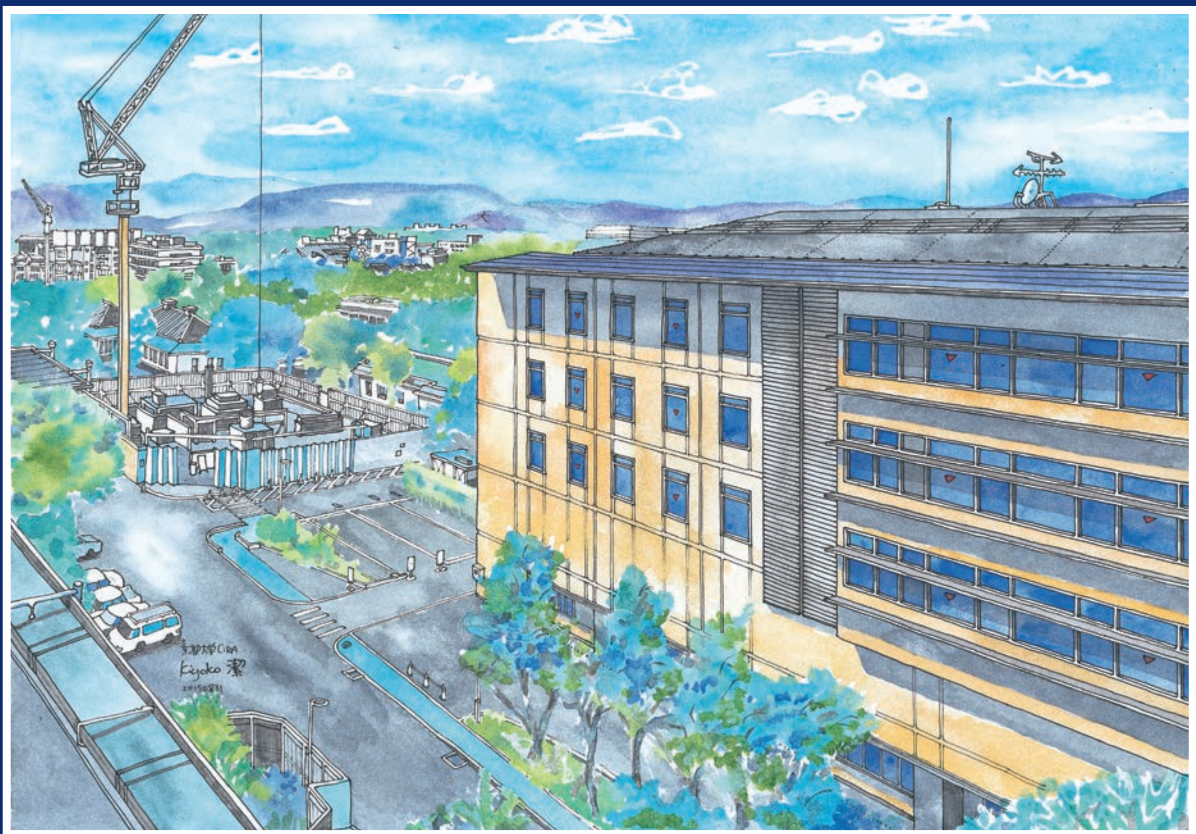
Kyoto University

Research Activities

Vol. 5 No. 2 September 2015

Special Feature:

Takeda-CiRA Joint Program for iPS Cell Applications and Industry-Academia Collaboration



京都大学

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Cover:

The main building of the Center for iPS Cell Research and Application (CiRA)

➡ p. 12

Message from the President

Serving Society through Innovation and Creativity

IN recent years, Japanese universities have been strongly encouraged to connect research results with industrial applications. Since its founding in 1897, Kyoto University has contributed to the advancement of industry and society by fostering talented human resources and pursuing innovative research to meet society's needs.

To cite one example, Dr. Sakuro Tanabe is known as one of the founders of modern Japanese civil engineering. In the early days of modern civil engineering, Dr. Tanabe's Lake Biwa Canal Project constructed a new canal connecting Kyoto City with Lake Biwa. The achievements of that project later led to the construction of Japan's first hydroelectric power plant, and contributed to the revitalization of industry in Kyoto, which had fallen into a decline after the Meiji Restoration. Another notable example is Dr. Ichiro Sakurada, who invented Vinylon, the first Japan-made synthetic fiber, in 1939. Vinylon greatly relieved the hardships caused by a lack of cotton in the wake of the Second World War.

Dr. Isamu Akasaki, who was awarded the 2014 Nobel Prize in Physics for the development of a blue light-emitting diode (LED), was also a Kyoto University graduate. In a commemorative lecture delivered at his honorary doctorate conferment ceremony in May 2015, Dr. Akasaki said "I remember the time when, as a new KU student, I heard the news of Dr. Hideki Yukawa receiving the 1949 Nobel Prize in Physics. I vowed that I too would accomplish something unprecedented—even a small feat. This led me to my research on the blue LED." Kyoto University has a long tradition of valuing research based on new ideas and concepts, and that innovative spirit has been the driving force behind many new discoveries and inventions.

This distinctive academic culture is also behind Kyoto University's dynamic engagement in industry-academia collaboration relating to iPS cell research. iPS cells are a type of stem cell developed by Dr. Shinya Yamanaka in 2006. In recognition of that accomplishment, Dr. Yamanaka was awarded the 2012 Nobel Prize in Physiology or Medicine. Kyoto University's Center for iPS Cell Research and Application (CiRA) has launched many collaborative research projects with leading pharmaceutical companies in Japan and overseas. The university's Graduate School of Pharmaceutical Sciences has also established a new research center for the development of new drugs using iPS cells.

This issue features reports on several of our industry-academia collaboration projects centering on iPS cells or other areas of medicine. The articles, written by our university's researchers themselves, are not only interesting from a science and technology point of view, but are also of general interest due to the wealth of new ideas and concepts they contain. Reading the features, I feel proud of our scholars, and of our university's tradition of academic freedom. As always, we are limited by the size of this publication, and the research covered herein represents only small a part of Kyoto University's activities. I hope that you will find this issue interesting, and that it will convey a sense of the pioneering spirit that drives our research.

September 2015

Juichi Yamagiwa
President, Kyoto University

FEATURE

Takeda-CiRA Joint Program and Industry-Academia Collaboration

MED-SCI

CiRA collaboration with Takeda: Billions of yen for iPS cell research

THE discovery of induced pluripotent stem cells (iPSCs) is anticipated to change medical research and treatment. Japan has invested heavily in this technology, beginning with the creation of CiRA, an institute devoted to the research and application of iPSCs at Kyoto University. Sharing investment has been industry. The most recent example is the comprehensive partnership between CiRA and Takeda Pharmaceutical Co. Ltd. announced last April.

Over the past decade, stem cells have captured the imagination of the public as a potential miracle cure. Stories abound about stem cell discoveries have hinted at the possibility of new treatments for patients suffering from debilitating diseases and injuries. Yet, stem cells have been used as treatments for decades. What distinguishes the recent stem cell excitement from the past?

Stem cells come in many types, but the latest attention is specifically about pluripotent stem cells (PSCs). PSCs emerge at the very early moments of development and have the ability to self renew and differentiate into various cell types of the adult body, which means they have the potential to replace any cell that is diseased or destroyed. Unfortunately, unlike other stem cells, PSCs do not exist in the adult body.

PSCs can be created in the laboratory, however. The first of these were embryonic stem cells (ESCs). More than any stem cell discovered before them, ESCs have shown remarkable curative potential for various diseases and injuries. However, their use has been subject to stringent laws, as their acquisition requires the destruction of fertilized embryos, which has created controversy among the public and led to relatively severe limitations in their use for research. More recently, another PSC type, induced pluripotent stem cells (iPSCs), was reported. Unlike ESCs, iPSCs can be generated from adult cells and avoid the aforementioned ethical concerns. Equally important, they share the same fundamental properties as ESCs and are therefore expected to have the same curative potential.

Somewhat paradoxically, while they can be acquired from the body, iPSCs do not actually exist in the body. They are created by Professor Shinya Yamanaka and other researchers at Kyoto University. Prior to iPSCs, it was believed that a cell develops unidirectionally, from a primitive to mature state, with no possibility of reversal. Thus, once a fertile egg differentiates into a somatic cell – for example, a skin cell – it will forever be a skin cell until it dies. Yamanaka and his team, however, showed that a cell's fate need not be final. They demonstrated that by inducing specific genes, they could reprogram a differentiated cell to the pluripotent state, i.e. an iPSC. Because iPSCs are pluripotent, they can be differentiated into different cell types of the body. In other words, one can reprogram skin cells into iPSCs, which can then be differentiated into any cell type of choice – neural cells, pancreatic cells, muscle cells, etc. Theoretically just about any cell type in the human body can be reprogrammed into any other cell type using Yamanaka's discovery.

The impact of this realization cannot be exaggerated. Since the first reports by Yamanaka on iPSCs from mouse fibroblasts in 2006 and human fibroblasts in 2007, there has been an explosion in cell reprogramming science. The potential of iPSCs as medical treatments has already been demonstrated in a long list of cells and tissues. Even though it has still not been 10 years since their birth, international conferences on iPSCs are abound, with the next one happening in Kyoto in March 2016.

In recognition of his discovery, Yamanaka was awarded the Nobel Prize in Physiology or Medicine in 2012, only six years after the first iPSC report. Moreover, the first clinical research involving iPSC-based cell therapy is already ongoing in Japan, as a patient suffering from age-related macular degeneration received a transplant of retinal cells derived from iPSCs generated from her own somatic cells. The advancement of cell reprogramming science has startled almost everyone in the field, including Yamanaka. "I am impressed with the rapid progress of iPSC research."

CiRA

In response, Kyoto University founded the Center for iPS Cell Research and Application (CiRA) in 2010 and appointed Yamanaka its director. Now in its sixth year, the institute has already seen its staff more than double. The core of CiRA research is to develop iPSC technologies for medical therapies, especially for intractable diseases. Over this time, CiRA researchers have established methods to generate and evaluate clinical-grade iPSCs for quality and safety so that they can be used in humans. In the next few years, CiRA is anticipating clinical research using iPSC-based therapies to treat Parkinson's disease and blood diseases, with treatments for other diseases expected thereafter. In addition, CiRA is building an iPSC stock for regenerative medicine, from which clinical-grade iPSCs will be made available to research institutes and companies around the world that are investigating new cell therapies.

Along with cell therapies, iPSCs have shown great value for drug discovery. Work by CiRA researchers has suggested that iPSCs can be used to separate subpopulations of diseased patients that respond positively to a drug from those that do not. More recently, a CiRA research team has shown the benefits of iPSCs for drug repositioning. The possibility of finding new drugs and reducing R&D costs has encouraged a number of pharmaceutical companies to explore iPSCs as a tool for drug discovery.

Prof. Jun Takahashi prepares clinical research for the treatment of Parkinson's disease using iPS cells.

Prof. Koji Eto prepares a clinical-grade platelets using iPS cell. (see p.16)

The Japanese government has responded unequivocally to the discovery of iPSCs, as it recognizes them a foundational technology on which to promote not only the nation's science and technology, but also economic growth. Appropriately, it has supported CiRA with abundant research funding. CiRA also distinguishes itself from other research institutes in Japan by the generous number of private donors that contribute money to its research.

However, even these funds are not enough for CiRA's ultimate goal of iPSC-based cell therapies when considering the cost of translating an academic discovery into a widely used treatment, a translation commonly known as the "Valley of Death" in commercialization. Consequently, CiRA has partnered with industry for the study of diseases and development of new therapies. Current examples include work with Sumitomo Dainippoin Pharma Co. Ltd. on treatments for fibrodysplasia ossificans progressiva, a rare but horrifying disease where tissue ossifies, and with Fujifilm Corp. for Alzheimer's disease, a form of the most common dementia. The latest, T-CiRA, was announced in April and is the largest yet.

Facility for iPS Cell Therapy at CiRA

POINTS OF INTEREST 1

CiRA Gallery and Tour

CiRA features a gallery in its main building where visitors can access information about CiRA and iPS cell research. The gallery is open to the public 8:30-17:15 on weekdays and 9:00-17:00 on Saturdays. CiRA also offers tours of its facilities to the general public. For details, please visit the CiRA website.

WEB www.cira.kyoto-u.ac.jp/e/about/contact/ (The tour schedule and availability are limited)

T-CiRA


Takeda Shonan Research Center

Takeda, Japan's biggest pharmaceutical company, teamed with CiRA to create T-CiRA, or Takeda-CiRA Joint Program for iPS Cell Applications. The program aims to combine the respective expertise in iPS cells of CiRA and drug development of Takeda for the innovation of iPS cell-based medicines. T-CiRA is extraordinary in its size and length, as Takeda has pledged 20 billion yen (app. $US 160 million) for 10 years plus another 12 billion yen for infrastructure.

Also making it extraordinary is the speed at which T-CiRA came to fruition. One of the first destinations Takeda President and Chief Executive Officer Christophe Weber visited after taking over his post in 2014 was CiRA. At the time, Yamanaka planned little more than a handshake and a smile. "I was just going to say, 'Hi. Welcome to Japan.'" Instead, the introduction quickly escalated into a partnership that Yamanaka hopes will redefine drug discovery research. Formal discussions about T-CiRA began the beginning of 2015 and were finalized in April. "T-CiRA is extraordinary in view of scale, time and budget," says Atsushi Onodera, one of the officials at CiRA responsible for the agreement.

T-CiRA aims to employ up to 100 researchers, with the two institutes directly hiring half each. The initial plan is to develop drugs in areas such as heart failure, diabetes, mellitus neuro-psychiatric disorders and cancer, which are all strengths of CiRA. However, as new scientists are hired, there is an expectation that the number of diseases for study will increase. T-CiRA projects will be located at the Takeda Shonan Research Center, which is much closer to Tokyo than it is to Kyoto, the home of CiRA. The reason, explained Yamanaka, is that he wanted a wall between the science done at T-CiRA and that done at CiRA alone. "I wanted a clear separation between T-CiRA and any other efforts." The purpose, he added, was to assure other potential industrial partners that collaborative projects with CiRA will in no way be encroached by this one.

