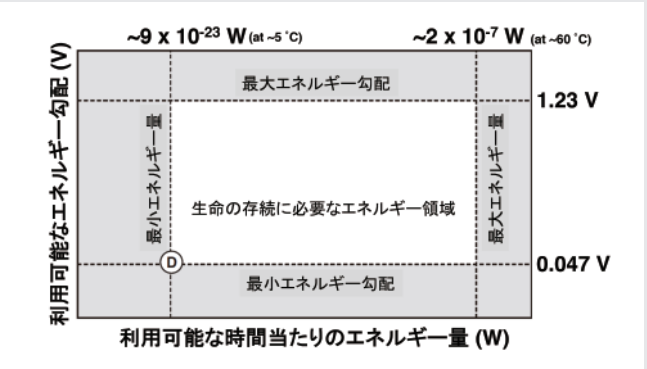

Extreme Environmental Biomolecular Research Group

KATO, Koichi

Organisms living in extreme environments such as deep-sea trenches develop unique ecological adaptation mechanisms. In addition, even in more familiar environments, some organisms develop peculiar adaptation mechanisms to extreme environmental conditions as exemplified by cryptobiosis. We conduct biomolecular analyses to elucidate the molecular processes underlying these biological adaptation mechanisms. Furthermore, we aim to develop biotechnological applications based on our knowledge of biomolecular systems involved in biological processes adapted to extreme environments. Moreover, we exploit extreme environmental conditions such as microgravity in outer space for controlling biomolecular processes including amyloid formation.

References：

- Yagi-Utsumi, M., Sikdar, A., Kozai, T., Inoue, R., Sugiyama, M., Uchihashi, T., Yagi, H., Satoh, T. and Kato, K. Conversion of functionally undefined homopentameric protein PbaA into a proteasome activator by mutational modification of its C-terminal segment conformation, Protein Eng. Des. Sel. 31, 29-36 (2018)
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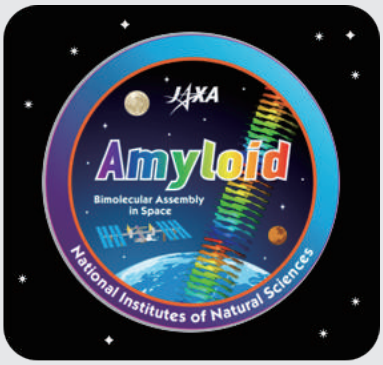
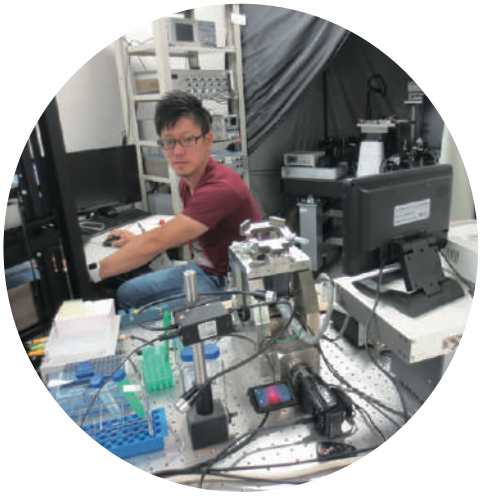


