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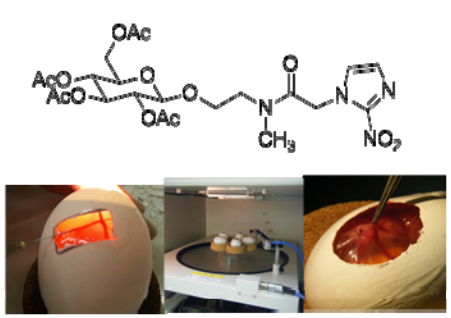
Tokushima University

Medicinal Chemistry Based on Developing Chicken Egg

Professor Yoshihiro Uto



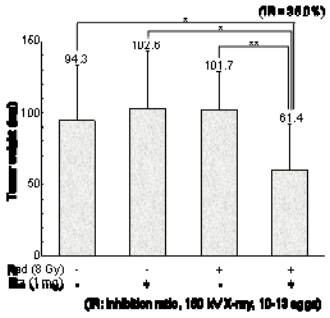
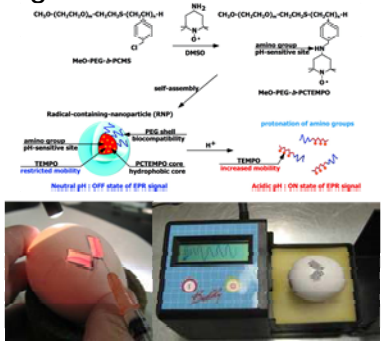


Fig. 1 Evaluation of radiosensitizing activity of TX2244



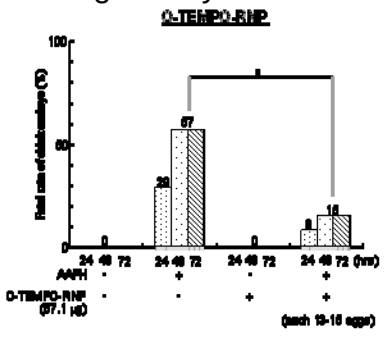
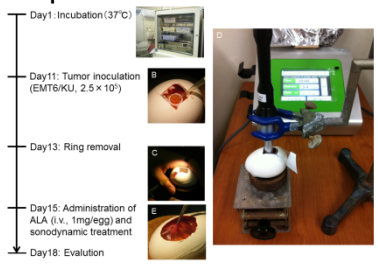


Fig. 2 Evaluation of antioxidative activity of redox nanoparticle



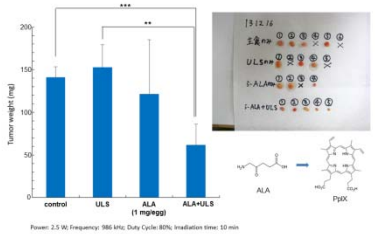


Fig. 3 Evaluation of sonosensitizing activity of 5-ALA

Content:

Although the animal experiments which used the mouse and the rat is indispensable to drug discovery, the use has been restricted for an ethical problem. The zebra fish is developed as alternative experimental animal in recent years. However, only a drug with comparatively high lipophilicity is absorbed and hard to control the amount of absorption using zebra fish. Therefore, development of other experimental animals is strongly required.

Then, we have tried to develop the drug evaluation method which used the developing chicken egg. The developing chicken eggs are the next-generation experimental animal which has many advantages that it is cheap, controllable only at temperature and humidity, individual specificity is small, allergic nature is low, and a special experimental institution is unnecessary. Until now, we have succeeded in the pharmacokinetic analysis and evaluation of biological activity of our designed radiosensitizer / radioprotector, an antiangiogenic / antimetastatic agent, a sonosensitizer, and an antioxidant using the developing chicken egg.

Keywords : developing chicken egg, radiosensitizer/ radioprotector, antiangiogenic/antimetastatic agent, sonosensitizer, antioxidant

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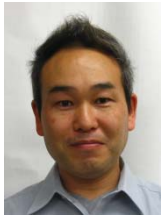


Faculty of Engineering
Tokushima University

Microbial production of functional lipids

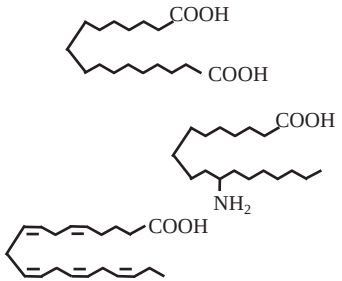
Professor Eiji Sakuradani

Screening of various organisms

Fungus
Basidiomycete
Plant
Microalga
etc.

- Genetic engineering
- Metabolic engineering
- Characterization of enzymes

Microbial production of functional lipids



Content:

Functional lipids such as polyunsaturated fatty acids, hydroxy fatty acids, and dicarboxylic acids are used for food, medicine, and raw materials of chemical compounds. Lipid-relating enzymes and their reactions have not been unclear.

We are trying microbial production of functional lipids by screening of valuable microorganisms, isolation of useful genes from various organisms, and breeding of genetically modified microorganisms. Our research also contains isolation and characterization of novel enzymes related with lipid conversion.

Keywords : microbial conversion, functional lipid, breeding

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Faculty of Engineering
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Macroalgae biomass: A renewable source for bioethanol

Professor Akihiko Tsuji

Macroalgae (seaweed)

Sea lettuce

Fast growth rate, high yield
Low percentage of lignin

Significant amount of sugar (at least 50 %)
Cellulose, starch, laminarin, agar, mannan, alginate etc.

Seaweed

↓

Saccharification

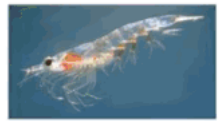
↓

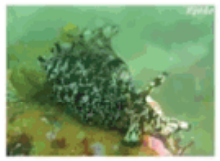
Fermentation

↓

Bioethanol

Discovery of novel enzymes





Enzymes from crustacean, mollusk

↓

Development of efficient enzymatic saccharification

Content:

Marine macroalgae is gaining wide attention as an alternative renewable source of biomass for production of bioethanol, which is grouped under “Third generation biofuels”. Growth rates and yields of material per surface area that can be obtained in seaweeds forests are significantly higher than those reported for terrestrial plants. However efficient digestive enzymes for saccharification of polysaccharides in seaweed is not available.

Marine invertebrates feeding seaweed possess various glucanases. The digestion system of crustacean and mollusk may thus provide useful clues for the establishment of an artificial process for saccharifying polysaccharide in seaweed.

In order to develop efficient enzymatic saccharification system for seaweed, we are now studying endo and exo-glucanases toward various polysaccharides from marine crustacean and mollusk.

Ref: Tsuji et al. (2013) PLOS ONE 8 (6) e65418

Keywords : <enzymes, saccharification, seaweed>

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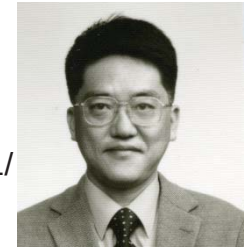

Faculty of Engineering
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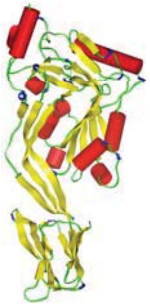
Comprehensive Research on Bacterial Bioactive Molecules

Professor Hideaki Nagamune

1. Search and characterization of BBM

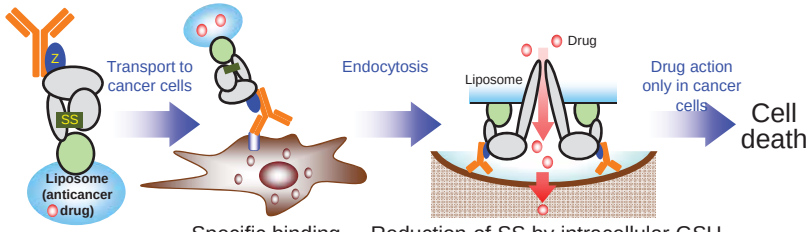
To clarify the molecular mechanism of pathogenicity of pathogenic bacteria and to overcome the infectious diseases, molecular investigations on BBM such as CDC are proceeding.

