Graduate School of
Biological Sciences

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SCIENCE and TECHNOLOGY

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Graduate School of Biological Sciences

CONTENTS

Introduction

to the Graduate School of

Biological Sciences

Looking at Cells from the Perspective of Molecules

The Graduate School of Biological Sciences undertakes advanced research to elucidate various functions of microorganisms, plants and animals at the molecular and cellular levels, and clarifies the basic phenomena of life and biological diversity.

In the 21st Century COE Program, we elucidated the dynamic networks of molecules that comprise cells, using information science techniques in exhaustive analyses of genome sequences and protein structures. Based on such advanced fundamental research, the Graduate School of Biological Sciences produces research and development that benefits human well-being and trains researchers for active roles in the international community.

Building on Excellence

The "Global Program for Frontier Biosciences: Adaptation and survival strategies in a changing global environment" was initiated in 2007 as a part of the Global COE Program commissioned by the Ministry of Education, Culture, Sports, Science, and Technology (MEXT). The school developed this project to create a globally pre-eminent center for training researchers capable of participating in the international community, while performing world-leading research in the biological sciences. With the outstanding results of this program as a start, we continue to forge ahead to further advance our school's position in the international science community.

Active and high-level faculty and staff

Our dynamic research and education programs are led by internationally active faculty. The Graduate School of Biological Sciences is one of the top institutes in attracting funds such as Grants-in-Aid for scientific research and the COE Program from the Japan Society for the Promotion of Science and Japanese government ministries, showing that our faculty and staff are of high repute both inside and outside Japan.

Abundant research facilities

Each department is equipped with a variety of state-of-the-art equipment. Furthermore, shared equipment on a par with the most advanced available for biological science research in Japan, is provided at numerous locations within the School.

Graduate school education with a comprehensive curriculum

We provide two graduate courses to meet students' needs for their future careers: a two-year Bio-Expert course, and a five-year Frontier Bio course. We also offer an international masters course that is taught completely in English, and a wide range of lectures covering the diverse fields of biological sciences.

Support for student research and life

We have a strong support system for students to enable them to engage in research without worrying about basic needs. We offer Global COE funding as well as scholarships from the Japan Student Services Organization and other public and private entities, and TA and RA funds for distinguished students in the doctoral program.

New education system for the graduate university

NAIST's efforts to reform graduate university education have been consecutively recognized in programs promoted by MEXT: the Initiatives for Attractive Education in Graduate Schools (2005–2006), the Support Program for Improving Graduate School Education (2007–2009), and the Global Initiatives Program for Promoting Overseas Collaborative Research Toward Graduate Education in Biological Science, Nano-science, and Information Technology (2011-2016). With support from these programs, NAIST helps students to develop autonomous and international outlooks as part of a graduate university education that is unparalleled in Japan.

Plant Science Research and Education Promotion Project

Under the Project for the Promotion of Plant Science Education between 2005 and 2009 and continuing with the Plant Science Research and Education Promotion Project from 2010, NAIST has begun to function as a nationwide center for the networking of leading plant scientists, in order to promote advanced education in plant science through graduate-level educator collaboration.

Research and Education Center for Genetic Information

We manage and operate campus-wide joint education and research facilities for radioisotope, animal and plant experiments at the Center. The Radioisotope Facility is responsible for the safety of radioisotopes used throughout NAIST as well as for user training. The Animal Experimentation Facility houses small animals and provides training for users. It also creates various transgenic mice to support research. The Greenhouses comprise both open and closed green-houses. This facility houses the individual plants necessary for research activities, including transgenic plants.

These facilities are an essential resource in advanced biological sciences. Technicians and other expert staff are employed to make sure the Center operates efficiently.

Graduate School of Biological Sciences

Departments & Faculty

Department of Plant Biology			
Laboratory	**Professor**	**Associate Professor**	**Assistant Professor**
Plant Molecular Genetics	Ko SHIMAMOTO		Hiroyuki TSUJI, Yoji KAWANO, Ken-ichiro TAOKA
Intercellular Communications	Seiji TAKAYAMA		Megumi IWANO, Yuko WADA, Kohji MURASE
Plant Cell Function	Takashi HASHIMOTO	Keiji NAKAJIMA	Takehide KATO, Tsubasa SHOJI
Plant Metabolic Regulation	Taku DEMURA		Ko KATO, Arata YONEDA
Plant Growth Regulation	Masaaki UMEDA		Yoko OKUSHIMA
Plant Morphological Dynamics	Masao TASAKA		Masahiko FURUTANI
Plant Differentiation and Morphogenesis	Akiho YOKOTA		Hiroki ASHIDA, Yuri MUNEKAGE
Plant Developmental Biology		Mitsuhiro AIDA	

Department of Biomedical Science			
Laboratory	**Professor**	**Associate Professor**	**Assistant Professor**
Molecular and Developmental Biology	Yoshiko TAKAHASHI	Kohsuke KATAOKA	Daisuke SAITOU
Molecular Signal Transduction	Hiroshi ITOH		Norikazu MIZUNO, Tetsuo KOBAYASHI
Neuronal Cell Morphogenesis		Naoyuki INAGAKI	
Functional Neuroscience	Sadao SHIOSAKA	Shoji KOMAI	Hideki TAMURA
Gene Function in Animals	Masashi KAWAICHI	Yasumasa ISHIDA	Chio OKA, Eishou MATSUDA
Molecular and Cell Genetics	Kenji KOHNO	Yukio KIMATA	Akio TSURU, Michiko SAITO, Kohta YANAGITANI
Tumor Cell Biology	Jun-ya KATO		Noriko KATO

Department of Systems Biology			
Laboratory	**Professor**	**Associate Professor**	**Assistant Professor**
Microbial Molecular Genetics	Hisaji MAKI	Masahiro AKIYAMA	Satoko MAKI, Asako FURUKOHRI
Systems Microbiology	Hirotada MORI		Toru NAKAYASHIKI
Genomics of Bacterial Cell Functions	Naotake OGASAWARA		Kazuo KOBAYASHI, Taku OSHIMA, Shu ISHIKAWA
Cell Signaling	Kaz SHIOZAKI		Hisashi TATEBE
Applied Stress Microbiology	Hiroshi TAKAGI		Nobuyuki YOSHIDA, Iwao OHTSU
Structural Biology	Toshio HAKOSHIMA		Ken KITANO, Yoshinori HIRANO
Biodynamics and Integrative Biology	Narutoku SATO (Thomas N. Sato)		Takashi AKANUMA, Norio TAKADA, Kyoji URAYAMA
Gene Expression Research	Yasumasa BESSHO		Takaaki MATSUI, Yasukazu NAKAHATA

Plant Global Educational Project			
Laboratory	**Professor**	**Associate Professor**	**Assistant Professor**
Plant Protein Analysis	Masao TASAKA	Noriko INADA, Tetsuya KURATA, Yoichiro FUKAO	Masayuki FUJIWARA

Affiliate Laboratories		
Laboratory	**Professor**	**Associate Professor**
Molecular Genetics of Human Diseases (with Osaka Medical Center for Cancer and Cardiovascular Diseases)	Kikuya KATO	
Neuronal Network Formation (with Osaka Bioscience Institute)	Kazuo EMOTO	
Tissue Development Dynamics (with the Center for Developmental Biology, RIKEN)		Erina KURANAGA
Cell Growth Control (with the Center for Developmental Biology, RIKEN)		Takashi NISHIMURA
Molecular Microbiology and Genetics (with Research Institute of Innovative Technology for the Earth (RITE))	Hideaki YUKAWA	

Laboratory

Plant Molecular Genetics

▶ URL: http://bsw3.naist.jp/eng/courses/courses101.html

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Outline of Research and Education

Rice is an important source of food for humans. Its genome has been completely sequenced recently. Furthermore, gene transfer is easy with rice, and many mutants are available. These features make rice a suitable material for studies of molecular biology. Our laboratory, “Plant Molecular Genetics” is aimed at clarifying various phenomena of plants at the molecular level, using rice as a material. It is also aimed to apply research outcomes for rice improvement in the future.

The research at this laboratory employs the following techniques: gene isolation by map-based cloning, transformation, RNA interference (RNAi), isolation of interacting proteins by the yeast two-hybrid method and affinity chromatography, proteomics using mass spectrometry.

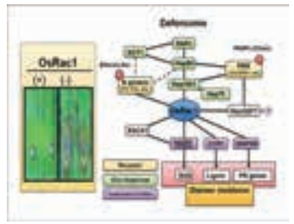

Fig.1 The Defensome complex containing small GTPase OsRac1 plays important roles in rice innate immunity

Major Research Topics

1. Plant innate immunity
 1) Role of small G-protein Rac in plant immunity
 2) Signal transduction pathways in plant immunity
2. Regulation of flowering
 1) Searching for the flower inducing hormone “florigen”
 2) Induction of flowering by day length (photoperiod)
3. Rice improvement by genetic engineering
 1) Disease-resistant rice
 2) Modification of flowering time
4. Bio-imaging of plant cells
 1) FRET biosensor
 2) In vivo imaging of protein-protein interaction

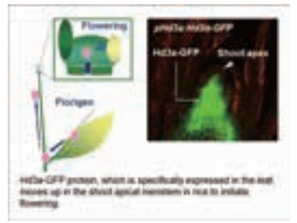

Fig.2 Florigen: the mobile flowering signal

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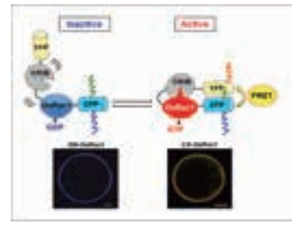

Fig.3 FRET biosensor monitors the activation state of OsRac1, a key regulator of rice innate immunity

Laboratory Intercellular Communications

▶ URL: http://bsw3.naist.jp/eng/courses/courses102.html


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Outline of Research and Education

Plants and animals have evolved multicellularity and cell-to-cell communication systems independently, each starting a different unicellular eukaryote, which in turn evolved from a common unicellular eukaryotic ancestor. Therefore, the mechanisms of signaling between cells in plants and animals have both similarities and differences. Our overall research interests are to understand these common and unique communication mechanisms working in plant cells.