Yamanaka expects T-CiRA will become the paradigm for successful translation of academic inventions to the clinic, not just iPSC-based ones. He also expects that the large investment will attract leading scientists from around the world to CiRA and the field of iPSCs. "This 10-year joint program with Takeda will become a powerful engine to realizing medical applications using iPS cells." Weber shares his enthusiasm."I am excited that we will be able to collaborate with CiRA, the world's leading institute dedicated to pioneering iPS cell research."

In part because the speed in which T-CiRA was formed, many of the details about the project, including how current CiRA staff will be involved, need to be clarified. Wherever T-CiRA leads, Yamanaka looks forward to hiring bright minds committed to iPSC research. "Any talented scientist will be welcome as long as he or she wants to find new cures to intractable diseases by using iPSCs."

MED-ENG

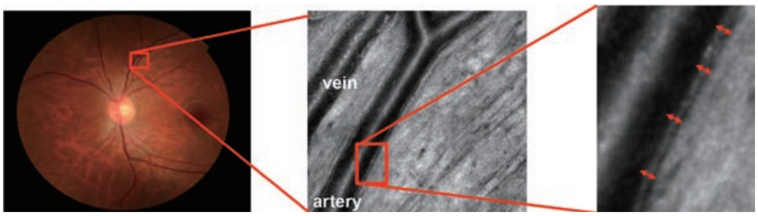
The CK Project: For the Unprecedented Aging Society to Come

The hope of all members participating in the CK project is to create a truly healthy society.

Innovative Techno-Hub for Integrated Medical Bio-Imaging Project for Developing Innovation Systems Creation of innovation centers for advanced interdisciplinary research area program, known as the CK Project is a ten-year national project supported by the Ministry of Education, Culture, Sports, Science, and Technology (MEXT). The project aims to create a healthy society through promoting cutting-edge research and development, improving quality of life (QOL), and reducing medical expenses for the future aging society. As of April 2015, one hundred

OCT / AO-SLO

◀ A high-level eye fundus diagnostic modality with the ability to detect signs of important sight threatening diseases appearing on fundi. The technique aims to deliver higher-level and more effective treatment.



▲ An arterial blood vessel wall is visualized with a simultaneous improvement in resolution and imaging speed.

A novel technology integrating ultrasound and optical imaging, Photoacoustic mammography (PAM) enables the visualization of neo-vascular cancer networks. Other related researches which are underway include development of the technique for the medical image fusion of ultrasound and MRI, and development of the disease-specific diagnostic agent for photoacaustic imaging.

teaching staff and researchers at Kyoto University, together with seventy-eight research staff at the Canon Corporation are involved in the project, making it a unique and unprecedented model of joint research and development between a university and a major commercial company. To date, a new form of optical coherence tomography (OCT) has been marketed, and a new method of photoacaustic mammography (PAM) is undergoing clinical research evaluation. The performance enhancement of both devices (OCT and PAM) will be carried out continuously through two new national projects; NeXTEP (Next Generation Technology Transfer Program established by JST) and ImPACT (Impulsing Paradigm Change through Disruptive Technologies Program established by Cabinet Office). In the course of this project, the researchers, together with the managing staff of Canon Corporation and Otsuka Pharmaceutical Co., Ltd., will decide whether the use of novel molecular probes for photoacaustic imaging will move into preclinical trials. Furthermore, the CK project and the AK project have recently initiated joint research into the creation of novel contrast agents consisting of nanoparticles. The CK project is also involved in close collaboration with the Training Program for Leaders of an Integrated Medical System for Longevity and a Fruitful and Healthy Society (LIMS), a program that is supported by the Japan Society for the Promotion of Science (JSPS), and which aims to foster talented researchers in the interdisciplinary research area of medicine and engineering (medico-engineering).

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Center for the Promotion of Interdisciplinary Education and Research WEB ckpj.t.kyoto-u.ac.jp/?lang=en

MED-SCI

Astellas Pharma-Kyoto University Project

Over thirteen drug targets discovered, ten drug discovery program targets achieved, and twenty-seven patent applications in ten years.

The Center for Innovation in Immunoregulative Technology and Therapeutics (The AK Project), an open innovation laboratory for drug discovery and development, was established in 2007 by Kyoto University and Astellas Pharma. The AK Project works in the field of immunology area to develop innovative therapeutics to overcome intractable diseases, e.g. allergies, autoimmune diseases, and chronic inflammation. The project seeks to invent a drug discovery model for the post genome era that is capable of producing game-changing drugs in Japan.

At the Fusion Laboratory on the Medical School Campus of Kyoto University, fifteen groups led by young principal investigators (PIs) and two groups from Astellas work closely with each other under the guidance of three key researchers from the Medical School: Prof. Shuh Narumiya, Prof. Nagahiro Minato, and Prof. Shimon Sakaguchi. Each group carries out independent research to identify unique targets. A prominent feature of the AK Project is collaboration with clinical departments, which search for biomarkers and verify the clinical significance of drug targets found in the Fusion Lab. A satellite laboratory located in the Astellas Research Institute in Tsukuba conducts high-throughput screening and compound optimization. The members share clinical information and samples, knowledge on molecular mechanisms, and drug discovery skills. The AK Project has an intellectual property (IP) office in the Fusion Lab, where two IP managers handle all IP matters, such as patent applications, publications, and contracts, on-site.

Thus far, we have successfully discovered over thirty drug targets and advanced over ten targets to drug discovery programs. We have also filed twenty-seven patent applications, including the Filaggrin production promoter for the treatment of atopic dermatitis. The AK Project turned out six professors and three associate professors, and aims to engage in excellent scientific research and drug discovery. Its motto is *Best Drugs on Best Science.*

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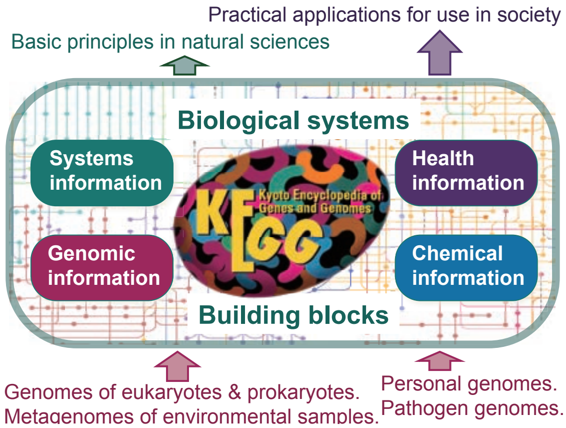
LIFE SCI

KEGG Resource for Deciphering the Genome

Bringing the genomic revolution to society.



KEGG: Kyoto Encyclopedia of Genes and Genomes

The Human Genome Project in the 1990s and early 2000s was an international effort to determine the entire DNA sequences and identify all the genes that constitute the human genome. Thanks to technological advancements, it is now a routine task to determine the genome sequence of an organism or an environmental sample that contains multiple organisms. However, it still remains a challenging task to understand biological meanings encoded in the genome. My laboratory in the Institute for Chemical Research at Kyoto University started the KEGG (Kyoto Encyclopedia of Genes and Genomes) database project in 1995, in anticipation of the need for a reference resource that can be used for biological interpretation of genome sequence data. Since then, KEGG has been an advanced bioinformatics resource for understanding the functions and utilities of biological systems, such as cells, organisms, and ecosystems, and has become one of the most widely used biological databases in the world.

Our current focus is translational bioinformatics to bring the genomic revolution to society. Genome sequencing has the potential to revolutionize healthcare, notably in personalized medicine using personal genome information and in combating infectious diseases using pathogen genome information. The latter may be more feasible and will have wider impacts, because the management of infectious complications, especially those caused by antibiotic-resistant bacteria, is a universal problem. KEGG is being expanded to enable the characterization of pathogens from their genome sequence data.

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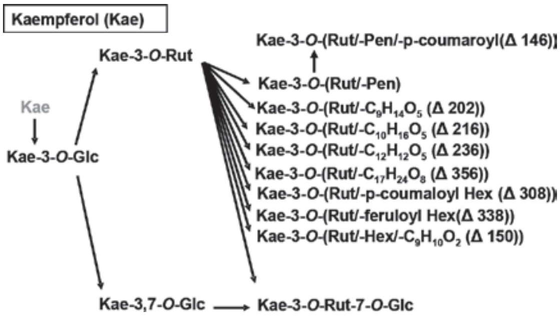
FOOD-SCI

Rediscovering the Goodness of Tomatoes

Searching for functional ingredients through metabolomics approaches

Finding functional or healthy components in food materials through metabolomics approaches is an emerging research area in food science. The findings will be key to developing new processing methods for functional foods. Tomatoes are known to have at least 5,000 metabolites (ingredients) in which functional or palatable chemicals are likely to be included.



Our lab is engaged in ongoing annotation of tomato metabolites detected by the-state-of-the-art liquid chromatography-coupled mass spectrometry with bioinformatics approaches. The data of the annotated metabolites are deposited in our metabolite database, and the information about tomato metabolites obtained in our lab is used in Prof. Teruo Kawada's lab (Division of Food Science and Biotechnology, Graduate School of Agriculture) to search for functional components. Functional components—those which function to prevent inflammation, oxidation stress, and metabolic syndromes—are evaluated genetically or in laboratory animals or cells. The tomato metabolite information is also used to develop functional foods in Prof. Yoshiki Matsumura's lab (Division of Agronomy and Horticultural Science, Graduate School of Agriculture), where tomato fruit undergoes food processing treatments, and the quality and palatability of the processed tomato is evaluated. All three labs, including ours, are involved in Kyoto University's collaboration with Kagome CO., Ltd.

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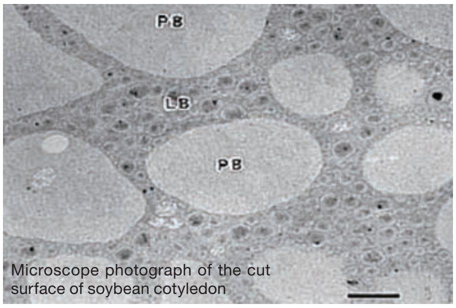
FOOD-SCI

Fuji Oil Soybean Renaissance Laboratory

Joint research to develop innovative soy foods.



Microscope photograph of the cut surface of soybean cotyledon


Field-flow fractionation system

Soybeans contain many nutrients. The fat and protein content is very high (20% and 35%, respectively) and the nutritional values of both are excellent. Soybeans are, therefore, a beneficial food for humans. Although globally 200 million tons of soybeans are produced per year, only 10% of that is utilized for human food, with most being used for animal feed. The quantity of soybeans used as a protein source for humans is very relevant in light of the food shortage problem caused by global population growth. As described above, however, the amount used for human food is small, and the major reason for this is that there are few soy food products which have an appealing taste and high applicability as food material.

In order to increase the usage of soybean for food, our joint research has begin to develop basic technologies for new soy food products which have an appealing taste and high applicability to various foods.

Fig. 1 shows a microscope photograph of the cut surface of soybean cotyledon. The photograph shows that the structure of cotyledon is not homogeneous. Many particles can be seen in soybean cotyledon, and each particle is covered by a membrane and contains various kinds of materials. These components are considered as effective factors in designing the taste and texture of soy food products.

Our research is investigating in detail the properties of soybean components, and the mutual interaction between them under different conditions using latest methods (for example, the field-flow fractionation system in Fig. 2). Soybeans contain many functional components beneficial to human health, especially for the prevention of metabolic syndrome. Therefore, the physiological effects on humans also require further study.

Eventually, we aim use our study results to propose innovative soy foods with excellent flavor and functionality. We have named our collaborative project the "Soybean Renaissance."

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WEB www.fujioil.co.jp/fujioil_e/news/150316.html

Achievements of History

Pioneer works to make products enhance quality of life.

Med-Sci Special Issue

Alinamin® and Dr. Motonori Fujiwara

The Takeda-Kyoto University partnership that created the best-selling vitamin supplement.

Prof. Emetitus Motonori Fujiwara of Kyoto University and the lineup of Alinamin®

SIXTY-FOUR YEARS before Takeda Pharmaceutical Co. Ltd. and the Center for iPS Cell Research and Application (CiRA) of Kyoto University started their extensive, 10-year joint program, collaboration between a Kyoto University School of Medicine scientist and Takeda researchers culminated in a nationally recognized vitamin supplement product: Alinamin®. This drug contains a vitamin B_1 derivative, fursultiamine, as its major active ingredient. The Alinamin® line-up includes over-the-counter tablets and nutritional drinks that have been best-sellers over a long period, as well as injectable solutions for use in clinical settings.

Humans rely on carbohydrates, lipids, and proteins as energy sources. Water-soluble vitamin B_1 is indispensable for metabolizing carbohydrates but absorbed in small amounts by the small intestine. Takeda Pharmaceutical marketed fursultiamine, a lipophilic vitamin B_1 derivative, which is more readily absorbed in large amounts in the small intestine and has a longer half-life than its active counterpart vitamin B_1. Fursultiamine is the main active component of Alinamin®.

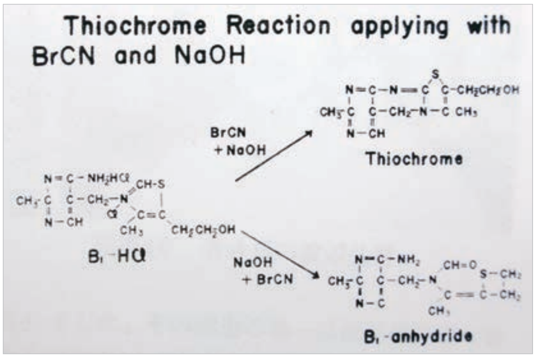
Since its market launch in 1954, Alinamin® has been one of Japan's best-selling commercial brands. Kyoto University researcher Dr. Motonori Fujiwara (1915-1994), then an assistant professor of medicine, played a critical role in the birth of this product. Dr. Fujiwara, born in Nagasaki, Japan, studied medicine at the Kyoto Imperial University College of Medicine and served the Imperial Japanese Navy as a medical officer during World War II. Shortly after the end of the war, he started his research career in public health at the Kyoto

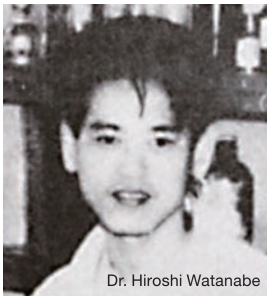
Medicine Building at the time

Imperial University College of Medicine. Throughout his life, he made important contributions to the development of public health and nutritional science in Japan. He had more than 220 books and journal articles published and theses and dissertations supervised, and was one of the frontrunners in vitaminology. His studies on vitamin B_1 (thiamine) were instrumental towards eradicating beriberi in the post-World War II period in Japan.