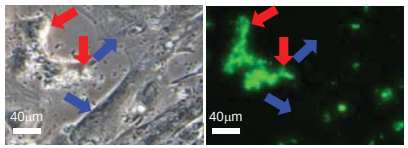


intermedilysin

2. Application: anti-cancer DDS by CDC variants

Based on the findings in CDC investigations, CDCs were remodeled as the variants for nano-biotool of DDS with a module for fixation of cancer-targeting molecule and controlled toxicity *in vivo*.

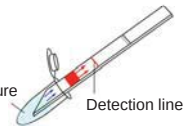




Targeting of fluorescent liposomes to cancer cells by an anti-CEA-CDC variant
Red arrow : HepG2 cell, Blue arrow : Human normal fibroblast

3. PCR immunochromatography for pathogen detection

After amplification and simultaneous labeling of marker gene(s) for various pathogens, the amplicon(s) is detected by immunochromatostrip within 10 min.



Content:

Bacteria produce various bacterial bioactive molecules (BBM) such as toxins, enzymes, chaperones, and small metabolites on their growth stage in the habitat/host. Our main interest is on these BBM in the aspects of understanding of pathogenicity and their application for medical and industrial fields. We currently investigate Gram-positive BBM. For example, we searched cytolysins as oral streptococcal virulence factors, discovered unique cholesterol-dependent cytolysins (CDC) with specificity and directivity to human cells (intermedilysin from *S. intermedius* and Sm-hPAF from *S. mitis*, respectively) and twin peptide cytolysins (*i.e.*, streptolysin S of *S. anginosus*), and characterized them. Our team is continuing further investigations on their molecular action mechanism, regulation of gene expression and roles in pathogenicity. Moreover, development of DDS for anticancer treatment is also proceeding by using nano-biotool: CDC variants designed to have cancer-targeting module and controlled toxicity only in intracellular condition. We are also promoting development of inexpensive and rapid PCR immunochromatography system for diagnosis and for hygiene control in food processing and medical facilities.

Keywords: bacteria, toxin, enzyme, DDS, diagnosis system

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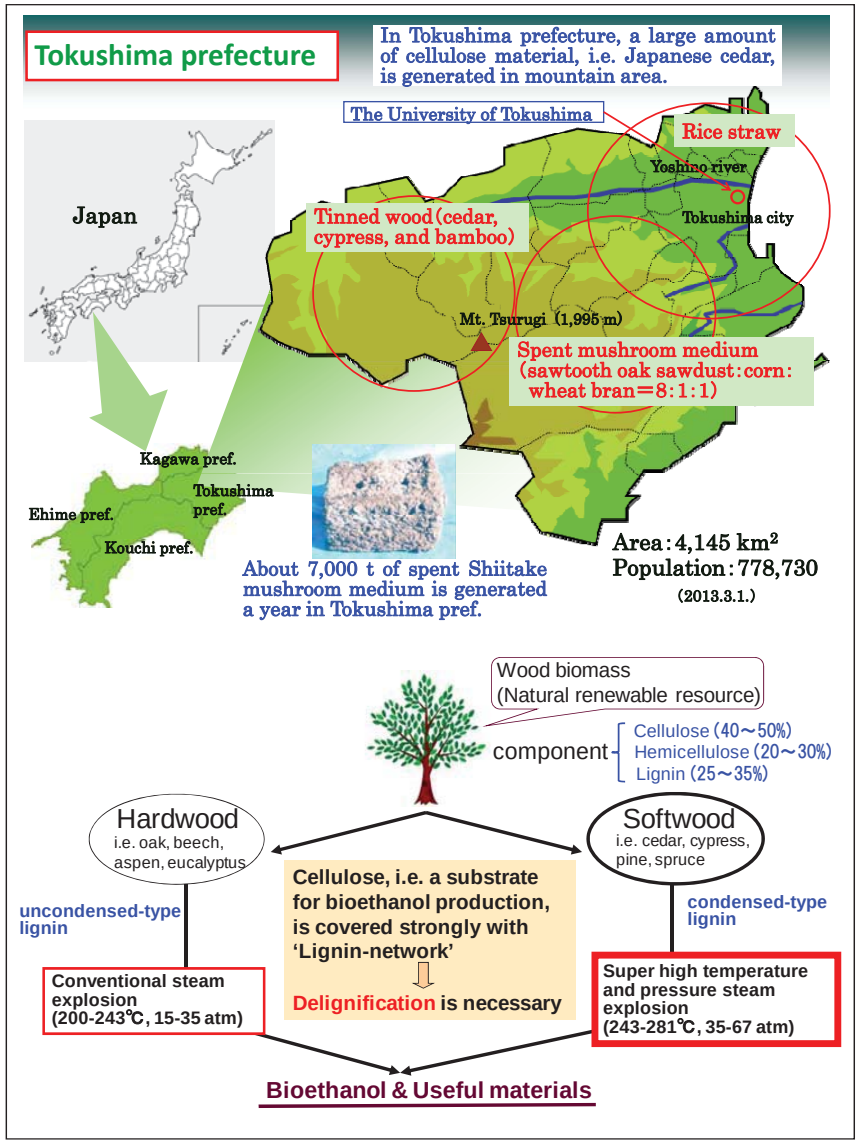
Effective Utilization of Cellulosic Biomass

Professor Yoshitoshi Nakamura



Content:

Steam explosion method has been recognized as one of the most effective pretreatments for delignification of wood biomass. This method seems to be very effective for hardwoods, but ineffective for softwoods that contain a comparatively large amount of condensed-type lignin. Therefore, the steam explosion with only ultrahigh temperature and pressure steam, i.e. up to 281 ◦C and 67 atm, that are significantly higher than the conventional steam explosion (200–243 ◦C and 15–35 atm), was applied for not only the pretreatment of softwood biomass but also the effective conversion into bioethanol and useful materials.

This investigation aims to develop the total conversion process structural components of softwood biomass into useful fuel and materials using Japanese cedar. The structural components, i.e. cellulose, water soluble material, methanol soluble lignin, and Klason lignin, in the softwood biomass treated by the steam explosion were converted into various biofuels and useful materials, i.e. antioxidant materials, electronic circuit board made of lignin, ethanol, methane gas, and cellulose nanofiber materials.

Keywords: Biomass Conversion, Bioremediation

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Bio-Membrane Engineering

Professor Hitoshi Matsuki

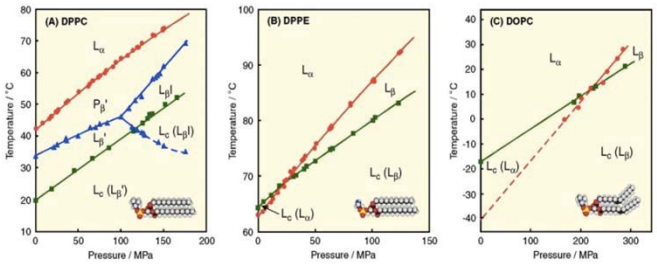

Fig. 1 Barotropic phase behavior of lipid bilayers

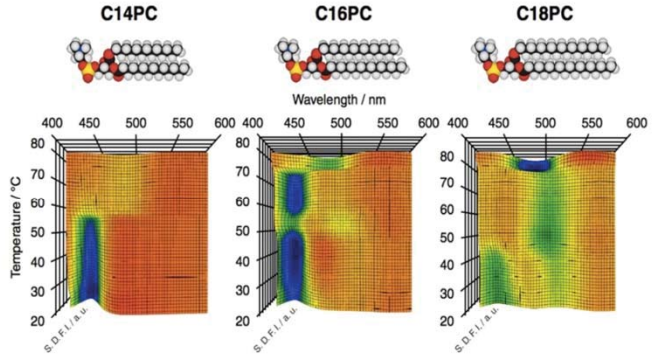

Fig. 2 Imaging of packing states of lipid bilayers

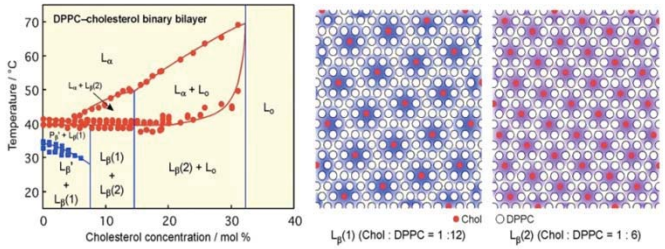

Fig. 3 Miscibility of lipid-cholesterol binary bilayer

Content:

In order to elucidate various phenomena of biological membranes such as phase transitions, nonbilayer formation, lipid raft, membrane fusion and fission, anesthetic action, studies on bio- and model membranes have been made by means of biophysical and surface-science approaches. One of characteristics of the research is that pressure as well as temperature and concentrations is used as an analytical tools for bio-membrane studies. Since the variables like temperature and concentrations always contain a diffusion process, there exist the propagation delay and the local differences. On the other hand, pressure acts uniformly and instantaneously due to Pascal's principle and brings about large mechanical fluctuation on biological membranes. Thereby novel phenomena that are not observable under atmospheric pressure are observable under high pressure. Pressure-induced interdigitation of phosphatidylcholine bilayers and the pressure reversal of anesthesia are the representative examples. Left hand side figures show barotropic phase behavior of lipid bilayers (Fig. 1), imaging of packing states of lipid bilayers (Fig. 2) and miscibility of lipid-cholesterol binary bilayer (Fig. 3), which were revealed recently.

Keywords : lipid bilayer membrane, phase transition, high pressure

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Phase separation within sterol-containing phospholipid bilayers

Associate Professor Nobutake Tamai

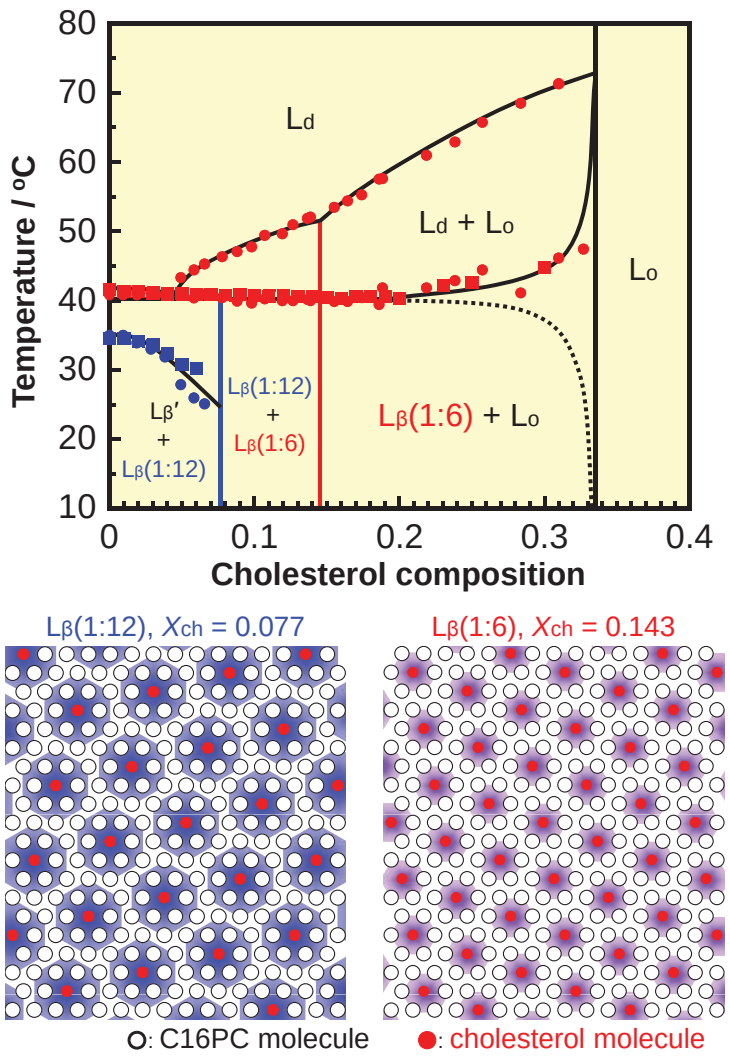

Fig. 1 Phase diagram of C16PC-cholesterol bilayer.

Content:

In 1990's, it was reported that domains composed of sphingolipids and cholesterol are formed within cell membranes, and they were termed *lipid rafts*. Such domains are thought to be relevant to lateral phase separation induced by cholesterol within membranes. Although tremendous efforts have so far been made to explain the phase behavior of cholesterol-containing binary bilayers, it has not been completely elucidated yet.

Recently, we have succeeded in constructing the compositional phase diagrams of diacylphosphatidylcholine-cholesterol binary bilayers using differential scanning calorimetry and Prodan fluorescence spectroscopy. On the basis of the diagrams, we could elucidate the membrane properties related to the aggregate structure of those binary bilayers, such as the distribution of cholesterol within the binary bilayer and the miscibility between phospholipid and cholesterol, from a thermodynamic standpoint.

Keywords : cholesterol, phase separation, raft domain

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Molecular biology of pathogenic streptococci

Associate Prof. Toshifumi Tomoyasu

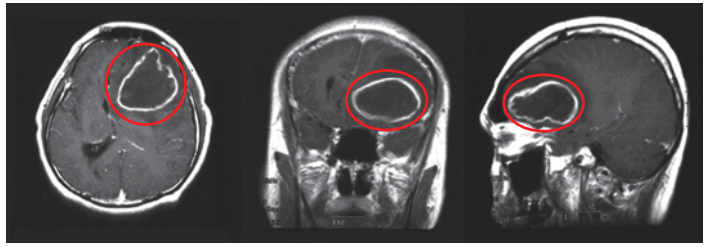

Fig. 1 Brain abscess by *S. intermedius*

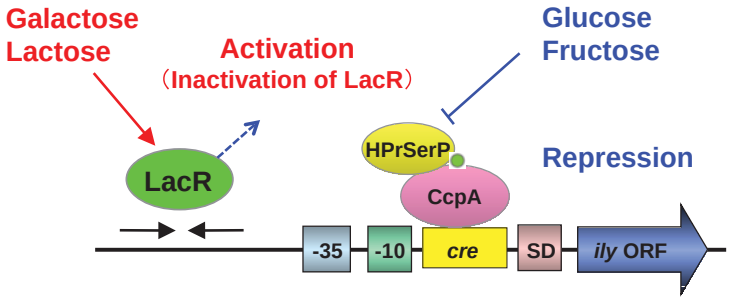

Fig. 2 Transcriptional regulation factors for *ily*

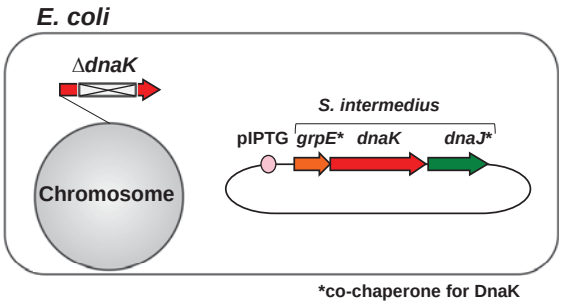

Fig. 3 Analyzing system for chaperone activity of G⁺ DnaK using *E. coli dnaK* knockout (Δ*dnaK*) mutant

Content:

Streptococcus intermedius is a part of the normal flora of the human oral cavity and a leading cause of deep-seated infections, including brain and liver abscesses (Fig. 1). We are investigating the mechanism involved in the regulation of transcription of *ily* (1) that encodes the human-specific cytolysin, intermedilysin, which is the major virulence factor. In addition, we are examining the quality control mechanism for cytosolic proteins by *S. intermedius* DnaK (2).

