



HOKKAIDO, JAPAN

Hokkaido's ambitious new face

Hokkaido aims to create one of the world's top health science and medical industry clusters, backed by strong industry-academia-government alliances.

Hokkaido is a land awash in natural beauty. With soaring mountain ranges, clear caldera lakes and natural hot springs, the northernmost island of the Japanese archipelago is renowned not only as a popular destination for summer visitors in search of cooler, alpine climes, but also as a haven for winter sports enthusiasts. Owing to its vast stretches of fertile arable land and abundant marine life, Hokkaido prefecture ranks first in the nation in the production of a wide array of fresh dairy, agricultural and seafood products.

Only recently have industry, academia and government bodies joined forces to begin tapping the potential of Hokkaido's natural resources in earnest, with the first wave of industrial cluster activities mobilized in 1998 as a means of invigorating the regional economy. Larger-scale collaborations are currently underway, focusing on biotechnology R&D, translational research and drug discovery, with the overarching goal of creating a new health science and medical care industry cluster in Hokkaido within a decade.

At the heart of the initiative to create a world-class biomedical hub is the Hokkaido University Research & Business Park (HU R&BP), an integrated research and business centre located in the heart of Sapporo. The HU R&BP is actively encouraging R&D and innovation, inviting companies and laboratories to

the park area and providing the infrastructure to foster bioventures and the commercialization of new technologies.

Backed by strong industry-academia-government partnerships, the HU R&BP aims to emerge as an internationally competitive Center of Excellence (COE) by 2020 as part of the Japanese government's Global COE Program. In addition, by integrating former prefectural research institutions and compiling data from established centres such as the Hokkaido Research Organization (HRO), the HU R&BP is strengthening its base as a cross-disciplinary research hub.

"Our current focus is to create a new Hokkaido by constructing an indispensable platform that supports food, environment, health care and cutting-edge medical technology," says Yasuhiro Koba, senior director of the Bureau of Science Promotion, Department of Policy Planning and Coordination at the Hokkaido Government. Koba affirms that drawing on the wealth of Hokkaido's primary commodities, securing and fostering innovative partnerships, and attracting high-calibre researchers in food and health sciences are key targets in propelling the initiative forward.

Japan's breadbasket

Spanning an area of 83,457 square kilometres, Hokkaido is the largest food-producing region in the country, earning



Hokkaido University in Sapporo

NOASTEC

its reputation as the breadbasket of Japan, with a gross regional production of ¥18.5 trillion (approximately US\$241.9 billion) as of 2008. Important crops produced in the prefecture include corn, rice, wheat, potatoes, soybeans, pumpkins and sugar beet. The harvest of paddy rice in the prefecture accounted for 7.3% of the nation's total production in 2008. The region's major marine products include salmon, trout and scallops. Scientists at the HRO have also introduced their salmon farming techniques overseas. "We have offered our salmon farming technology to Chile to help expand the country's aquaculture industry," says Norihito Tambo, president of the HRO.

Extensive land cultivation began in Hokkaido in 1869, one year after the Meiji Restoration that catapulted Japan forward as a modern nation. The

region was formerly known as Ezochi, home to the indigenous Ainu people, whose ancestors originally subsisted on hunting and fishing. During the tumultuous early Meiji period, two Americans played a key role in developing Hokkaido's roads, ports and harbours, as well as coal mining, intensive farming and introducing a new higher education system. Both men hailed from Massachusetts; Horace Capron, then commissioner of the US Department of Agriculture, was appointed as a special advisor to develop Hokkaido's economy, and William S. Clark, then president of the Massachusetts Agricultural College, was instrumental in establishing the Sapporo Agricultural College, later to become Hokkaido University.

"Hokkaido was the Japanese equivalent of America's Wild West," says Tambo,



The American-style neo-baroque Old Government Building in Sapporo

“and the Americans who came here to help in those early days brought with them that frontier spirit.” The legacy left behind by Capron and Clark is considerable—as well as introducing new techniques in agriculture, fishing and animal husbandry, Clark himself promoted freedom and equality, and urged his students to think independently. These principles had a lasting impact on many notable alumni of the college, and Clark’s departing words to his students—“Boys, be ambitious”—have become the famous motto of today’s Hokkaido University.

Driving innovation

The new biotech cluster activities at HU R&BP not only mark a new era in the funding of innovative research in Hokkaido but also underline the significance of the life sciences and biomedical industries to Japan. The HU R&BP has been selected by the Japanese government as one of nine projects receiving targeted support to flourish as centres of international competitiveness, paving the way towards a projected five-year budget of ¥1 billion (US\$13 million) as part of the Regional Innovation Cluster Program implemented by the Japanese government.

“We have studied ways to become economically independent, learning from science parks such as Technopolis in Finland, as it has a similar climate to that of Hokkaido,” says Masaru Tsunetoshi, executive director

at the Northern Advancement Center for Science & Technology (NOASTEC) Foundation, one of the core organizations involved in promoting science and technology in the region.

Three innovative projects are bolstering HU R&BP’s efforts to deep-

en collaborations between academic research groups and the private sector. The first is an alliance between Hokkaido University and leading companies, including Shionogi and Hitachi, named the Matching Program for Innovations in Future Drug Discovery and Medical Care, which received government funds of ¥3.15 billion (approximately US\$41.2 million) from fiscal 2006 to 2011. The second is the Sapporo Biocluster ‘Bio-S’ project, designed to bring together academic and industry expertise in food and health science, which has received a total of ¥3.1 billion (US\$40.5 million) in government grants from 2007 to 2011. The third is the All-Hokkaido Translational Research Project for Advanced Medicine, which was awarded government funds of ¥1.3 billion (approximately US\$17 million) over the same period.

Crucially, the decision to locate the HU R&BP in the northern part of Hokkaido University’s 1.8 square-kilometre Sapporo campus has the key advantage of facilitating communication between existing university facilities and newly formed public and private research institutions, incubation buildings and various support centres, so as to form a fully integrated R&D hub.

Already the Sapporo campus has won widespread acclaim for developing the world’s first isotope microscope system, as

a result of a research project led by Hisayoshi Yurimoto at the university’s Graduate School of Science. Most recently, the campus celebrated the awarding of the Nobel Prize in Chemistry 2010 to emeritus professor Akira Suzuki for his groundbreaking research in organic synthesis.

New frontiers

In further significant steps to support medical research at the HU R&BP, the government has awarded ¥3.6 billion (approximately US\$47.1 million) to the Advanced Radiation Therapy Project led by Hiroki Shirato at the Hokkaido University Graduate School of Medicine. The project involves real-time tumour tracking based on molecular imaging techniques and was selected for inclusion in the government’s Funding Program for the World-Leading Innovative R&D on Science and Tech-



Statue of William S. Clark in Sapporo

nology’. This year has also seen the completion of a new facility at the business park to launch the Platform for Research on Biofunctional Molecules.

Hokkaido University itself was awarded ¥4.31 billion (approximately US\$56.3 million) as part of Japan’s Grants-in-Aid for Scientific Research in 2010, with seven of its projects selected to be part of the government’s Global COE Program. Research grants awarded to the Hokkaido Research Organization doubled to ¥201 million (approximately US\$2.6 million) between 2007 and 2009.

Other strong cluster activities in the region include the Marine Cluster in Hakodate project, with a budget of ¥1.5 billion (US\$19.6 million) over five years, and the Tokachi Agricultural Bioscience Cluster national project, with a ¥1.24 billion (US\$16.2 million) grant over nine years. A business lobby for biotechnology set up five years ago focusing on processed foods in cooperation with the Hokkaido bureau of the Ministry of Economy, Trade and Industry and the Hokkaido and Sapporo City governments is also making a significant impact. “The number of manufacturers is still very small,” says Kenichi Kosuna, chairman of the Hokkaido Association for Bio-Business. “However, we are aiming to make value-added products using Hokkaido’s agricultural and marine products to help stimulate the regional manufacturing industry.”

Burgeoning interest in food and health-related sciences is spurring new research into the development of functional foods and nutritional biomarkers, with projects like the Bio-S initiative actively involved in evaluating the functionality of food ingredients sourced in Hokkaido. Evaluating the safety of recombinant DNA-derived foods is an on-going research topic for bio-businesses operating in the region. At a time when Japan is focusing on revitalization and restoration efforts following the March 11 disaster, addressing safety issues surrounding food, energy and the environment and establishing consumer confidence are priorities that cannot be ignored.

Imbued with the ‘frontier spirit’ on which the land was founded, Hokkaido is uniquely positioned to embrace forward-thinking creativity and attract a new generation of pioneers in bioscience and technology. ■



HOKKAIDO UNIVERSITY

Hokkaido's ambitious frontier spirit

Academic institutions, just like people, can be ambitious. Ever since opening its doors in 1876, Hokkaido University has epitomized the pioneering spirit of ambition instilled in it by its founding fathers. Now in its 135th year, those ambitions are becoming ever more global, yet the university's fundamental focus remains deeply rooted in Hokkaido's rich natural beauty and long history of agricultural innovation.

For centuries, Hokkaido has been renowned throughout Japan for its quality produce and idyllic natural environment—attributes that made the region a natural choice for establishing the country's first agricultural college specifically for the development of modern agricultural practices in 1876. The charter of the Sapporo Agricultural College as it was called, and which in 1947 would become known as Hokkaido University, was to develop a food supply system as part of the government's desire to explore and cultivate Hokkaido's natural agricultural resources, fulfilling a pioneering role in Japan on many fronts. "Sapporo Agricultural College was the first modern academic institution in Japan, and also the first institution in the country to award bachelor degrees," says Hiroshi Saeki, president of Hokkaido University.

As the Japanese government of the day lacked experience in managing such institutions and the country had little home-grown expertise in modern academic practices, it looked to Europe and the United States for help. In the US at that time, William Smith Clark—a former colonel in the country's civil war and a professor in chemistry, botany and zoology—was championing the technological modernization of America's farming industry through his innovative leadership of the Massachusetts Agricultural College. Inspired by Clark's zeal and ideas, the Japanese government invited him to Japan to help establish the Sapporo Agricultural College. Clark readily accepted, regarding Hokkaido as Japan's equivalent of the American frontier, and in less than a year founded the college, established the

first American-style farm in Japan and introduced new crops and techniques in agriculture, fishing and animal husbandry. On his departure in 1877, Clark famously addressed the faculty and students of the college in the countryside outside Sapporo, where in parting he shouted, "Boys, be ambitious!"—words that to this day are taken as Hokkaido University's motto and guiding principle.



