

# Investigation and synthesis of functional aroma compounds

## Pharmaceutical applications of physiologically active compounds

**R**esearch interests range widely among a variety of physiologically active compounds in nature. In particular, analysis and synthesis are my main tools for the demonstration of the chemical ecology. We are currently investigating pheromones and allelochemicals in marine organisms.

Citrus fruits and herbs are found worldwide, and the essential oils are widely utilized in foods and beverages and as fragrances in cosmetics. The essential oils can have relaxing or stimulating effects on humans. Our odor descriptions and physiological analyses reveal the relationships between odor and the human brain.

Research interests

- 1) Investigation and synthesis of pheromones and allelochemicals in marine organisms
- 2) Flavor chemistry of citrus fruits, herbs, and flowers
- 3) Elucidation of mechanistic pathways for the biogeneration of volatile aroma compounds
- 4) Relaxation effects of aroma on humans
- 5) Isolation and synthesis of physiologically active compounds
- 6) Development of functional foods and cosmetics



Diversity of naturally occurring compounds.

### About Researcher

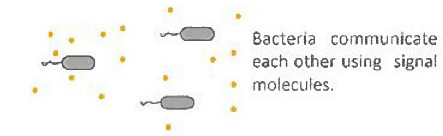


AKAKABE Yoshihiko, Ph.D.

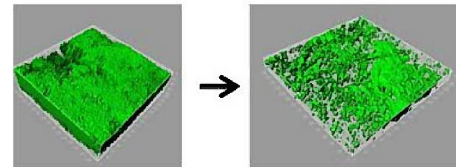
Ph. D., 1994 Okayama University of Science

## Pathogenic bacterial adhesion and colonization of host cells

**W**hen pathogenic bacteria infect animal and plant hosts, they must adhere to host surfaces. These bacteria have various adhesion factors against host defense mechanisms. Additionally, most of these bacteria communicate each other within biofilm community. Employing biochemistry and molecular biology techniques, we aim to uncover the mechanisms governing pathogenic bacterial communication and colonization. Particularly, we aim to investigate the mechanism of bacterial adhesion and colonization of animal and plant host cells and screen for inhibitors of biofilm formation. Dissecting the mechanism of bacterial communication will provide insights into managing and even preventing biofilm formation, which is necessary to prevent diseases and maintain quality in various industrial fields.



Bacteria communicate each other using signal molecules.



Inhibition of bacterial communication affects their biofilm formation.

Inhibition of bacterial communication affects biofilm formation.

### *About Researcher*



**AZAKAMI Hiroyuki, Ph.D.**

Ph. D., 1994 Hiroshima University

# Anti-Aging and Life Span Extension

**O**ur main subject of research is the understanding of the aging process and the development of effective methods for **anti-aging** and **life span extension**. Because we have a limited understanding of the aging mechanism, we investigate it in terms of oxidative stress. With regard to the aging process, we emphasize on reactive oxygen species (**ROS**) generated inside the body and the antioxidant systems protecting against **ROS**-mediated oxidative stress. We study the benefits as well as the damages of **ROS**. In addition to these research themes, we attempt to reveal the anti-aging strategy of long-lived termites. Ongoing research projects in our laboratory are

1. Understanding the ROS-induced aging process using superoxide dismutase-deficient mice.
2. Identifying functional food components for anti-aging and **life span extension**.
3. Analysis of the long-lived termite from the standpoint of the antioxidant system.
4. Edible insects as a functional food for health.



## About Researcher



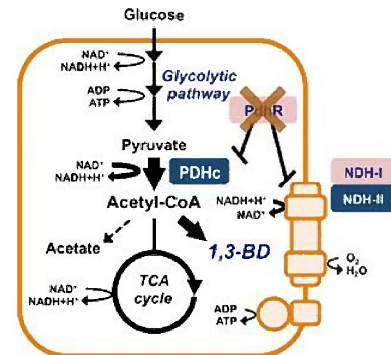
IUCHI Yoshihito, Ph.D.

Ph. D., 1995 Hiroshima University

# The role of microbial physiology and metabolic engineering in fermentation

**O**ur laboratory mainly focuses on the “fermentation physiology” and “metabolic engineering” of microbes. Acetic acid bacteria, such as *Gluconobacter* spp. and *Acetobacter* spp., and amino acid-producing bacteria, such as *Corynebacterium* spp., are industrially important microbes used for the fermentative production of vitamin C, acetic acid, amino acids and so on. These microbes produce various chemical compounds through their respective metabolic processes. We are studying the dynamics of this “fermentative physiology” to molecularly understand these metabolic process.