(1)Transcriptional control mechanism for *ily*

We found two transcriptional regulation factors for *ily*, catabolite control protein (CcpA) and lactose phosphotransferase system repressor (LacR) (Fig. 2). In addition, we reported that ILY-overproducing strains isolated from deep-seated abscesses such as brain and liver abscesses have a loss-of-function mutation in the *lacR*.

(2) Cytosolic protein quality control mechanism

Previous studies have shown that DnaK from gram-positive (G^+) bacteria was unable to show the activity in gram-negative (G^-) *Escherichia coli*, which is the model bacterium for studying the chaperone function. Therefore, many cellular functions of G^+ DnaK remain to be elucidated. We successfully created the system, which could activate the G^+ *S. intermedius* DnaK in *E. coli* (Fig. 3), and thus we have been analyzing the function of G^+ DnaK using our system.

Keywords：Streptococci, Molecular biology, Pathogen, Molecular chaperone

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Analysis of Adaptation and Evolution Mechanism and Its Utilization

Associate Professor Hideaki Maseda

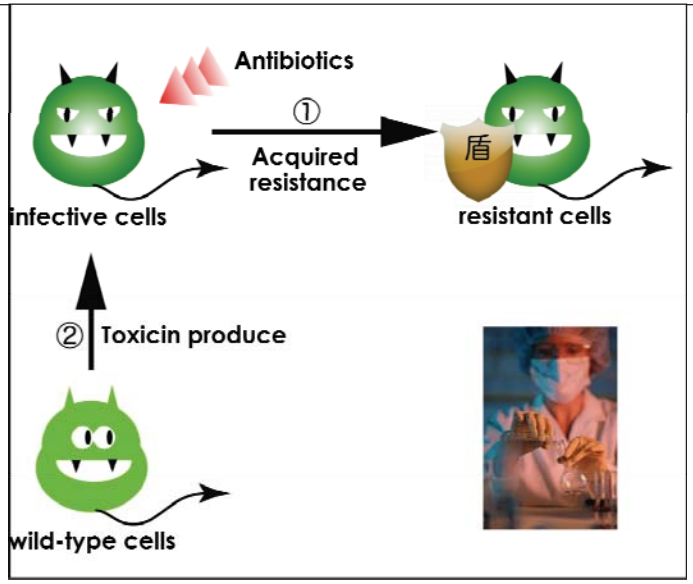

Fig. 1 Acquirement process of antibiotic resistance

Fig. 2 Blue-green algae

Content:

Since the life was born on the earth, the living thing has adapted and evolved to various environments. Now, there are no less than 30 million sorts of living thing in the earth in case of including small living things like bacteria. And they have lived for a long time with interacting mutually, and support each other at a certain time, but attack mutually at other times

Our group analyze that the mechanisms of adaptation and evolution which occur as a result of involving the various living things in such SEITAI (a living body and ecology) in detail on the genetic level, and want to know the mystery of biodiversity. Finally, we aim at using those knowledge for artificial control of a microbe such as effective production of useful substances and control of bacterial infection.

We are enhancing the following researches; ① Analysis of adaptation and evolution mechanism of bacteria to antibiotics, and ② Analysis of co-evolution of the production gene of toxicin in cyanobacteria and its specific degradative gene in bacteria.

Keywords：adaptation, evolution, resistance, toxicin

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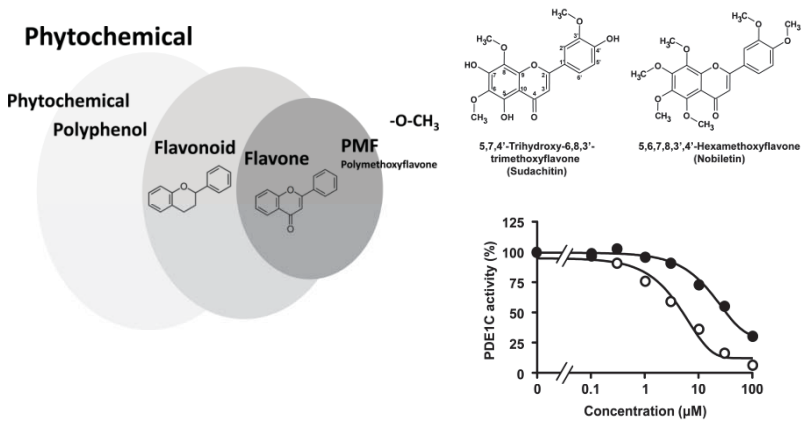
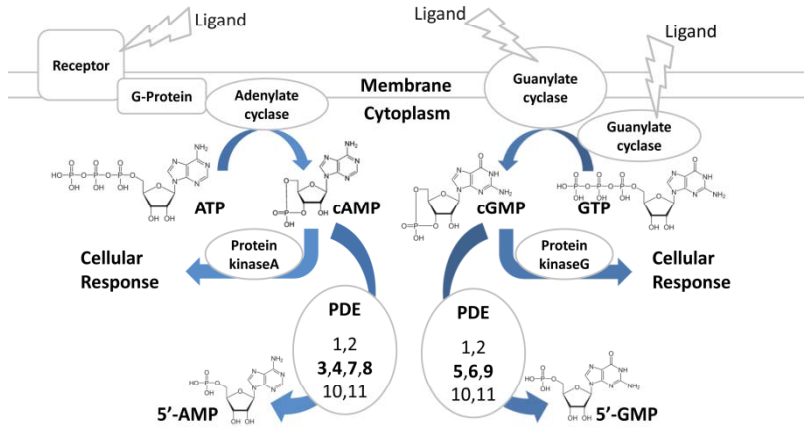
Development of New Functional Food Materials based on the PDE Inhibitory Activity

Associate Professor Keizo Yuasa



PDE：cyclic nucleotide phosphodiesterase



Content:

Although several thousand polyphenols have been identified in plant, most of them are not effectively used. In the pericarp of *Citrus sudachi*, a well-known fruit in Tokushima Prefecture in Japan, sudachitin is found, but its biological activity has not been analyzed yet. On the other hand, nobiletin, a typical polymethoxyflavone from the pericarp of *Citrus depressa*, possesses a wide range of pharmacological activities. Nobiletin stimulates cAMP signaling through inhibition of cyclic nucleotide phosphodiesterase (PDE), which catalyzes the hydrolysis of cAMP and cGMP. Mammalian PDEs are composed of 21 genes and are closely related to the regulation of numerous physiological functions through alteration of intracellular cyclic nucleotide levels. Therefore, PDE selective inhibitors are expected to be useful for the treatment of various diseases.

We analyze the inhibitory effects of a variety of polyphenols including sudachitin on PDE activities, and are tackling the development of new functional food materials based on the inhibitory activity.

Keywords: polyphenol, functional food material, cyclic nucleotide phosphodiesterase

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Creation of High Value-Added Materials from Plant Biomass

Associate Professor Chikako Asada

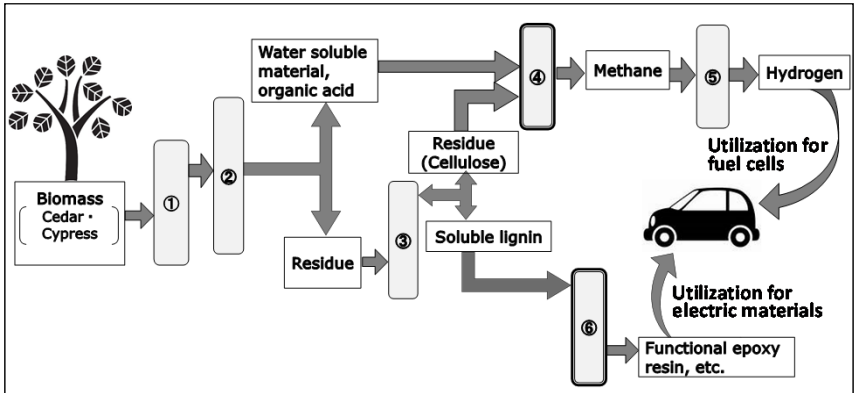

Fig.1 Collaborative creation system of hydrogen and resin from plant biomass. ① Steam explosion, ② Water extraction, ③ Acetone extraction, ④ Methane fermentation, ⑤ Steam reforming, ⑥ Resinification.