How did Dr. Fujiwara become involved in the development of Alinamin®? After serving in the military, Dr. Fujiwara was assigned a teaching post at Kyoto Imperial University in June 1945. During the wartime and post-war periods, overcoming beriberi caused by nutritional deficit was on the national agenda. The Vitamin B Research Committee was established as a government initiative, with Dr. Fujiwara a founding research member. His assignment was to determine the recommended minimum daily intake of vitamin B_1, later determined to be in the range of 0.2-0.3 mg per 1000 kcal. In the course of his research, Dr. Fujiwara developed a new vitamin B_1 quantification method.[1)]

While preparing the final report of his results, he discovered by chance another important chemical reaction for vitamin B_1. One day, Dr. Fujiwara experimented with a variety of reagents available in his laboratory and left the test tubes by the window. Exposed to sun's UV rays, one of the tubes glowed in




Dr. Hiroshi Watanabe


Dr. Kiyoo Matsui

the waning late-afternoon daylight and caught his eyes. Dr. Fujiwara found that vitamin B_1 was converted to fluorescent thiochrome when mixed with BrCN under alkaline conditions (NaOH). This characteristic thiochrome (B_1-BrCN-NaOH) reaction proved to be very useful for vitamin B_1 quantification. Then, together with new laboratory members such as Dr. Hiroshi Watanabe (later appointed as professor at Mie University) and Dr. Kiyoo Matsui (later promoted to the Director General of Hyogo Prefectural Institute of Environmental Science), Dr. Fujiwara embarked on a project to identify vitamin B_1-decomposing substances present in bracken fern using this thiochrome reaction. Work by American scientist P. H. Weswid had previously shown that bracken fern contained substances capable of breaking down vitamin B_1, although their identities were totally unknown. Using the B_1-BrCN-NaOH reaction, Dr. Fujiwara and his colleagues discovered the heat-sensitive vitamin B_1-decomposing enzyme aneurinase (thiaminase) in bracken fern that was already known to be present in fish and shellfish. They also discovered the presence of heat-resistant vitamin B_1-degrading factors. Moreover, they found that substances that convert vitamin B_1 into compounds unresponsive to the thiochrome reaction are present in plant parts such as sweet potato vine, burdock root, butterbur stalk, and garlic bulbs, as well as materials of animal origin including saliva and bile juice.

Reflecting on this series of new findings, Dr. Fujiwara had a hunch that *garlic bulbs* must have

Motonori Fujiwara (1915-1994) was a medical researcher who pioneered vitamin research in post-war Japan. After graduating from Kyoto Imperial University College of Medicine in 1940, he obtained his medical license the same year. In 1945, he was appointed as a research assistant at Kyoto Imperial University College of Medicine. He was promoted to professor in 1959. He received an honorarium for developing Alinamin® from Takeda Pharmaceutical, and used the award to establish the Fujiwara Memorial Foundation in 1960. He received the Japan Academy Award in 1959. He was a renowned amateur tennis player and served as the student chair of Shiran-kai Tennis Club during its inception period. This was an on-campus organization for undergraduate and graduate medical students.

Dr. Fujiwara (second left) and Research Members

additional features of biological importance worthy of investigation. The reactive potential of garlic bulb was so powerful that only 0.1 g were sufficient to convert 1 mg of vitamin B_1 (the recommended daily dose) into a derivative unresponsive to the thiochrome reaction. Based on this finding, he reasoned that if this reaction involved vitamin B_1 decomposition, as was the case with aneurinase, people eating garlic bulbs regularly should suffer vitamin B_1 deficiency, but this idea contradicted the time-tested reputation for garlic as a performance enhancer. His reasoning proved correct. *In vitro* and *in vivo* studies showed that although the addition of garlic extract to vitamin B_1 solution rendered it unresponsive to the thiochrome reaction, the mixture recovered powerful thiamine activity when administered to animals or mixed with reducing agents such as cysteine. Dr. Fujiwara termed the garlic-processed vitamin B_1 derivative unresponsive to the thiochrome reaction as "garlic B_1." He found the same phenomena in long onion and other Allium species.

Thinking that he had completed the main part of the vitamin B_1 research project, Dr. Fujiwara proposed the laboratory members to sample the garlic B_1 juice to commemorate their progress. His idea was to measure the urinary levels of the unresponsive vitamin B_1 derivative in human volunteers orally given the vitamin B_1 solution treated with Allium plant extracts.

Whole laboratory filled with pungent smell of onion and scallion!

After the start of the joint vitamin B_1 project, piles of onion, scallion, and other pungent plants were brought into the Matsubara Group's laboratory rooms, releasing a powerful odor. The smell was a marker of newly started activities and added to the lively atmosphere of the laboratory. Of course, the people at the Department of Public Health, Kyoto University, were also not exempt from the battle against that unusual smell!

Each member took and swallowed the bitter-tasting vitamin B_1 cocktail of their preference, containing garlic, chive, or scallion, thinking that this "toasting" ceremony would mark the end of the project. To their amazement, however, the results completely betrayed their expectations. "We were so astonished," the self-appointed "toastmaster" later described.

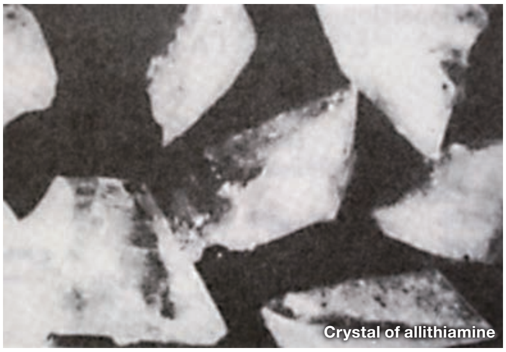
> *"I went to the fluorescence apparatus to measure the emission intensity. I tested again, same results. We were so astonished. The results showed that the levels of vitamin B_1 excreted into urine via unresponsive vitamin B_1 (= garlic B_1) were 10 times higher than typical plasma vitamin B_1 levels. I once encountered a similar case with S-B_1, an artificial vitamin B_1 analog synthesized by Dr. Taizo Matsukawa, former Director of Research Department, Takeda Pharmaceutical. S-B_1 was an exogenous product that had no thiamine activity. Animal studies have demonstrated that garlic B_1 is reduced to biologically active vitamin B_1 in vivo. The logical conclusion drawn from our unexpected results was that garlic B_1 was absorbed from the intestine highly efficiently."* [2]

Dr. Fujiwara continues:

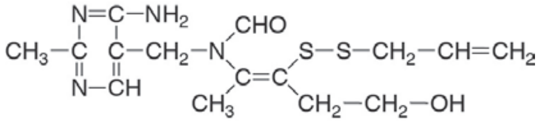
> *"On 15 September 1951, I went up to Tokyo to attend the Vitamin B Research Committee held at Japan Women's University for presenting our interesting results. It was a rainy day from early morning. In the Toden streetcar I took, I ran into Dr. Matsukawa from Takeda Pharmaceutical and started to share that day's presentation with him. This inspired him to make a formal offer for a joint research some time later."* [3]

Coffee gets rid of garlic breath

The Japanese market release of 5 mg Alinamin® Sugar Coated Tablets in 1954 met with great success. However, the garlic-like smell, attributable to the main active ingredient prosultiamine, was a big problem for both consumers and production line workers. Takeda Pharmaceutical started research to create less smelly compounds with similar efficacy. In an office conversation with his co-workers one day, one researcher questioned why the garlic breath from eating a steak disappears after drinking a cup of coffee. This question provided an important clue, and the non-smelling vitamin B_1 derivative, fursultiamine, was developed by analyzing coffee's flavor components.



Crystal of allithiamine



2-(2-methyl-4-amino-5-pyrimidylethyl)-formamdo-5-hydroxy-Δ^2-pentenyl-(3)-allyl disulfide

allithiamine

Takeda Pharmaceutical had been producing bulk vitamin B_1 products by extraction since 1936 and by chemical synthesis since 1938. As explained above, Dr. Matsukawa at Takeda Pharmaceutical had discovered a new synthetic scheme for vitamin B_1 in 1949. He was one of Japan's top-ranking vitamin B_1 researchers, which Dr. Fujiwara acknowledged. Dr. Matsukawa's expertise in vitamin B_1 chemistry and the most advanced resources of his laboratory made him the best research partner for Dr. Fujiwara with medical and clinical perspectives. At the same time, Dr. Matsukawa had a great interest in garlic B_1's potential as a new drug.

The first goal of the joint project was to isolate garlic B_1 in a crystal form. Initially, Dr. Matsukawa estimated that it would take one year before garlic B_1 could be crystallized. However, with the help from Dr. Jutaro Okada, assistant professor at Kyoto University Faculty of Pharmaceutical Sciences, Dr. Fujiwara was successful in two months (30 December 1951). Two weeks after the crystal was obtained, Shojiro Mangi at Takeda determined its chemical structure. These results were presented by the joint team at the meeting of the Vitamin Society held on 8 March 1952, where the new compound was called "allithiamine." The prefix "alli-" before thiamine (vitamin B_1) was derived from

Dr. Matsukawa

Dr. Shojiro Mangi

"Allium" species to which garlic and many other plants with similar activities belong. After the discovery of allithiamine, a variety of derivatives were chemically synthesized at Takeda, including prosultiamine. Meanwhile, the Allithiamine Subcommittee was formulated within the Vitamin B Research Committee.[4)]

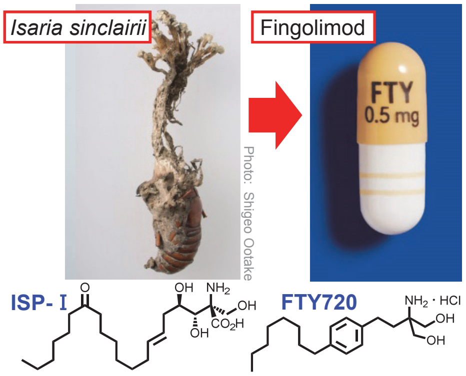
This subcommittee investigated the following aspects of allithiamine over the next two years: physical chemical properties, quantification method, animal toxicities and mechanism of action in humans, tissue distribution, pharmacokinetics, and clinical application. Taking note of the research results of the Allithiamine Subcommittee, Takeda Pharmaceutical launched 5 mg Alinamin® Sugar Coated Tablets in March 1954, which contained prosultiamine as the major active ingredient. Because prosultiamine had an unappealing garlic-like odor, fursultiamine was created to minimize the smell. In order to increase chemical stability, fursultiamine hydrochloride was subsequently developed, which is the main active component of Alinamin® F. Initially, Alinamin® was used in clinical settings for the treatment of beriberi and malnutrition or for vitamin B_1 supplementation. Over the years, it has attained the status of a best-selling non-prescription medication, owing to the post-war economic and industrial boom in Japan, commercial advertisements on television and other media, increased awareness of health and well-being among the general population, and discovery of new pharmacologic actions for fursultiamine. For over half a century, Alinamin® has served as a springboard for Takeda Pharmaceutical.

Acknowledgments The author thanks Prof. Shu Narumiya, Kyoto University Graduate School of Medicine, for his comments on the manuscript. The author also thanks Takeda Pharmaceutical Co., Ltd. for the presentation of valuable materials. Almost all of the figure and picture are from *Vitamin* (Japan), **73**(3), 177-197 (1999). The author express deep gratitude to the Vitamin Society of Japan and Public Utility Foundation for the Vitamin & Biofactor Society.

1) Dr. Fujiwara's new approach stirred up controversy from scientists who supported the Fujita method, considered the "golden standard" for quantitative vitamin B1 determination at that time. The debate ended in his favor. 2) Source: Dr. Motonori Fujiwara Recollections from the discovery of allithiamine to the establishment of Fujiwara Memorial Foundation. 1981. 3) Source: Motonori Fujiwara, 1981. 4) The members are Takashi Inoue and Masaya Araki of Kyoto Prefectural University of Medicine, Shinji Ito of Hokkaido University, Yoshito Sakurai and Norio Shimazono of the University of Tokyo, Toichiro Sawada of Kyushu University, Tomihide Shimizu and Eiji Hamamoto of Okayama University, Isamu Tachi and Motonori Fujiwara of Kyoto University, Ichiro Nakagawa of The Institute of Public Health, Harutada NInomiya and Yoshito Nishizawa of Osaka University, Taizo Matsumoto of Takeda Pharmaceutical Company Limited.

Blockbuster Drug to Treat Multiple Sclerosis

FTY720, the world's first drug for multiple sclerosis developed at Kyoto University.




Dr. Tetsuro Fujita

The invention of a new drug can sometimes save millions of lives, and research for the development of blockbuster drugs for diseases that have no effective treatment can bring hope to people suffering from various illness around the world. Dr. Tetsuro Fujita, professor emeritus of Kyoto University, played a key role in the development of Fingolimod Hydrochloride (Product Name: IMUSERA®, GILENIA®), the world's first medicine for multiple sclerosis, which has been long an intractable disease.

Dr. Fujita had been engaged in a long period of research on bioactive substances in plants when he was offered a professorship in the department of medicinal plant chemistry in Kyoto University's Faculty of Pharmaceutical Sciences. Upon taking up his new post, however, he decided to shift his focus to a research area directly related to medicine. This was around the time that organ transplant treatments were beginning to garner attention as a new medical technology, and Dr. Fujita embarked on research to explore substances that are able to suppress immune response. He focused on vegetative wasp, which is a parasitic fungus found on moth larvae. Vegetative wasp is named *Dōng chóng xià cáo* (冬虫夏草) in Chinese, which means "winter-worm, summer-grass," because its shape resembles a worm in winter and a grass in summer. The fungus has long been valued as herbal remedy in traditional Chinese medicine and it is used as an ingredient in traditional medicinal dishes.