Due to increased concerns about the depletion of fossil resources and ensuing environmental problems, biological production of platform chemicals from renewable sources has attracted much attention as a viable alternative to petroleum-based manufacturing. “Metabolic engineering” is one of the most promising means to respond to this demand. In this field, metabolically and genetically well-studied microbes, such as *Escherichia coli* and *Corynebacterium glutamicum*, are engineered to produce the desired products, i.e., platform chemicals. Thus, we aim to produce valuable chemical compounds via “metabolic engineering” approaches, such as constructing the synthetic pathways to generate platform chemicals on a large scale.



Metabolic engineering strategies to enhance 1,3-butanediol (1,3-BD) production

## About Researcher



KATAOKA Naoya, Ph.D.

Ph. D., 2013 Hiroshima University

## Molecular mechanism for the reducing power supply system in the plastids of plants and malaria parasites

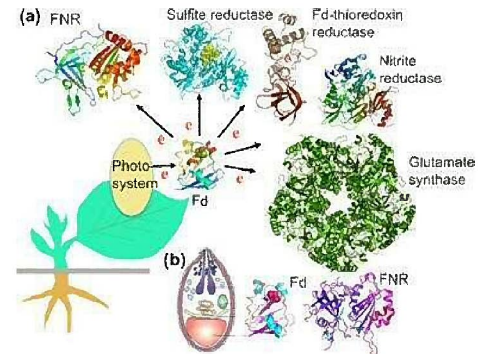
We are interested in the way plants utilize light energy to synthesize various biomolecules which nourish life on earth. We have been focused on the mechanism by which high-energy electrons (reducing power), provided from photosystems, are properly distributed into various biosynthetic metabolisms depending on the environmental and physiological demands (Figure). A small stromal electron carrier protein, **ferredoxin** (Fd), which receives electron from photosystem I, plays a key regulatory role. On this front, we are currently working on identifying;

1) molecular mechanism for the distribution of reducing power in the plant plastids, in terms of **protein-protein interactions** and electron transfer between ferredoxin and its dependent metabolic enzymes.

Recently, malaria parasites were found to possess a system for supplying reducing power, of which protein components (ferredoxin and its dependent NADP<sup>+</sup> oxidoreductase) are homologous to those of plants. Therefore, we are also working on;

2) characterization of the system for reducing power supply in the plastids (apicoplasts) of malaria parasites.

We are studying these molecular mechanisms using biochemical and physicochemical methods, for the purpose to regulate the energy flow into their plastids, and also, from the viewpoints of their physiological significances and evolutionary development of plastids in the parasitic organisms.



Electron distribution in chloroplasts (a) and the homologous system of ferredoxin (Fd) and Fd-NADP<sup>+</sup> reductase (FNR) in malaria parasites (b)

### About Researcher



KIMATA Yoko, Ph.D.

Ph.D., 1993 North Carolina State University

# Functional analyses of biosynthetic enzymes involved in plant specialized metabolites

**P**lants biosynthesize many specialized metabolites (secondary metabolites) including volatile compounds that serve as attractants for pollinators or for defense against herbivores and bacterial pathogen for adaptation to their ecological niches. Since antiquity, humans have used plant metabolites as commercial resources, such as medicinal, food flavoring agents, and perfumes. However, the biosynthetic pathways leading to these metabolites and their regulatory mechanisms are largely unknown. My goal is to investigate the biosynthetic pathways involved in the production of specialized plant metabolites and the enzymes that catalyze them. Genetic engineering of plant production systems with such enzymes could offer high potential for the introduction of new scents and flavors into various plant species.



Research overview

## About Researcher



KOEDUKA Takao, Ph.D.

Ph.D., 2005 Tottori University

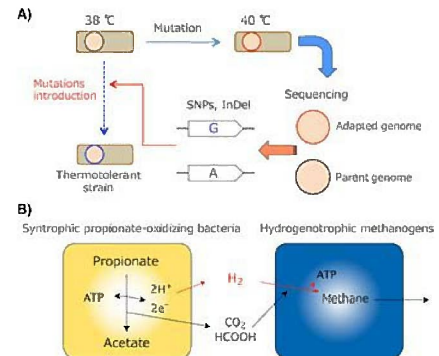
# Application of genomics to physiological analysis of microorganisms

**I**t has become increasingly important to learn the procedures of extracting information from genomic sequence and exploiting this information for a better understanding of biological phenomena. Although bioinformatics using genomic information can expand the understanding of metabolic mechanisms of microorganisms, it is dependent on biological studies for most of this information. Thus, our researches provide to the increasing need for the systematic merger of genetic and genomic information with physiological analysis.