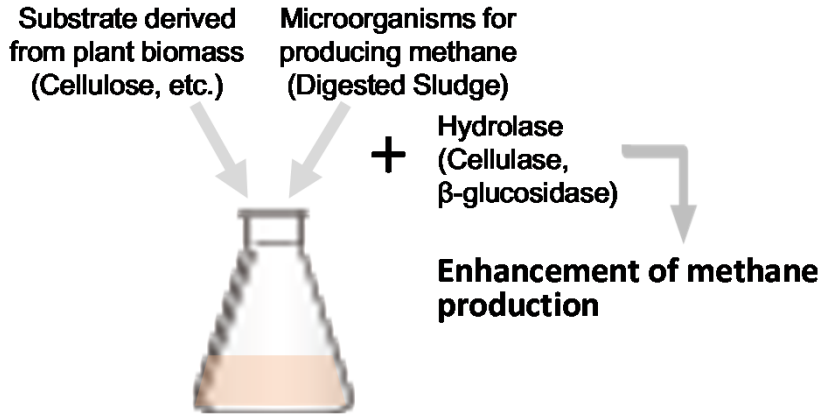

Fig.2 Utilization of cellulose-degrading enzyme that is produced in large quantities by recombinant *E. coli*.

Content:

To develop alternative material of oil substitute has been requested until present while increasing since an oil crisis. It is over 30 years since the second oil crisis that a biomass fuel attracts attention, but it is hard to say the energy from using biomass is effective for CO_2 reduction, and suitable for reality use of industrial system.

In Japanese mountain, a large quantities of softwood (cedar or cypress) has left unused and unattended. Because softwood material is difficult to pretreat for de-lignification more than other biomass due to the strong lignin network structure of softwood, we attempted to use this softwood material for effective utilization.

About the energy conversion of the biomass, methane ferments to produce methane becoming the source of hydrogen which is the energy source of the fuel cell. The hydrogen production is prepared by the steam reforming method of methane included in natural gas mainly, but the use of biomethane is expected now to solve problems such as the drying up or the global warming of fossil resources. The material (cellulose and hemicellulose) are converted into methane, and the synthesis of functional epoxy resin is attempted using other component, i.e. lignin.

Keywords : methane fermentation, biomass, high temperature-resistant enzyme

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Production of useful chemicals from branches pruned from Japanese pear tree

Associate professor Chizuru Sasaki

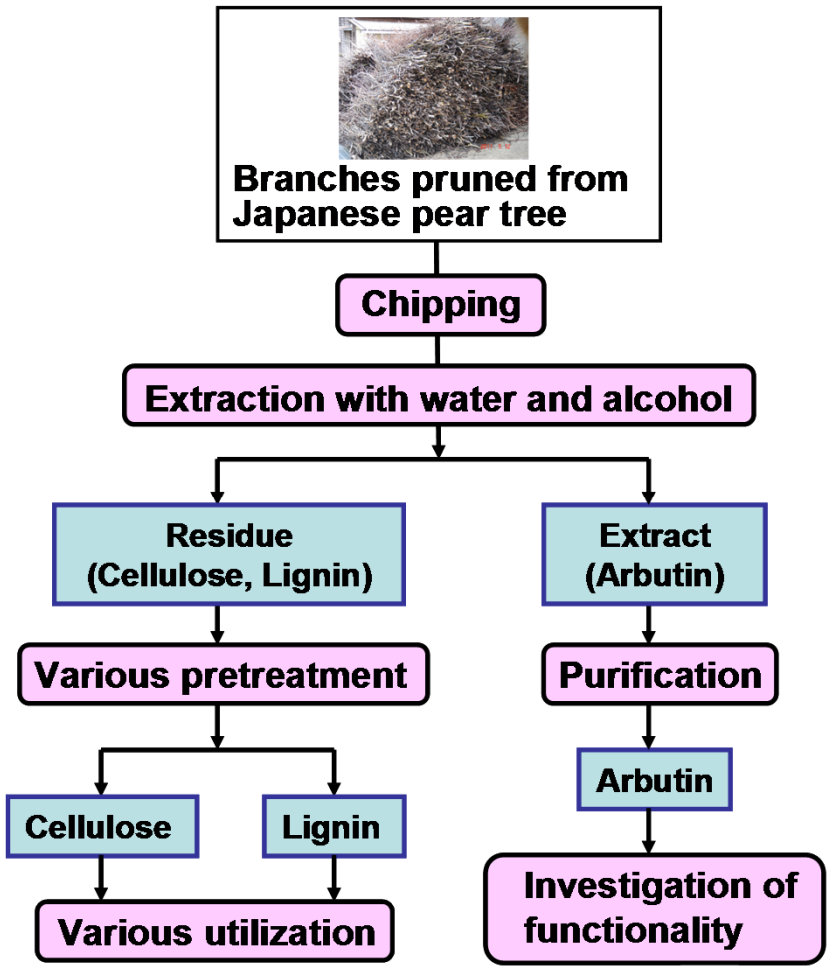

Fig. Production of useful chemicals from branches pruned from Japanese pear tree

Content:

Branches pruned from fruit trees are byproduct of fruit cultivation and a abundant source of biomass. Large quantities of this material remain unutilized and thus accumulate on farms. Especially, branches pruned from Japanese pear tree are one of the unutilized discarded byproducts, since pear plantation farms are located in urban areas, it should be possible to limit the transportation and collection costs of this unutilized biomass.

This study aims to identify efficient ways of using discarded pear branches. The main components of lignocellulosic biomass, i.e. pear branches, are cellulose and lignin. The cellulose can be converted into bio-liquid fuel and resource of plastics, the lignin also can be a resource of plastics. Moreover, recently, we found out the functional polyphenol, arbutin, from branches pruned from Japanese pear tree. Arbutin has been widely used as a whitening agent in cosmetics, because of its tyrosinase-inhibiting qualities. Thus, discarded woody biomass are promissing resource for various useful chemicals.

Keywords：cellulose, lignin, polyphenol

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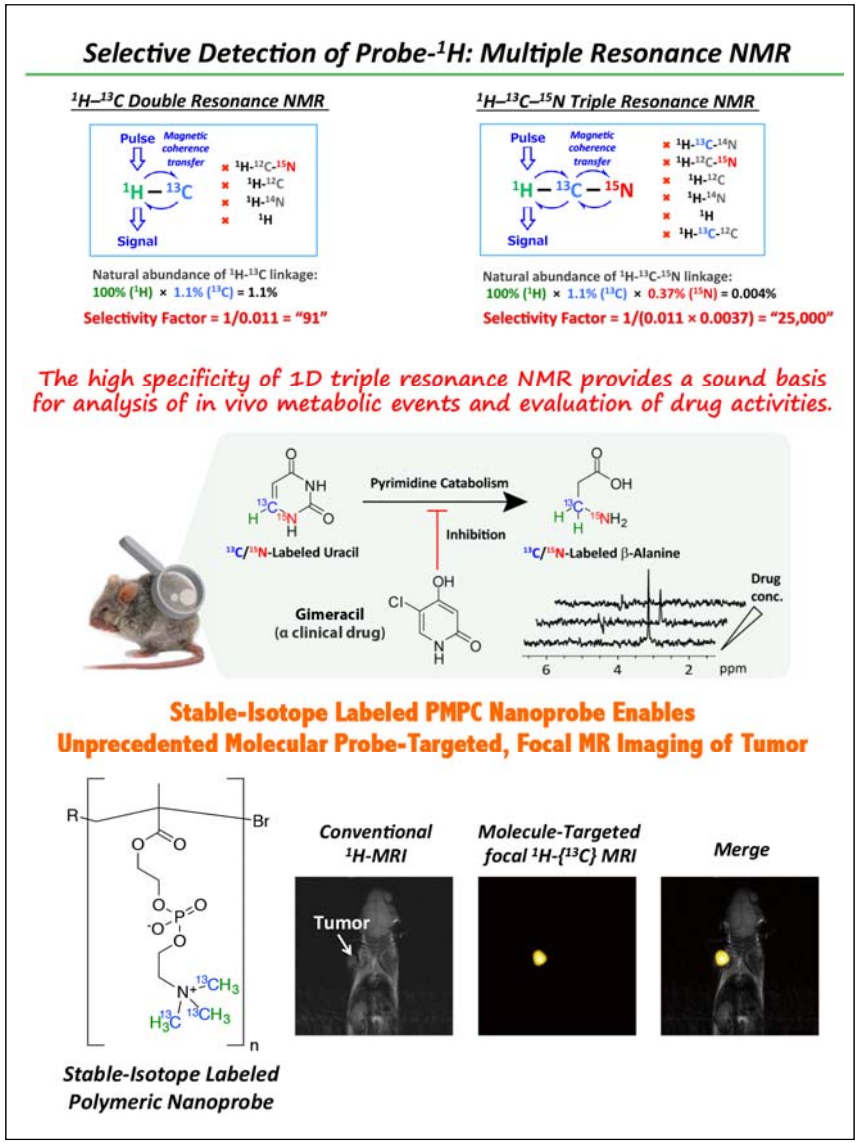
Development of New Tools for Molecule-Targeted MR Imaging