Hiroshi Saeki, president of Hokkaido University

Over the last 135 years, the university has undergone a number of transformations that have seen it expand considerably from an institution with a single agricultural faculty in 1876 to one of Japan's largest national universities with 12 undergraduate schools, 18 graduate schools, 26 research institutes and centres and a total of more than 18,000 undergraduate and graduate students supported by more than 3,800 staff.

A recent influx of international students has given Hokkaido University the largest increase in student numbers of any national university in Japan. Saeki attributes this to Hokkaido's comfortable northern climate and the natural beauty and ease of living in Hokkaido. The short walk or bicycle ride from nearby dormitories and apartments to the university is a stark contrast to the hot, humid and crowded commute endured by students at universities in Japan's famously cramped metropolises. Yet Hokkaido University's countrified reputation does not make it a sleepy hollow—many of the facilities

on the campus, such as the library and cafeterias, are open until late at night.

The rise in the number of international students has helped Hokkaido University come closer to realizing its ambitions of becoming a 'university open to the world'. To further develop this concept, the university is focusing on expanding its researcher development system to include international researchers by advertising five-year research positions to applicants worldwide. "One of the major benefits of this system is that any kind of research is possible, which allows researchers a great deal of freedom," says Saeki.

The university's core philosophies—of frontier spirit, a global perspective, practical learning and all-round education—resound throughout its academic curricula. Practical learning has been emphasized ever since its early days as Sapporo Agricultural College, when academic learning was used as a means of utilizing Hokkaido's natural agricultural resources for the benefit for the rest of the country.

Much of the research conducted at the university still focuses on the rich natural bounty that exists on and around the island. Sustainable development is an important core activity for the university, and since 2007 it has held annual sustainability events to promote research and education on sustainable development. And to reinforce its message, the environmental impact of the event itself is offset by expanding one of the many forests throughout Hokkaido that are owned by the university. "We believe that the best way of demonstrating the importance of sustainable development to students is to take the lead ourselves," says Saeki.



HOKKAIDO
UNIVERSITY

Hokkaido University
N8, W5, Kita-ku, Sapporo,
Hokkaido 060-0808, Japan
Tel: +81-(0)11-716-2111
www.hokudai.ac.jp/en/index.html



HOKKAIDO UNIVERSITY OFFICE OF INTERNATIONAL AFFAIRS

HOKKAIDO
UNIVERSITY

Research outside the box

The opening in July 2010 of Hokkaido University's Office of International Affairs to consolidate and integrate all of the international affairs functions throughout the university was a significant step in the university's development and one that puts it on the road to ever greater participation in international collaborative research. With the support of the office's wide-ranging activities, Hokkaido University researchers are broadening their horizons and leading innovative international research aimed at addressing some of the world's biggest issues.

When the Meiji government came into power in Japan in 1868, it faced the monumental task of modernizing the country after 260 years of isolation from the outside world. One of its first moves was to introduce modern agricultural technology, for which Hokkaido was chosen as a testing ground. This initiative led to the establishment in 1876 of Sapporo Agricultural College—Hokkaido University's predecessor—under the presidency of William Smith Clark, an American who was invited by the Japanese government to lead the college after developing innovative agricultural programs as president of the Massachusetts Agricultural College. "I believe that the government's decision was successful because Hokkaido is now one of the most important prefectures in Japan for agriculture as well as fisheries and food production," says Takeo Hondo, vice-president for international affairs at Hokkaido University.

The expertise in agricultural science accumulated over its 135 years is something that Hokkaido University is now eager to export to the rest of the world. This international focus is supported by the recently created Office of International Affairs, and by the university's commitment to increasing the numbers of international students it teaches—numbers are increasing significantly every year and now stand at 8% of the total 18,000 students currently studying at the university. Although the majority of the international students hail from China, 80 nationalities in total are represented.

One of the countries that Hokkaido University has maintained particularly strong ties with for many years is Zambia. The university sends its researchers to Zambia and in return accepts many Zambians to come and study in Sapporo. The dean of veterinary medicine at the University of Zambia is in fact a graduate of Hokkaido University, and his



Takeo Hondo, vice-president for international affairs at Hokkaido University

return from Sapporo to eventually become a leader in the Zambian scientific community is an example of how Hokkaido University is making a contribution to the advancement of science abroad. To help promote similar developments in the future, the university would like to see the number of international students rise beyond 10% over the next few years.

Another of the university's major goals is the development of researchers who are experts in sustainable development—an issue Hondo believes is one of the most pressing currently facing global society. "Although having researchers who are experts in very specific fields is important with respect to publishing highly cited research," he says, "in order to be sustainable, researchers need to consider the environment in their research."

Environmental issues are not restricted by national borders, meaning that an international outlook is crucial. Over the past ten years, researchers from Hokkaido University have been collaborating

with colleagues from research institutes in China and Russia on research in the Sea of Okhotsk north of Hokkaido. Situated between Japan and the Russian Kamchatka Peninsula, the Sea of Okhotsk marks the most southern extent of sea ice in the northern hemisphere. The joint research team has discovered in recent years that pollution has threatened the bioproductivity of the area, where sea ice plays an important role. "It is important from a sustainability perspective that this sea ice-supported ecosystem is preserved," says Hondo, "which is why our researchers are transferring their knowledge into action in this area."

Every year, the researchers from China and Russia who take part in the Sea of Okhotsk project are invited to participate in a consortium held at Hokkaido University as part of a two-week event known as the 'Sustainability Weeks'. In 2010, over 11,000 people participated in the event, which was accompanied by several mini-events that were held jointly with nine overseas partner institutions. Celebrating its fifth year in 2011, the event is scheduled to take place from 24 October and will comprise approximately 40 separate mini-events to encourage researchers at Hokkaido University to look beyond their own narrow field of research and try to understand other areas—and thereby contribute to sustainability.

"When we first started the Sustainability Weeks, researchers were quite narrow in their thinking, but over the past five years we have seen some of them think outside the box and collaborate with researchers from different disciplines," says Hondo. "At Hokkaido University, we will continue to actively promote this way of thinking and get researchers to think not only about knowledge but also about action."

**Office of International Affairs,
Hokkaido University
N15, W8, Kita-ku, Sapporo,
Hokkaido 060-0815, Japan
Tel: +81-(0)11-706-8023
www.hokudai.ac.jp/en/relations/office.html**



HOKKAIDO UNIVERSITY

Bringing home the Nobel Prize

The awarding of the 2010 Nobel Prize in Chemistry to Hokkaido University professor Akira Suzuki marked the pinnacle of a glittering 60-year academic career at the institution. Suzuki is the first Nobel Laureate from Hokkaido University and only the 14th Japanese researcher to have been recognized with science's highest accolade.

The announcement by the Nobel Prize committee that the Chemistry prize for 2010 was to go to Akira Suzuki in recognition for his pioneering work in the development of palladium cross-coupling reactions came as a surprise to few researchers in the field. The impact of the methodology developed over the course of 40 years' study by Suzuki—and his co-recipients Richard Heck of the University of Delaware and Japanese-born Ei-ichi Negishi of Purdue University—had revolutionized the science of organic synthesis and had been flagged by many as being worthy of Nobel status for some time.

For Suzuki himself however, the announcement and the international accolade that accompanied it was far from a foregone conclusion: "There are so many chemists carrying out great chemistry throughout Japan that there really is no reason why the Nobel Prize Committee should choose me over them," he says.

The work for which the three chemists were awarded equal shares in the Nobel Prize allows the construction of complex molecular systems by linking together separate 'aromatic' chemical entities to give coupled products with a precisely defined geometry with high efficiency and under mild reaction conditions. Prior to this, such molecules could only be generated inefficiently in an uncontrolled fashion that produced a string of undesired side products. Suzuki's contribution to the field, known as the Suzuki reaction to chemists, involves the union of an unsaturated organic molecule containing a carbon-halogen bond, and a hybrid molecule of carbon and boron known as a boronic acid under the influence of a minute quantity of palladium with remarkable efficiency and geometric predictability.



Akira Suzuki (left) accepts the 2010 Nobel Prize in Chemistry

Suzuki first encountered the field of organoboron chemistry in the early 1960s when he became interested in the research then being carried out at Purdue University in the US by H. C. Brown, who himself would also go on to be awarded the Nobel Prize in 1979. Joining the Brown group as a postdoctoral researcher in 1963, Suzuki found that whilst his colleagues were studying the generation and structures of organoboranes, there was little enthusiasm for investigating their utility as synthetic intermediates due to their perceived low reactivity. Returning to Hokkaido after his two years at Purdue, Suzuki concentrated on exploiting boronic acids as synthetic chemical intermediates, finally publishing his landmark paper in *Tetrahedron Letters* in 1979.

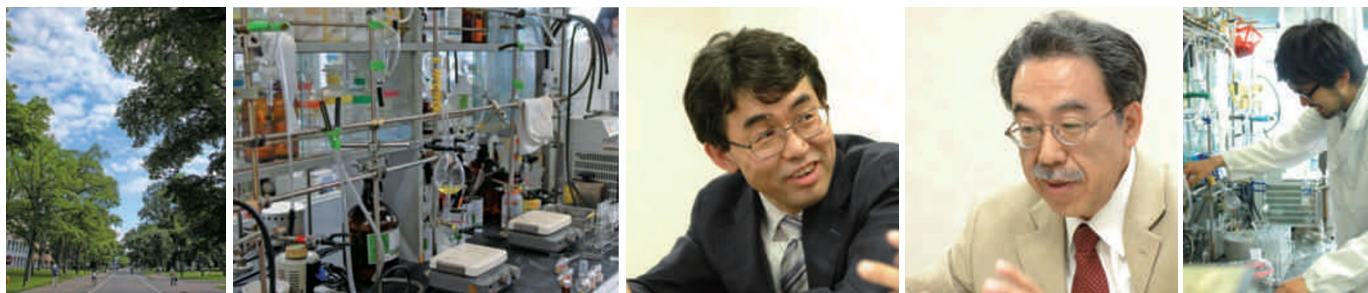
The reaction quickly became a standard part of the synthetic toolkit of academic and industrial chemists alike and is now used globally in the industrial synthesis of such products as pharmaceuticals, agrochemicals, liquid crystals and coatings for electronics. "I regularly receive inquiries from pharmaceutical companies that want to use my cross-coupling reaction," comments Suzuki, who benefits personally from the methodology he developed. "I have relatively high blood pressure and I use an antihypertensive that Merck manufactures using my cross-coupling reaction," he says. Another

antihypertensive drug, Valsartan, produced by Swiss pharmaceutical giant Novartis using Suzuki's cross-coupling reaction, is taken by 22 million people worldwide.