We presently focus on studying several microbiological aspects of fermentative microbes, especially thermotolerant and syntrophic microorganisms.

A) For thermotolerant microorganisms, we have investigated several ethanol-producing bacteria, of which relatively thermotolerant strains have been analyzed to elucidate the thermotolerance mechanisms based on their genetic differences with mesophilic microorganisms. In addition, we attempt to identify the differences in these mechanisms by observing the effects of genetic and genomic modification.

B) For syntrophic microorganisms, we have investigated methane fermentation, in particular propionate oxidation performed by syntrophic propionate-oxidizing bacteria and hydrogenotrophic methanogens. These microorganisms inhabit anaerobic environments, and their genetic modification is difficult. Genomic, physiological, and biochemical analyses are performed to identify the mechanisms and procedures that are important for achieving syntrophic association under these energy-limited conditions.



A) Research of thermotolerant microorganisms.

B) Schematic diagram of syntrophic propionate oxidation in methane fermentation.

## About Researcher



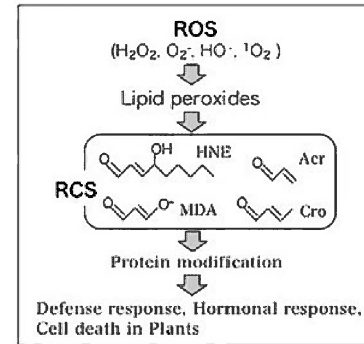
**KOSAKA Tomoyuki, Ph.D.**

Ph.D., 2003, Kyushu University



# Investigation of the mechanisms of plant responses to and defense against environmental stress

**I**nvestigating basic plant biology provides insights into applications to improve human health. Plants are affected by environmental changes, which induce oxidative stress due to increased levels of reactive oxygen species. We recently revealed that reactive carbonyl species (RCS), products of lipid peroxides, are mainly responsible for 'oxidative injury' in plant cells. RCS are a group of compounds commonly found in living organisms, and their biological functions are as versatile and important as those of reactive oxygen species. Our current aims are: (1) to elucidate RCS regulation in plants, (2) to define the physiological functions of RCS in plants, and (3) to discover compounds to scavenge RCS in plants. Detailed understanding of RCS functions will give us insights into the critical importance of these compounds in plant cells. In addition, if we identify RCS scavenging compounds, they may be viable nutritional supplements for human consumption.



Reactive carbonyl species are critical compounds in plant cells.

## About Researcher



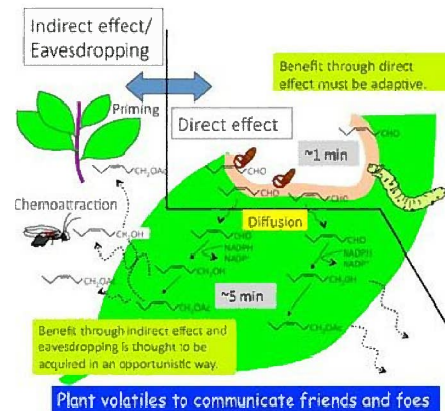
MANO Junichi, Ph.D.

Ph. D., 1991 Kyoto University



# Volatile compounds as tools for plants to communicate with animals, other plants, and microbes

**A**lmost all living organisms produce volatile compounds that elicit odor. In our laboratory, we are particularly investigating why plants emit volatile compounds and the dynamics of such volatile compound emissions upon various stimuli. We are also investigating how plants communicate with other plants, animals, and microbes in their ecosystem. Using molecular biological techniques and ecological experiments, we aim to holistically dissect the landscape of the volatile compounds emitted by plants.



## About Researcher



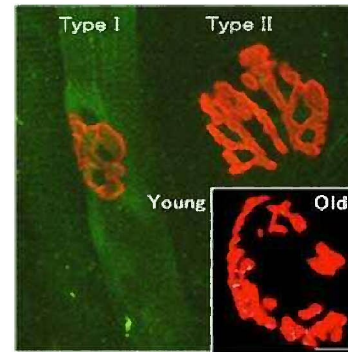
MATSUI Kenji, Ph.D.