Associate Professor Hisatsugu Yamada



My current research interest is focused on the development of new molecular probes for minimally invasive and diagnostic imaging. NMR/MR is one of the most promising techniques for the analysis of biochemical/biomedical reactions, but it has a couple of problems if it is to be applied to complicated living systems. We first aimed at the application of multiple-resonance NMR to in situ monitoring of a particular cellular reaction. Multiple-resonance NMR is a method that correlates three successive NMR-active nuclei with different Larmor frequencies (^{1}H-^{13}C-^{15}N in the present case). This method, which is applicable, in principle, to various HCN compounds, should markedly suppress background noise. Recently, we revealed that (1) multiple-resonance NMR is applicable to metabolic analysis of ^{13}C/^{15}N-labeled uracil, (2) integration of stable isotopes into the biocompatible polymer-tag (^{13}C/^{15}N-PMPC) enabled observation of the selective triple resonance NMR signal of ^{13}C/^{15}N-PMPC at a nano-molar level in a mouse liver lysate, and (3) application of a multiple-resonance NMR technique to a MR imaging allows us to obtain the selective MR image of ^{13}C/^{15}N-PMPC without endogenous noise signals. A final goal of our research is the application of this strategy to molecule-targeted functional MRI.

Keywords: Multiple-resonance NMR, Probes, Imaging

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Design, production and quality improvement of antibody

Assistant prof. Masayoshi Onitsuka

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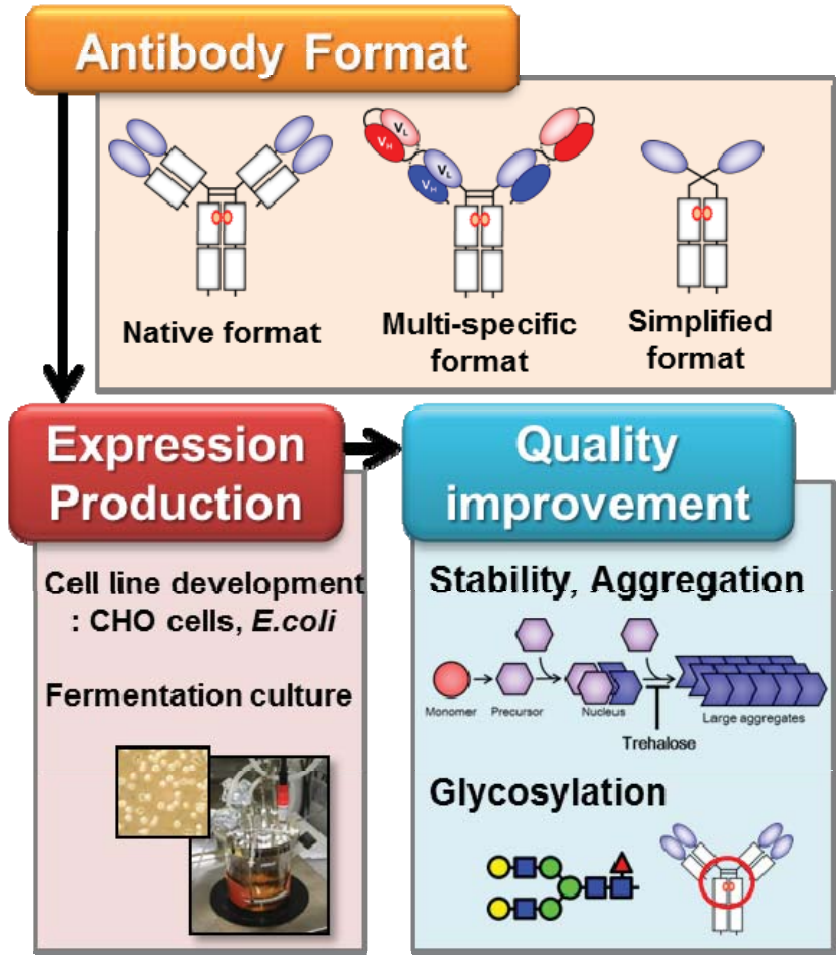

Content:

Recently, engineered formats of antibody (such as multi-specific and simplified formats) have been emerged as promising candidate for next-generation therapeutic antibody. However, the strategies for their industrial production are not successfully constructed, because little is known about biophysical characteristics of the engineered formats.

The aim of the study is to develop the production process based on the characteristics of the engineered formats. Research topics are as follows:

1) Stability and aggregation analysis of engineered formats, 2) Cell line development for production of recombinant antibody using CHO cells and *E.coli*, 3) Development of chemical chaperone medium for anti-aggregation in cell culture, 4) *N*-glycosylation analysis of antibody and its improvement.

The study is performed as part of research interests of professor Takeshi Omasa.

Keywords : antibody production, Chinese hamster ovary (CHO) cells, antibody aggregation

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Phase behavior of phospholipid bilayers under high pressure

Research Associate Masaki Goto

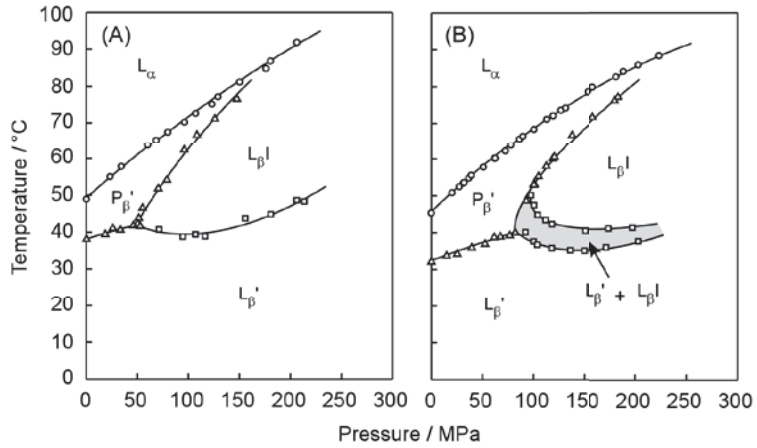

Fig.1 Pressure-temperature phase diagrams of asymmetric PC bilayers.