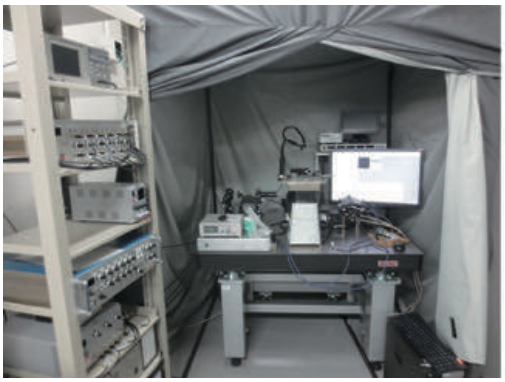
Joint Research Projects of ExCELLS

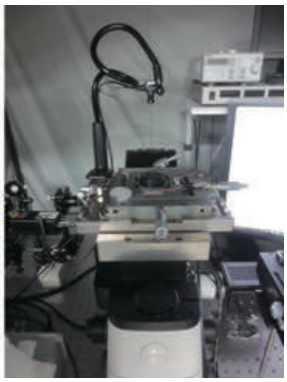
The Exploratory Research Center on Life and Living Systems (ExCELLS) promotes collaborative research with researchers from other institutes and universities. Various researchers can use ExCELLS equipment to perform their own research through joint research projects along with ExCELLS researchers.



ExCELLS Equipments

(1) Combined system of high-speed atomic force microscopy and fluorescence microscopy





(2) Q-TOF mass spectrometer for native MS

Notes

When presenting the results of their joint research project, researchers must note that the results were achieved through the ExCELLS joint research initiative (an example is provided below).

※Example
This research was supported by the Joint Research of the Exploratory Research Center on Life and Living Systems (ExCELLS). (ExCELLS Programme No.***), where *** is your programme number. (The programme number will be provided if your application is successful.)

Travel expenses in Japan may be paid based on the budget set out in the NINS regulations.
Travel expenses in foreign countries will not be reimbursed.

Please refer to the joint research project guideline for other notes.

(3) High-speed live imaging system

(4) Total internal reflection fluorescence (TIRF) microscope

(5) Multifunctional super-resolution fluorescence microscope NEW

Symposium

Frontier Bioorganization Forum 2018

Date
July 8 (Sun) – 11 (Wed), 2018

Venue
Exploratory Research Center
on Life and Living Systems (ExCELLS),
National Institutes of Natural Sciences, Okazaki, Japan
(5-1 Higashiyama Myodaiji, Okazaki, Aichi,
444-8787, Japan)

Organizing Committee
Koichi Kato (ExCELLS, IMS)
Shigetoshi Aono (ExCELLS, IMS)
Motohiro Nishida (ExCELLS, NIPS)
Kazuhiro Aoki (ExCELLS, NIBB)
Maho Yagi-Utsumi (ExCELLS, IMS)

Co-organizers
IMS Asian International Symposium
10th Korea-Japan Seminar on Biomolecular Science

Joint partner
JSPS Grant - in - Aid for Scientific Research on Innovative Areas

ExCELLS Young Scientists Forum 2018

Date
July 10 (Tue), 2018

Venue
Exploratory Research Center on Life
and Living Systems (ExCELLS),
National Institutes of Natural Sciences,
Okazaki, Japan
(5-1 Higashiyama Myodaiji, Okazaki, Aichi,
444-8787, Japan)