Ph.D., 1991 Kyoto University

## Muscle and Motoneuron Plasticity

**O**ur research interests encompass several areas of motoneuron and **muscle** plasticity, including 1) accommodation of skeletal **muscle** and motoneuron functions during altered use; 2) neurophysiology of locomotion and respiratory motor system during development and **aging**; and 3) optimal training stimulation for **muscle** adaptation in **mammals**. We conduct research employing histochemical, biochemical, and basic electrophysiological techniques.

Several ongoing research projects in the laboratory include 1) morphological changes in the endplate of aged rat diaphragms; 2) training and detraining effects on satellite cell responses after exhaustive exercise in thoroughbred horses; 3) **muscle** fiber properties in **mammals**, including humans; and 4) effect of eccentric **muscle** contraction on satellite cell activation in human anti-gravity **muscles**. We are embarking on collaborative research efforts within Yamaguchi University, the Japanese Racing Horse Society, and the Mayo Clinic (USA).



One of our research projects is assessing the aging of the 3D endplate in aged rats.

### *About Researcher*

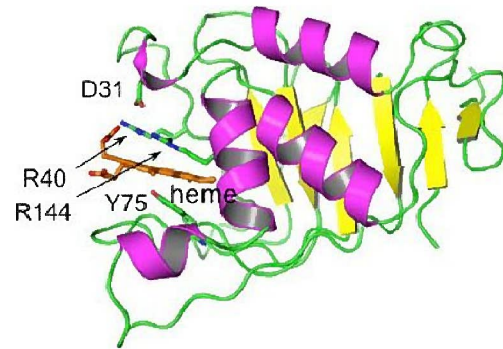


**MIYATA Hirofumi, Ph.D.**

Ph.D., 1992, Osaka University

## Structure and Function of Metalloproteins

**I**ron is an essential metal element in most living organisms, including bacteria. Pathogenic bacteria have developed diverse mechanisms to survive under iron-limited conditions. For example, gram-negative bacteria produce siderophores, which have high affinity for Fe(III). Siderophores chelate iron and transport it into the bacteria. However, iron atoms in host cells are tightly bound to proteins such as transferrin or ferritin. Very low concentrations of free iron pose severe challenges to pathogenic bacteria. Under such circumstances, heme could be a major iron source and some bacterial pathogens use hemophores for iron uptake from heme. Heme acquisition system A (HasA) is known as a hemophore in several gram-negative pathogens including *Pseudomonas aeruginosa*, *Serratia marcescens*, and *Yersinia pseudotuberculosis*. Using spectroscopic, crystallographic, and kinetic techniques, we have shown that iron-tyrosine coordination is critical for prompt heme capture by HasA from *Y. pseudotuberculosis*. We have also shown that interactions of the guanidinium group of the distal arginine with propionates and the heme plane contribute to the retention of heme in this hemophore.



The Structure of Heme Acquisition System A from *Y. pseudotuberculosis*

### *About Researcher*



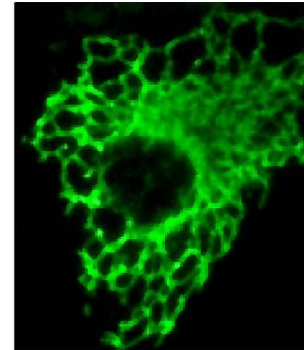
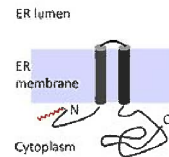
OZAKI Shinichi, Ph.D.

Ph.D. 1992 Texas A&M University

# Analysis of post-translational modifications of proteins and its application for genetic and protein engineering

**P**ost-translational modifications of proteins play critical roles in the structure and function of proteins. In our laboratory, we are investigating lipid modifications of proteins. Lipid modification involves the covalent attachment of lipids, such as fatty acids, isoprenoids, or phospholipids, to a protein. Wide ranges of proteins, including many proteins involved in human diseases, are modified by lipids. Therefore, identification and characterization of lipid-modified proteins will be useful for the discovery of disease marker proteins, disease associated proteins or therapeutic target proteins. For the identification of novel human lipid-modified proteins, we have established a systematic strategy by using metabolic labeling of proteins. In this strategy, using cDNA as starting material, the susceptibility of the protein to lipid modification was evaluated by metabolic labeling in a cell-free protein synthesis system or in transfected mammalian cells. Using this strategy, we have succeeded in discovering more than 100 novel human lipid-modified proteins. We are currently studying the specific role of lipid modification on the function of disease-associated proteins.