Aside from his two-year stint at Purdue University, Suzuki has spent almost all of his six decades in academia at Hokkaido University and has a unique perspective on why the university is so special. "When I joined it was one of the biggest imperial universities in Japan," says Suzuki. "We used to have two separate chemistry departments, but since they were both located on the same campus, communication between different chemists was easy." The close proximity of the two departments was also cherished by Suzuki's contemporaries at the university, including Norio Miyaura, a professor in the Graduate School of Engineering who has worked with Suzuki for over 30 years. "It was different from many other universities in Japan at the time, which had departments spread over multiple campuses," says Miyaura. Continuing this tradition of stimulating inter-departmental communication, the recently opened Hokkaido University Graduate School of Science and Engineering combines the chemistry and engineering departments in a top-level interdisciplinary amalgam that is rarely encountered in Japan.

The continuing development of his beloved Hokkaido University is something that Suzuki, now 80, is watching with keen interest as befits someone who, despite having received chemistry's most prestigious honour—as well as the Person of Cultural Merit and the Order of Culture bestowed upon him by the Japanese emperor—is first and foremost a researcher at heart. "This is a very high-level prize that is awarded to chemists at the cutting edge of their field," Suzuki says. "But I just think of myself as a simple chemist."

**GCOE Administration Office of Chemistry,
Graduate School of Engineering,
Hokkaido University
N13, W8, Kita-ku, Sapporo,
Hokkaido 060-8628, Japan
Tel: +81-(0)11-706-6788
www.eng.hokudai.ac.jp/gcoe/eng/**



HOKKAIDO
UNIVERSITY

HOKKAIDO UNIVERSITY GRADUATE SCHOOL OF CHEMICAL SCIENCES AND ENGINEERING

Nano-scale robots work their magic

An award-winning chemist at Hokkaido University has created a molecular catalyst that allows for the efficient, cost-effective and environmentally friendly synthesis of important pharmaceutical compounds—an achievement that promises to revolutionize the pharmaceutical industry.

Nobel Prize-winning chemist Akira Suzuki is not the only chemist in the Graduate School of Chemical Sciences and Engineering at Hokkaido University who is making waves in industrial circles. Organic chemist Takeshi Ohkuma has developed a molecular catalyst that drastically improves the efficiency and speed at which certain reactions take place. “The catalyst that I have manufactured is superior to existing ones because it is more active and only a tiny amount is necessary,” says Ohkuma.

The main objective of Ohkuma’s research is to develop reactions that produce substrates for medicine in an efficient, cost-effective and environmentally friendly way. In particular, he has been focusing on how he can improve the development of optically active alcohols, which are in high demand as raw materials in the production of pharmaceutical products.

In 2007, Ohkuma won the Japan Society for the Promotion of Science Prize for his achievement in modifying a reaction commonly used by industry to create optically active alcohols, the asymmetric hydrogenation of organic compounds known as ketones. The difficult part of this reaction lies in synthesizing the desired enantiomer—one of two

mirror-image ‘chiral’ forms that certain molecules, particularly optically active ones, can adopt. In the pharmaceutical industry, having the correct enantiomer is crucial, as the opposite chiral forms of an otherwise identical compound can have markedly different pharmacokinetic properties.

Ohkuma has developed a molecular catalyst that is able to control the chirality of the optically active alcohol to the extent that the method can

guarantee 99.5% enantiomeric purity, which leads to less waste and a more efficient production process. “My molecular catalyst is so active that it takes just one molecule of the catalyst to create 100,000 alcohol molecules,” says Ohkuma, “which is why I call it a ‘nano-scale robot’. In the future, I would like to develop a wider variety of substrates to create more compounds that can be converted to medicinal applications.”

Reconstructing nature’s secrets

Hokkaido University’s Graduate School of Chemical Sciences and Engineering is carrying out a collaborative project that builds upon recent advances in genomic DNA sequencing technology to develop an alternative method for the synthesis of bioactive compounds using biosynthetic enzymes.

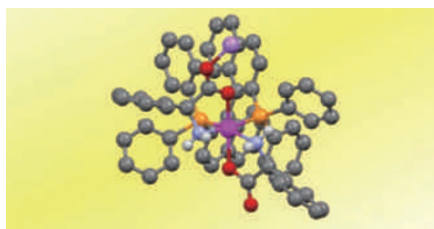
Despite his wealth of experience in organic chemistry, Hokkaido University’s Hideaki Oikawa knows when he has to rely on his colleagues for help. In collaboration with 40 researchers who come from a wide range of scientific and engineering backgrounds, including those involved in bioinformatics and expression systems, he is leading a project entitled ‘Biosynthetic Machinery: Deciphering and Regulating the System for Creating Structural Diversity of Bioactive Metabolites’. This project, sponsored by the Japanese government, aims to reproduce the genetic blueprints found in organisms that produce useful natural products in order to synthesize novel molecules for a variety of purposes. “Since the completion of the human genome, the post-genomic era offers scientists like myself many exciting opportunities,” says Oikawa.

Due to run until 2014, Oikawa has many objectives that he would like to pursue under the umbrella of the project. His team is investigating ways to develop a methodology for the rational

decoding of substrate structure and biosynthetic pathways obtained from genomic data based on chemical structures and the bioinformatics of natural product biosynthesis. Existing and newly developed methods will be used to introduce multiple biosynthetic genes into model hosts to synthesize naturally bioactive products. Through this research, Oikawa and his team will explore the methodology behind the reconstitution of biosynthetic machinery involving representative skeletal modification enzymes and widespread modification enzymes. “We will also explore the intriguing diversification of natural products with regards to molecular evolution through the engineering of biosynthetic machinery,” says Oikawa.

At the culmination of the project, it is hoped that Oikawa’s team will have successfully developed a versatile methodology for the reconstruction of artificial gene clusters. According to Oikawa, this will provide a novel way to synthesize molecules with new functions, which could be used, for example, to create useful drugs to fight drug-resistant bacteria and tumours.

Graduate School of Chemical Sciences and Engineering, Hokkaido University
K13, N8, Kita-ku, Sapporo,
Hokkaido 060-8628, Japan
Tel: +81-(0)11-706-7246
www.cse.hokudai.ac.jp/english/



A molecular model of an organometallic catalyst that behaves as a ‘nano-scale robot.’



HOKKAIDO UNIVERSITY GRADUATE SCHOOL OF MEDICINE, DEPARTMENT OF CANCER PREVENTIVE MEDICINE

Dealing with the root cause of cancer

Gastric cancer is the second most common cause of cancer-related deaths in the world behind lung cancer, and remains one of the most difficult forms of cancer to cure. Research by Masahiro Asaka and his colleagues in the Department of Cancer Preventative Medicine of the Hokkaido University Graduate School of Medicine is giving hope for highly effective preventative measures that will not only save billions of dollars in treatment costs but which are also expected to save the lives of hundreds of thousands over the next decade.

Although gastric cancer is one of the most common forms of cancer worldwide, its particular prevalence in Japan, Korea and China has earned it a reputation for being a peculiarly East Asian disease. In Japan, most cases of gastric cancer are preceded by atrophic gastritis—chronic inflammation of stomach lining as a result of an infection by the bacterium *Helicobacter pylori*. Crucially, it is estimated that this bacterium is present in almost half the Japanese population. “In order to eliminate all traces of gastric cancer in Japan and other countries, we have to win the battle against *Helicobacter pylori*,” says Asaka.

In recent years, Asaka has co-authored two highly acclaimed research papers that contain results so conclusive that the Japanese Society for Helicobacter Research renewed their guidelines in 2007 to include a strong recommendation that all cases of *H. pylori* should be treated when discovered.

The first paper presented the findings of a trial in which 500 patients with early-stage gastric cancer were divided into two groups: those treated for *H. pylori* infection and those who weren't. The researchers found that the occurrence of secondary gastric cancer in patients who had been freed of *H. pylori* infection was close to three times lower than for the group that did not receive treatment for the bacterial infection. In their other published research, Asaka and his colleagues described how

deaths from gastric cancer in Japan can be prevented by combining *H. pylori* treatment for primary prevention with endoscopic follow-up for secondary prevention. The combination of these primary and secondary prevention measures is expected to prevent about 150,000 deaths from gastric cancer over five years.

Asaka is optimistic that with the help of these breakthroughs, gastric cancer will have been

completely eradicated in Japan within the next 10 to 20 years. “I am confident that we can start by preventing gastric cancer in Japan and then in the rest of the world,” he says. “Because prevention costs far less than treatment.”

Department of Cancer Preventive Medicine,
Graduate School of Medicine, Hokkaido University
N 12, W7, Kita-ku, Sapporo, Hokkaido 060-0812, Japan
Tel: +81-(0)11-706-3363
www.med.hokudai.ac.jp/index-e.html

HOKKAIDO UNIVERSITY GRADUATE SCHOOL OF MEDICINE, DEPARTMENT OF RADIATION MEDICINE

Pinning down a moving target

World-leading advancements in proton beam therapy for highly targeted tumour radiotherapy by researchers at Hokkaido University's Department of Radiation Medicine promise to expand this next-generation treatment option to include a wider range of cancer types.

Radiotherapy is one of the three pillars of cancer treatment along with surgery and chemotherapy. In the past, radiotherapy has been performed using a beam of X-rays or electrons, but both methods tend to expose a considerable amount of healthy tissue to radiation damage. The introduction of proton beam therapy (PBT), however, revolutionized the field by allowing unprecedented precision in the targeting of tumours in the body.

Proton beam therapy is now a mainstream technology that allows patients to be treated in the time of a normal consultation, with almost no pain and minimal damage to healthy tissue and bodily functions. Its highly targeted nature, however, also means that it has been very difficult to use this form of therapy for tumours that cannot be immobilized, such as tumours in the lung, which move with each breath of the patient.