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Maho Yagi-Utsumi (ExCELLS, IMS)
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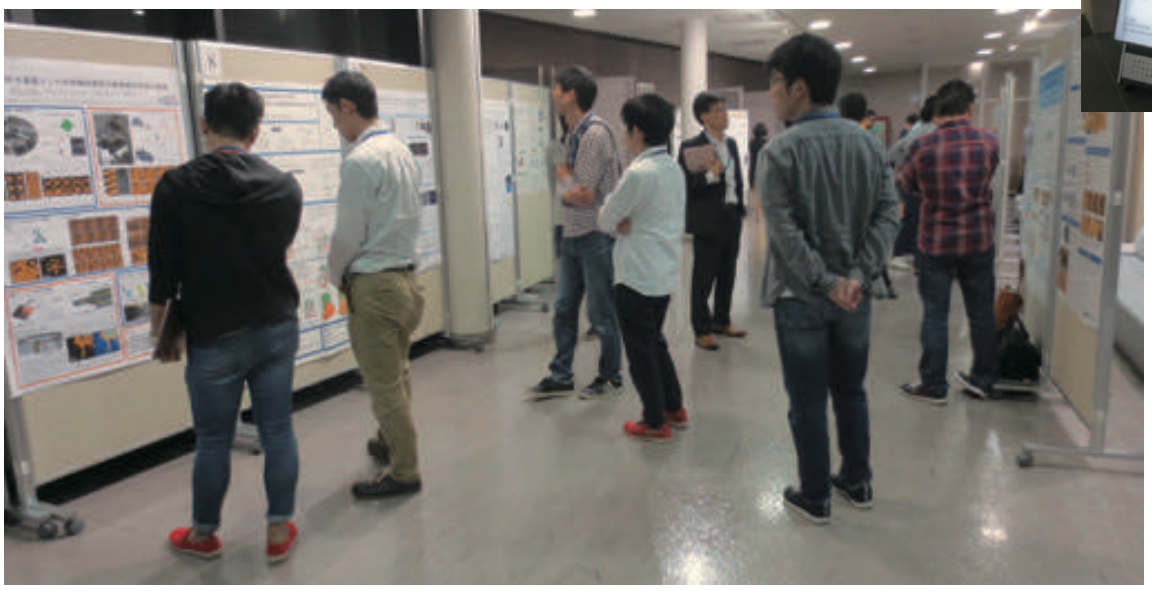
Yohei Kondo (ExCELLS, NIBB)
Haruko Miura (Kyoto University)
Rina Yogo (Nagoya City University)
Taichiro Sekiguchi (SOKENDAI)

Co-organizers
Frontier Bioorganization Forum 2018

Symposium

The 1st ExCELLS Symposium



Date
15th Oct. 2018 (Mon) – 16th Oct. 2018 (Tue)

Venue
Okazaki Conference Center
(Address: Azatenma 8-1, Myodaiji, Okazaki
444-0864, Japan)

Organizing Committee
Motohiro Nishida (ExCELLS, NIPS)
Shin-ichi Higashijima (ExCELLS, NIBB)
Hisashi Okumura (ExCELLS, IMS)

※Language: Japanese

ExCELLS Seminar

The 1st ExCELLS Seminar
Date: 2nd,July, 2018
Speaker: Dr. Satoshi Toda
(Department of Cellular and Molecular Pharmacology
University of California, San Francisco)

The 2nd ExCELLS Seminar
Date:2nd August, 2018
Dr. Ryuji Kawano
(Tokyo University of Agriculture and Technology)