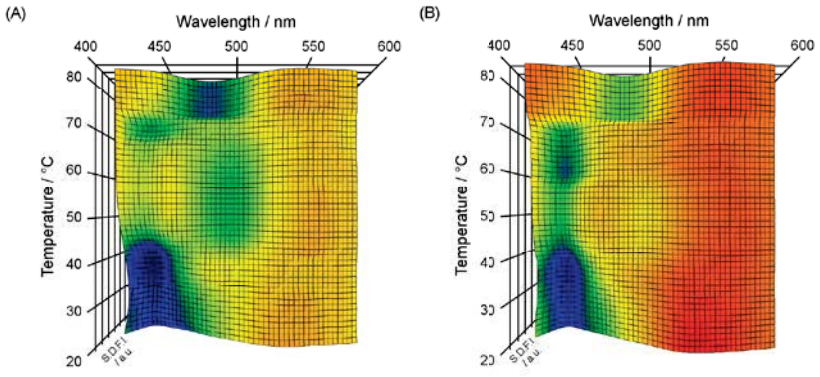

Fig. 2 3D image plots of asymmetric PC bilayers.

Content:

Phospholipids form bilayer aggregates called vesicles or liposomes in aqueous solution. The aggregates induce structural changes called phase transitions depending on temperature, pressure, pH and added salts. Studies concerning the effect of the environmental variables on lipid membranes concentrate on that of temperature and concentration of added salts and there are few reports of pressure effect.

We have focused our attention on pressure as experiment variables and constructed the thermodynamic quantities including the volume information and temperature-pressure phase diagrams of various phospholipid bilayers. Recently, we have established a high-pressure fluorescence technique using the fluorescent probe Prodan, which enables us to observe precise phase transitions, especially bilayer interdigitation. Further, we have also showed that a three-dimensional image plot based on the second-derivative of the Prodan fluorescence provides a correlation between the probe location in the bilayer and the state of the bilayer.

Keywords : phospholipid, phase transition, high pressure

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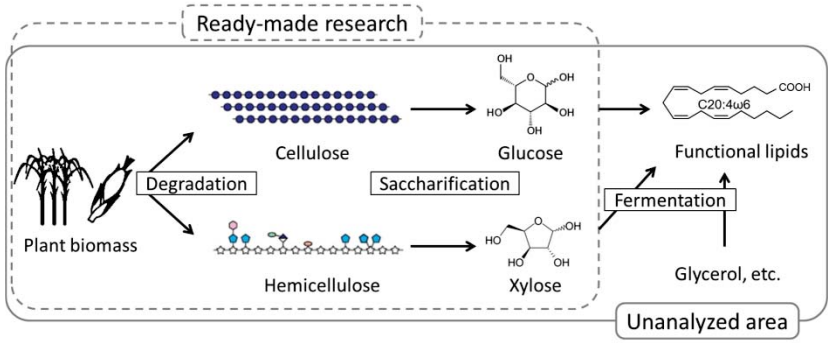
Fermentative production from unused resources

Assist. Prof. Takaiku SAKAMOTO

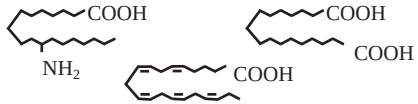


・Plan

Sampling of wood-rotting fungi

・Lipid analysis
・Genetic engineering
・Metabolic engineering, etc.

Microbial production of functional lipids



Content:

Ligninolytic and cellulolytic enzymes from wood-rotting fungi have been actively studied as the key tools for degradation and saccharification of the plant biomass. Most microorganisms including yeasts produce various compounds through fermentation by using saccharified biomass. Therefore, we try to construct the consistent process that includes all of phases, degradation, saccharification and fermentation.

Functional lipids such as polyunsaturated fatty acids, hydroxy fatty acids, and dicarboxylic acids are used for food, medicine, and raw materials of chemical compounds. We are trying to isolate the fungus which produce functional lipids by screening of valuable wood-rotting fungi, and to construct the consistent process of biomass-fermentative production using the fungus.

Keywords : microbial conversion, functional lipid, breeding

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Development of novel biocides and methods to sterilize harmful microbes

Assistant Professor Akihiro Shirai

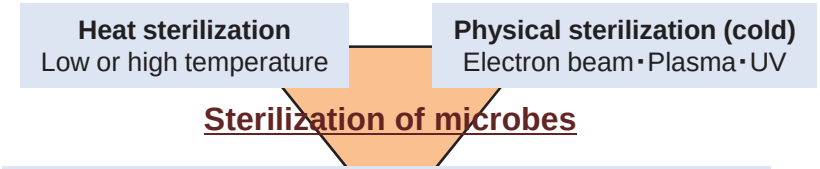

Fig. 1 Sterilization methods against harmful microbes

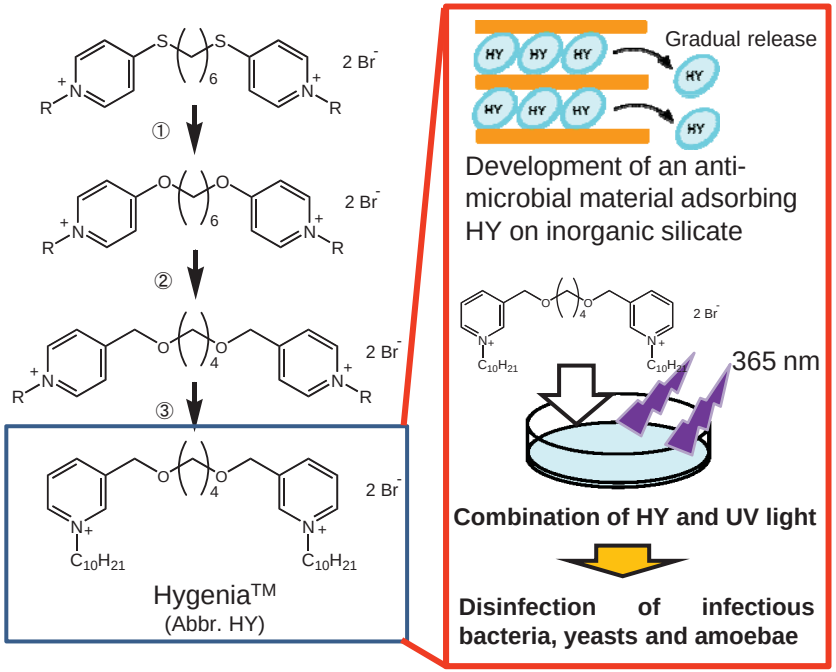

Fig. 2 Optimization of new biocides and applied research of Hygenia™

Content:

Sterilization of microbes is classified into heat- and cold-sterilizations, and there are physical- and chemical-sterilizations in the cold sterilization (Fig. 1). Their methods have been constructed to sterilize harmful microbes effectively on clothing, food and housing, pharmaceuticals and environmental sanitation. Focusing on chemical sterilization, many scientists have developed new biocides and studying their formulations and applications for a long time. However, the infectious diseases caused by harmful microbes and the deterioration of quality of products by microbes have occurred, even if chemical sterilization is carried out continuously, and moreover, excessive use of biocide causes emergence of resistant microbes. Therefore, I am developing new biocides and their application to construct effective sterilization method.

I have reported "Hygenia™" as a biocide and its antimicrobial material, and a sterilization method by combination of Hygenia™ and UV light (Fig. 2). The present subject is the development of new biocides which transform into active molecule by being treated physically, such as light irradiation, and of sterilization methods applied with their biocides.