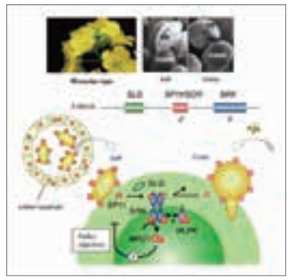
Fig.1 Mechanism for self-incompatibility in the Brassicaceae

Major Research Topics

1. Molecular mechanisms for plant self-incompatibility
 1) Self-recognition system in the Brassicaceae (Fig. 1)
 2) Nonself-recognition system in the Solanaceae (Fig. 2)
2. Molecular mechanisms for plant sexual reproduction process.
3. Mechanisms for epigenetic gene regulation in plants (Fig.3)

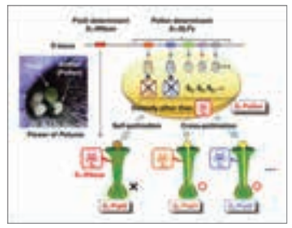
Fig.2 Mechanism for self-incompatibility in the Solanaceae

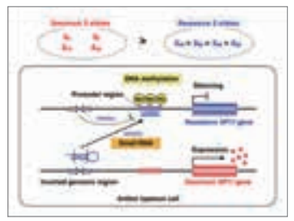
Fig.3 Models for epigenetic control of dominant/recessive relationship

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Laboratory Plant Cell Function

▶ URL: http://bsw3.naist.jp/eng/courses/courses103.html


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Outline of Research and Education

We are conducting extensive research, ranging from basic to applied, concerning the cellular function, signal transduction and regulation of gene expression in higher-plants, making effective use of molecular genetics and imaging technologies on Arabidopsis thaliana, tobacco, and tomatoes.

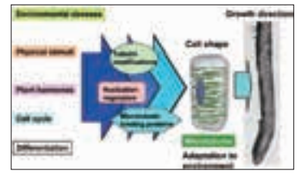
Fig.1 The plant microtubule cytoskeleton remodels in response to developmental and environmental signals, and controls plant cell shape

Major Research Topics

1. Dynamic reorganization of microtubule cytoskeletons in response to environmental stimuli and during plant growth
 1) Pattern formation of bio-polymer networks
 2) Regulators of microtubule dynamics
 3) Left-right asymmetry establishment in cell shape

2. Molecular mechanisms of cell differentiation and reprogramming
 1) MicroRNA-mediated developmental signaling
 2) Mechanisms of cell reprogramming during embryogenesis
 3) Cell differentiation control in the root meristem

3. Biosynthesis of bio-active natural products
 1) Enzymes and transporters for nicotine in tobacco
 2) Herbivory activation of wound-signaling pathways for defense compound biosynthesis
 3) Novel natural products in crop plants

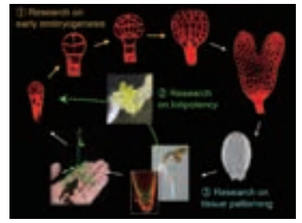
Fig.2 Beautiful tissue patterns are formed from a single cell, the zygote, through highly organized cell division sequences. These tissue patterns are essential for plant functions, such as photosynthesis and nutrient uptake.

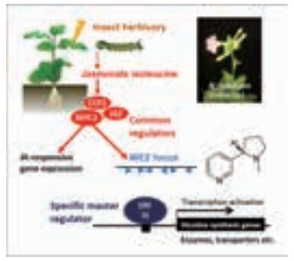
Fig.3 Jasmonate-responsive ERF transcription factor genes clustered at NIC2 locus regulate nicotine biosynthesis in tobacco.

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Laboratory Plant Metabolic Regulation

▶ URL: http://bsw3.naist.jp/eng/courses/courses104.html



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Outline of Research and Education

Our laboratory is engaged in research and education pertaining to the biotechnology needed to resolve the issues for human beings in the 21st century such as food, environments and energy. Using methods of molecular biology based on genomic information, we are clarifying the mechanism for regulation of gene expression in plants and molecular breeding of stress-resistant plants and trees making use of biological functions.

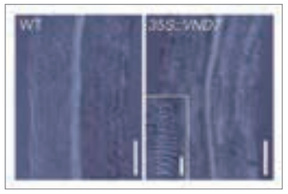

Fig.1 VND7 acts as a key regulator of the xylem vessel differentiation Overexpression of VND7 induces transdifferentiation of epidermal cells into xylem vessel elements with spiral structure of secondary wall thickening (arrows) in hypocotyle. Bar=100 μm.

Major Research Topics

1.Analysis of molecular mechanism controlling xylem cell differentiation

2.Molecular and cell biological approaches to trees

3.High-efficient expression systems of transgenes in higher plants

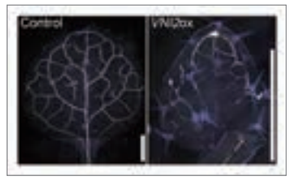

Fig.2 VNI2 is a negative regulator of the xylem vessel differentiation VNI2 has been isolated as an interacting protein with VND7. The discontinuous structure of xylem vessels is observed in VNI2 overexpression line. Bar = 1 mm.

Fig.3 Molecular breeding for obtaining trees with useful traits

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Laboratory Plant Growth Regulation

▶ URL: http://bsw3.naist.jp/eng/courses/courses105.html


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Outline of Research and Education

Because plant cells are surrounded by a rigid cell wall, they cannot - unlike animal cells - move within organs. Therefore, plants control cell division in a precise, spatiotemporal manner to achieve proper development of organs. However, little is known about how the cell cycle is regulated during morphogenesis and under various environmental conditions. We focus on the molecular mechanisms underlying cell cycle control in response to internal and external signals, such as phytohormones and environmental stresses. Our studies will broaden our understanding of plant survival strategies, and provide insights for molecular breeding that will yield an increase of plant biomass.

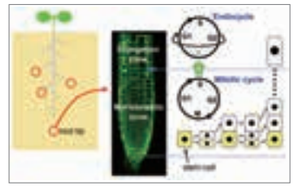

Fig.1 Cell cycle regulation in root growth.

Major Research Topics

1. Cell cycle regulation in root growth (Fig. 1)
 1) Hormonal control of the transition from the mitotic cycle to the endocycle
 2) Time-lapse imaging of the cell cycle in different cell types
2. DNA damage signaling in roots (Fig. 2)
 1) DNA damage signaling mediated by the transcription factor SOG1
 2) Crosstalk between DNA damage response and phytohormone signaling
3. Control of organ size by adjusting cytokinin biosynthesis in the vasculature (Fig. 3)
4. Developing technologies for plant productivity improvement by inducing DNA polyploidization

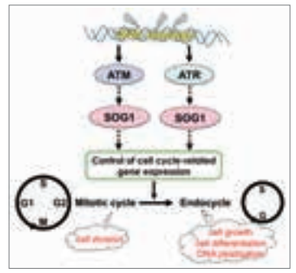

Fig.2 DNA damage signaling in plants.

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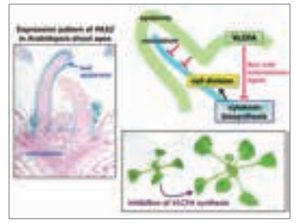

Fig.3 Epidermis-derived signals control organ size. VLCFA, very-long-chain fatty acids; *PAS2, PASTICCINO2.*

Laboratory

Plant Morphological Dynamics

▶ URL: http://bsw3.naist.jp/eng/courses/courses106.html

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Outline of Research and Education

During embryogenesis in higher plants, special tissues called the shoot and root meristems are formed at the upper and lower ends, respectively. After germination, the shoot meristem forms above-ground organs such as leaves, stems and floral organs, while the root meristem produces underground roots. Both genetic controls and diverse external environmental factors such as light or gravity influence the formation of the plant body. By using Arabidopsis thaliana, a model crucifer plant suitable for molecular genetic analyses, we are studying the molecular mechanisms that regulate plant development.

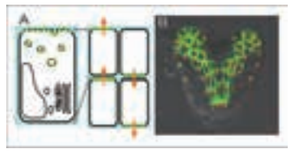

Fig.1 (A) Auxin efflux carriers (green) are localized in the plasma membrane with polarity and auxin is transported to a neighboring cell (orange arrow). (B) Localization of GFP-tagged auxin efflux carrier (green) and presumptive auxin flows (orange arrows) in Arabidopsisembryo.

Major Research Topics

1. Mechanisms of polar auxin transport

2. Formation and function of the shoot meristem

3. Molecular mechanisms for auxin-dependent gene transcription

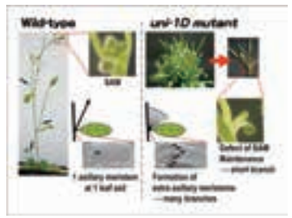

Fig.2 Wild-type Arabidopsis normally forms one axillary mersitem (AM) at each leaf axil (arrowhead) and as a result one branch elongates there (arrow). On the other hand, uni-1D mutants form multiple AMs at each axil (arrowheads), resulting in formation of many branches. Hence, the shoot apical meristem (SAM) at tips of branches of uni-1D plants displays low activity, resulting in short branches.