Dr. Fujita suspected that the vegetative wasp might contain an immune-suppressive compound-suspicions that were validated when he succeeded in extracting active substances with strong immune-suppressive qualities from *Iscaria sinclairii*, a kind of vegetative wasp. He formed a collaborative research team in cooperation with Taito Co., Ltd. (now Mitsui Sugar Co., Ltd.), a company with advanced culturing techniques, and Yoshitomi Pharmaceutical Industries, Ltd. (the present Mitsubishi Tanabe Pharma), a company skilled in pharmacological evaluation and drug discovery. The three-way research collaboration resulted in the discovered of FTY720, which was derived from a natural immunosuppressive product (ISP-I) through chemical modification utilizing synthetic organic chemistry techniques. FTY720 was named after the initials of Fujita, Taito, and Yoshitomi, and was later renamed Fingolimod. After international clinical trials, Fingolimod was approved in the US in 2010 and in Japan in 2011 as the world's first drug for multiple sclerosis. Multiple sclerosis is a disease affecting the central nervous system and causing different nerve

About the Cover

Main Building of CiRA

The Center for iPS Cell Research and Application building is located in the southwest area of Yoshida Campus, near the famous Kamo River, which flows north to south through Kyoto City. The third, fourth, and fifth floors of the building are laboratory spaces for research experiments, each with a large open laboratory at their center. The second floor and first basement contain facilities for animal experiments and cell culture manufacture, which are collectively called the Facility for iPS Cell Therapy (FiT). The ceiling and floor of the open laboratories are a distinctive blue color, providing a bright spacious atmosphere in keeping with CiRA's aim of creating a bright future. On the left, we see the new "Preemptive Medicine and Lifestyle Disease Research Center" under construction, funded by Himedic Inc, planned to be one of the largest facilities of its kind in the country.

Painter: **Kiyoko Yamaguchi, PhD** *Alumnae of Kyoto University* kiyoko-yamaguchi.com/

abnormalities. There was previously no effective treatment for the disease, so the discovery of Fingolimod was tremendous news for long-suffering patients. The drug has now become highly successful around the world.

The discovery of ISP-I, from which Fingolimod was derived, came about through a combination of serendipity and Dr. Fujita's foresight and rigorous research abilities. Dr. Fujita and his colleagues' passion to develop a new drug to help patients resulted in the development of Fingolimod (FTY720), which has greatly alleviated the suffering of many. Dr. Fujita's magnetic personality and ability to inspire others brought the collaborative research team together. Although he is now over eighty-five years old, Dr. Fujita is still active, and occasionally delivers lectures about the development of Fingolimod.

I took over the department of Medicinal Plant Chemistry Course (currently, the department of Synthetic Medical Chemistry) as the third successor of Prof. Fujita. My specialty is synthetic organic chemistry, and my research includes studies of the chemical synthesis of bioactive natural products from plants or microorganisms, the molecular design of more useful compounds, and development of new reactions giving biological active compounds synthesis for high value-added. Following the spirit of Prof. Fujita, I hope that my research in Kyoto University's Graduate School of Pharmaceutical Sciences will help as many people as possible by leading to the production of innovative new drugs for the treatment of diseases.

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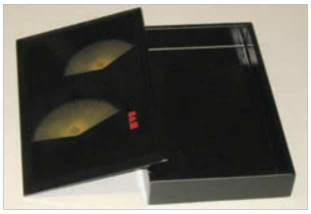
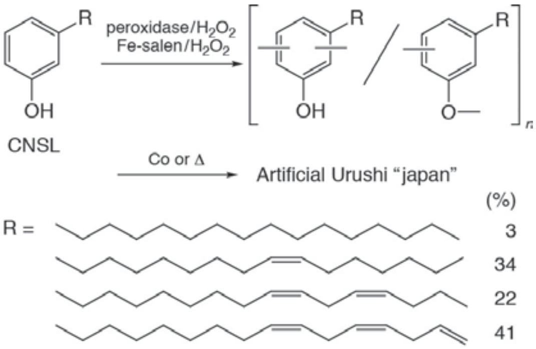
POL-CHEM

Japanese Lacquer Made of Cashew Nutshell Liquid

Green polymer chemistry produces artificial urushi lacquer.

Cashew nuts are a popular snack and food ingredient, especially in Indian cuisine. The oil extracted from cashew nut shells is a byproduct, meaning that cashew nutshell liquid (CNSL) is a cheap renewable raw material. Using CNSL, Prof. Emeritus Shiro Kobayashi developed a method to prepare artificial *urushi* lacquer through enzymatic polymerization. The physical properties of the artificial *urushi* lacquer, including its elasticity are good as genuine Japanese lacquer, and it can therefore be widely utilized for beautiful and robust coating materials. The advantages of the artificial *urushi* lacquer are as follows: i) instead of natural urushiol which has become hard to obtain in recent years, cheap renewable CNSL can be used, ii) the enzymes as well as the starting materials used in the preparation method are environmentally benign, and iii) urushiol causes an allergic skin irritation but CNSL causes little allergic reaction. In cooperation with Toyo Ink Co., Ltd., the technology patents were registered in Japan, the US, and Europe. At the moment, commercial products using the artificial *urushi* lacquer are not so common, but it has great advantages as a renewable material for sustainable societies.





Since retiring from Kyoto University, Prof. Emeritus Kobayashi continues to undertake research and provide research guidance to students as a distinguished professor of the Kyoto Institute of Technology. He is currently involved in research on artificial *urushi* lacquer.

From the Editor Prof. Emeritus Shiro Kobayashi received the Japanese government's Medal with Purple Ribbon in 2007 and the Order of the Sacred Treasure, Gold Rays with Neck Ribbon in 2015.

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Professor, Graduate School of Engineering
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NAT-CHEM

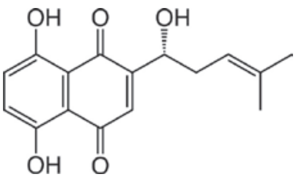
Shikonin and Dr. Mamoru Tabata

Shikonin, a revolutionary plant metabolite developed in the 1980s.

Dr. Mamoru Tabata

Lithospermum erythrorhizon

PHOTO: Research Institute of Medicinal Plant Resources, Shinnihonseiyaku Co., Ltd.



Plants produce a large variety of specialized metabolites that have been used as medicines, fragrances, and pigments. The supply of such natural compounds can be limited when they are derived from endangered species. Shikonin is a red naphthoquinone pigment that can only be produced from a few boraginaceous plants, one of which is *Lithospermum erythrorhizon*. The late Prof. Mamoru Tabata established a shikonin-producing cell culture from this plant and applied it to the industrial production of this lipophilic pigment in collaboration with Mitsui Petrochemical Industries, Ltd. (now Mitsui Chemicals Inc.) in the early 1980s. The shikonin produced was used for the popular "BIO" brand of lipstick, manufactured by Kanebo Co. Ltd. In the 1990s, this achievement triggered a plant biotechnology research boom around the world.

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FOOD-SCI

Distinctive Beers Bring the Taste of Ancient Egypt to Japan

A fusion of plant genetics research, Egyptian archeology, and Kyoto brewing technology.

White Nile, an original craft beer jointly developed by Kyoto University, Waseda University, and the long-established Kyoto brewing company Kizakura Co. Ltd., was launched in 2006 and has subsequently expanded into a range of beers that has proven popular, and achieved cumulative sales of 500,000 units and a total sales value of 200 million yen (as of May 2015). This is an unprecedented achievement for a university-developed beverage product.

In 2002, Egyptian archeologist Dr. Sakuji Yoshimura, then a professor at Waseda University (currently professor emeritus of Waseda University and President of Higashi Nippon International University) elucidated the production process of ancient Egyptian beers in a collaborative research project with a beer company. He discovered that emmer wheat[1] had been used to make beers in ancient Egypt. Although, today, emmer wheat is rarely grown anywhere in the world, and is therefore difficult to obtain, rare seed samples were being held by the Laboratory of Crop Evolution of

POINTS OF INTEREST 2

Research Promotion Institution for COI Site

The Research Promotion Institution for COI Site is a new hub for industry-academia cooperative research on Kyoto University's Yoshida Campus. The five-story building has one basement level, and a total floor area of 11,000 square meters. Its total construction cost was approx. 4 billion yen[1]. The facility contains the offices and laboratories of IT companies and manufacturers, including pharmaceutical companies, as well as Kyoto Prefecture and Kyoto City offices, an exhibition space and lounge. Visitors are welcome.

The opening ceremony was held on 25 May 2015.

1) The establishment of the facility was financially supported by the Ministry of Education, Culture, Sports, Science, and Technology of Japan (MEXT)

WEB www.coi.kyoto-u.ac.jp/en/access

Kyoto University's Graduate School of Agriculture.

The Laboratory of Crop Evolution was founded as a private laboratory[2)] in 1942 by the late Prof. Hitoshi Kihara, an internationally recognized wheat expert and professor in Kyoto University's Faculty of Agriculture. The laboratory holds and maintains approximately 10,000 different wheat strains collected from Japan and abroad. The emmer wheat seeds were collected in Ethiopia by the Kyoto University Scientific Expedition to the Sahara and its Surrounding Area (KUSES) in 1967-1968. Thanks to the emmer wheat seeds, provided by Associate Prof. Taihachi Kawahara[3)], The beer company's project succeeded in reproducing ancient Egyptian beer using the same raw materials and production process of that time.

Inspired by their success, Dr. Kazuo Oike, Kyoto University's president at the time, had the idea to put the research achievements to practical use. However, the authentically reproduced ancient Egyptian beer did not suit modern people's tastes, and so Kyoto and Waseda Universities jointly developed original craft beers in collaboration with the Kizakura brewing company. The concept behind the "Nile" series of beers is "good-tasting modern beer made of ancient wheat and utilizing advanced brewing technologies," which was suggested by Dr. Toru Fushiki, a professor in Kyoto University's Graduate School of Agriculture at the time (currently professor emeritus of Kyoto University and professor of Ryukoku University.)

In 2005, they succeeded in developing the first original beer made of durum wheat, which is a commercially available species related to emmer wheat. The beer was named "White Nile" after the primary tributary of the river Nile, and for the beer's characteristic white turbidity. Kyoto University's

Experimental Farm later established a method of cultivating emmer wheat, leading to the establishment of a mass production system by Tanaka Farm, a limited company in Tottori Prefecture. This facilitated the production of a new form of White Nile, made of emmer wheat, which was launched in 2007.

Currently, the product line comprises *Blue Nile*, a fresh-scented low-malt beer flavored with *yuzu* (a citrus fruit popular in Japan) and coriander, *Ruby Nile*, a high-alcohol beer with a mild but rich flavor, and *Cipher Nile*, a non-alcoholic beer with a fresh and rich taste. We urge you to enjoy the gift of Hathor, the ancient Egyptian goddess of beer, now being reborn as modern beer thanks to the collaboration between Kyoto University, Waseda University, and the Kizakura brewing company.

WEB www.kyoto-u.ac.jp/static/ja/news_data/h/h1/news7/2009/090420_1.htm

1) In his research, Assoc. Prof. Kawahara found that emmer wheat was established in south-eastern Turkey in approximately 8000 B.C.
2) Koichiro Tsunewaki, *Res. Act.* 4, No.3, 6-9 (2014)
3) Kawahara's research, *Res. Act.* 5, No.1, 23 (2015)

THIS ARTICLE'S KEY WORDS

Kyoto University Scientific Expedition to Sahara and its Surroundings (KUSES)

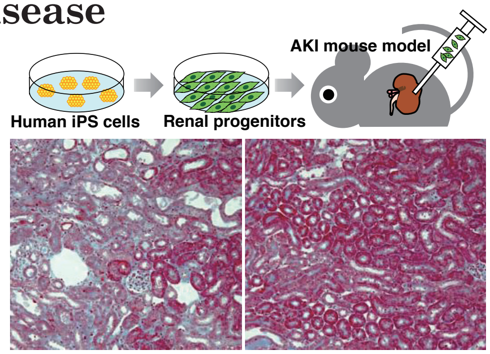
The Kyoto University Scientific Expedition to the Sahara and its Surroundings (KUSES) was an expedition formed to collect extensive information about the northern Africa. The expedition spanned thirteen countries, covering the Sahara Desert, Lybian Desert, West Africa, and the Abyssinian Highlands, and lasted for half a year from November 1967 to April 1968. Led by Kosuke Yamashita, the expedition comprised seven groups dedicated to different areas of study: plants, agricultural culture, art and archeology, language, humanity, and medicine. The plant study group chose the Abyssinian Highlands as the main location for their studies. The area is an important location with regards to the origin and differentiation of cultivated plants, and the team collected approximately 3,800 specimens there. They also collected wild plants, and conducted investigations into agriculture, landholding systems, and ethnobotanical studies.

Cutting-Edge Research Aiming to Contribute to the Society

MED-BIOL

iPS Show Promise for Kidney Disease

Acute kidney injury can be ameliorated by cell therapy.



Kidney without treatment (left) shows high levels of damage (blue). Cell transplantation therapy using iPS cell-derived renal progenitors significantly ameliorates the kidney damage (right).

Acute kidney injury (AKI) is defined as a rapid loss of renal function due to various etiologies and has a high mortality rate, especially in intensive care patients. In addition, AKI has also been reported as a cause of chronic kidney disease (CKD) and a risk factor for cardiovascular diseases. Despite urgent needs, a treatment for AKI remains to be developed. In a new study in collaboration with Astellas Pharma Inc., our group recently succeeded in attenuating the symptoms of AKI mouse models induced by ischemic injury by cell transplantation therapy using renal progenitors differentiated from human iPS cells. The result suggests promise that the iPS cell-derived renal cells could be used for cell therapy and drug discovery to remedy AKI. The research group is also aiming to develop cell therapy for CKD and generating metabolically or physiologically functional renal tissues from human iPS cells to develop regenerative treatments for kidney diseases.