Hiroki Shirato, a professor of the Department of Radiation Medicine at the Hokkaido University Graduate School of Medicine, is leading a project that aims to develop the world's first real-time (RT) tumour-tracking PBT in collaboration with Hitachi. The project, funded by the Japanese government's FIRST program for the establishment of a technical foundation for technologies of the future, is due for completion in 2014.

The RTPBT system will combine PBT technology with Hokkaido University's internationally patented technology for real-time tracking of tumours using a gold marker. By monitoring the position of the gold marker, which is inserted by endoscope to the tumour site, the proton beam can be set to activate only when the tumour is in the region of the beam target. This means for the first time that patients with advanced lung and other cancers will have access to the benefits of PBT. “I have promised the Japanese government that this new treatment will cure tumours located in moving organs and improve the quality of life of our patients,” Shirato says.

FIRST Program Coordinator's Office,
Graduate School of Medicine, Hokkaido University
N15, W7, Kita-ku, Sapporo, Hokkaido 060-8638 Japan
Tel: +81-(0)11-706-7440
<http://rtpbt.med.hokudai.ac.jp/index-e.html>



HOKKAIDO UNIVERSITY SUPPORT OFFICE FOR SPACE SCIENCE AND ENGINEERING

Elucidating the mysteries of space

Since its establishment in 2008 by 100 scientists from Hokkaido University, the Support Office for Space Science and Engineering (SOSSE) has been supporting the university's space research and coordinating new cross-disciplinary research. Through these activities, researchers from Hokkaido University have developed scientific instruments that are now used aboard an unmanned spacecraft orbiting Venus, discovered how certain compounds form in space, and even constructed a novel hybrid rocket.

Exploring Venus

Launched in 2010, the Japanese unmanned spacecraft known as Akatsuki or the Venus Climate Orbiter (VCO) contains onboard scientific instruments that were developed by two researchers from the Hokkaido University's Department of CosmoSciences, Shigeto Watanabe and Yukihiro Takahashi. The VCO will circle the Venusian equator in an elliptical orbit for at least two years, monitoring the atmosphere at different altitudes. The data obtained will allow researchers to reconstruct a three-dimensional model of the Venusian atmosphere's structure and dynamics, which will hopefully shed some light on the mysteries in which Earth's sister planet is shrouded.

One of the instruments, the Lightning and Airglow Camera (LAC) developed by Takahashi, will measure lightning flashes and airglow emissions on the nightside disk of Venus. It is hoped that the information gained from the lightning observations will answer once and for all how lightning can occur in Venus's hot, dry atmosphere without ice crystals, which on Earth drive the generation of static electricity responsible for lightning.

Another high-tech camera, the Ultraviolet Imager (UVI) developed by Watanabe, will be used to study the distribution of atmospheric gases at the tops of clouds surrounding Venus by measuring ultraviolet radiation. The data are anticipated to provide valuable insights into the energy balance and dynamics of the Venusian atmosphere.

Watanabe and Takahashi's ambitions do not stop there, however. In 2013, a microsatellite named RISING-2 developed by their group with the support of engineers from Hokkaido University and Tohoku University will be launched to observe the atmosphere of Earth and other planets.

Analysis of space matter

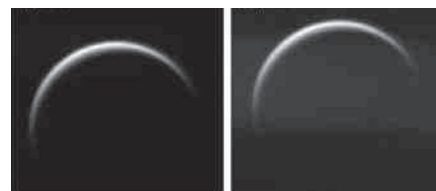
The Institute of Low Temperature Science (ILTS) at Hokkaido University consists of a team of researchers from a wide range of backgrounds, including physics, chemistry, geoscience and biology. These researchers collaborate on various unique research themes within the ILTS and also often conduct research in cooperation with institutions in other countries, including Catania University in Italy and Seoul University in Korea.

One of the ILTS's best-known achievements in the field of astronomy is its work on the formation mechanism of formaldehyde, methanol, water and hydrogen molecules in interstellar molecular clouds. Naoki Watanabe and Akira Kouchi, researchers in the Ice and Planetary Science Group of the ILTS, discovered the formation mechanism of these molecules and showed that surface reactions between methanol and heavy hydrogen atoms speed up the formation of deuterated methanol. Based on this finding, their group has proposed a novel heavy-hydrogen fractionation process that has been announced in several international journals.

In research that provides insight into the way stars work, Hisayoshi Yurimoto, a researcher in the Isotope Imaging Laboratory, has developed an isotope microscope that analyses presolar grains, isotopically distinct clusters of material, found in meteorites. His successful analysis of a meteorite sample brought back by the Japanese space probe Hayabusa from the 25143 Itokawa asteroid will shed light on the nucleosynthesis processes that drive the stellar machine.

Hokkaido University's hybrid rocket

In collaboration with scientists at one of Japan's core institutes for space science research, the



JAXA/ISAS

First observations of Venus using the Ultraviolet Imager (UVI) in 2010

Institute of Space and Astronautical Science (ISAS), Harunori Nagata has led a team of researchers in Hokkaido University's Division of Mechanical and Space Engineering in the development of a hybrid rocket known as CAMUI, or the Cascaded Multi-state Impinging Jet, which dramatically reduces manufacturing and operation costs.

Costs have been kept low by replacing the expensive explosives normally used as a propellant with a combination of liquid and solid materials. A novel combustion method has been devised to overcome the crucial problem of the slow combustion of solid fuel that normally occurs with hybrid rockets—the main reason why hybrid rockets have been overlooked in the past.

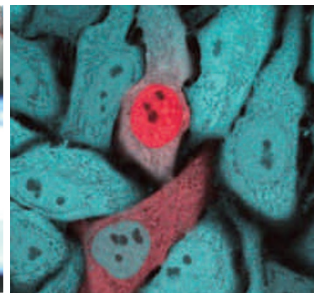
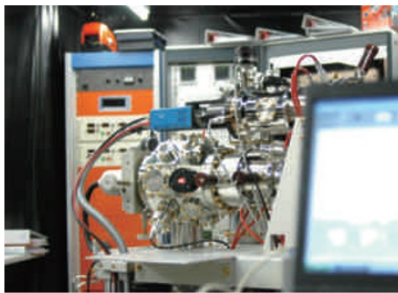
Non-explosive, non-hazardous liquid oxygen is injected into the combustion chamber of the CAMUI, which collides with fuel blocks to generate a combustion gas that flows along the body of the rocket, accelerated by an impinging jet that generates a thrust density three times greater than conventional designs. Successfully launched in 2002 and 2003, the CAMUI has already undergone engine flight tests, and will be used for atmospheric and space science research in the future.

Support Office for Space Science and Engineering, Creative Research Institution, Hokkaido University

N21, W10, Kita-ku, Sapporo, Hokkaido 001-0021, Japan

Tel: +81-(0)11-706-9244

www.cris.hokudai.ac.jp/sosse/en/



HOKKAIDO UNIVERSITY RESEARCH INSTITUTE FOR ELECTRONIC SCIENCE

Shedding new light on technology for the future

Cutting-edge research at the Research Institute for Electronic Science (RIES) at Hokkaido University is breaking new ground in light-related research. From advanced solar cell technology to quantum computing and molecular imaging, RIES researchers are bringing technologies of the future ever closer to reality.

The RIES, established in 1992, is located on the northern outskirts of Hokkaido University's Sapporo campus and plays a major role in operating the Hokkaido Innovation Through Nanotechnology Support (HINTS) project funded by the Japanese government as a part of the Nanotechnology Network Project. HINTS aims to coordinate the wealth of experience among its participants and provide support for strategies related to new research, technology, manufacturing and development.

Hiroaki Misawa, a representative of HINTS at Hokkaido University, leads his own group of researchers as professor and director of the RIES. "We carry out many types of research at our centre and we are at the cutting-edge of light-related research," he says.

Limited natural resources and climate change are driving a rapid expansion in research on renewable energy sources. Such research has become of particular importance to Japan, which now finds itself under extraordinary pressure to develop alternative sources of energy for electricity production following the double shock of a massive natural disaster and nuclear crisis. Misawa's research group at the RIES has for years been studying solar cells in an effort to increase their efficiency and make them more attractive for large-scale commercial use. Now, renewable energy technologies such as solar cells have become a major part of the RIES research portfolio.

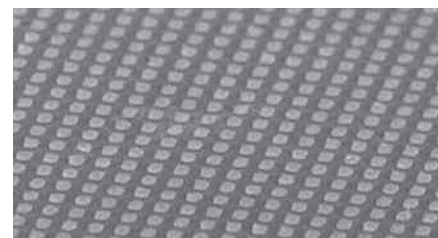
"Existing silicon solar cells commonly only have photoelectric conversion efficiencies of less than 20%. In order for solar energy to be a viable renewable energy source, however, this conversion efficiency must be increased to at least 60%," says Misawa.

One of the ways in which researchers at the RIES are hoping to increase this light-to-energy conversion efficiency is through better utilization of the energy available in sunlight. About 40% of the total solar energy that makes it to the Earth's surface falls in the infrared region. Unfortunately, the photoelectric conversion efficiency of the amorphous silicon commonly used in solar cells peaks at visible wavelengths and drops dramatically in the infrared region. Misawa's research group at the RIES has now developed a photovoltaic system that responds to solar light across a broad spectrum ranging from visible to near-infrared, considerably increasing the photoelectric conversion efficiency of the solar cell.

The new solar cell developed by Misawa's group consists of gold nanorods that are elaborately arrayed on the surface of single-crystal titanium dioxide using a top-down nano-structuring process. The nanorods introduce an effect known as 'plasmonics' that increases light conversion remarkably. Although additional product development is required in order for this breakthrough to be converted into solar cells suitable for industrial production, Misawa is confident of the technology's potential. "We will soon be able to develop a completely new genre of solar cell that will be well placed to meet the renewable energy demands of the future," he says.

Other research at the RIES is more fundamental in nature but no less revolutionary. Shigeki Takeuchi, a professor of the RIES Quantum Information Photonics Laboratory, has successfully developed an optical quantum gate device that can be operated by a single photon of light. The technology is very promising for future quantum-based computational devices and has the advantage over other quantum schemes of requiring very little energy for operation—traditional optical quantum gates are so energy-intensive that powerful lasers need to be used.

By putting together a combination of these gates, Takeuchi has constructed one of the world's largest optical quantum circuits capable of filtering a certain state of quantum entanglement, which is essentially the information 'bit' of quantum



Solar cells of the future: Gold nanorods on titanium dioxide increase the photoelectric conversion efficiency of solar cells.

computing. Takeuchi's research has attracted worldwide attention and could prove to be a pivotal development in the progression toward practical quantum computing.