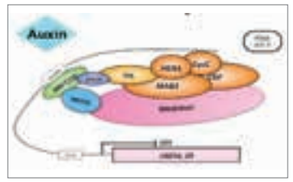

Fig.3 A schematic diagram of auxin-dependent transcription. The transcription factor AUXIN RESPONSE FACTOR (ARF) binds to an auxin-responsive element AuxRE in the promoter region of target genes. A mediator complex transmits information from the ARF to RNA polymerase II.

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Laboratory

Plant Differentiation and Morphogenesis

▶ URL: http://bsw3.naist.jp/eng/courses/courses107.html

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Outline of Research and Education

Our research focuses on the photosynthetic mechanism and its environmental responses. Our research has three projects which involve (1) the photosynthetic CO2-fixing enzyme, RuBisCO, (2) the evolutional process of C4 photosynthesis, and (3) the simultaneous improvement of the sink and source organ functions. Based on our research results, we are trying to increase plant photosynthetic capacity and productivity by improvement of photosynthetic mechanisms.

Fig.1 Outline of our research

Major Research Topics

1. CO2-fixing enzyme, RuBisCO (Fig. 2)

2. Evolutional process of C4 photosynthesis(Fig.3)

3. Simultaneous improvement of the sink and source organ functions.

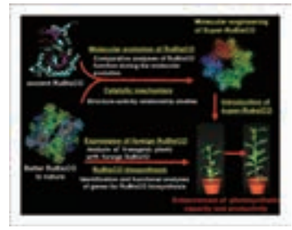

Fig.2 RuBisCO research project

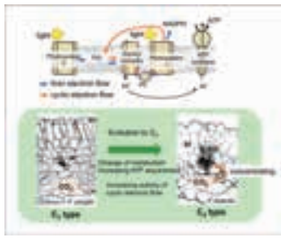

Fig.3 Evolutional process of C4 photosynthesis

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Laboratory Plant Developmental Biology

▶ URL: http://bsw3.naist.jp/eng/courses/courses108.html

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Outline of Research and Education

Why can plants continuously grow upwards throughout their lifetime? How do plant organs such as leaves and floral organs acquire their diverse shapes that we see around us? To answer these questions, we focus on a small tissue called the shoot meristem, which is located at the tip of the stem (Fig 1). The shoot meristem contains a group of undifferentiated cells in its center. These cells proliferate to produce differentiated organs while they renew themselves to maintain their entity. Cells in the meristem thus possess characteristics of "stem cells", a common strategy for generating complex structures in multicellular organisms. The self-maintaining ability of the meristem is remarkable: in some species, its activity can last for more than a thousand years to produce a tall tree that reaches 100 meters in height. The activity of the shoot meristem is modified upon developmental and environmental cues so that it can produce appropriate types of organs with different shapes. The aim of our research is to understand molecular and cellular mechanisms that control the activity of this fascinating tissue, using the model plant *Arabidopsis thaliana*.

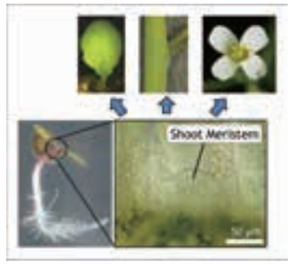

Fig.1 Shoot meristem is the main source of all aerial organs, such as leaves, stems and flowers.

Fig.2 Left: *Arabidopsis* embryo at the globular stage. The arrowhead indicates the site of shoot meristem formation.
Center: Localization of a protein (green) encoded by one of the CUC1 and CUC2 downstream genes in the heat stage embryo.
Right: A mutant that lacks both CUC1 and CUC2 activity. Cotyledons are fused and no shoot meristem is formed.

Fig.3 Top: Although homeotic genes are known to turn a leaf into individual floral organs, how they do this is still largely unknown.
Bottom left: The shoot meristem (central dome) produces floral meristems.
Bottom right: PUCHI protein (green) marks two early flower primordia successively produced from the shoot meristem.

Major Research Topics

1. Shoot meristem establishment during embryogenesis
2. Flower development and meristem activity
3. Specification and morphogenesis of carpels

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Laboratory Molecular and Developmental Biology

▶ URL: http://bsw3.naist.jp/eng/courses/courses201.html

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Outline of Research and Education

We attempt to reveal the molecular mechanisms of cell differentiation and maintenance of their specific functions, particularly focusing on the control of gene expression, intra- and inter-cellular signaling, and cell migration. Our goal is to understand how cells such as pancreatic β-cells, parathyroid cells, and germ cells are formed and how breakdown of the molecular system induces diseases such as diabetes and cancer.

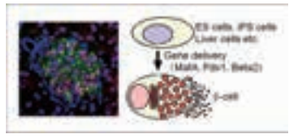

Fig.1 (left) Immunostaining of pancreatic islet of a mouse. MafA (magenta) is found only in β-cells that express Insulin (green). (right) An example of cell-reprogramming approach to convert ES or iPS cells to functional β-cells.

Major Research Topics

1. Pancreatic β-cell differentiation and diabetes

2. Oncogenic function of Maf transcription factors

3. Primordial germ cell migration in avian embryos

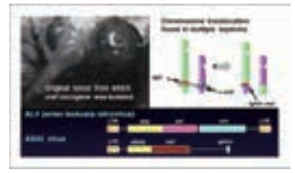

Fig.2 Original tumor formed in a chicken leg (left) from which AS42 retrovirus carrying maf oncogene has been isolated (bottom). Later, maf was found to induce multiple myeloma in humans by chromosome translocation (right).

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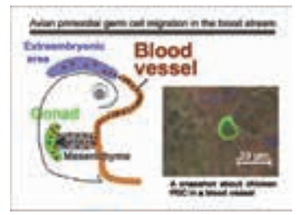

Fig.3 We are currently investigating the mechanism underlying extravasation (cell emigration from blood vessels), which avian PGC undergoes.

Laboratory — Molecular Signal Transduction

▶ URL: http://bsw3.naist.jp/eng/courses/courses202.html



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Outline of Research and Education

Signal transduction is indispensable for organ development and homeostasis. Hormones and neurotransmitters induce a variety of cell responses mediated through membrane receptors and intracellular signaling pathways. Impairment of the signal transduction often causes disease. Many drugs targeted at the signal components are widely used today. Our laboratory is interested in cellular signaling systems with special emphasis on heterotrimeric G proteins. In our laboratory, faculty and graduate students are dedicated to cutting-edge scientific research and work towards a better understanding of how the human body functions and to alleviate human disease.

Fig.1 Signal transduction mediated by G protein-coupled receptor

Major Research Topics

1. Cellular functions and regulatory mechanisms of G protein signaling
2. Molecular mechanisms of self-renewal, differentiation, and migration of neural stem cells
3. Monoclonal antibodies against orphan adhesion GPCRs involved in tumorigenesis and neural function
4. Molecular and cellular mechanisms that regulating formation of primary cilia in mammalian cells

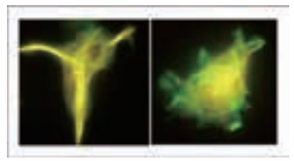

Fig.2 G protein/PKA signal-regulated dynamics of cytoskeleton in neuronal progenitor cells

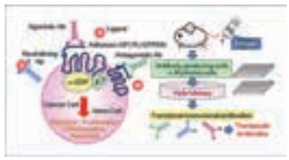

Fig.3 Monoclonal antibody against orphan GPCR as a tool for signal analysis

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Laboratory — Neuronal Cell Morphogenesis

▶ URL: http://bsw3.naist.jp/eng/courses/courses204.html

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Outline of Research and Education

During morphogenesis, biological systems self-organize their simple shape into more complicated and beautiful ones. The goal of our studies is to understand deeply such a miraculous phenomenon, cellular morphogenesis. There are fundamental questions to be answered. Symmetry breaking (change of a symmetric shape to an asymmetric one) is an essential process of morphogenesis: theoretical models suggest that feedback loop and lateral inhibition may be involved in it, but how do the cellular molecules indeed give rise to these processes? Generation of mechanical forces is required to create cellular shape, but how? How do cells sense cellular length and size in order to regulate their size and morphology? Transport and diffusion of intracellular molecules would create unhomogeneous distribution: Do they play a role in cellular pattern formation? Is stochasticity utilized in cellular morphogenesis? All these questions are fascinating for us.

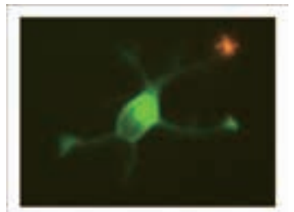

Fig.1 Shootin1 is a key molecule involved in neuronal symmetry breaking

To untangle these issues, our group is focusing on neuronal morphogenesis and the proteins Shootin1, Shootin2 and Singar1, which we identified by proteome analyses. We are analyzing the molecular mechanisms for neuronal polarization, axon/dendrite formation and cell migration, using up-to-date methods including systems biology. We expect that these analyses will give us a new window into therapeutic strategies for neuronal diseases, such as nerve injury.