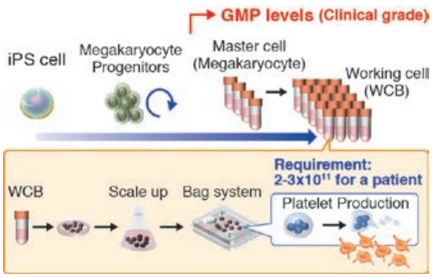
From the Editor Prof. Osafune received the Oshima Award 2014 from the Japanese Society of Nephrology for his research achievements, including this study.

Kenji Osafune, MD, PhD *Professor, Center for iPS Cell Research and Application (CiRA)*
www.cira.kyoto-u.ac.jp/j/research/osafume_summary.html

MED-SCI

Manufacturing Marketable Blood

Platelet packaging supply using human iPS cell-based technology.



Blood transfusion has a long history as the most successful form of cell therapy, but it is totally dependent on donors. In addition, platelets have a short shelf-life, which means that donors are constantly needed. In Japan, it is anticipated that its blood banks will fail to meet the demand for blood by up to twenty percent in ten to fifteen years. For this reason, my colleagues and I, with the involvement of industrial partners, are developing a system to produce marketable platelets. One challenge in cell therapies is providing a sufficient number of cells, and so we are currently seeking ways, using iPS cell technology, to achieve the required numbers by designing unipotent progenitors (immortalized megakaryocytes) that can generate platelets. These can be cryopreserved and expanded when required. In this way, they can be preserved for many months, instead of the few days for which blood cells can be normally stored.

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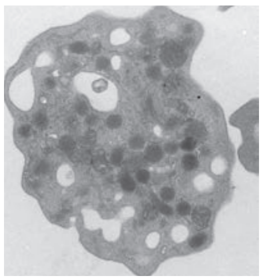
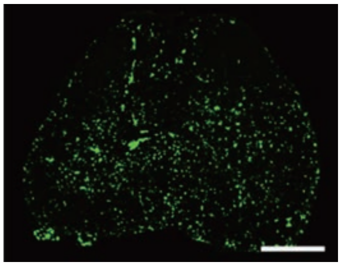


Regenerative medicine for ALS using human iPS cells

Transplanted glial cells improve the disease environment in spinal cords of ALS mice.



Transplanted cells expressing green fluorescent protein in spinal cords of ALS mice (Kondo *et al.*, *Stem Cell Reports*, **3**, 242-249 (2014).

There is currently no effective cure for amyotrophic lateral sclerosis (ALS), which is characterized by a loss of motor neurons. Diseased glial cells are thought to accelerate motor neuron degeneration. My colleagues and I have found that transplanted healthy glial cells derived from human induced pluripotent stem cells (iPSCs) can protect motor neurons in spinal cords and prolong the lifespan of ALS mice. Despite the hurdles ahead for human trials, all possible avenues provided by iPSC technology should be considered and tested to combat this pervasive disease.

Schema of spinal cord transplantation

Haruhisa Inoue, MD, PhD *Professor, Center for iPS Cell Research and Application (CiRA)*
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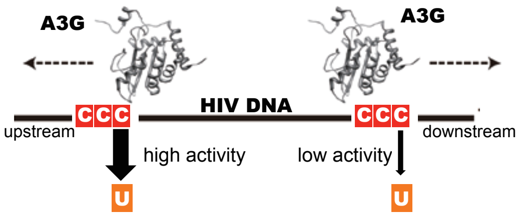
STRUCT-BIOL

Behavior of a Guard Against HIV (AIDS)

Real-time monitoring of anti-HIV enzymatic activity by NMR.



Mutation by A3G coupled with sliding along HIV DNA

Human APOBEC3G (A3G) protein deaminates and mutates cytosine bases of HIV genes and thus destroys the genetic information of HIV. This is how A3G, a guard against HIV, exhibits anti-HIV activity. I developed a method to monitor the enzymatic activity of A3G in real-time by nuclear magnetic resonance (NMR) in collaboration with the Suntory Foundation for Life Sciences. The method enabled us to elucidate the dynamic behavior of A3G in action for the first time. A3G slides along HIV DNA to find a target cytosine. When A3G finds the target, A3G deaminates it. The catalytic rate of deamination is dependent on the sliding direction: the rate is higher when A3G slides upstream than it when sliding downstream. These properties of A3G are beneficial for effective destruction of the genetic information of HIV. Comprehensive understanding of the behavior of A3G may lead to the development of an anti-HIV drug.

Masato Katahira, PhD *Professor, Institute of Advanced Energy*
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MED SCI

KEGG MEDICUS Drug Information Service

Making drug interactions easier to understand.

The aging population in Japan has led to a growing demand for medicines. In order to raise awareness of the drugs taken by each individual, my laboratory has developed the KEGG MEDICUS drug information service as part of our KEGG (Kyoto Encyclopedia of Genes and Genomes) project. It contains package insert (drug label) information for all prescription and over-the-counter drugs marketed in Japan, and is integrated with scientific data and information about diseases and drugs, as well as a database of adverse drug interactions. Its users can create personal medication lists in a web browser tool or an iPhone app, and the lists are automatically checked for any adverse interactions. This is a new form of the medication notebook (called *okusuri-techo* in Japanese) that is commonly used in Japan, which encourages more active involvement by each individual in managing their own medication plan.

Minoru Kanehisa, PhD
Project Professor, Institute for Chemical Research
www.kanehisa.jp/en/kanehisa.html

HEALTH SCI

Device for Mild Hyperbaric Oxygen and its Effect

New product for the maintenance and improvement of health and prevention of aging and metabolic disease.

In cooperation with Medical O_2 Co., Ltd. (Kumamoto, Japan), my laboratory has developed a device (Japanese patent number: 5076067; Inventor: Akihiko Ishihara; Registration date: September 7, 2012) that can maintain conditions at 1.25 atmospheres absolute with 36% oxygen (mild hyperbaric oxygen). Mild hyperbaric oxygen raises the level of dissolved oxygen in plasma and increases blood flow due to vasodilation, thereby enhancing metabolism effectively and safely. In addition, mild hyperbaric oxygen stabilizes the activity of the autonomic nervous system.

The chamber consisted of two instruments: an oxygen tank in which a single participant could lie down and a control box containing an oxygen concentrator and an air pump.

Space travel induces degenerative changes such as muscle atrophy in the neuromuscular system. We observed that preconditioning with mild hyperbaric oxygen inhibits disuse-induced muscle atrophy (2008, 2010). We also observed that mild hyperbaric oxygen in experimental animals effectively treats type 2 diabetes (2006, 2007, 2010), diabetes-induced cataracts (2011), hypertension (2010), and type II collagen-induced arthritis (collaborative project with NH Foods Ltd., Tsukuba, Japan, 2010).

In human clinical studies, we observed that mild hyperbaric oxygen inhibits ultraviolet B irradiation-induced melanin pigmentation and diminishes senile spot size (collaborative project with Kao Corporation, Tokyo, Japan, 2011). Recently, we determined that mild hyperbaric oxygen is beneficial in the treatment of infertility (collaborative project with Suwa Maternity Clinic, Hospital for Obstetrics, Gynecology, and Pediatrics, Suwa, Japan, 2013, 2014). The rates of clinical pregnancy in thirty-seven women with intractable infertility were 4.9% and 13.8% before and after mild hyperbaric oxygen treatment, respectively. Finally, women treated with mild hyperbaric oxygen gave birth after *in vitro* (five subjects) and natural (two subjects) fertilization. Currently, we are examining the effects of mild hyperbaric oxygen on mental conditions such as depression, autism, and autonomic ataxia.

Akihiko Ishihara, PhD *Professor, Graduate School of Human and Environmental Studies*

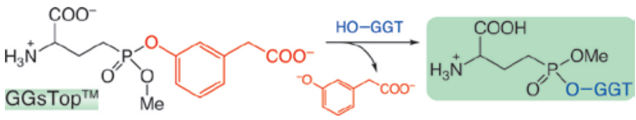
kyouindb.iimc.kyoto-u.ac.jp/e/xF8oJ

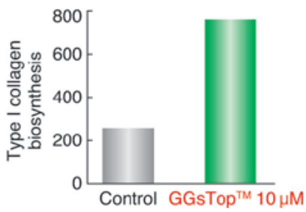
BIO-ORG CHEM

γ-Glutamyl Transpeptidase Inhibitor Marketed

γ-Glutamyl transpeptidase inhibitor as an innovative ingredient in anti-aging cosmetics.

Glutathione (γ-Glu-Cys-Gly, GSH) is a natural anti-oxidative and detoxifying agent against reactive oxygen species (ROS) and toxic xenobiotics. In its metabolism, γ-glutamyl transpeptidase (GGT) plays a critical role as the sole enzyme that degrades glutathione. We developed phosphorus-containing mechanism-based inhibitors of GGT for controlling cellular redox status. The most potent inhibitor GGsTop™ was found to increase the biosynthesis of collagen, elastin and HSP47 in fibroblasts in human skin. After careful examination of efficacy *in vivo* (human) and toxicity tests, we founded a venture company called Nahls Corporation in 2012, and marketed the GGT inhibitor as an innovative anti-aging cosmetic ingredient under the registered trade name of Nahlsgen®. Nahlsgen® increases skin elasticity and keratin water content. Nahlsgen® has gained a reputation as a unique anti-aging cosmetic agent based on a novel concept, and has penetrated the cosmetic market not only in Japan, but also in other Asian countries.



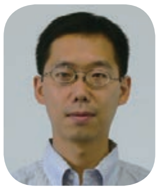


From the Editor For the production and sales of Nahlsgen®, the Nahls Corporation received the NBK Grand Prize and the Director of Kinki Economic Industries Prize from the New Business Conference Kansai (NBK) in 2012.

Jun Hiratake, PhD (left) **and Bunta Watanabe, PhD**

Professor (left), and Assistant Professor, Institute for Chemical Research

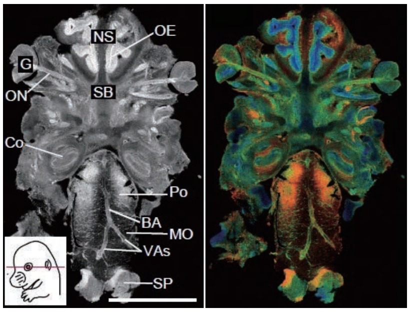
www.scl.kyoto-u.ac.jp/~hiratake/index-j.html



MED-SCI

Seeing "in a Living Mouse" is Believing

Live imaging of molecular activities by cutting-edge microscopy.



With the advent of microscopy and the discovery of green fluorescent protein (GFP), even molecular activities can be visualized in tissue culture cells. However, does what we see in the tissue culture cells occur also in living tissues? To seek answers to this question, I have generated transgenic mice expressing GFP-based biosensors for the molecular activities. Furthermore, in collaboration with Olympus Co., I developed imaging instruments designed specifically for the observation of living mouse tissues. Now, we can see how protein activities are regulated in inflamed tissues or cancer cells in living mice. More recently I have even been able to visualize molecular activities in the brains of awake-behaving mice.

From the Editor Prof. Matsuda and his colleagues observe and document *in vivo* behaviors of bacterial materials which express fluorescent proteins. Videos of their work can be viewed on their laboratory website (www.fret.lif.kyoto-u.ac.jp/movie.htm).

Michiyuki Matsuda, MD, PhD *Professor, Graduate School of Biostudies*
www.fret.lif.kyoto-u.ac.jp/e-phogemon/index.htm

BLDG ENG

Seismic Retrofit of Wooden Houses

What's the best way to reinforce houses to withstand nearby earthquakes?

Prof. Kawase explaining the structure and functions of the seismic retrofitting for an NHK broadcast. This research has been receiving increasing attention from the media.

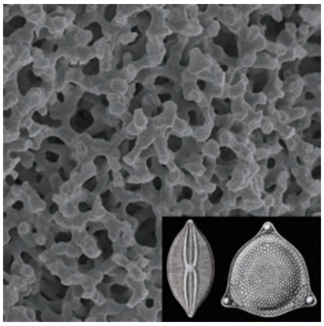
After the Hyogo-ken Nanbu (Kobe) earthquake disaster in 1995, we found that the heavy damage in Kobe was caused by relatively long-period (approx. 1 second) ground motions typical for earthquakes occurring nearby, in which both peak accelerations and velocities are quite high. The current building codes and retrofit methods for old buildings consider only how to cope with high acceleration input, for which any rigid structure can survive. We performed two different kinds of shaking table experiments, one to examine tolerance to high acceleration input and the other to examine high acceleration and velocity input. It turned out that the conventional method for reinforcing wooden houses seemed effective to the former, but not to the latter. On the other hand, our newly developed "Wall-of-Columns" technique can make houses survive both inputs. We are promoting this technique to retrofit as many wooden houses as possible in preparation for subsequent earthquakes.

Hiroshi Kawase, PhD *Professor, Disaster Prevention Research Institute*
zeisei5.dpri.kyoto-u.ac.jp/en/index.html

INORG-CHEM

An Artificial Diatom?

Porous Silica Monolith by Sol-Gel. purifies chemical substances.



Microstructure of monolithic silica with uniform-sized pores (inset: Diatom [taken from Ernst Häckel, *Kunstformen der Natur*, 1904])

A microorganism called a "diatom" utilizes silica to support its body, and a variety of sponge, network or slit morphologies are found in nature. My study started with synthesizing silica gels from a solution, through a sol-gel process, to obtain spongy solids in a bulk form, "monoliths." Diatom-like porous structures are obtained with the aid of water-soluble polymers. Similar materials consisting of various metal oxides, such as titania and alumina, are also available now. Monolithic silica with uniform-sized pores allows solutions to quickly flow through and can purify chemical substances by a method called "liquid-chromatography (LC)." The "monolithic silica LC column" was commercialized in 2000, and I have since explored many extended applications with my venture companies.

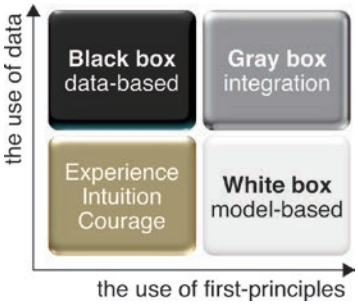
From the Editor This achievement earned Dr. Nakanishi the 2010 Commendation for Science and Technology, awarded by MEXT.