Light also has its biological uses. In collaboration with the RIKEN Brain Science Institute, RIES researcher Takeharu Nagai has developed a new technology that allows light to be used to image the inner workings of the body in animals. He has developed ultra-sensitive calcium ion indicators that can detect subtle changes in the intracellular concentrations of these ions, which play a diverse range of roles in cellular processes.

This combination of indicators and light-based imaging will for the first time allow the detection of spatial and temporal changes in ion concentration in living cells, which will make it possible for researchers to monitor neural activity in the cerebral cortex with unprecedented sensitivity.

The benefits for clinicians and patients could be dramatic, particularly for the diagnosis of conditions such as bipolar disorder and cardiovascular disease. "This is a significant step in treating illnesses, because after all, a picture is worth a thousand words," says Misawa.

**Research Institute for Electronic Science,
Hokkaido University**
N20, W10, Kita-ku, Sapporo,
Hokkaido 001-0020, Japan
Tel: +81-(0)11-706-9400
www.es.hokudai.ac.jp/english/



HOKKAIDO UNIVERSITY RESEARCH CENTER FOR ZOOONOSIS CONTROL

Japan's control centre for infectious diseases

The opening of Hokkaido University's Research Center for Zoonosis Control in April 2005 fulfilled a pressing need for an organization that specializes in the control of zoonoses — infectious diseases that can be transmitted between animals and humans. As such diseases originate in the wild, monitoring for potential hosts and transmission routes is a never-ending task but one in which zoonosis researchers at Hokkaido University lead the world.

Among the long list of infectious diseases that are prevalent around the world, influenza is the one that affects more people than any other. Hiroshi Kida, director of the Research Center for Zoonosis Control at Hokkaido University and one of the leading zoonosis experts in the world, has dedicated decades of research to deciphering how influenza spreads. "Over the last 100 years, four instances of pandemic influenza have occurred in humans—the Spanish flu, the Asian flu, the Hong Kong flu and the 2009 swine flu," Kida says. "Through surveillance carried out over many years, we are now in a position to propose a mechanism for the spread of such pandemic flu."

Kida initially focused his attention on the H3N2 Hong Kong influenza virus. Since 1977, he has isolated both of the two subtypes of the virus, H1-16 and N1-9, from migratory ducks and discovered that the virus replicated in their colon to be shed in faeces for up to a week. When the ducks migrated to southern China from their summer nesting grounds in Siberia, they spread the virus via water-borne transmission. Through genetic research Kida concluded that the migratory ducks are the natural host for the avian influenza A virus.

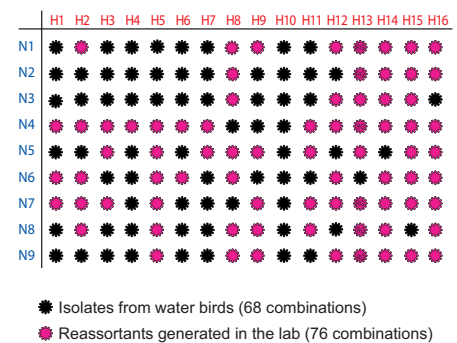
The discovery of a closely related H3N2 virus in the upper respiratory tract in pigs in southern China was then surprising given that the pigs could have had no direct interaction with the migratory ducks. This suggested to Kida that there had to be an intermediate host, and his research eventually revealed a convoluted progression

involving the infection of domestic ducks through water-borne transmission from migratory ducks, and then subsequent infection of pigs who shared the same water source as the infected domestic ducks. The virus could then be transmitted from pigs to humans by inhalation of respiratory pathogens suspended on droplets coughed into the air by the pigs.

Pigs are also central to a theory that Kida believes explains the worldwide propagation of the Spanish flu in 1918, which is reported to have killed up to 40 million people worldwide. The mechanism proposed by Kida suggests that the swine flu originated in Illinois in the United States, from where infected soldiers were dispatched to Europe, initiating the international spread of the virus. This theory indicates that pig infections could be a critical precursor for the emergence of a pandemic strain of influenza. "Conversely, this also suggests that if a virus does not infect pigs, it is unlikely to become a pandemic strain," says Kida.

Many leading zoonosis experts agree that the worldwide spread of influenza strains often originates in southern China. Kida, however, has his own ideas. In two separate four-year surveys conducted in Alaska and Siberia, Kida discovered that many subtypes of the influenza virus are perpetuated in the water of lakes close to the Arctic circle where ducks nest in summer. Viruses in the lakes are preserved when the water freezes over, and so are available to re-infect birds when they return to the lakes from the south. "I believe that this mechanism of the perpetuation of viruses in nature is a very important finding," Kida says.

Since 2003, a total of 62 countries have reported occurrences of highly pathogenic avian influenza in poultry and wild birds, and 15 of those countries have reported human infection with the virus. The largest proportion of the reported cases and deaths occur in China, Vietnam, Indonesia and Egypt, where vaccines are used as the primary tool for the control of avian flu. Japan was successful in controlling the outbreaks of avian influenza



An influenza A virus library of vaccine strain candidates: Influenza viruses of 68 combinations of the HA and NA subtypes have been isolated from faecal samples of ducks (black). Seventy six other combinations have been generated by genetic reassortment procedures in the lab (red).

in 2004 and 2007, as well as the latest outbreaks in 2011. "In all three cases, my recommendation to the Japanese Ministry of Agriculture that we should cull all affected chickens stopped the infections in their tracks," he says. Vaccinations, Kida believes, should be used as an additional measure to culling, not the primary measure as some authorities have advocated.

In an effort to promote the development of vaccines and diagnoses for the control of animal and human influenza, in 2008 Kida established the Influenza Virus Database System, which comprises more than 1,200 vaccine strain candidates. Importantly, the database is made openly available, allowing anyone to access the data and biological materials and share their own. "I was asked if I would like to patent the database but I refused," says Kida. "This information is for the common benefit of all humanity."

**Research Center for Zoonosis Control,
Hokkaido University
N20, W10 Kita-ku, Sapporo,
Hokkaido 001-0020, Japan
Tel: +81-(0)11-706-5207
www.hokudai.ac.jp/czc/index-e.html**



HOKKAIDO UNIVERSITY RESEARCH FACULTY OF AGRICULTURE

Feeding the world

The Research Faculty of Agriculture at Hokkaido University is the university's oldest with a 135-year history of progressive and innovative research focused on improving productivity, quality and competitiveness in Hokkaido's renowned agricultural industry. That mission has now become global.

When it was founded in 1876, Hokkaido University, then known as Sapporo Agricultural College, had one faculty and one goal: to introduce and develop modern agricultural technology in order to bring the agricultural industry of Hokkaido and Japan back to international competitiveness after centuries of isolation. In the twenty-first century, however, that mission has become much broader. "Our research now covers the environment, food production and nutrition," says Hirokazu Matsui, dean of Hokkaido University's Research Faculty of Agriculture.

The university's ambitions now also extend beyond Japan's borders. Takashi Hirano, one of the key members of the faculty, is part of an international project on wildfire and carbon management in peat forests in Indonesia, through which he hopes to help reduce carbon dioxide emissions. Owing to accelerated deforestation and drainage since the 1990s, the tropical peat land in the Central Kalimantan Province of Indonesia has become a major source of greenhouse gas emissions. "Over the past ten years, our team has determined the exact levels of carbon dioxide emitted from the peat land in Kalimantan, which will now allow us to formulate ways to reduce those emissions," says Hirano.

Microbiology and molecular biology support many of the studies on food production and nutrition that are conducted in the faculty. For example, Hiroshi Hara has found that an oligosaccharide called epilactose produced by a unique enzyme from gut microbiota promotes human health. "Epilactose has the ability to increase the efficiency of absorption of iron and calcium, which are often lacking in the human diet," he says. Junpei Takano, on the other hand, has been conducting research on the mechanism by which plants absorb nutri-

ents, particularly boron. Using fluorescent protein labelling, he has discovered that the transporters involved in helping nutrients travel through cell membranes in plants are not evenly positioned. "In the future, I want to work out how the transporters are controlled so that this information can help us grow vegetables like cucumbers and tomatoes in land where there are few nutrients," says Takano.

Such research contributes to securing the wor-

ld's food supply, which is considered by Matsui to be one of the main responsibilities of his faculty. "We are currently struggling to feed 6.9 billion people, so if we don't do something now how can we expect to feed a world that in the future may be inhabited by 10 billion people?"

Research Faculty of Agriculture, Hokkaido University
 N9, W9, Kita-ku, Sapporo, Hokkaido 060-8589, Japan
 Tel: +81-(0)11-706-2420
shomu@agr.hokudai.ac.jp

HOKKAIDO UNIVERSITY FACULTY OF ENVIRONMENTAL EARTH SCIENCE

Training scientists for the future

Hokkaido University's Faculty of Environmental Earth Science is nurturing the next generation of researchers in the knowledge that without people, science will not survive into the future.

The world is an ever-changing place, and no-one can be sure of what developments the future may hold. Preserving and perpetuating the expertise built at Hokkaido University over the past 135 years is therefore something that Yasuhiro Yamanaka, a professor of the university's Faculty of Environmental Earth Science, does not intend to leave to chance. "If we do not develop the next generations of researchers, our scientific work could be lost forever," he says.

Yamanaka heads a Global Center of Excellence program entrusted with ensuring that the university's science and technology is perpetuated for generations to come. One of the program's main activities is the continuous development of researchers in both Japan and abroad. Hokkaido University has set up liaison offices in Mongolia, Siberia and Indonesia to establish equal partnerships with researchers in those countries. Participants are currently developing personnel to contribute to the '100-year observation network', a long-term environment observation project. "Japan may currently be more developed than, for example,

Mongolia, but who knows what will happen in the future — the roles might be reversed," says Yamanaka. He regards it as one of the duties of Hokkaido University's Japanese researchers to try to instil in the people of these countries the ambitious frontier spirit that epitomizes the university's approach to teaching and research.