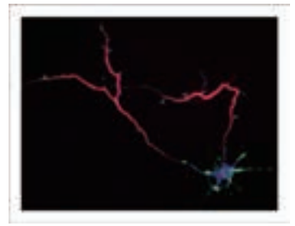

Fig.2 Singar knockdown leads to formation of surplus axons

Fig.3 Diffusion-based neurite length sensing by shootin1

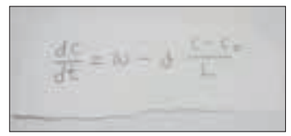

Fig.4 An equation to describe neurite length sensing by shootin1

Major Research Topics

1. Axon/dendrite formation, neuronal polarization and migration.
2. Generation of mechanical forces for neurite outgrowth and migration.
3. Sensing of cellular length and size.
4. Symmetry breaking.

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Laboratory Functional Neuroscience

▶ URL: http://bsw3.naist.jp/eng/courses/courses205.html



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Outline of Research and Education

1. Our current research and education are focused on the neural functions of the hippocampus, amygdala, and prefrontal cortex using techniques of neuroanatomy, electrophysiology, biochemistry and behavioral neuroscience.
Major topics are (1) the mechanisms of structural plasticity in the neuronal circuits for memory and learning, (2) a mechanism for signal transduction in the limbic system, and (3) a mechanism for synaptic tagging through molecular based studies of synaptic potentiation and efficiency control.
2. To study the neural activity and the neuronal plasticity observed during animal behaviors depending on its experiences, it is necessary to perform multi-faceted research covering extensive fields, ranging from molecules to behaviors. At our laboratory, we are attempting to achieve this goal by taking single-cell recordings from the brains of behaving animals, making use of patch clamping in vivo.

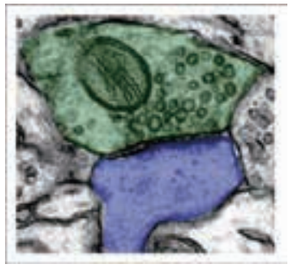

Fig.1 Electron microscopic profile of a synapse in the hippocampal pyramidal layer. The presynapse is colored green and the postsynapse is blue.

Major Research Topics

The synaptic contacts are composed of cell adhesion and extracellular matrix molecules (CAMs and ECMs) which are sensitive to intracellular and extracellular signaling. It has been unveiled that proteases cleave CAMs and ECMs and the cleaving process might regulate the synaptic potentiation relating cortical and limbic brain functions. In our laboratory, several novel secretory-type serine proteases were cloned and we have analyzed their functions in detail. To date, we have demonstrated that neuropsin (also referred to as klk8) plays a significant role in the regulation of early phase of long-term potentiation (E-LTP), and regulates intracellular signals of the limbic brain.
However, there are many unresolved questions over how this protease affects the signals from outside into inside of the cells and how it regulates the synaptic function via proteolysis processing. Moreover, it is unknown what roles this mechanism plays in acquisition and/or retention of memories. Our research is currently in progress to resolve these questions concerning the molecular mechanisms of behavioral memory.

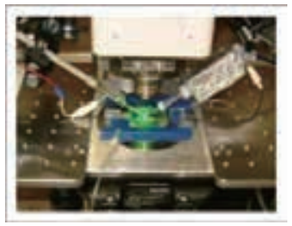

Fig.2 Electrophysiological analysis f of synaptic functions. Electrodes are inserted into a hippocampal slice and membrane currents or potentials are recorded.

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Fig.3 Behavioral analysis of memory and learning. Animals (mice) are given various learning tasks and the course of their learning is observed in detail.

Laboratory Gene Function in Animals

▶ URL: http://bsw3.naist.jp/eng/courses/courses206.html


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Outline of Research and Education

Many human diseases are caused by disturbances in gene function and expression. Understanding of gene function and modes of regulation is important to developing new cures for diseases. We are identifying and analyzing genes involved in the onset of human diseases. We are especially interested in diseases closely related to aging processes. Furthermore, in view of the post-genomic age, we are developing new techniques capable of rapid and systematic analysis of animal gene function through experiments involving randomized gene destruction of ES cells. We conduct research on one particular gene isolated by this technique. This gene encodes a novel methyl DNA binding protein and regulates various aspects of human development.

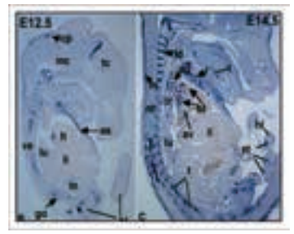

Fig.1 HtrA1 gene involved in the onset of arthritis is primarily expressed in the skeletal system of mouse fetuses and regulates the differentiation of cells in cartilage and bone.

Major Research Topics

1. Research on genes which are involved in the onset of human diseases, such as osteoarthritis, age-related macular degeneration, familiar brain infarction, preeclampsia and cerebellar ataxia (Fig. 1)
2. Development and application of the gene trap technique which enables efficient, random disruption of every mouse gene in ES cells (Fig. 2)
3. Functional analysis of methylated DNA binding transcription factors with regard to the regulation of cell differentiation, proliferation, and carcinogenesis (Fig. 3)

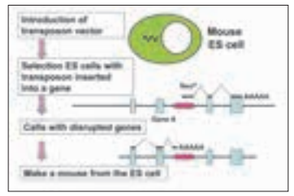

Fig.2 Gene trap technique. Every gene in the mouse ES cell is randomly disrupted by insertion of transposon DNA. The phonotype of the mouse produced from the ES cell will be analyzed to reveal the function of the gene.

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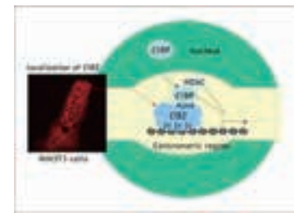

Fig.3 CIBZ suppresses transcription by recruiting CtBP (a transcription suppression cofactor used commonly for various transcription suppressing mechanisms) and histone deacetylase to the heterochromatic area of the centromere.

Laboratory Molecular and Cell Genetics

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Outline of Research and Education

The endoplasmic reticulum (ER) is an important organelle in which newly synthesized secretory and membrane proteins are correctly folded and assembled. We are conducting studies, with a goal of clarifying the signal transduction pathways (UPR: unfolded protein response) from the ER to cytosol/nucleus, the quality control of protein folding in the ER, and the physiological roles of UPR at the molecular, cellular, and individual animal level. We are also interested in the study of diseases caused by UPR dysfunction.
In other work, we have developed a simple and highly sensitive method for conditional cell ablation in transgenic mice, called "toxin receptor-mediated cell knockout (TRECK)". We have created mouse models of hepatitis and diabetes mellitus and are conducting studies on regenerative medicine by using these TRECK-Tg mice.

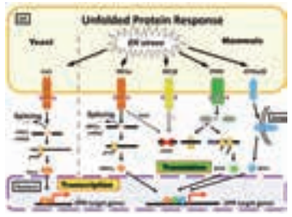

Fig.1 Unfolded Protein Response in yeast and mammals.

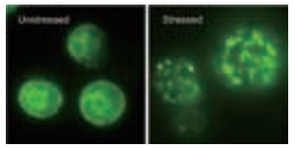
Fig.2 Cluster formation (right) of yeast Ire1 under ER stress.

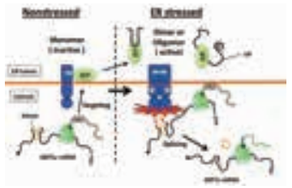
Fig.3 Unconventional splicing of *XBP1* mRNA in mammalian IRE1α -XBP1 pathway.

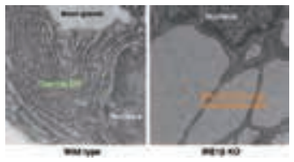
Fig.4 The ER in IRE1β KO goblet cells is distended with misfolded mucin accumulation.

Major Research Topics

1. ER quality control and Unfolded Protein Response (UPR)
   1) ER stress-sensing mechanism by IRE1.
   2) Molecular analysis of unconventional splicing in mammals.
   3) Physiological functions of IRE1α and IRE1β using KO mice.
   4) Analysis of a novel ER chaperon molecule DNAJB12.
2. Regenerative medicine, using TRECK-Tg mice

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Laboratory Tumor Cell Biology

▶ URL: http://bsw3.naist.jp/eng/courses/courses208.html


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Outline of Research and Education

We focus on the molecular mechanisms controlling proliferation, differentiation, and death of mammalian cells, and study the connection between cell cycle progression and oncogenesis, as well as differentiation, proliferation, and leukemogenesis in hematopoietic cells. The findings can be applied to regenerative medicine and cancer research. We use the following experimental systems: (1) an in vitro culture system using mouse and human cell lines, (2) an in vitro differentiation system using ES cells and primary cultures, and (3) a mouse model system using knockout mice and transgenic mice.

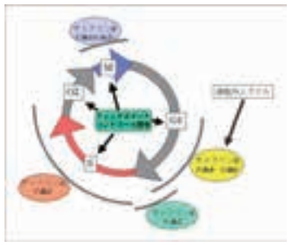
Fig.1 Cell cycle and cyclin/Cdk complexes

Major Research Topics

1. Cell cycle control and oncogenesis

2. Leukemogenesis

3. Hematopoietic stem cells

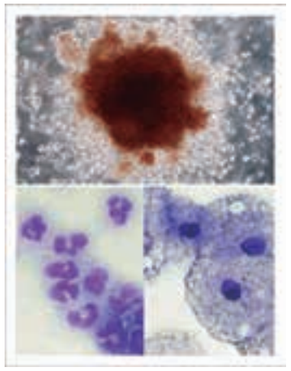
Fig.2 A group of erythrocytes and leukocytes (upper), neutrophils (lower left) and macrophages (lower right), which were induced to differentiate from ES cells in vitro.