Kazuki Nakanishi, PhD *Associate Professor, Graduate School of Science*
kuchem.kyoto-u.ac.jp/mukibutsu/en/

PROCESS SYS ENG

Virtual Sensing Technology

How to predict and control product quality in real time.



We must control product quality, but is it always measured in real time? Unfortunately, the answer is no. Thus, virtual sensing technology, which predicts difficult-to-measure product quality from easy-to-measure process variables, plays a key role in industrial processes. We have developed a "just-in-time" modeling technique, which can predict product quality with high accuracy even when process characteristics change abruptly due to equipment maintenance. The idea is that we build a local approximation model every time prediction is required. In addition, we have developed a unified framework of gray-box modeling, in which first-principle (white-box) models and statistical (black-box) models are integrated in three ways. The developed modeling method has been applied to various industrial processes such as petrochemical processes at Showa Denko, semiconductor processes at Sony Semiconductor and Toshiba, steel processes at Nippon Steel & Sumitomo Metal, and pharmaceutical processes at Daiichi-Sankyo. Through this technique, product quality, productivity, and process stability have been improved in real industrial processes.

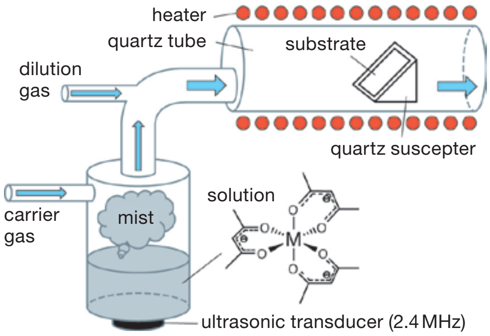
From the Editor For this work, Prof. Kano and his colleagues received the Technology Award from the Society of Instrument and Control Engineers (SICE), the Outstanding Paper Award from the Journal of Chemical Engineering of Japan (JCEJ), and the Instrumentation, Control and System Engineering Research Award from the Iron and Steel Institute of Japan (ISIJ).

Manabu Kano, PhD *Professor, Graduate School of Informatics*
human.sys.i.kyoto-u.ac.jp/

ELEC-ENG

Using Green Technology to Manufacture Green Devices

Reducing the energy use of electronic devices to help save the environment.



Electronic devices have a key role to play in saving environment, as highlighted by the Nobel Prize awarded for the development of blue LED technology in 2014. It should be noted that huge amounts of energy (electricity, waste disposal, etc.) are used in fabricating electronic devices, and that efforts to lower the energy used is now an important issue. We have developed a mist chemical vapor deposition as an environmentally-friendly and non-vacuum-based growth technology for nanoscale-controlled thin films and devices (see schematic illustration). A variety of metal-oxides, metal-sulfides, and organic films have been grown under nanometer-scale control without using vacuum systems and dangerous sources.

Through collaborative research and development with a lot of companies, as well as patent management by Kyoto University's Office of Society-Academia Collaboration for Innovation (SACI), this technology is becoming more widely used for fabricating solar cells, high-voltage devices, functional coating, and applications. With the support of the New Energy Development Organization (NEDO), the further development and application of this technology is rapidly progressing.

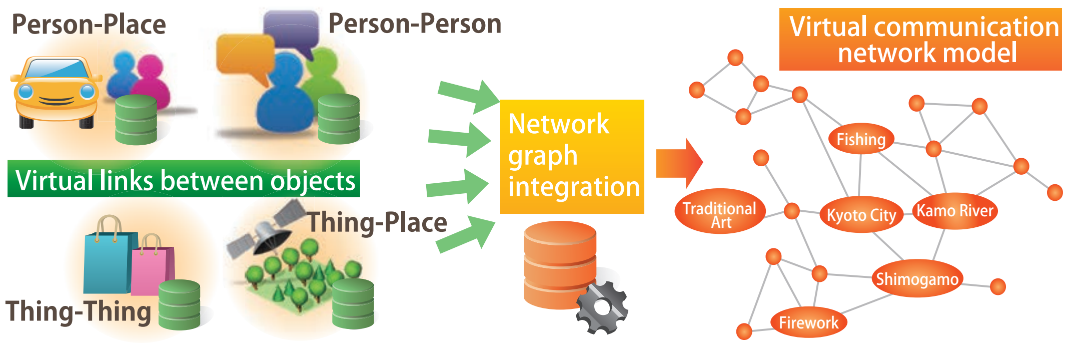
Shizuo Fujita, PhD *Professor, Graduate School of Engineering*
pesec.t.kyoto-u.ac.jp/ematerial/index.html

LIFO

A Virtual Link to Behavior Modeling

Communication-network behavior modeling and prediction.

My research has mainly focused on how to model the behaviors of communication-network users and how to predict their future behaviors. My findings suggest that people's behaviors are affected mainly by economic and social factors. First, people are more likely to choose more economically beneficial options: users simply prefer a faster or a more-battery saving connection for their mobile communication. For this reason, a discount-coupon type mechanism might work to provide incentive for users to suppress their data traffic when the network is congested. Second, people use communication network applications like phone calls, e-mail, chat, and SNS, to



establish, maintain, and develop social relationships with their family, friends, colleagues, and business partners. They also use communication networks to obtain information that they are socially interested in. My research results have shown such economic and social models of communication-network users work effectively to solve complex problems in related research fields.

One of the most promising solutions produced from my research results is the "virtual communication network model," in which we can numerically measure relationships between any two objects, i.e., people, things, or places, if we assume everything is virtually equipped with its own communication device, and each pair devices is virtually interconnected via a "virtual" link. In such a virtual communication network model, the strength of each virtual link between each pair of two objects temporally varies according to their interaction, while those virtual links are integrated to a huge network graph. Surprisingly, this model enables us to predict people's behaviors, i.e. who they will meet, what they will want, and where they will go, because the structure of the network graph reflects how it will change in the near future. Behavior prediction attracts many business fields like market analysis, advertising, e-commerce, content delivery, navigation systems, healthcare, etc. In 2011, I co-founded an industrial forum called the Mobile and Socialized Systems Forum (MSSF, http://mssf.jp/en/), in which over sixty private companies in Japan have been actively developing and promoting a commercialized system based on the virtual communication network model.

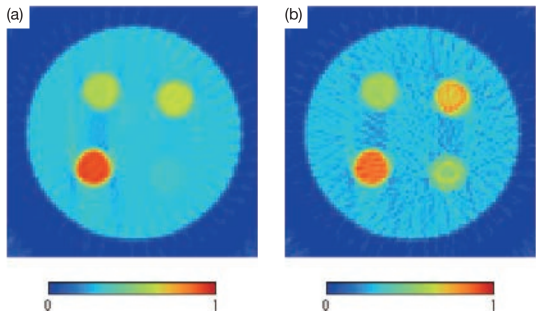
Ryoichi Shinkuma, PhD *Associate Professor, Graduate School of Informatics*
kyouindb.iimc.kyoto-u.ac.jp/e/uA1dL

RAD-PHYS

Material Inspection with Fixed X-ray Colors

Energy-resolved computed tomography with a current-mode transXend detector.

X-rays emitted by an X-ray tube have polychromatic energy distribution. The average energy, i.e., color, of X-rays becomes higher as they pass through materials. In the observation of cancer being marked by an iodine contrast agent, the signal of X-ray absorption by the iodine is smaller when the cancer is in a Japanese Sumo wrestler than it is in a boxer: the Sumo wrestler has much more X-ray absorbing stomach, which changes the color of X-rays not very sensitive to iodine. The energy-resolved computed tomography (CT) uses X-rays with specific colors, and CT images obtained are not affected by the thickness of the subject. Our invention the "transXend detector" makes the energy-resolved CT practical. A two-dimensional transXend detector for future human applications is currently under construction through a collaborative study with Mitsubishi Chemical.



CT images observed by (a) the conventional CT measurement method, in which the color of the X-rays changes and (b) the energy-resolved CT, in which materials are inspected by the fixed-color X-rays. The CT subject is 30 mm diameter cylindrical acrylic with four 5 mm diameter holes. In the bottom left and bottom right holes, iodine and tungsten solutions are filled with the thicknesses of 30 μm and 8 μm in 5 mm X-ray pass length (diameter of holes), respectively. The top left and top right holes have mixed solutions with the thicknesses of iodine being 15 μm and tungsten 2 μm, and iodine 15 μm and tungsten 4 μm in 5 mm in length, respectively.

From the Editor The Atomic Energy Society of Japan presented a paper associated with this study with their Best Paper Award in March 2015.

Ikuo Kanno, PhD *Professor, Graduate School of Engineering*
www.ne.t.kyoto-u.ac.jp/en/information/laboratory/person/kannoikuo-fold?set_language=en

ROBOTICS

Why Can Snakes Move Without Legs?

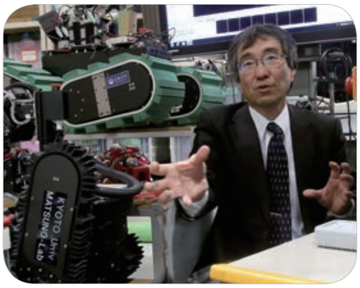
Developing rescue robots based on an understanding of animal behaviors.

KOHGA3

At a harver in Rikuzentakata, Iwate

Our laboratory has been engaged in two broad and connected areas of research that relate to human surroundings: "bio-inspired robotics" and "rescue robotics." Living creatures have survived and been optimized by natural selection. An understanding of the functions of living things is very useful in creating new artificial robots. In our lab, we are interested in analyzing the beautiful skills and behaviors of living things, and we are trying to find solutions to the following questions, among others: Why can living snakes move without legs? Why do quadrupeds change their gait patterns (for example, walk, trot, gallop) depending on their speed of movement? What is the mechanism of the flocking behaviors of birds and fish? How can small ants build a big anthill? Why can human beings walk with two legs? Based on our understanding of these phenomena, we can apply our knowledge to create robots to solve industrial problems. We have also been engaged in collaboration with several companies, through projects such as the swarm control of multiple moving robots, the "Murata Cheerleading Robots," with Murata Manufacturing, and the development of walking-assist carts with RTWorks and Funai Electric.

We believe that rescue robot systems are another important application of robotic technology. During my time as an employee at Kobe University, one of my masters' student, Mr. Motohiro Kisoi, was killed in the Great Hanshin-Awaji Earthquake on 17 January 1995. I have been putting my great efforts into the development of useful rescue robot systems and the establishment of rescue engineering. When the Great East Japan Earthquake occurred in 2011, we dispatched and utilized the rescue robots KOHGA3 (upper photo) to inspect damaged buildings in Hachinohe and Aomori, and we dispatched underwater robots to search for bodies in Minamisanriku, Miyagi, and Rikuzentakata in Iwate (bottom photo). My dream is to establish an international rescue robot team, like the popular TV show *Thunderbirds*, using advanced robotic technologies. If we can dispatch rescue robots from Japan to disaster sites everywhere in the world for disaster response and recovery, it will be a strong contribution to the world. I established the Motohiro Kisoi Fund to encourage and support students, from elementary school through to the university and graduate school-level, who are interested in rescue robotics, and young researchers who are dedicated to research on rescue engineering, emergency medical care, and mental care.



Fumitoshi Matsuno, PhD *Professor, Graduate School of Engineering*
www.mechatronics.me.kyoto-u.ac.jp

John Mung Program*

Opportunities to Explore Global Frontiers

The project to support mid- and long-term research by junior faculty members at leading academic institutions overseas.

*The program is named after the Japanese sailor, Nakahama Manjirō, also known in English as "John Mung," who was the first Japanese to set foot on American soil in 1841.

LAW

What Are Fair Conditions of Employment?

Court checks on the fairness of employment conditions.

Yuko Shimada, JD
Associate Professor,
Graduate School of Law
kyouindb.iimc.kyoto-u.ac.jp/e/eI6sF

MAT-SCI

Ceramics for Nuclear Core Safety

Silicon carbide composites for nuclear reactor core materials.

Fracture surface of SiC composites

Everything has changed following the Great East Japan Earthquake, resulting tsunami and subsequent damage to the Fukushima Daiichi nuclear power plant complex. Enhancing the accident tolerance of light water reactors (LWR) has become significantly important internationally and in Japan. Silicon carbide (SiC) ceramics are considered as the safest nuclear core material due to their superior stability in high temperature steam. One of issues regarding SiC ceramics is their brittle nature. In collaboration with the Toshiba Corporation, we are developing ductile SiC ceramics by reinforcing SiC fibers (SiC composites) for LWR application. We have successfully developed SiC composites with enhanced corrosion resistance to high temperature water and high temperature steam with precise control of their processing.

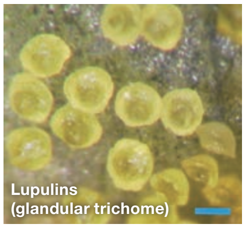
Tatsuya Hinoki, PhD *Associate Professor, Institute of Advanced Energy*

www.iae.kyoto-u.ac.jp/conv/hinoki/index.html

BIOCHEM

A Key Gene to Add Bitterness to Beer

Aromatic prenyltransferase for bitter acid biosynthesis in hops.


Lupulins (glandular trichome)


Hop cone (female flower)

Hops are an indispensable ingredient in beer production. The characteristic flavors and bitter taste of beer are given by hops, which are the female flowers of hop plants widely cultivated for brewery. Prenylated phloroglucinol derivatives of humulone (α-bitter acid) and lupulone (β-bitter acid), contained in lupulin glands in hop cones, are responsible for the bitter taste, and the former compound in particular contributes to the taste of beer. In the biosynthesis of humulone, the prenylation enzyme of phloroglucinol ring has remained a missing piece of the puzzle for many decades. Our group first opened this "black box" of the aromatic substrate prenyltransferase family in 2008 by identifying the first flavonoid-specific prenyltransferase. Then in collaboration with Kirin Holdings, a Japanese brewery company, we found the hop's prenyltransferase HlPT-1 for phloroglucinol substrate in 2012. This membrane intrinsic enzyme is also involved in the biosynthesis of xanthohumol, another hop-specific functional metabolite showing anticancer activities. More than five years are required for the breeding of new hop cultivars. HlPT-1 will be a powerful tool as a new molecular marker of hop breeding.