Yamanaka himself acts as co-chair of the international Marine Ecosystem Model Intercomparison Project (MAREMIP). Established in October 2009, the project is large enough for tens of researchers to gather at international conventions. In addition to building a community around marine ecosystem models, the project aims to promote interactions among modelers and document the evolution of marine ecosystem models. Climate change is a pressing concern of MAREMIP scientists, which Yamanaka believes can kick off a damaging domino effect felt not only by human beings but also by marine life. "Any change in the climate brings about a change in the biogeochemical cycle that can in turn influence the marine ecosystem and end up adversely affecting the fisheries industry, which forms a crucial part of the economy of Hokkaido."

GCOE Unit, Faculty of Environmental Earth Science,
Hokkaido University
 N10, W5, Kita-ku, Sapporo, Hokkaido 060-0810, Japan
 Tel: +81-(0)11-706-4861
www.ees.hokudai.ac.jp/gcoe/en/index.html



BIOIMMULANCE

Taking the fight to cancer

Every year cancer kills approximately 7.6 million people worldwide. Although many therapies have been devised to aid in the fight against the disease, the search for a comprehensive therapy remains the major focus of global life science research. Bioimmulance, a biotechnology company in Hokkaido, believes that it may have come up with a combination of a cancer vaccine called 'H/K-HELP' and cell therapy that gives patients the best chance yet to fight off the disease.

Takashi Nishimura, the founder and chair of Bioimmulance and a researcher who has devoted his career to understanding the critical role of immune balance in protecting the human body from disease, believes that he has found the key to tackling cancer: activate the type 1 helper T cell (Th1) immune system. "Cancer treatments that work by increasing the strength of the immune system produce fewer side effects, giving hope to both patients and their families," says Nishimura, who is also a professor at Hokkaido University's Institute for Genetic Medicine.

Based on his expert knowledge of Th1 cells, a key part of the immune system, Nishimura has for many years been convinced that using these cells could provide a breakthrough in the fight against cancer. A few years ago, he led a team of researchers that artificially synthesized a helper/killer-hybrid long peptide cancer vaccine called H/K-HELP containing 40 amino acids that simultaneously stimulates both helper and killer T cells. "H/K-HELP has proved effective at eliminating cancer cells in terminal cases in exploratory clinical trials," he says. This is in stark contrast to the relatively poor therapeutic effect achieved by other cancer vaccine therapies, which focus on activating killer T cells but not helper T cells.

The efficacy of the H/K-HELP vaccine has been tested in exploratory clinical trials with cancer patients at Hokkaido University Hospital and Kinki University Hospital near Osaka. The results of the trials have been very promising. Eleven out of 13 of

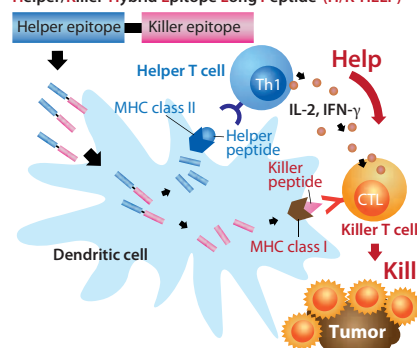
the patients in the trials showed a heightened Th1-dependent cellular and humoral immune response after vaccination with H/K-HELP, and one patient at Kinki University Hospital experienced a complete remission of refractory breast cancer after receiving the vaccine, despite little or no response to previous treatments with anticancer drugs and chemotherapy. The vaccine also inhibited the growth of lung metastatic colon cancer in a patient at Hokkaido University Hospital. "I would like to continue carrying out exploratory clinical trials for colorectal and breast cancer patients with the aim of putting the vaccine into practical use as soon as possible," says Nishimura. With phase II efficacy trials planned for this year, Nishimura is now looking for pharmaceutical companies to collaborate in the further development of the H/K-HELP vaccine.

Although the H/K-HELP vaccine has proved to be very promising, Nishimura has found that it is less effective for cancer patients with severely weakened immune systems. In such cases, H/K-HELP is suboptimal to fully activate killer T cells. Looking to overcome this, Bioimmulance has developed two other complementary immune-cell therapies—Th1 cell therapy and a dendritic cell (DC) based therapy.

Th1 cell therapy, proposed by Nishimura, involves administering cancer-specific Th1 cells expanded with the H/K-HELP *in vitro* from the cancer patient's own lymphocytes. This therapy is able to create Th1 cells, which facilitate the generation of killer T cells to destroy cancer and cancer-specific memory T cells and prevent the recurrence of cancer. Mice with cancer treated with this therapy exhibited a strong killer function against cancer and 80% were completely cured. "The combination of H/K-HELP and Th1 cell therapy is effective because it induces a systemic anti-tumour immunity," says Nishimura. The Th1 cell therapy is currently in exploratory clinical trials and Nishimura is confident that it will be ready for clinical use within four years.

The DC-based therapy exploits the important role of DCs in inducing Th1-dependent killer T cells. Dendritic cells break down unique protein

Helper/Killer-Hybrid Epitope Long Peptide (H/K-HELP)



A potent therapy for cancer: The helper/killer-hybrid epitope long peptide (H/K-HELP) stimulates T cell responses to fight cancer with remarkable efficacy.

antigens of cancer cells into smaller peptide pieces and then present these peptide antigens to helper T cells, which in turn activate killer T cells to destroy the antigen-expressing cancer cells. To develop a more efficient cancer therapy by combining H/K-HELP and DC-based cell therapy, Bioimmulance is collaborating with the Japanese research and development company Tella Inc., which has already made good progress in DC-based cell therapy. "H/K-HELP-pulsed DC-based cell therapy will be a potent cancer therapy because it accelerates Th1-dependent killer T cell activation, which is essential for curing cancer patients," says Nishimura.

H/K-HELP, discovered by Nishimura and developed by Bioimmulance and Tella Inc., is a novel basis for promising cancer vaccine therapies on its own or in combination with other cell therapies.



Bioimmulance
Hokudai Business Spring, N21, W12-2,
Kita-ku, Sapporo, Hokkaido 001-0022, Japan
Tel: +81-(0)11-736-6033
ytogashi@bioimmulance.com



NORTHERN ADVANCEMENT CENTER FOR SCIENCE & TECHNOLOGY, NATIONAL INSTITUTE OF ADVANCED INDUSTRIAL SCIENCE AND TECHNOLOGY

Building the world's first transgenic plant factory

A transgenic plant factory under development by the Northern Advancement Center for Science & Technology (NOASTEC) and the National Institute of Advanced Industrial Science and Technology (AIST) in Hokkaido will be unique in the world, providing the unprecedented opportunity to grow genetically modified plants under controlled conditions for the production of pharmaceutical compounds.

Many of the pharmaceuticals that we now rely on are produced from complex compounds that only occur in nature. Others can be produced synthetically but at high cost. For this reason, pharmaceutical companies are turning to the use of genetically modified plants to obtain natural drug compounds in higher yield and to produce synthetic compounds more economically. With the support of the Japanese government, NOASTEC has embarked on a remarkable project that aims to establish a system for the mass cultivation of transgenic plants while at the same time addressing the regulatory concerns regarding genetically modified crops.

The Transgenic Plant Factory, a new, comprehensive, fully enclosed facility to be constructed on the grounds of the AIST Hokkaido Center in Sapporo at a cost of one billion yen, will integrate the entire process from transgenic plant cultivation to the formulation of pharmaceuticals under one roof. The project builds on the government-supported work on plant production by the AIST, which already maintains an advanced plant factory facility run by the Plant Molecular Technology Research Group, to establish a low-cost mass-production system for value-added substances for pharmaceuticals, including interferons and base compounds for vaccines, herbal drugs and cosmetics, using genetically modified plants.

"The new factory will be the world's top facility for mass-producing high-value pharmaceutical compounds using transgenic plants in a completely artificial environment. It will also be the only facility in the world that integrates research

and plant production technology in a single location," says Masaru Tsunetoshi, executive director of NOASTEC. In the long term, NOASTEC plans to use the factory to produce the base compounds for both clinical and veterinary medicine, such as influenza vaccines, and establish the facility as the world's core research and development hub for pharmaceutical transgenic plant research and production. "I want it to become a centre of excellence where researchers, companies and investors from Japan and abroad come together to develop plant technology," adds Tsunetoshi.

The 915-square-metre plant factory will be used to develop transgenic plants that produce high value-added substances, cultivate those plants using a hydroponic culture system for high yield in an artificial environment, and extract and purify the desired products for use as raw materials in pharmaceuticals. A further aim of the project is to undertake comprehensive analyses of the functionality of the substances produced by the factory, and by taking the research results to industry to establish venture businesses based on these high-value products.

One of the transgenic plants developed by the AIST using their advanced plant factory is a line of strawberries expressing canine interferon—a base compound used in the treatment of periodontal disease in dogs. "Veterinary medicines produced using 250 kilograms of the transgenic strawberries can be used to treat about one million dogs with periodontal disease, all of which will be completely cured," says Takeshi Matsumura, group leader of the Bioproduction Research Institute at the AIST Hokkaido Center.

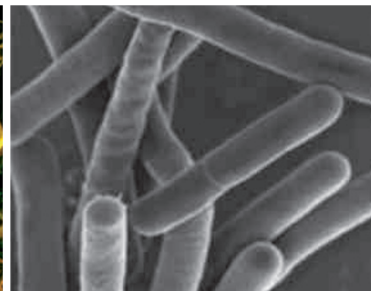
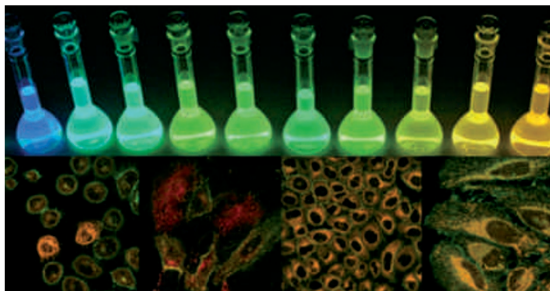
The research institute has also developed molecular technologies to produce a transgenic potato expressing avian influenza vaccine and other valuable substances such as antibodies, cytokines and vaccine components using various transgenic plant species. The advantages of producing pharmaceuticals from plants include low risk of contamination, ease of transport and storage, lower production costs and suitability for mass production.

The AIST's advanced plant factory facility consists of a transgenic plant cultivation area and a pharmaceuticals production area. The cultivation area provides complete containment of the modified genes and so ensures full compliance with the relevant biosafety regulations. The facility features complete control over the cultivation environment, including temperature, humidity, light intensity and composition, carbon dioxide concentration and nutrient liquids. The adjacent pharmaceuticals production area is also a controlled environment and is microorganism-free to prevent contamination.