Fig.3 A chimeric mouse generated by infusion of genetically modified ES cells

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Laboratory Microbial Molecular Genetics

▶ URL: http://bsw3.naist.jp/eng/courses/courses301.html


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Outline of Research and Education

At our laboratory, we have been studying how genetic information is precisely transmitted from parent cells to daughter cells and, conversely, how mutation is induced by inaccurate transmission of genetic information. To approach these questions, it is important to understand molecular mechanisms of genomic stability and molecular functions of DNA replicative apparatus. We are also exercising our best efforts in the international education of young students who are highly interested in basic issues related to DNA transaction and the molecular mechanisms of organism evolution. We want to help our laboratory members become globally active individuals who act and think independently.

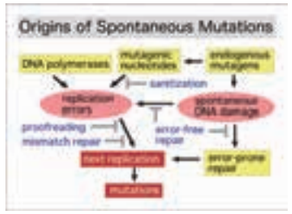

Fig.1 Multiple mechanisms suppress mutations. However, spontaneous DNA lesions serve as major causes of mutation under normal growth conditions.

Major Research Topics

1. Mechanisms for spontaneous mutation and its suppression (Fig. 1)
 1) Onset of DNA replication errors and their repair
 2) Generation of DNA damage due to oxygen radicals and its repair
 3) Spontaneous mutation induced by cellular growth environments

2. Molecular mechanisms for genetic stability (Fig. 2)
 1) Control mechanisms for genetic recombination
 2) Roles of DNA damage response and cell cycle checkpoint control

3. Molecular functions of DNA replicative apparatus (Fig. 3)
 1) Biochemical activities of DNA polymerases
 2) Replication fork arrest and its recovery processes
 3) Dynamics of DNA replication machineries

Fig.2 When DNA replication occurs without repair of DNA lesions, replication fork progression is inhibited. Mechanisms to rescue arrested replication forks include recombination repair, regression of replication forks and translesion DNA synthesis.

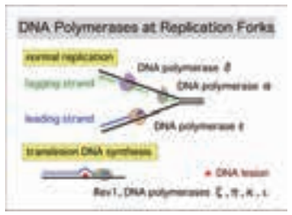

Fig.3 Multiple DNA polymerases ordinary work together for efficient DNA replication, thereby replication errors are suppressed. Special DNA polymerases work in both eukaryote and bacteria for translesion DNA synthesis (References 4 & 5).

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Laboratory Systems Microbiology

▶ URL: http://bsw3.naist.jp/eng/courses/courses302.html


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Outline of Research and Education

Genome biology and technology innovation have accelerated development and expansion of biology dramatically for 20 years. In physics, many laws were established during the 16th to 17th century based on the analysis of previously accumulated observations; Now is the period for biology to change by establishing new rules from the accumulation of vast amounts of data with the concept of the systems approach. Before the genome era, small numbers of targets were focused on for analysis but now, thanks to genome and post-genomic projects, entire sets of genes in many organisms can be investigated from global aspects and points of view. In other words, we biologists can now expand our research from "for the parts (genes)" to "for the systems". In the last half century, many analyses have been done in molecular biology to open biology to the molecular level. In the beginning of the 21st century, new concepts of biology are now showing steady progress. They are systems and synthetic biology.

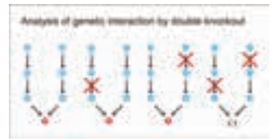

Fig.1 Concept of genetic networks.
Normally a cell has multiple pathways to produce an essential substrate for cellular life. Single gene knockout destroys one path but another route is still active and the cell can survive. The opposite case may be expected to show the same situation. But both pathways shut down together, and the cell cannot survive. These two genes are defined as having a genetic interaction.

Major Research Topics

1. Analysis of genetic interaction networks
2. Quantitative metabolic network analysis
3. Development of cross-transfer systems of huge DNA

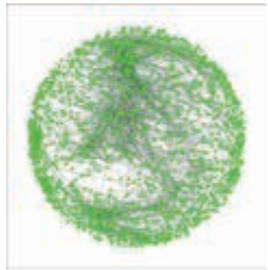

Fig.2 The genetic network structure of central metabolic genes
We performed genetic interaction analysis using genes related to glycolysis, TCA cycle and pentose phosphate pathways as query genes. Green nodes represent genes and arches show genetic interaction. Short arches means they have similar genetic interaction profiles.

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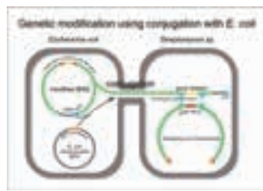

Fig.3 Transfer system between species
RPs is a plasmid carrying a wider range of host organisms than the F plasmid conjugation system. In this case, the BAC plasmid carrying transfer origin of RP4 might be transferred into the production strain, such as Streptomyces sp. by conjugation supplied from the tra genes operon on the host cell chromosome.

Laboratory

Genomics of Bacterial Cell Functions

▶ URL: http://bsw3.naist.jp/eng/courses/courses303.html

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Outline of Research and Education

With the availability of complete genome sequences, microbial research has entered a new era of study based on comprehensive gene information. We study networks of genes and proteins to understand the basic cellular functions of model bacteria, Bacillus subtilis and Escherichia coli, as a system (Fig. 1). Utilizing the results, we recently promote collaborations for the advancement of industrial applications and deeper understanding of pathogenicity.

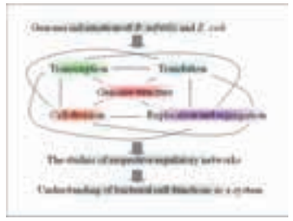

Fig.1 Outline of our research

Major Research Topics

1. Studies on the regulatory network of gene expression in *B. subtilis* and *E. coli*

2. Studies on systems controlling the bacterial cell cycle

3. Studies on higher-ordered nucleoid structures of bacterial genomes

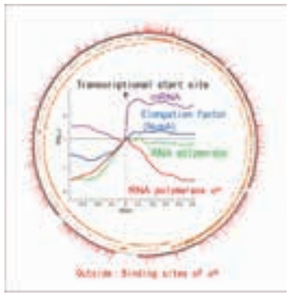

Fig.2 Average distribution of RNA polymerase

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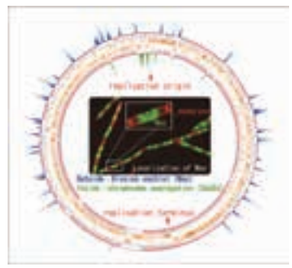

Fig.3 Binding of Noc & Spo0J proteins on the *B. subtilis* genome

Laboratory

Cell Signaling

▶ URL: http://bsw3.naist.jp/eng/courses/courses304.html

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Outline of Research and Education

Our research aims to elucidate intracellular signaling networks that sense and transmit diverse extracellular stimuli, with particular focus on the signaling pathways involved in cancerous cell proliferation and metabolic syndromes such as diabetes. To identify and analyze novel components of the signaling pathways, the studies utilize the fission yeast *Schizosaccharomyces pombe* (Figure 1), which has been successfully used as a genetically amenable model system to investigate cellular regulatory mechanisms conserved from yeast to human. Students in our laboratory are encouraged to design multifaceted approaches that logically combine research tools in molecular genetics, cell biology and biochemistry. Originally established in 1998 at University of California-Davis, our laboratory has been training researchers that can serve the international scientific community.

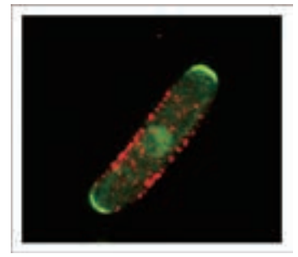

Fig.1 Fission yeast *Schizosaccharomyces pombe.*

Major Research Topics

1. TOR (Target Of Rapamycin) signaling pathway (Figure 2)

2. Stress-responsive MAP kinase cascade

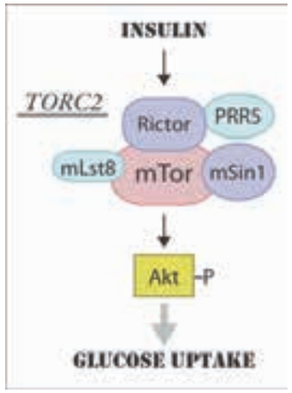

Fig.2 TOR complex 2 (TORC2) mediates insulin signals that induce cellular uptake of glucose.

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Laboratory Applied Stress Microbiology

▶ URL: http://bsw3.naist.jp/eng/courses/courses305.html

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Outline of Research and Education

Our research involves in "Applied Molecular Microbiology". The aims of our laboratory include basic studies in microbial science, particularly cellular response and adaptation to environmental stresses, and practical applications in new biotechnology. To understand in depth microbial cell functions under stress conditions, we analyze and improve various mechanisms of microorganisms from molecular, metabolic, and cellular aspects. In the best scenarios, novel findings of our basic studies can be applied to the molecular breeding of useful microorganisms (yeasts, bacteria), the production of valuable biomaterials (enzymes, amino acids), and the development of promising technologies to solve environmental issues (bioethanol, CO_2 fixation).