The book what Prof. Yazaki is a co-author, *Shokubutu-aroma-saiensu-no-saizennsen (Forefront of the Plant aroma-science)* (Tokyo: Fragrance Journal LTD., 2014)

Kazufumi Yazaki, PhD

Professor, Research Institute for Sustainable Humanosphere

www.rish.kyoto-u.ac.jp/lpge/

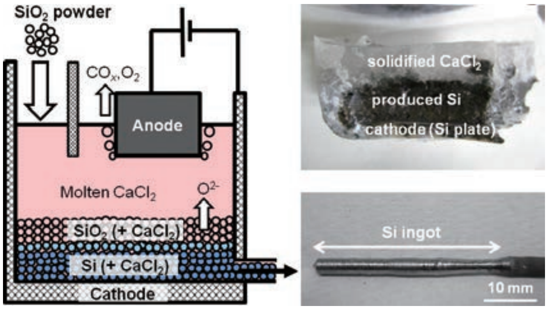
We work mainly for our livelihoods, but also in order to engage with society. The conditions of our employment, e.g., wage benefits and holidays, play an important role. However, most of us are not involved in determining such employment conditions, as they are usually decided by our employers. Most employees must accept the conditions offered by their employers. But, what happens, if the conditions which employers one-sidedly determine are unfair? For example, if an employment condition stipulates that employers can arbitrarily retract benefits? In such a case, the lives of the employees would become unstable. If unfair conditions of employment are prevalent in society, the society itself will become unstable, and it will become difficult to maintain public order. In Germany, I have been engaged in research into a system whereby the court checks the fairness of employment conditions.

From the Editor Dr. Shimada has been engaged in research as a Humboldt Research Fellow since May 2015.

INORG-CHEM

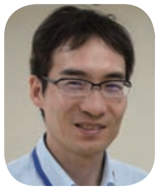
Make Solar Power the Main Energy Source for Mankind

Innovation for solar-silicon production by molten salt electrolysis.



A new method of producing solar-grade silicon through the electrochemical reduction of silica in molten salt.

Solar power generation is one of the most promising renewable energies. However, the percentage of photovoltaic (PV) power in the world's total primary energy production is still less than 1%. Silicon (Si) solar cells are most quickly spreading type of solar cells in the world owing to the advantages of their high efficiency, high durability, and harmlessness to the environment. However, the conventional production method of high purity Si (or solar Si, 99.9999% purity) has the disadvantages of low energy efficiency, low productivity, and high cost. Against this background, my colleagues and I have proposed a new method for the producing solar Si from purified silica (SiO_2) feedstock by using molten salt electrolysis. We have already verified the principle of the method, and are now conducting practical research with the aim helping to make solar power the main energy source for mankind.

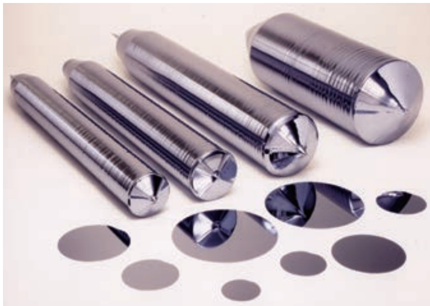


Toshiyuki Nohira, PhD *Professor, Institute of Advance Energy*
www.iae.kyoto-u.ac.jp/chemical/a-10_j.html

PROC SYS ENG

Super-Flat Epitaxial Silicon Wafer

Efficient data-based method for improving wafer flatness



Flatness of thick-film epitaxial silicon wafers is crucial in manufacturing power semiconductor devices. The time-consuming adjustment of flatness is frequently required because parts of the manufacturing equipment are routinely replaced. To standardize the adjustment procedure and improve productivity, we developed a flatness adjustment method based on a statistical model that relates wafer flatness to manipulation of the converted equipment. The statistical model was derived through design of experiments (DoE). The proposed method reduced the adjustment time by 75%. Consequently, we successfully increased productivity and decreased the operational risk.

From the Editor For this achievement, they received the Technology Award from the Division of Systems, Information and Simulation Technologies of the Society of Chemical Engineers, Japan (SCEJ).

Masahiko Mizuta (left) **and Manabu Kano, PhD**
SUMCO Corporation (left), Professor, Graduate School of Informatics
human.sys.i.kyoto-u.ac.jp/

LAW

A Page of Medieval History

Daily legal life reflected in medieval court records.

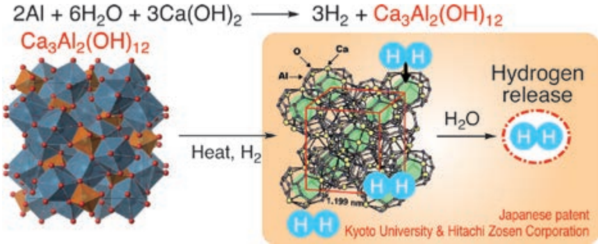
I am currently studying in Göttingen as a visiting fellow. My research deals with the Magdeburgian Law, a representative German medieval town law. It is a well-known fact that medieval towns created many legal institutions. To understand the law, it is essential to work with medieval manuscripts, such as court records. As may be expected, the records contain many civil conflicts. However, those who lived in medieval towns apparently visited courts for rather peaceful purposes—in order to avoid potential problems. Whenever I read the court records, I feel that people have always had similar tendencies, regardless of era or country. My research mainly contributes to the field of legal history, but it could also contribute to contemporary jurisprudence and a reexamination of existing legal systems.

Dan Sato, LLD *Associate Professor, Graduate School of Law* kyouindb.iimc.kyoto-u.ac.jp/e/iS2uO

INORG-CHEM

Save, Recycle, and Reuse Efficiently

Recycling waste using the chemical reactions of aluminum, calcium hydroxide, and water.



In this age in which we are vulnerable to global warming, it is important to make the maximum effective use of natural resources."Save, recycle, and recover" is a slogan for energy-saving and the effective use of resources in the future. We are working to recycle different types of waste using chemical reactions to produce new materials, new properties, or reuse them. One of the waste products is generated by a reaction between aluminum and calcium oxide with water to produce hydrogen. This reaction produces aluminum oxide, calcium aluminate compound, and other materials. With this simple process, we have transformed the waste product into a ceramic which is capable of storing hydrogen in its structure and surface. This ceramic has more advantages than conventional hydride materials used to store hydrogen, such as being lightweight and low cost.

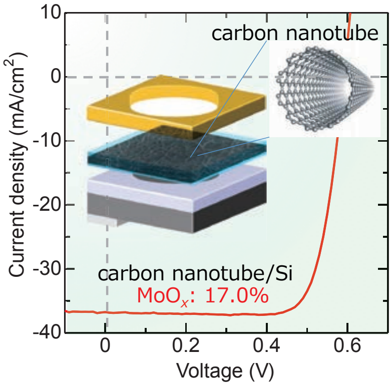
Heidy Visbal, PhD *Researcher, Graduate School of Engineering*

www1.kuic.kyoto-u.ac.jp (The laboratory to which she belongs)

NANO-SCI

Renewable Energy Research for the Next Generation

Development of high performance solar cells using carbon nanotubes.

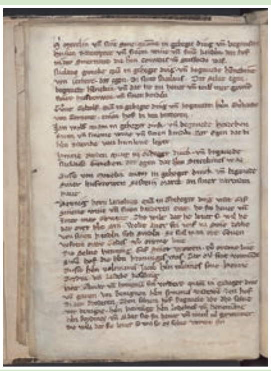


Recently, innovative research and development of renewable energy sources are strongly required to ensure a sustainable society in the future. Solar light is a major clean renewable energy source, and so it is important that we use it efficiently to generate energy. High-performance solar cells with new functionality are key devices for solar light utilization. I have developed a new class of solar cells using carbon nanotubes in collaboration with the Hitachi Zosen Corporation. Right figure shows a schematic picture of my carbon nanotube/Si solar cell, which has a very high level performance (i.e. power conversion efficiency of 17.0%). This value (performance) is currently the highest among solar cells using carbon nanotubes. I am proceeding to develop new solar cells with flexibility and lightweight properties using the insights obtained from this research.

From the Editor Based on this research, Prof. Matsuda co-authored a paper with Mr. Feijiu Wang, for which Mr. Wang received the Young Author's Award at the 28th International Microprocesses and Nanotechnology Conference.

Kazunari Matsuda, PhD *Professor, Institute of Advanced Energy*

www.iae.kyoto-u.ac.jp/conv/en/#



Halle, Universitäts- und Landesbibliothäk, Yd 2° 31 (1), "Hallisches Schöffenbuch Bd. I", fol. 24v.

RESCUED by an American whaler after a terrible shipwreck in 1841, Nakahama Manjirō, also known in English as "John Mung," set foot in America. He enthusiastically learned about new technologies, laws, and customs. After he returned to Japan, he became a pioneering figure in developing the country's international relations. Inspired by his colorful life story, the program seeks to give junior faculty, staff members, and students opportunities to explore new academic and professional frontiers throughout the world.

PHOTO: Wikipedia

International Recognition of Kyoto University's Research

Topic

Prof. Emeritus Shigekazu Nagata Elected Foreign Associate of the National Academy of Science

For his distinguished research achievements, Prof. Emeritus Shigekazu Nagata was elected Foreign Associate of the United States' National Academy of Science (NAS) in April 2014. Dr. Nagata is a molecular biologist, best known for his research on apoptosis, the process of programmed cell death occurring in multi-cellular organisms. As a member of Dr. Charies Weissmann's Laboratory at the University of Zurich, he succeeded in the first cloning and expression of an interferon gene. He also identified Granulocyte colony-stimulating factor, a death factor (Fas receptor) and its ligand (Fas ligand), and elucidated their physiological and pathological roles in apoptosis. He was appointed as an endowed research department professor at Osaka University in April 2015.

WEB www2.mfour.med.kyoto-u.ac.jp/~nagata/english/index.html (Prof. Nagata's Lab)

Topic

Prof. Shimon Sakaguchi Awarded Canada Gairdner International Award

Prof. Shimon Sakaguchi of Kyoto University's Institute for Frontier Medical Sciences and distinguished professor of Osaka University, was awarded the 2015 Canada Gairdner International Award.

One of the most prestigious scientific prizes in the world, the Canada Gairdner International Award is presented by Canada's Gairdner Foundation to recognize and celebrate the work of the world's leading biomedical researchers. Prof. Sakaguchi received the award "for his discovery of regulatory T cells, characterization of their role in immunity and application to the treatment of autoimmune diseases and cancer." The award ceremony is scheduled to take place in Toronto, Canada in October 2015.

WEB www.frontier.kyoto-u.ac.jp/bf03/index-j.html (Prof. Sakaguchi's Lab)

TOPIC

Prof. Tsuyoshi Nakaya Awarded 6th Yoji Totsuka Prize

Prof. Tsuyoshi Nakaya of the Graduate School of Science was awarded the 6th Yoji Totsuka Prize. Prof. Nakaya shares the prize with Prof. Masato Shiozawa of the Institute for Cosmic Ray Research (ICRR), and Prof. Takashi Kobayashi of the Institute of Particle and Nuclear Studies, High-Energy Accelerator Research Organization (KEK).

The Yoji Totsuka Prize was established by the Heisei Foundation for Basic Science in 2009. The prize acknowledges researchers who have made distinguished achievements in the fields of experimental and theoretical particle physics, particularly in the area of neutrino and non-accelerator physics.

The three recipients of the 6th prize were honored for "the observation of electron neutrino appearance in a muon neutrino beam." The three scientists have played a leading role in the Tokai to Kamioka (T2K) collaborative project, which is conducting a long-baseline neutrino oscillation experiment.

WEB kyouindb.iimc.kyoto-u.ac.jp/e/cI4gH (Profile of Prof. Nakaya)

TOPIC

Profs. Jun-ichi Yoshida and Masahiro Morikura Awarded the Medal of Honor with Purple Ribbon

Profs. Jun-ichi Yoshida of the Graduate School of Engineering and Masahiro Morikura of the Graduate School of Informatics were each awarded the Medal of Honor with Purple Ribbon (*Shiju Hōshō*) by the Government of Japan in April 2015. The award is conferred by the Emperor of Japan for meritorious deeds or excellence in the fields of science, art or sport.


Prof. Jun-ichi Yoshida


Prof. Masahiro Morikura

Prof. Yoshida, an organic chemist, is recognized as one of the leading scientists in the field of organic synthesis based on time integration and space integration of reactions using unstable reactive intermediates. He also received the Manuel M. Baizer Award from the Electrochemical Society (ECS) in 2014.

Prof. Morikura is a researcher in the fields of electronics, information, and communication engineering. As an NTT researcher, he is engaged in a research and development project on wireless local area networks (LAN). Through the project, he proposed a method of digital modulation called "orthogonal frequency division multiplexing" in collaboration with Lucent Technologies Inc., a US telecommunications equipment company. He also played a leading role in formulating "IEEE802.11a" which is a standard for wireless LAN communication.

WEB www.sbchem.kyoto-u.ac.jp/yoshida-lab/en/index.php?yoshida-lab (Prof. Yoshida's Lab)

WEB www.s-ee.t.kyoto-u.ac.jp/en/information/laboratory/gsi/cce/imc/6885539f-59277949?set_language=en (Prof. Morikura's Lab)

TOPIC

Prof. Susumu Kitagawa Awarded the Marco Polo Prize

Prof. Susumu Kitagawa, director of Kyoto University's Institute for Integrated Cell-Material Sciences (iCeMS), a leading researcher in the field of Chemistry, was awarded the Marco Polo Prize for Italian Science at a ceremony in Kyoto in April 2015. This prize was established by the Italian government in 2011 to acknowledge researchers who have made outstanding contributions to scientific and technological collaboration between Italy and Japan in the field of nanotechnology. Prof. Hiroshi Kitagawa of iCeMS was awarded the prize in 2013.