The construction of the new, comprehensive plant factory is part of Hokkaido's 'food cluster' activities promoting the Hokkaido Food Complex International Strategic Comprehensive Special Zone framework. This initiative is intended to boost the regional economy and help make the region economically independent by establishing an industry based around the production of high-added-value foods using the intellectual assets of local universities and laboratories. NOASTEC has played a pivotal role in the Hokkaido food cluster initiatives for over ten years by supporting research and development projects, promoting industrial cluster activities, and connecting companies, government bodies, universities and research labs to create new business opportunities. With collaborators including the Hokkaido Bureau of Economy, Trade and Industry, the Hokkaido government, the Hokkaido Economic Federation, and the Japan Agricultural Cooperatives Hokkaido Chuokai, the framework aims to make Hokkaido a world-class hub for research and development on food and health.

NOASTEC
Northern Advancement Center for Science & Technology

AIST
National Institute of Advanced Industrial Science and Technology
2-17 Tsukisamuhigashi, Toyohira-ku, Sapporo, Hokkaido 062-8517, Japan
Tel: +81-(0)11-857-8492
www.aist.go.jp/index_en.html



NORTHERN ADVANCEMENT CENTER FOR SCIENCE & TECHNOLOGY

Collaboration breeds innovation

The Hokkaido University Research & Business Park (HU R&BP), an innovation hub supported by 12 organizations including the Northern Advancement Center for Science & Technology (NOASTEC) through the HU R&BP Project Promotion Council, serves as a base for cutting-edge research and development (R&D) through collaborations among industrial, academic and government partners. By bringing together R&D in food and medical care, the HU R&BP aims to become a world-class centre of innovation for the health science industry.

Since 1998, the industrial, academic and government communities in Hokkaido have been actively promoting the activities of industrial clusters to help boost the regional economy and increase employment opportunities. The HU R&BP, established as a major focus of such industrial cluster activities, developed as an initiative of the Hokkaido Economic Federation in partnership with Hokkaido University, the Hokkaido government, the City of Sapporo, the Hokkaido Bureau of Economy Trade and Industry, the Hokkaido Regional Development Bureau and NOASTEC, who together established the HU R&BP Project Promotion Council in 2003.

The research and business park is located on the campus of Hokkaido University and now hosts 16 collaboration facilities including university centres such as the Research Center for Zoonosis Control and the Institute of Low Temperature Science, as well as incubation facilities and the Hokkaido Industrial Research Institute. The park acts as an arena for the construction of a coherent cluster system to support the R&D and commercialization of new technology through industry-academia-government collaborations. Using the intellectual assets of universities and other academic institutions, the HU R&BP project aims to create venture businesses and new industries that will invigorate the regional economy.

The HU R&BP Project Promotion Council seeks opportunities to form R&D projects, and assists in the transfer of research results and intellectual

assets to the private sector. It is also active in recruiting corporate research facilities and other research organizations to the program, as well as promoting business startups and university spin-offs. To ensure the longevity of the program, the promotion council has made it a priority to develop and maintain a fulfilling lifestyle and community environment for researchers and businesses alike.

In 2009, the HU R&BP was formally recognized by the Japanese government as a global innovation hub. "The HU R&BP initiative is now expanding into

a solid platform to support R&D on health innovation based on food and medical care utilizing the cutting-edge biotechnology and life science technology currently available in Hokkaido," says Masaru Tsunetoshi, executive director of NOASTEC.

The HU R&BP now supports three national projects, in food, translational science, and drug discovery/medical care, and Tsunetoshi is very optimistic for the project's future. "We are seeking to make Hokkaido the world's best health science and medical care integration hub within ten years."

Functional food leads the way

The Sapporo Biocluster 'Bio-S', launched in 2007, is one of nine globally oriented regional innovation cluster programs established by the Japanese government under the Knowledge Cluster Initiative. Food is the primary focus of the Bio-S project, supported by R&D in immune, cognitive and metabolic functions and many other cross-disciplinary fields with contributions by 20 professors from 8 universities and more than 40 companies, 20 of which represent the local community.

One of the main goals of the Bio-S project, one of three national projects supported by the HU R&BP, is to stimulate local primary industry by scientifically evaluating the functionality of foods grown in the Hokkaido area leading to the development of a health sciences industry hub. By devising systems to evaluate the functionality of foods and developing diagnostic test kits and business centres for functional evaluation, the project aims to add value to food produced locally and develop 'functional' foods with proven health promotion properties.

"To commercialize research themes, we pursue scientific innovation in order to come up with distinctive patents, to strive for commercialization and marketing support, and to construct evaluation

bases for food innovation," says Fumio Suzuki, project director of Bio-S. "When a system for evaluating the functionality of food is developed, such as diagnostic test kits, we can both sell the kits and start up functional evaluation businesses for food."

The discoveries of prophylactic biomarkers for Alzheimer's disease and atherosclerosis are examples of the basic but important research conducted by Bio-S businesses. These biomarker candidates form the basis for the development of new assay kits for measuring the functionalities of foods. "We are also currently building research centres for antioxidant analysis, advanced lipid analysis, gut function analysis, clinical evaluation of foods and also for cohort studies involving foods." These five research centres are expected to contribute to the creation of a seamless innovation platform for the development of functional foods and also stimulate contract research business based on cutting-edge science.



Northern Advancement Center for Science & Technology
 N21 W12, Kita-ku, Sapporo,
 Hokkaido 001-0021, Japan
 Tel: +81-(0)11-708-6525
 info_noas@noastec.jp



HOKKAIDO RESEARCH ORGANIZATION

Feeding Hokkaido, feeding Japan

The Hokkaido Research Organization (HRO) was established in 2010 to bring together and coordinate 22 former prefectural research institutions—many being over 100 years old. Together, these research institutes have amassed an enormous collection of data that in the words of HRO president Norihito Tambo represents “a treasure-trove for Japanese researchers”. Research being conducted by the organization targets the development of technologies that can boost food supply and so increase Japan’s food self-sufficiency.

With a total of 700 researchers stationed throughout the island, the research institutes of the HRO have developed a deep knowledge of Hokkaido’s natural environment and are pursuing a range of projects with the aim of enhancing Hokkaido’s food production capacity and the long-term sustainability of the local industry. The HRO’s three leading research institutes, the Salmon and Freshwater Fisheries Research Institute, Abashiri Fisheries Research Institute and Kamikawa Agricultural Experiment Station, are each conducting research that make the most of Hokkaido’s premium produce.

Salmon’s circle of life

The people of Hokkaido have relied on the local chum salmon for thousands of years. Spawning in the island’s freshwater streams, salmon soon migrate out to sea where they will spend most of their lives ranging for thousands of kilometres. Every autumn, however, the salmon return to their own spawning grounds in one of the most remarkable feats of navigation in nature. Through this circle of life, salmon make an often-overlooked but vitally important contribution to the ecosystem, and without it Hokkaido would be deprived of one of its most important industries. As early as the 1600s, the growing salmon fishing industry was one of the main drawcards that enticed people from the main island of Honshu to come to Hokkaido, which

at the time was very much Japan’s wild frontier. In the late 1800s, the decision was made to import technology that allows salmon to be bred artificially in hatcheries, after which the juveniles would be released into Hokkaido’s rivers.

The use of this method, however, initially resulted in a drop in the numbers of salmon returning to Hokkaido each autumn. It was not until the early 1970s that researchers discovered that this drop was due to a mistake in the timing of release. “The mistake was corrected and the numbers of salmon increased rapidly from the 1980s to a peak in the 2000s of about 60 million each year,” says Toshio Izawa, director of the Salmon Fisheries Research Division at the HRO’s Salmon and Freshwater Fisheries Research Institute. “In recent years, however, the numbers have fluctuated.” Hokkaido’s fixed-net salmon fishing industry today has an annual turnover of close to ¥50 billion, and any aberration in the numbers of returning salmon is cause for concern. As the livelihoods of many locals are affected by these fluctuations, Izawa feels that it is crucial to determine their cause.

Leading a team of researchers at the Salmon and Freshwater Fisheries Research Institute in Eniwa near Sapporo, Izawa has come up with a number of possible theories for the fluctuations in salmon numbers. The tagging of juvenile salmon has shown that they are more likely to survive in some coastal regions where the sea water temperature is relatively high. One strategy being considered by the researchers is therefore releasing the young when the water has become warmer. Izawa also insists that since about 80% of all the juveniles released die in the coastal regions, they need to intensify their research in these areas.

Although Hokkaido’s artificial spawning programme has been in place for over a hundred years, naturally spawned wild salmon with ‘pure’ genes of the original native variety continue to be found in some of Hokkaido’s rivers. Preserving the genetic identity of these true wild salmon is of utmost importance to Izawa and his colleagues. “Unfortunately, these salmon are often fished before they



Maintaining the circle of life: Artificially hatched salmon

can lay their eggs, which affects the sustainability of their genetic gene pool,” says Izawa. “We are now in the process of establishing an ecological-based management system that preserves the purity of wild salmon genes.”

Sowing a stronger scallop industry

Over 40% of the world’s naturally raised scallops are caught in Japan, mostly in the Sea of Okhotsk just north of the island of Hokkaido. The scallop fishing industry grew through the introduction of aquaculture technology in the 1970s that led to a rapid increase in the region’s capacity for scallop production. Other major contributing factors include the geographical character of the Sea of Okhotsk, which is relatively calm and generally highly productive, and the biological characteristics of the scallops themselves, which grow quickly in the cold waters of this northern sea. Maintaining the quality and yield of scallops is the focus of research at HRO’s Abashiri Fisheries Research Institute on Hokkaido’s north coast, where advanced methods for fishery management and environmental monitoring of scallop fields are under development.

Scallops in the Sea of Okhotsk are primarily raised using a sowing culture method in which young scallops are released from a moving boat and distributed over a defined area at sea. The mature scallops are then harvested by surface dredging in the same area three to four years later.



A steady increase in the surface temperature of the coastal sea from 1980 to 2010, however, has researchers worried. "We are concerned that this temperature rise will adversely affect the production of scallops," says Akira Miyazono, director of the Resources Management and Enhancement Division. If the temperature continues to increase, there is a possibility that the area of sea ice production will shrink, which will lower the brine content in the intermediate cold water layer and in turn detrimentally affect the primary production of scallops.