Major Research Topics

1. Stress response and tolerance in yeast *Saccharomyces cerevisiae* (Fig. 1, 2)
 1) Proline: Metabolic regulation, transport mechanism, physiological functions
 2) *N*-Acetyltransferase Mpr1: Antioxidative mechanism, structural and functional analyses
 3) Arginine/Nitric oxide (NO): Characterization of yeast NO synthase, downstream pathway and physiological roles of NO
 4) Ubiquitin system: Quality control of stress-induced abnormal proteins, regulation of the uniqutin ligase Rsp5 activity
2. Physiological roles and metabolic regulation of cysteine in Escherichia coli (Fig. 3)
3. Novel CO_2-fixation systems in extremely oligotroph *Rhodococcus* sp. (Fig. 4)

Fig.1 Novel oxidative stress-tolerant mechanism in *S. cerevisiae*

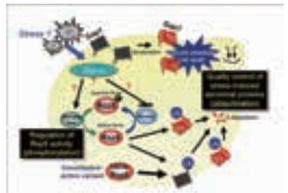

Fig.2 Ubiqitin system in *S. cerevisiae* under stress conditions

Fig.3 The cysteine/cystine shuttle system in *E. coli*

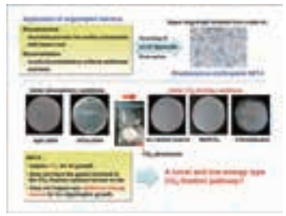

Fig.4 Novel CO_2-fixation system in *R. erythropolis* N9T-4

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Laboratory Structural Biology

▶ URL: http://bsw3.naist.jp/eng/courses/courses306.html

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Outline of Research and Education

Proteins are folded into specific three dimensional (3D) structures. These structures are essential for imparting functions such as molecular recognition and catalysis. Without precise knowledge of their 3D-structures, we are unable to understand how proteins execute their respective molecular functions. It is virtually impossible to predict protein 3D-structures from amino acid sequences alone. Thus, the experimental determination of protein 3D-structures represents the hallmark of structural biology. Structural biology in our laboratory is performed using X-ray crystallography to determine the 3D-structures of proteins and molecular complexes at atomic resolution, and biochemical/biophysical analyses are performed to delineate the mechanisms by which proteins function at the atomic, molecular, and cellular levels.

Our general goal is to contribute towards our understanding of the nature of life. Our long-term objective is to understand the molecular functions of proteins and other biological macromolecules and their complexes in terms of molecular structures. Our efforts are directed towards defining the manner by which protein interactions and 3D-structures determine specificity and how structural changes enable functional switches in living cells.

Major Research Topics

1. Structural molecular medicine
2. Structural cell biology
3. Structural molecular biology
4. Structural plant biology

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Fig.1 A crystal of histidine protein phosphatase (left), crystallized in our laboratory and part of its electron density map at 1.9 A resolution obtained from X-ray crystal structure analysis

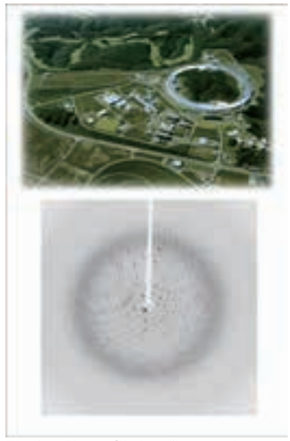

Fig.2 The SPring-8 synchrotron radiation facilities at Harima, Hyogo. We perform X-ray intensity data collection at SPring-8 for structure determination.

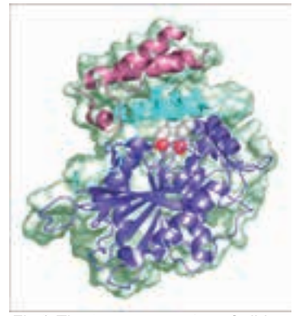

Fig.3 The ternary complex of gibberellin (space-filled model in white and red)-bound receptor GID1 (blue and cyan) trapping its downstream effector protein DELLA protein (pink) from our recent Nature article [2].

Laboratory

Biodynamics and Integrative Biology

▶ URL: http://bsw3.naist.jp/eng/courses/courses307.html




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Outline of Research and Education

Our long-long term goal is to understand the dynamic and complex nature of biological systems in a quantitative manner, and eventually to develop a quantitative theorem that unifies a variety of biological processes. We also apply our experimental and theoretical findings to uncover the mysteries of human diseases. We use not only classical molecular and cellular biological tools, but also import and use concepts, principles, and tools from other disciplines such as physics, engineering, chemistry, computer science, mathematics to challenge fundamentally significant questions in life science. Because of this cross-disciplinary nature of our approaches, we have a number of on-going collaborations at both domestic and international levels. Prof. Sato is an accomplished scientist at the international level and has significant experience in research and education in top research institutions and universities in the USA for over 20 years and he currently holds adjunct professor positions at Cornell University, USA, and Centenary Institute in Sydney, Australia. Students and scientists in this laboratory will gain experience and training to become pioneers and future leaders at the international level.

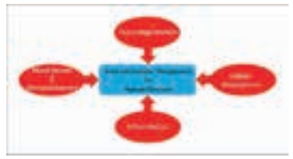

Fig.1 Molecular mechanisms of human diseases.

Major Research Topics

1. Molecular mechanisms of human diseases（Fig. 1）
2. Interdisciplinary approaches towards inventing next-generation tissue engineering tools for regenerative medicine（Fig. 2）
3. Mechanisms of stochasticity and its buffering in biology and disease（Fig. 3）

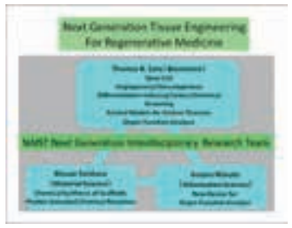

Fig.2 Interdiciplinary approach towards inventing next-generation tissue engineering tools for regenerative medicine.

Fig.3 Mechanisms of stochasticity and its buffering in biology and disease.

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Laboratory

Gene Expression Research

▶ URL: http://bsw3.naist.jp/eng/courses/courses308.html

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Outline of Research and Education

Organisms are composed of a number of cells arranged in a well-coordinated manner. A fertilized egg repeats cell division and differentiates into the animal body in embryogenesis, in which various phenomena take place in a pre-determined order controlled by the inherent “biological clock” in each living body. We attempt to clarify the principles of animal morphogenesis through investigating the mechanism of the “biological clock” that controls various life phenomena during embryonic development.

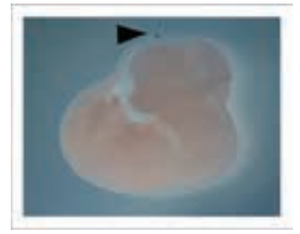

Fig.1 Transcription factor Hes7, serving as a molecular clock, is specifically expressed in the primordium of somites.

Major Research Topics

Research on somitogenesis in vertebrates as a model system for the biological clock

The mouse body is composed of a metameric structure along the anteroposterior axis. For example, the spine is made up of the accumulation of multiple vertebrae, each of which is similar in shape. Such metamerism is based on the somite, which is a transient structure in the mid-embryogenesis. Somites are symmetrically arranged on both sides of the neural tube as even-grained epithelial spheres that give rise to vertebrae, ribs, muscles and skin.

The primordium of somite, located at the caudal tip of the mouse embryo, extends posteriorly. The anterior extremity of the somite primordium is pinched off to generate a pair of somites in a two-hour cycle, resulting in the formation of repeats of a similar size structure. On the basis of this finding, it has been considered that there is a biological clock, which determines the two-hour cycle, in the primordium of somites. The expression of several genes oscillates in the primordium of somites, corresponding to the cycle of somite segmentation, which serves as molecular evidence of the biological clock. We are exploring the mechanism of the biological clock on the basis of such oscillatory gene expression.

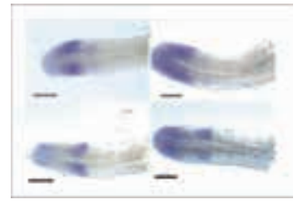

Fig.2 The expression of Hes7 oscillates in the the primordium of somites.

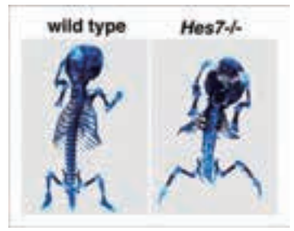

Fig.3 In Hes7 knockout mice, somite segmentation does not occur cyclically and the metameric structures along the anteroposterior axis are lost.

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Laboratory

Plant Protein Analysis

▶ URL: http://bsw3.naist.jp/eng/courses/courses901.html

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Outline of Research and Education

Our laboratory started in 2010 within the framework of the Plant Science Global Top Education Program, supported by the Ministry of Education, Culture, Sports, Science and Technology. The aims of this program are to establish an educational system linking nationwide universities and institutes, and to cultivate young plant researchers for the promotion of future plant science in Japan.

With the goal of promoting education on frontier technologies, we focus on rapidly advancing research fields such as genome-transcriptome analysis, biochemical and proteomic analysis of intracellular protein complexes, and visualization of those protein-protein interactions in living cells. Four researchers are assigned to this education purpose; Dr. Tetsuya Kurata has expertise in genome-transcriptome analysis with high-throughput next generation sequencer; Dr. Masayuki Fujiwara is a biochemist whose focus is on protein purification by various biochemical methods; Dr. Yoichiro Fukao specializes in proteomic analysis using the latest mass spectrometers; Dr. Noriko Inada is an expert of bioimaging using confocal and multiphoton microscopies.

Every year, we select ~30 graduate students who have applied with their own research proposals employing genome-transcriptome analysis, biochemical and proteomic analysis, or bioimaging analysis investigating plant protein function. These selected graduate students will benefit from one week of training in the above-mentioned cutting-edge technologies as well as avid interaction with other participating graduate students from various universities and institutes.