Prof. Kitagawa (right) receiving the award from Mr. Daisaku Kadokawa, mayor of Kyoto City

WEB www.icems.kyoto-u.ac.jp/e/pr/2015/04/03-tp.html

TOPIC

Prof. Akihide Kasai Awarded the Uda Prize of the Japan Society of Fisheries Oceanography

Prof. Akihide Kasai, a former associate professor in Kyoto University's Field Science Education and Research Center (FSERC), was awarded the Uda Prize by the Japan Society of Fisheries Oceanography (JSFO) for his research titled "Study on the Mechanism of Material Cycle and Biological Production in Coastal Seas." The Uda Prize was named after Prof. Michitaka Uda, the first president of JSFO, and has been annually awarded to scholars in Japan and overseas in recognition of outstanding achievements in fisheries oceanography research. Prof. Kasai, a specialist in marine biological environment is currently working in the Graduate School of Fisheries Sciences of Hokkaido University (since April, 2015).

WEB www2.fish.hokudai.ac.jp/modules/labo/content0118.html (Hokkaido University)

POINTS OF INTEREST 3

Princess Maha Chakri Sirindhorn of Thailand Visits iCeMS

On 20 April 2015, Her Royal Highness Princess Maha Chakri Sirindhorn of Thailand paid a visit to Kyoto University's Institute for Cell-Material Sciences (iCeMS) during her week-long visit to Japan to observe top-level research institutes focused on science and technology. In his welcome speech to the Princess, President Yamagiwa expressed his hope that Kyoto University strengthens its academic partnerships with Thai institutions. Princess Sirindhorn interacted with the iCeMS team about the institute's role as a global hub for scientific collaboration between industry, government, and academia.

iCeMS was founded in 2007 as one of five research centers within the World Premier International Research Center Initiative (WPI) program. A team of 19 principal investigators (PIs) and 160 researchers, a third of whom are drawn from overseas, concern themselves with the science of biochemical and biophysical processes within DNA, proteins, cells and beyond. To develop new approaches to benefit society, iCeMS is establishing a research environment that attracts the world's best scientists, where its community extends to 14 global partner institutions, English is the official language and ample support for funds acquisition is provided.

WEB www.icems.kyoto-u.ac.jp/e/pr/2015/04/30-tp.html

Princess Sirindhorn listening to a presentation by Assistant Prof. Shimpei Yamamoto of iCeMS

Topic

Prof. Ryoichi Inami Awarded the Yomiuri Prize for Literature

Prof. Ryoichi Inami of the Institute for Research in Humanities was awarded the Yomiuri Prize for Literature for his book *Dream of the Red Chamber: A New Translation* (Tokyo: Iwanami Shoten, 2013). Established in 1949 by the Yomiuri Shinbun newspaper company to contribute to Japan's standing as a "cultural nation," the Yomiuri Prize for Literature (*Yomiuri Bungaku Shō*) is one of Japan's most prestigious literary awards.

Dream of the Red Chamber, also called *The Story of the Stone* is one of China's "four great classical novels." It was written by Cao Xueqin during the Qing Dynasty in the mid-18th century, and is generally acknowledged to be the pinnacle of Chinese fiction.

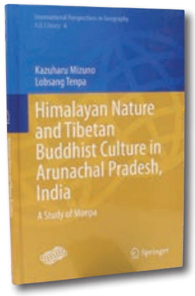
WEB www.zinbun.kyoto-u.ac.jp/zinbun/members/inami.htm (Profile of Prof. Inami. Japanese only)

Topic

Prof. Kazuharu Mizuno Awarded the 2014 Association of Japanese Geographers Award in the Publication Category

Prof. Kazuharu Mizuno

Prof. Kazuharu Mizuno of Kyoto University's Graduate School of Letters, an ecological geographer, was awarded the 2014 Association of Japanese Geographers award in the publication category. The award was presented in recognition of his book titled *Arunachal Pradesh, India: Nature of Assam Himalaya and Tibetan Society* (published by Showado, 2012), which is the first book to systematically describe the nature, society, and history of Arunachal Pradesh state of northeast India. The English version of the book, co-authored with Lobsang Tenpa, was published this summer by the Springer Publishing Company. Prof. Mizuno also serves as vice-chair of the International Geographical Union (IGU) Commission on Biogeography and Biodiversity.



Kazuharu Mizuno, Lobsang Tenpa, *Himalayan Nature and Tibetan Buddhist Culture in Arunachal Pradesh, India: A Study of Monpa* (Tokyo: Springer Japan KK, 2015).

WEB www.bun.kyoto-u.ac.jp/geography/geo-staff/

Topic

RISH's MU Radar Receives the IEEE Milestone Award

The middle and upper atmosphere radar (MU radar) at Kyoto University's Research Institute for Sustainable Humanosphere (RISH) was developed by Kyoto University in collaboration with Mitsubishi Electric Corporation and has been in use since 1984. It is the world's first mesosphere, stratosphere, and troposphere (MST) radar with an active phased array antenna system. In 13 May 2015, the radar was awarded the IEEE Milestone by the Institute of Electrical and Electronic Engineers (IEEE), one of the world's largest academic societies. The award was presented in recognition of the radar's contributions to atmospheric science and radar engineering.

From left: Masaki Sakuyama, president and CEO of Mitsubishi Electric Corporation, Juichi Yamagiwa, president of Kyoto University, and Howard E Michel president and CEO of IEEE

Under computer control, the MU radar is capable of emitting an ultra-fast 400 μs scanning beam in all directions, enabling real-time monitoring of the atmosphere at an altitude of up to several hundred kilometers, making it one of the most powerful instruments of its kind in the world. As a joint-use facility accessible to all universities and research institutions in Japan, it has contributed to the advance of atmospheric science and radar technology by playing a role in numerous research projects in a broad range of related fields, including aeronomy, meteorology, astronomy, electrical engineering, electronics, and astrophysics.

The MU radar seen from above

The IEEE Milestones in Electrical Engineering and Computing program was launched in 1983 to acknowledge significant innovations in relevant fields of technology that occurred at least 25 years ago, and which have made major contributions to regional and industrial development.

WEB www.kyoto-u.ac.jp/en/research/events_news/department/seizonken/news/2015/150513_1.html

TOPIC

Prof. Emeritus Sin Hitotumatu Awarded the 2015 MSJ Publication Prize

A committed researcher and educator in the field of mathematics, Prof. Emeritus Sin Hitotumatu has authored a large number of books and textbooks in his field for scholars of all levels of experience. He has also translated several major works, including Martin Gardner's *Mathematical Magic Show* (see the article in the Points of Interest section for further details). In recognition of his outstanding contribution to mathematical research and education in Japan though his writing activities, Prof. Hitotumatu was awarded the 2015 MSJ Publication Prize by the Mathematical Society of Japan (MSJ).

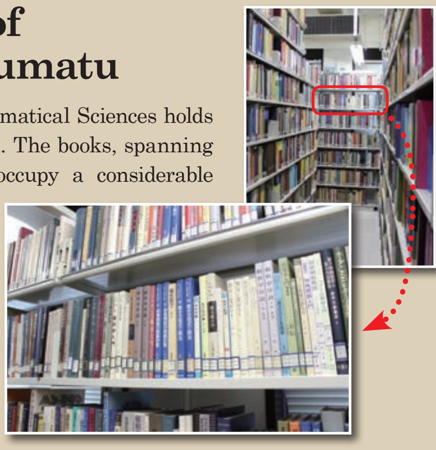
One of his excellent work, *Kaisekigaku-josetsu* (Tokyo: Shokabo Co., Ltd., 1981), vol. 1, vol. 2.

WEB mathsoc.jp/publicity/pubprize2015.html

POINTS OF INTEREST 4

The Remarkable Works of Prof. Emeritus Sin Hitotumatu

The Library of Kyoto University's Research Institute for Mathematical Sciences holds a collection of books written by Prof. Emeritus Sin Hitotumatu. The books, spanning specialized academic works to books on self-improvement, occupy a considerable portion of the library's "Japanese Books H-J" shelf. The library as a whole holds 100,196 books and 1,582 different of journal on mathematics, applied mathematics, computer science, and theoretical physics, as well as valuable lecture notes and preprints. The library is open to all researchers as a Joint Usage / Research Center. Please see the website below for details on how to visit the library.



WEB www.kurims.kyoto-u.ac.jp/~library/eng_index.html

HONORS

Award Winning Researchers in Kyoto Univ.

The following is a list of just some of the Kyoto University researchers who have received international awards —— a testimony to the university's intellectually fertile environment and culture of academic freedom.

Nobel Prize

in Physics

Hideki Yukawa (1949), **Sin-Itiro Tomonaga** (1965), **Makoto Kobayashi** (2008), **Toshihide Maskawa** (2008), **Isamu Akasaki*** (2014)

*Photo provided by Meijo University

in Chemistry

Kenichi Fukui (1981), **Ryoji Noyori** (2001)

in Physiology or Medicine

Susumu Tonegawa (1987), **Shinya Yamanaka** (2012)

Fields Medal

Heisuke Hironaka (1970), **Shigefumi Mori** (1990)

Gauss Prize

Kiyosi Itō (2006)

Lasker Award

Susumu Tonegawa (1987), **Yasutomi Nishizuka** (1989), **Yoshio Masui** (1998), **Shinya Yamanaka** (2009), **Kazutoshi Mori** (2014)

Japan Prize

Kenichi Honda* (2004), **Makoto Nagao*** (2005), **Masatoshi Takeichi*** (2005)

*Photos provided by the Japan Prize Foundation

Kyoto Prize

Yasutomi Nishizuka (1992), **Chushiro Hayashi*** (1995), **Kiyosi Itō*** (1998), **Alan Curtis Kay** (2004), **Isamu Akasaki** (2009), **Shinya Yamanaka*** (2010), **Masatoshi Nei*** (2013)

*Photos provided by the Inamori Foundation

Die Schaudinn-Hoffmann-Plakette ◆ **Shin-ichi Matsumoto** (1965)

Huxley Memorial Medal ◆ **Junichiro Itani** (1984)

Canada Gairdner International Award ◆ **Kimishige Ishizuka** (1973), **Susumu Tonegawa** (1983), **Yasutomi Nishizuka** (1988), **Shinya Yamanaka** (2009), **Kazutoshi Mori** (2009), **Shimon Sakaguchi** (2015)

Order of the White Elephant - 3rd Class ◆ **Yoneo Ishii** (1987)

Ross G. Harrison Prize ◆ **Tokindo S. Okada** (1989)

Salem Prize ◆ **Mitsuhiro Shishikura** (1992)

Robert Koch Prize ◆ **Shigekazu Nagata** (1995), **Shinya Yamanaka** (2008), **Tasuku Honjo** (2012)

The Keio Medical Science Prize ◆ **Shigetada Nakanishi** (1996), **Masatoshi Takeichi** (2001), **Koichi Tanaka** (2002), **Yoshinori Fujiyoshi** (2005), **Shimon Sakaguchi** (2008), **Kenji Kangawa** (2009)

Frank Nelson Cole Prize ◆ **Hiraku Nakazima** (2003)

John Dawson Prize ◆ **Tetsuya Sato** (2005)

Yuri Gagarin Medal ◆ **Hiroshi Matsumoto** (2006)

Booker Gold Medal ◆ **Hiroshi Matsumoto** (2008)

The Ulysses Medal ◆ **Shuh Narumiya** (2008)

L.S.B. Leakey Prize ◆ **Toshisada Nishida** (2008)

Prix du Rayonnement de la langue et de la littérature françaises ◆ **Kazuyoshi Yoshikawa** (2010)

de Gennes Prize ◆ **Susumu Kitagawa** (2013)

L'Oréal-UNESCO Awards For Women in Science ◆ **Tomiko Yonezawa** (2005), **Kayo Inaba** (2014)


H. Yukawa


S. Tomonaga


H. Hironaka


K. Fukui


S. Tonegawa


Y. Nishizuka


S. Mori


C. Hayashi


Y. Masui


R. Noyori


K. Honda


M. Nagao


M. Takeichi


K. Ito


M. Kobayashi


T. Maskawa


S. Yamanaka


M. Nei


K. Mori


I. Akasaki

Author Index

This information is also available online. WEB www.kyoto-u.ac.jp/ja/issue/research_activities

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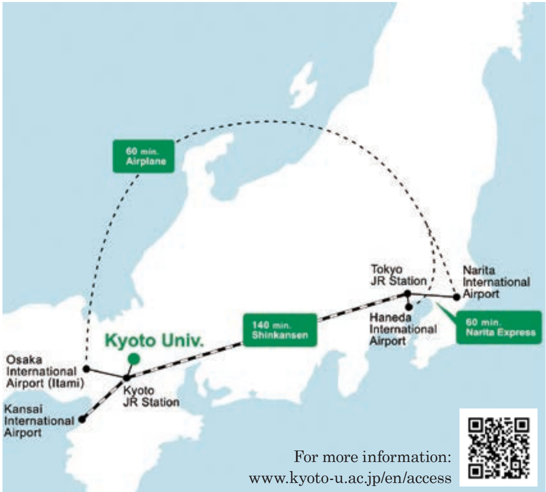

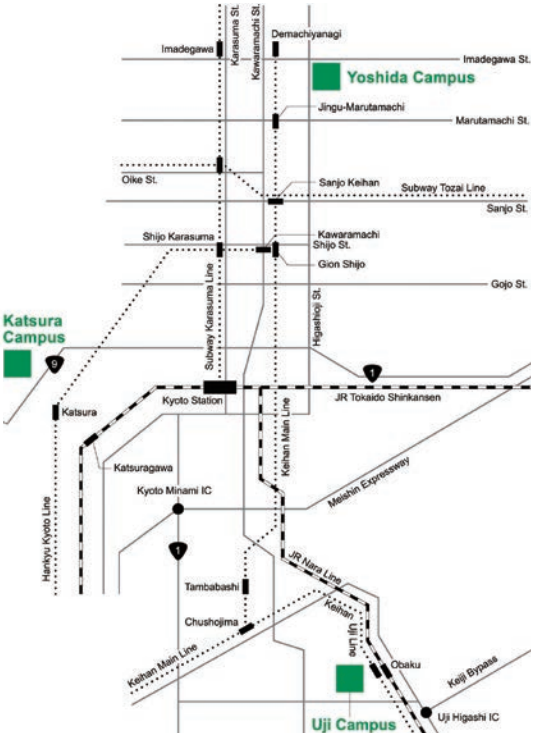

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