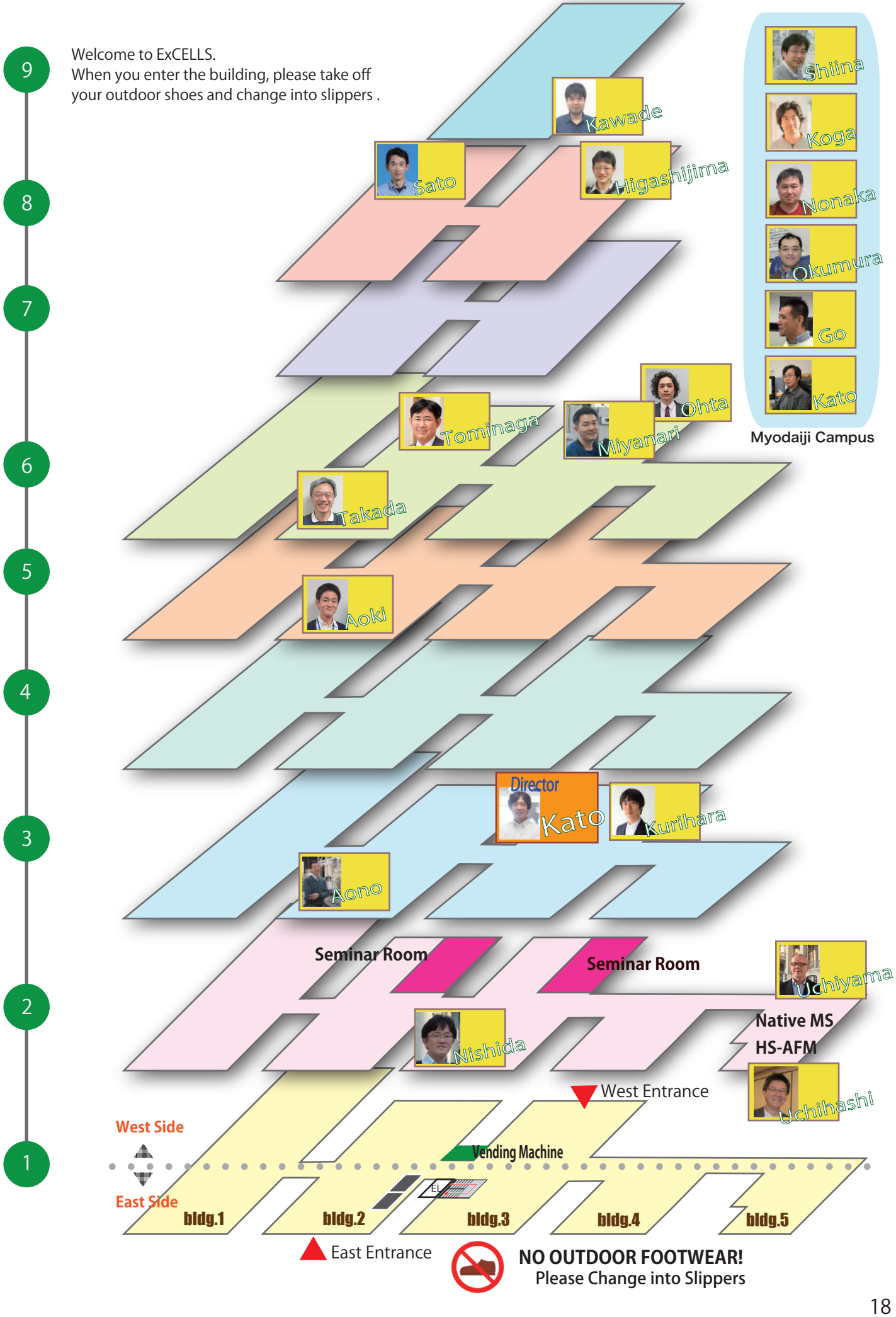
The 3rd ExCELLS Seminar
Date: 21st September, 2018
Dr. Ken Takai
(JAMSTEC)

The 4th ExCELLS Seminar
Date: 21st December, 2018
Prof. Dr. Azusa Kamikouchi
(Nagoya University)

ExCELLS Research Meeting

The 1st ExCELLS Research Meeting
"Dormant and Metabolism Research Meeting"
Date: 15th, November, 2018
Speaker:
Prof. Dr. Yoshifumi Yamaguchi (Hokkaido University)
Dr. Genshiro Sunagawa (Riken)
Prof. Dr. Toshihiko Fujimori (NIBB)
Prof. Dr. Tohru Ishitani / Dr. Masayuki Oginuma(Gunma University)
Dr. Masamitsu Fukuyama (The University of Tokyo)

Welcome to ExCELLS.
When you enter the building, please take off your outdoor shoes and change into slippers .