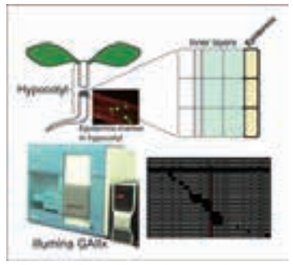

Fig.1 Coordinated growth among cell layers in Arabidopsis hypocotyl, and data from NGS.

Fig.2 LTQ-Orbitrap XL and TSQ-Vantage.

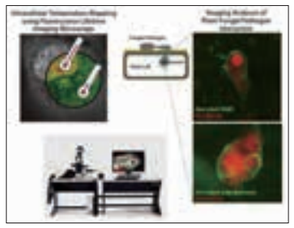

Fig.3 Imaging cellular temperature and powdery mildew-Arabidopsis interaction.

Major Research Topics

1. Genome-Transcriptome analysis (Tetsuya Kurata)
2. Purification and Analysis of Protein complex (Masayuki Fujiwara)
3. Proteome analysis (Yoichiro Fukao)
4. Bioimaging analysis (Noriko Inada)

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Affiliate Laboratory

Molecular Genetics of Human Diseases

(with Osaka Medical Center for Cancer and Cardiovascular Diseases)

▶ URL: http://bsw3.naist.jp/eng/courses/courses501.html

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Outline of Research and Education

Following recent advances in bioscience, particularly molecular biology, it is becoming possible to directly analyze cancer tissue in individual patients. Our laboratory is aimed at establishing new oncology, making use of not only conventional gene manipulation technology but also techniques of genomic science and bioinformatics. In parallel to these efforts, we are also conducting research on the application of basic research outcomes to bedside practice (so-called translational research).

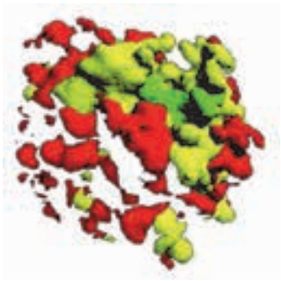

Fig.1 Diversity of cancer cells within a tumor

Major Research Topics

1. Analysis of cancer tissue architecture

Cancer is not an assembly of monoclonal cancer cells but is composed of various subclones involving different somatic mutations. In most cancers, non-cancerous cells are interposed. Depending on the site, environmental factors (oxygen concentration, etc.) vary, indicating limitations in the applicability of the conventional view that the entire cancer tissue can be regarded as a homogeneous tissue. At our laboratory, several areas of a given cancer tissue are sampled separately for analysis of gene expression and mutation in individual areas, with the goal of clarifying how the entire cancer tissue is formed in individual areas. To put it more concretely, we will investigate how the sensitivity to anti-cancer drugs of the entire cancer tissue is determined by the features of individual subclones, since the sensitivity is naturally expected to differ among different subclones.

2. Development of methods for diagnosis and treatment making use of gene expression profiles

Chemotherapy plays an important role in the treatment of cancer. However, about half of all patients with cancer fail to respond to chemotherapy. Because anti-cancer agents often induce severe adverse reactions, the stress on patients will be alleviated if their responses to treatment can be predicted in advance. This is called personalized medicine (tailor-made medicine). If gene expression profile analysis, a technique of genomic science, is used, pre-treatment evaluation of patients' responses may be possible. At present, efforts are being made not only to apply gene expression profiles to the prediction of patients' sensitivity to anti-cancer agents but also to develop methods of diagnosis and treatment making use of gene expression profiles for patients with mammary, hepatic, esophageal, pulmonary, cerebral and other cancers. The outcomes from these studies have been published on Cancer Gene Expression Database (CGED, http://cged.hgc.jp).

3. Development of gene analysis technology

We have succeeded for the first time in the world in developing high-throughput quantitative PCR (adaptor-tagged competitive PCR; ATAC-PCR) and have been applying this technique of PCR to cancer expression profile analysis. At present, we are conducting research for the application of ATAC-PCR to genomic structure analysis.

Fig.2 Personalized medicine (tailor-made medicine)

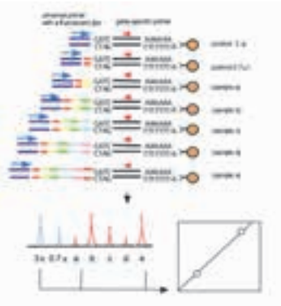

Fig.3 Adaptor-tagged competitive PCR (ATAC-PCR)

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Affiliate Laboratory

Neuronal Network Formation

(with Osaka Bioscience Institute)

▶ URL: http://bsw3.naist.jp/eng/courses/courses502.html

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Outline of Research and Education

The human brain receives, processes, stores, and transmits complex information with great fidelity. The neuronal network that underlies these functions is comprised of an estimated 1011 neurons linked by over 1014 synaptic connections between two structurally and functionally different neurites, axons and dendrites. Precise patterning of dendrites as well as axons is essential for the correct wiring and function of neural circuits. We combine genetics, imaging, and biochemical approaches to investigate the interplay between genetic and epigenetic control of neural morphogenesis, and deduce the functional importance of these regulatory systems in disease etiology. We use fruitfly and mice as research models.

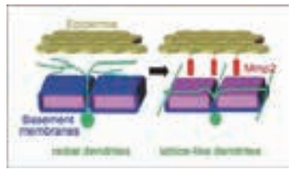

Fig.1 Dendrite reshaping in Drosophila sensory neurons.

Major Research Topics

1. Structural plasticity of neuronal circuits

Neuronal circuits in the brain are not static. In many systems, especially during critical periods of development, neurons exhibit a period of juvenile plasticity in which connectivity can be modified in response to sensory input or following specific experiences, thereby providing neurons with new response properties tailored to the new environment. To achieve these changes in connectivity, certain neurons modify the shape of their axon and dendritic arbors in response to various stimuli. We have identified novel mechanisms that regulate the structural plasticity of dendritic arbors in fly sensory neurons. We are investigating how these mechanisms are related to the sensory-evoked plasticity in fly and mouse nervous systems.

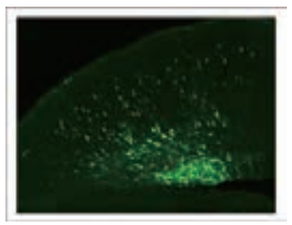

Fig.2 Migration of newborn neurons in the adult mice brain.

2. Adult neurogenesis in the brain

Neural stem cells have been found in certain areas of the adult brain. Although the adult neurogeneis likely plays an important role in learning and memory, the information is still limited. We are investigating the roles of newly born neurons in the mice and fruitfly brain.

3. The neural basis for decision-making

Animals always make appropriate decisions based on environmental information. How one can make distinctive decisions based on the same sensory information remains elusive. We utilize Drosophila larvae as model animals to dissect the neural circuits responsible for decision-making.

Fig.3 Light preference of Drosophila 3rd instar larvae.

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Affiliate Laboratory

Tissue Development Dynamics

(with the Center for Developmental Biology, RIKEN)

▶ URL: http://bsw3.naist.jp/eng/courses/courses503.html

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Outline of Research and Education

The development of multicellular organisms involves the collective effect of multiple events at the level of the individual cell, such as proliferation, differentiation, adhesion, and migration. Programmed cell death, for example, is a process by which cells are selected for death at set times in development, allowing for the sculpting of tissue, and is used in the adult organism to maintain homeostasis by eliminating cells that have developed abnormalities. Perturbations in cell death signaling can thus affect an organism's physiological stability, and result in developmental defects, tumorigenesis, or neurodegenerative disease. Cell death plays an important role in maintaining the cellular society not only by eliminating unneeded cells at given sites and stages, but in other functions, such as regulating the proliferation and migration of neighboring cells, as well. Such cellular behaviors give rise to cell networks capable of organizing into tissues, the study of which requires a experimental approach to spatiotemporal information in living systems, such as can be obtained through the real-time live imaging of biological phenomena. Our research goal is to elucidate the physiological roles of cell death and the basic mechanisms for regulating organogenesis using molecular, genetic and bioimaging approaches.

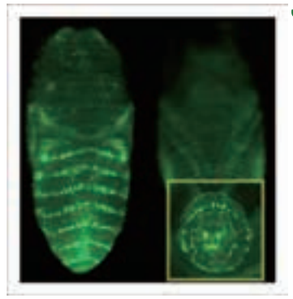

Fig.1 Dorsal (left) and ventral (right) views of Drosophila pupae that express fluorescent protein in cells located in the posterior component of each segment. Location of male genitalia is shown in the yellow square.

Major Research Topics

We have chosen the fruit fly Drosophila melanogaster as our primary research model, seeking to take advantage of its utility in developmental studies and wealth of genetic data in studying the coordination of histogenesis through live imaging and genetic screens. To elucidate the role of cell death in histogenetic processes, we will analyze caspase mutant phenotypes in which the exterior male genitalia (terminalia) develops abnormally. In normal Drosophila development, the terminalia rotates 360 degrees as it forms, but in caspase mutants, this revolution is incomplete. Image analysis reveals that in wildtype, the speed of this rotation is variable, with distinct initiation, acceleration, deceleration, and termination stages; caspase inhibition results in loss of the acceleration phase, and failure in terminalia development. We will seek to identify how caspase function and cell death control acceleration of the rotation through searching for associated genes and live imaging analysis. It has further been predicted that cell death alone cannot account for the rotation that maintains tissue area, suggesting other mechanisms are also at work. We will conduct single-cell analyses to determine whether other behaviors such as proliferation or migration are also altered. Through the use of the extensive Drosophila genetics toolset and live imaging technologies, we hope to be able to address questions that have proven technically challenging in the past, and by visualizing the activities of individual cells, develop a better understanding of how cellular network systems work in histogenesis.