## Protein Lunapark



Discovery of an N-myristoylated transmembrane protein that induces endoplasmic reticulum (ER) morphological change

## About Researcher

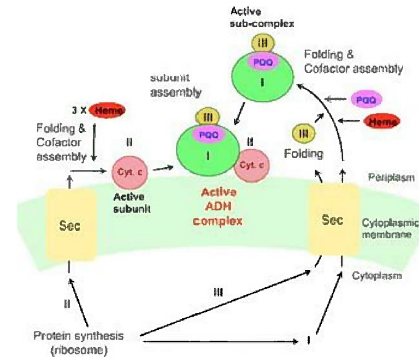


UTSUMI Toshihiko, Ph.D.

Ph.D., 1988, Kyushu University

# Biochemical function, physiological role, and molecular architecture of membrane proteins in bacteria

**W**e are interested in the fermentation process orchestrated by bacteria, such as acetic acid bacteria. Particularly, we are assessing the molecular architecture of membrane-bound bacterial enzymes involved in fermentation (such as alcohol dehydrogenase), via genetic engineering, molecular biology, biochemistry, and structural biology. Understanding the basic properties of these enzymes in fermentation may provide insights into the development of enzyme-based technologies, such as biosensors and fuel cells, and may improve fermentation processes.



Molecular architecture of membrane-bound alcohol dehydrogenase in acetic acid bacteria

## About Researcher



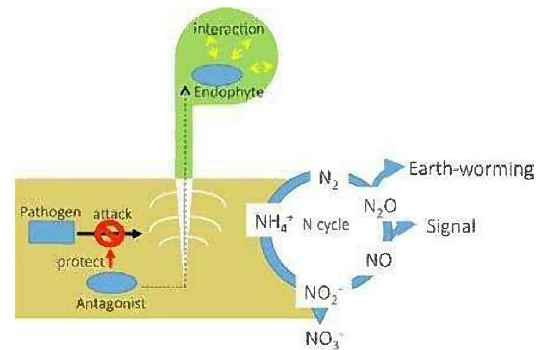
YAKUSHI Toshiharuru, Ph.D.

PhD, 1998, University of Tokyo

# Investigating soil microbial ecology to advance crop production and protect the environment

**I** study the following aspects of soil microbial ecology: Microorganisms in soil are essential for the cycling of plant nutrients.. Particularly, nitrogen is a major plant nutrient. Various soil microorganisms mediate **nitrogen transformation**. Additionally, both nitrification and denitrification contribute to the dynamics of nitrous oxide (N<sub>2</sub>O), which degrades ozone and acts as an earth-warming gas. To mitigate N<sub>2</sub>O emission, we are assessing the properties and regulation of nitrification and denitrification in agricultural soil. Microorganisms in soil interact with each other for either being detrimental or beneficial to the soil ecosystem. Studying the means to enhance crop protection from soil-borne microbial diseases will identify ways to control the growth of **antagonistic microorganisms**.

Some soil microorganisms invade plants and promote growth without disease symptoms. These microorganisms, called **endophytes**, affect plant growth in various manners. Notably, some **endophytes** induce environmental stress resistance in the host plant. This aspect of **endophytes** is currently being studied.



Importance of soil microbial ecology for crop production

## About Researcher



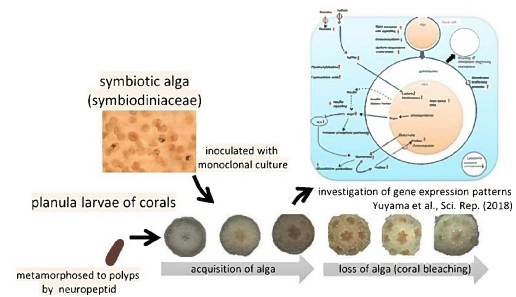
YOKOYAMA Kazuhira, Ph.D.

Ph. D., 1989 Kyushu University

# Functional analysis of symbiotic microorganisms

**R**esearch in my laboratory focuses on the characterization of environmental microorganisms and symbiotic microorganisms. So far, we have used scleractinian corals to clarify the role of symbiotic microorganisms. In this study, we are conducting incubation experiments, transcriptome analysis, immunohistological analysis, and physiological analysis. My current research interests include the following:

- Effects of bacterial communities on stress tolerance of corals.
- Identification of genes involved in the establishment of symbiotic relationship, and genes related to the stress response.
- Establishment of new monoclonal culture collections of coral symbiotic microorganisms.



Experimental system for investigating symbiotic relationships between coral and algae

## About Researcher



YUYAMA Ikuko, Ph.D.

Ph. D. 2009, The University of Tokyo