Keywords : disinfection, antimicrobial agents

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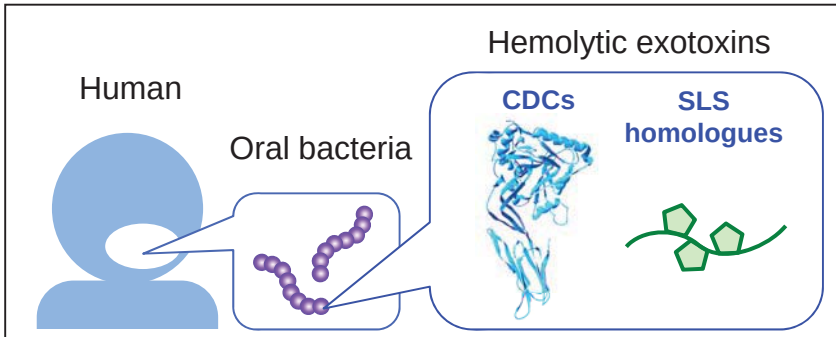
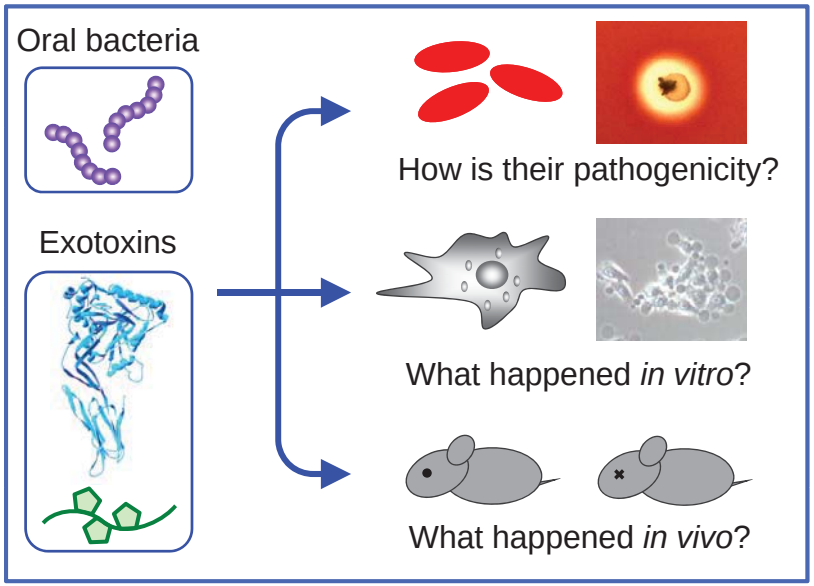
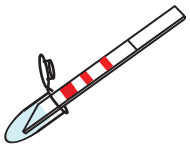
Mechanism for Action of Bacterial Toxin and Host Response

Assistant Professor Atsushi Tabata







Detection system for pathogens using “PCR immuno-chromatography” is also developing.

Content:

Background: Various bacteria including streptococci are persistent in oral cavity of human. In general, an oral streptococci had been accepted with low- or no-pathogenic potential except for *Streptococcus mutans*, responsible for the oral disorders such as dental caries. However, the non-oral disorders caused by other oral streptococci is also reported recently. In addition, some clinical oral streptococci is known to produce a hemolytic toxin. From these situations, the importance of the appropriate oral care is received increasing attention, and it is needed to be re-evaluated to maintenance and enhance our health.

Overview and feature of study: We are investigating about the function of streptococcal exotoxins [cholesterol-dependent cytolysins (CDCs) and streptolysin S (SLS) homologue] produced from Anginosus group streptococci (AGS). The mode of action of these exotoxins and the pathogenic potential of exotoxin-producing AGS are also investigated both *in vitro* and *in vivo*. Furthermore, the system to detect the various pathogenic bacteria is also developing using the method of “PCR immune-chromatography”.

Keywords: Bacterial toxin, Mechanism of action
Host response

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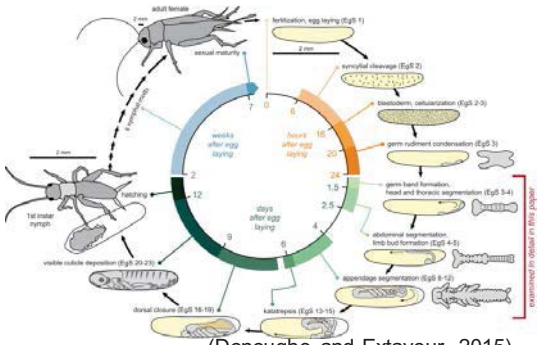
Study on genome function involved in developmental and regeneration processes

Assistant Professor Taro Mito

Life cycle of a cricket

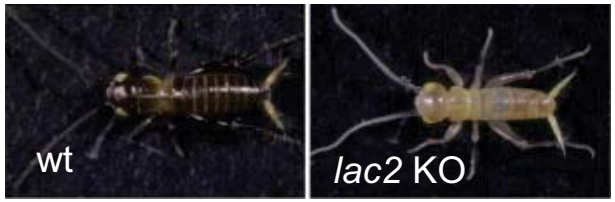


(Donoughe and Extavour, 2015)

Leg regeneration in a cricket nymph

Transgenesis in crickets

Gene knockout using genome editing



We have been studying on developmental and regeneration mechanisms and their evolution, using an insect model system. The two spotted cricket *Gryllus bimculatus* is a principal model species in our study. We are conducting whole genome sequencing of this species as well as developing techniques for genome function analysis.

We have successfully introduced RNA-interference, transgenic, and genome-editing technologies into the cricket system. Using the genome-editing technology, greatly sophisticated genome modification is becoming possible.

Using the above technologies, we aim to reveal molecular mechanisms of morphogenesis in developmental and regeneration processes. Making disease model insects and application to regenerative medicine are also included in our future plans.

Keywords：genome modification, morphogenesis, Insect model

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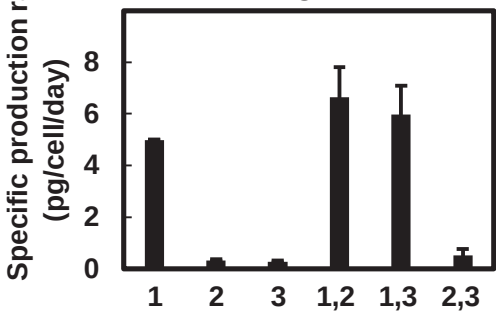
Cell engineering for therapeutic antibody production

Designated Assistant Professor Noriko Yamano

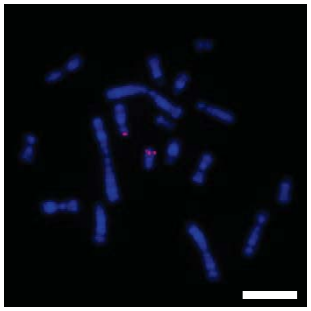
Rotation culture of CHO cells

Determination of antibody concentration

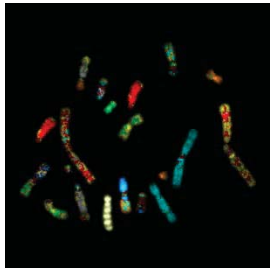
Productivity differences within the vector integration sites



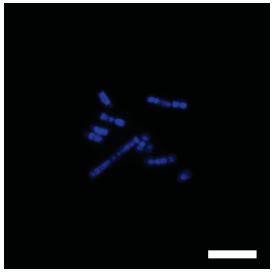
BAC-FISH

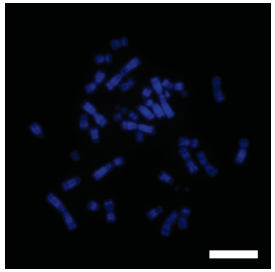


Multicolor-FISH



Chromosome aneuploidy





Scale bars; 10 μm

Chinese hamster ovary (CHO) cell lines are widely used in the field of biotechnology to produce therapeutic antibodies. Chromosomes of CHO cell are unstable and variation of chromosome number occurs in the CHO cells.

I focus on genomic instability of CHO cells to establish productive cell lines.

We have previously constructed a CHO genomic BAC library which enables us to distinguish all the 20 individual chromosomes in CHO cells. Using this material, I am working on the stability of each chromosome and would like to examine the differences in antibody productivity within various expression vector integration sites. I am also interested in the favorable chromosome distribution in antibody production, effects of chromosomal instability itself, and modifications of the cell function by genetic engineering.

Through these studies, the final goal of my research is to construct new cell lines that can more efficiently produce therapeutic antibodies.

Keywords : CHO cells, genomic instability, genetic engineering

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