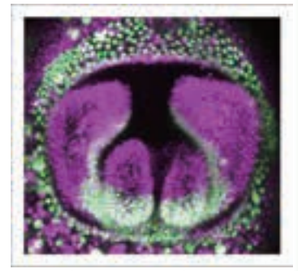

Fig.2 Caudal view of a Drosophila male terminalia showing cells in the posterior compartment (green).

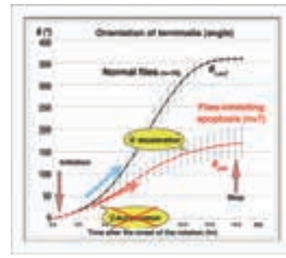

Fig.3 Comparison of the speed of genitalia rotation between normal flies and flies-inhibiting apoptosis.

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Affiliate Laboratory

Cell Growth Control

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Outline of Research and Education

The processes of animal development, including organ size and body size, are genetically predetermined, but these processes are also influenced by environmental factors such as nutrition and temperature. The close link between cell and tissue growth control and environmental cues ensures that developmental transitions occur at the appropriate time during animal development. Our lab's research aims to shed light on the molecular basis for growth control and developmental timing at the cellular and tissue/organ level using the fruit fly Drosophila melanogaster and mammalian cell culture as model systems. We combine biochemical and genetic approaches, along with quantitative and qualitative imaging and cell-biological analysis, to identify and characterize the relevant signal transduction pathways.

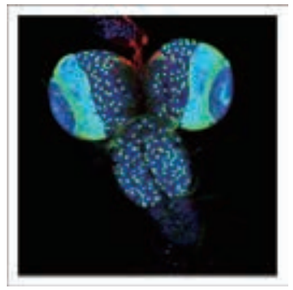

Fig.1 Larval central nervous system in Drosophila. Neural stem cells (green) and insulin-producing cells (red) are shown.

Major Research Topics

1. Molecular mechanisms of division arrest in neural stem cells

2. Molecular mechanisms of systemic growth and developmental timing

3. Molecular mechanisms of amino acid signaling

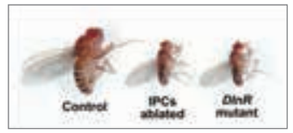

Fig.2 Drosophila mutants defective for systemic growth. Down regulation of the insulin signaling leads to the formation of small flies. The picture shows brain insulin-producing cells (IPCs) ablated flies and Drosophila insulin receptor (DInR) mutant flies.

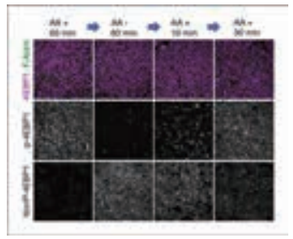

Fig.3 Amino acids response in cultured mammalian cell lines. The phosphorylation level of 4EBP1, a downstream target of the TOR kinase, is used as a readout of amino acids (AA) dependent activation of the TOR. Top panels indicate total 4EBP1 levels. Middle panels indicate phosphorylated 4EBP1, while lower panels indicate non-phosphoryated pools of 4EBP1.

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Affiliate Laboratory

Molecular Microbiology and Genetics

(with Research Institute of Innovative Technology for the Earth (RITE))

▶ URL: http://bsw3.naist.jp/eng/courses/courses505.html

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Outline of Research and Education

Global warming resulting from elevated CO_2 and global energy supply problems has been in the limelight in recent years. As these problems originate from rapid economic expansion and regional instability in parts of the world, broad knowledge of global economic systems as well as R&D is required to solve these problems. Fundamental research employing microbial function to tackle the adverse effects of global climate change and mitigate energy supply problems is carried out in our laboratory.

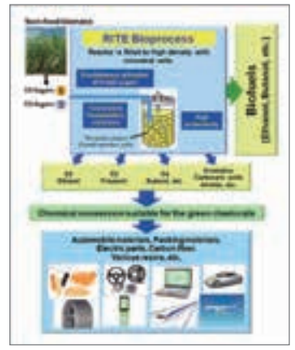

Fig.1 Biorefinery concept

Major Research Topics

1. Biorefinery

Biorefinery is a concept which describes production of chemicals and fuels from renewable biomass via biological processes. Biorefinery R&D is considered of national strategic importance to the U.S.A. (Figure 1). Biorefinery can be divided into two processes; a saccharification process to hydrolyze biomass to sugars and a bioconversion process to produce chemicals and fuels from the sugars. Based on a novel concept, we have pioneered a highly-efficient "growth- arrested bioprocess" as a bioconversion technology to produce chemicals and fuels (Figure 2). It is based on Corynebacteria that are widely used in industrial amino acid production. The key to high efficiency is the productivity of artificially growth-arrested microbial cells, cells with which we evaluate production of organic acids and biofuels. To efficiently produce these products, the cells are tailored for the production of a particular product using post genome technologies like transcriptomics, proteomics and metabolome analyses (Figure 3).

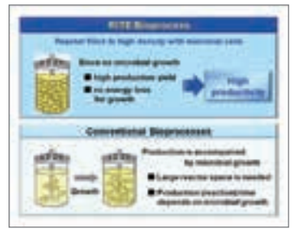

Fig.2 Novel features of the RITE Bioprocess

2. Bioenergy and green chemicals production

Having established the fundamental technology to produce bioethanol from non-food biomass, we are now partnering with the automobile and petrochemical industries to explore commercial applications. We have also developed the platform technology to produce biobutanol, the expected next-generation biofuel, as well as a variety of green chemicals such as organic acids, alcohols and aromatic compounds from which diverse polymer raw materials used in various industries are produced.

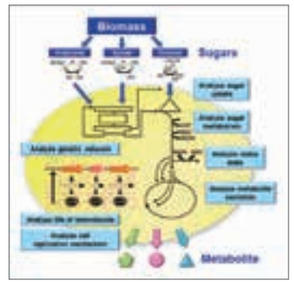

Fig.3 Breeding of recombinant strains using system biology

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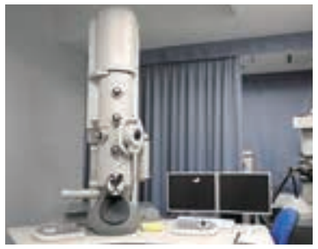
Graduate School of Biological Sciences

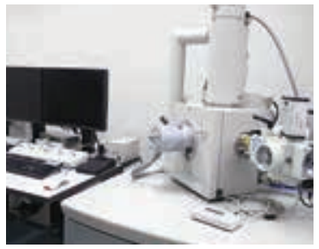
Research Facilities and Equipment

Abundant Research Facilities

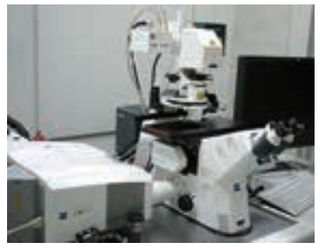
Each department is equipped with a variety of state-of-the-art equipment.
Shared equipment, among the most advanced available for biological science research in Japan,
is provided at numerous locations within the School.



Transmission Electron Microscope

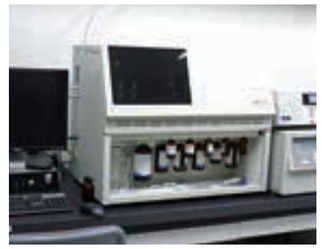


Scanning Electron Microscope



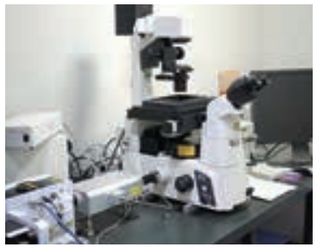
Confocal Laser Scanning Microscope

TSQ Vantage

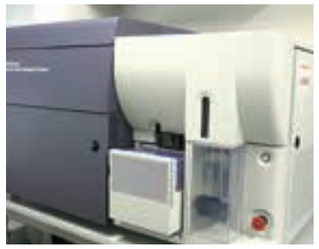


Protein Sequencer

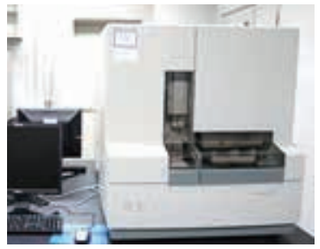
MALDI-TOF MS



Spinning Disk Confocal Microscope

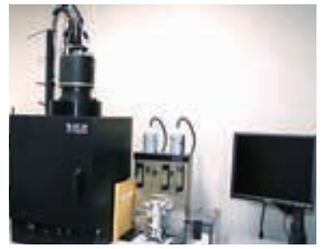


Flow Cytometry System

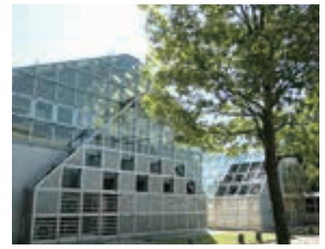


DNA Sequencer

GC-MS

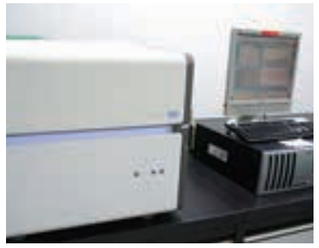


In vivo Imaging System



Botanical Greenhouses

Genome Analyzer IIx System



Real-Time PCR System

LTQ Orbitrap XL

Animal Experimentation Facility

Liquid Nitrogen Cryopreservation System