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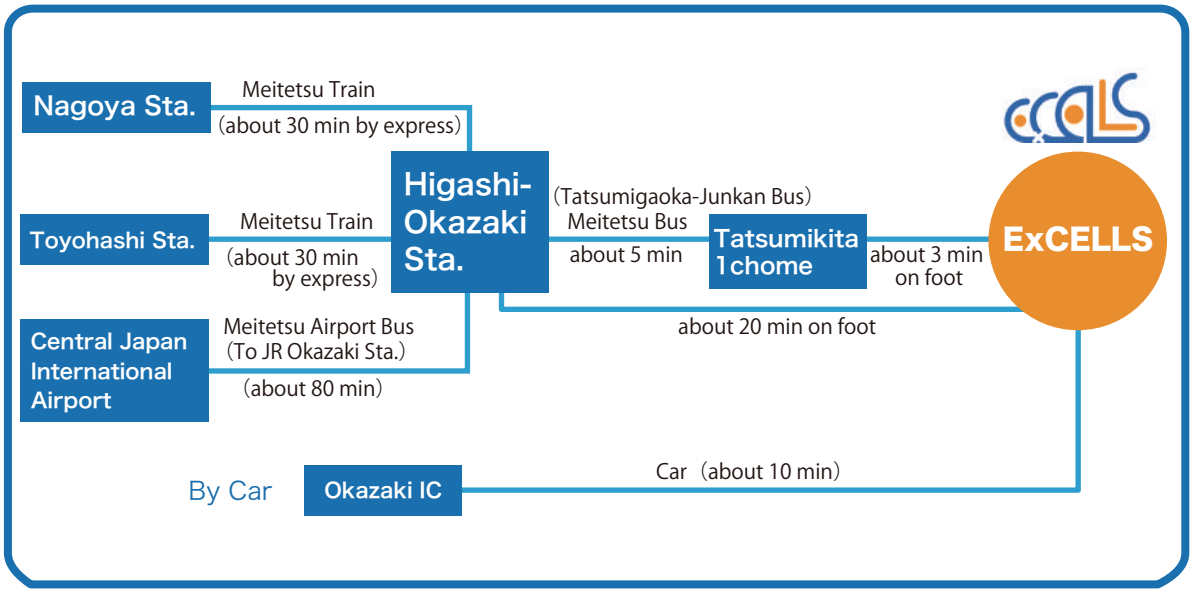
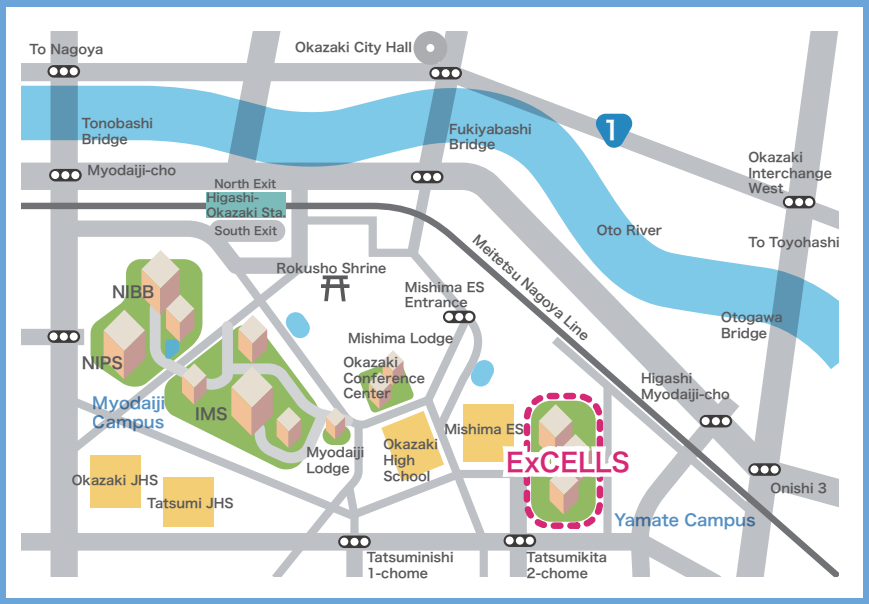


From the south exit of Higashi-Okazaki station,

- By taxi : About 7 min.
- By bus : Take Tatsumigaoka-jyunkan, which departs from No11 bus station, and get off at Tatsumi-kita-1chome (about 5 min), and walk to the east for about 3min.
- On foot : About 20 min.



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Issued in February 2019 Edited by ExCELLS