Miyazono believes that the only way to maintain the current level of scallop production will be to obtain an accurate picture of the scallops' food environment, though he admits that this may be difficult. "Farmers who tend fields can easily check the development of their crops, but in our case this is much trickier," he says.

Cutting-edge visual equipment will be introduced in the hope that it will give an accurate picture of the underwater environment. For example, the amount of phytoplankton, an important food source for scallops, will be determined by mooring a chlorophyll sensor with data logger at a depth of 42 metres for phytoplankton-related measurements. "We also plan to deploy a moving automatic image analysis system to take underwater video footage that will allow us to accurately measure the concentration of scallops, which is one of the key elements in the monitoring of the scallops' environment," he says.



A world-class industry: Scallop harvesting in the Sea of Okhotsk

Helping rice to thrive

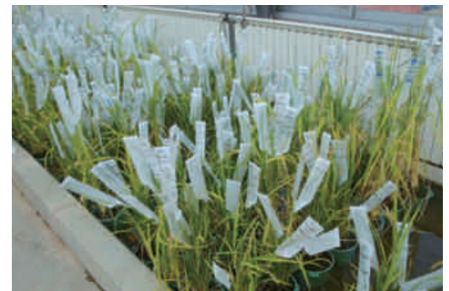
Even in Hokkaido, the coldest region in Japan, farmers have successfully grown rice for centuries. The cold climate, however, is certainly an obstacle, a fact noted by the visiting American special agricultural advisor Horace Capron in the late 1800s. "Capron reportedly suggested that the area was not suitable for rice and that Hokkaido would be better to focus on mining and livestock," says Tambo. Yet today, Hokkaido can boast the widest variety of high-quality rice to be found anywhere in Japan. In fact, the lower summer temperatures in Hokkaido result in better-tasting rice and a bigger harvest than elsewhere in the country.

The success of Hokkaido's rice industry has not come easily though. In the 1980s, Hokkaido's rice farmers were struggling in the face of poor sales. This situation led farmers, companies and researchers—including the Hokkaido Prefectural Agricultural Experiment Station—to form a consortium to develop rice strains that not only offer superior taste quality, but through the employment of the latest scientific techniques, such as DNA markers, are also resistant to the cold and disease.

One of the consortium's strategies was to reduce the percentage of amylose, a type of starch found in rice, from 23% to 18% and thereby give their varieties of rice a stickier texture, which is preferred by the Japanese consumer. Eventually, through the introduction of cutting-edge equipment, they were able to reduce the amylose content to an average of 19%. One of the varieties of rice developed as part of this project, Yumepirika or 'beautiful dream', actually contains just 15% amylose.

Another major breakthrough of the project was the development of a method to breed rice strains using a culture based on anther—part of the pollen-producing organs of a flower. "This method shortened the time to develop a rice strain from ten to seven years," says Takashi Sato, a senior research manager at the Kamikawa Agricultural Experiment Station.

Although the obstacle of the cold has been largely overcome, it still exacts a toll. Over the



A high-quality product: Developing new rice varieties

past 120 years, the annual rice crop has been severely damaged by low temperature weather on average once every four years. Using a set of DNA markers to identify the parts of various rice strains that are resistant to the cold, Sato and his team of researchers have identified three genes that they have experimented with to create a rice strain with improved cold resistance.

Also in the last two years, researchers at the Kamikawa Agricultural Experiment Station have developed strains of rice that are resistant to the rice blast disease. Several gene types with the potential to display resistance were identified and tested in rice strains, and the most successful of those are now under further development.

The Hokkaido rice industry has grasped the obstacles it has faced and turned them into opportunities. With continuous improvements to the local rice strains, Japanese consumers can look forward to a more varied choice of high-quality rice than ever before.



Hokkaido Research Organization
N19, W11, Kita-ku, Sapporo,
Hokkaido 060-0819, Japan
Tel: +81-(0)11-747-0200
www.hro.or.jp/en/



FUTURE UNIVERSITY HAKODATE

Working with society towards a smarter future

The increasingly global and complex information environment has made society more productive and more informed than ever before. At the same time, however, the rapid progress in information and communication technologies has far outpaced the development of academic and institutional learning systems, which remain fundamentally rooted in traditional educational paradigms. The Future University Hakodate (FUN), located on the southern peninsula of Hokkaido, was established in 2000 with the aim of founding a future-oriented educational system to help explore the uses of information and communication technology in society.

Located on a hillside overlooking the bay in Hakodate, FUN brings together the fields of information and communication technology and complex systems within a guiding concept of 'human values'. The university's curricula are highly focused in these areas, making it a unique institution devoted to studying the role and use of information and communication technology in society. It is also distinct in its future-oriented vision, promoting research that will help ensure that emerging information and communication technologies are strategically and wisely designed and mediated such that their cumulative effects bring positive benefits to society.

Supporting this endeavour is FUN's universal emphasis on social and educational innovation. The university has a compulsory project-based

learning course, through which all students at FUN spend a year as part of a project team working in collaboration with local communities on experimental applications of information and communication technology in society. One such project that was officially inaugurated in 2011 is the Smart Access Vehicle System (SAVS), which sees FUN students and researchers working hand-in-hand with the Hakodate community to develop systems that will help citizens, and particularly seniors, live more comfortably and conveniently.

"The SAVS is an integrated transportation system that plays the role of a brain and nerves to help control the whole city organically," says Hideyuki Nakashima, president of FUN. "The system will become far smarter and more flexible with central computer management, and that will help coordination with services such as restaurants, hospitals, libraries and tourist spots."

The goal of the SAVS is to provide an automated system for booking public transport by coordinating various public services. For example, by registering a doctor's appointment with the system, the SAVS automatically arranges the time for pickup by taxi or group bus at the home of the patient and informs the clinic or hospital on the patient's arrival. Similarly, registering that the appointment is over will automatically trigger a pickup request to take the patient home. The project is a social innovation experiment and is the first trial of its kind in Japan. The Hakodate area, with a population of 300,000, is a convenient size for the experiment. The project is now seeking special government endorsement to operate vehicles that combine the services of taxis and buses.

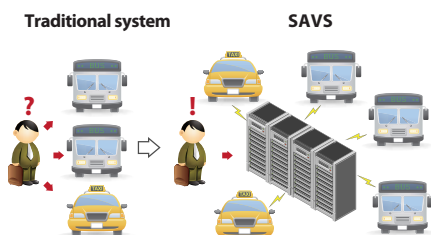
Marine information technology (IT) is another area in which FUN works with Hakodate city on experiments in social innovation. This study aims to apply information and communication technology in the fisheries industry in order to improve efficiency and enhance value.

"We are developing a small, oceanographic observation buoy system designed for ubiquitous sensing," says Nakashima. "The system will help fisheries workers by, for example, allowing them

to check the water temperature in scallop beds remotely using a system that can be implemented at a tenth of the cost of existing buoy systems. It is something that has been requested by the local scallop industry." FUN is also experimenting in the application of marine broadband networks to help support the fishing industry by constructing a wireless broadband environment through collaboration with local fishery unions. With broadband internet access at sea, fisheries workers can maintain web-based fishing diaries, including the locations and numbers of fish schools using iPad terminals. Such a system allows every vessel to share locations and fishing information in real time. "FUN is now receiving inquiries from other countries, such as South Korea and Oman, to help with the introduction of marine IT," says Nakashima.

Epitomizing the unusual, thought-provoking and insightful research that is being pursued by FUN researchers is the work of Toshiyuki Nakagaki, a professor of the Department of Complex and Intelligent Systems. Nakagaki and his colleagues have shown that slime mould *Physarum Polycephalum*, despite having no measurable intelligence of its own, can in fact solve a maze puzzle and even design a railroad network — both problems generally considered to require computational solutions. For their work, Nakagaki's team has twice won the Ig Nobel Prize, which is awarded annually for research that is unusual and imaginative, and at the same time stimulates thought and interest in science.

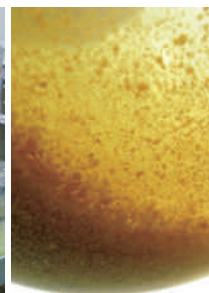
"It is rare for a researcher to win the Ig Nobel Prize twice. The concept of using slime mould to solve problems is yet to be made practical, but it is very intriguing," says Nakashima.



The Smart Access Vehicle System (SAVS): An integrated transport system for the future.



Future University Hakodate
 116-2 Kamedanakano-cho, Hakodate,
 Hokkaido 041-8655, Japan
 Tel: +81-(0)138-34-6448
www.fun.ac.jp/en/



HOKKAIDO ASSOCIATION FOR BIO-BUSINESS

A boost for functional foods

The Hokkaido Association for Bio-Business is implementing a five-year plan to increase sales of Hokkaido's agricultural and marine products by promoting their functions and creating innovative functional foods.

Hokkaido in northern Japan is blessed with a natural environment that generates a plentiful supply of food and marine products. "Hokkaido is so naturally rich in food that it has a self-sufficiency rate of 200%," says Ken-ichi Kosuna, president of the Hokkaido Association for Bio-Business. The membership of the association includes 42 bio-related companies as well as retail companies and financial institutions. The objective of the association is to increase sales of Hokkaido food products by ¥1 trillion by 2015—an ambitious target particularly considering the general acceptance that the food production capacity of the region is already at its peak. "For this reason, we intend to increase sales revenue of food products by giving them extra value, which can be achieved by emphasizing their functionality," says Kosuna.

Adding functionality to food products or enhancing the functionality they may already have is the primary focus of the association's activities. An example of this enhanced functionality is a new type of onion developed with the support of the association that contains three times the normal amount of quercetin, a plant-derived flavonoid that is reported to reduce blood pressure and increase metabolism. Onions of this variety can sell for five times the price of regular onions or even more. The development of functional foods by the incorporation of specific beneficial supplements is another approach being pursued by the association. The 'supplemental donuts' currently being sold at a major hotel in downtown Sapporo are examples of the functional foods that have been developed with the support of the Hokkaido Association for Bio-Business.

"We are looking at ways to expand our product portfolio by developing ingredients from plants that can be used to create functional foods," says Hiroshi Ishimoto, president of Hokkaido Mitsui Chemicals.

Tsutomu Inoue, vice-president of Hokkaido System Science, also proudly explains how his company has "established an evaluation platform to determine the safety of functional foods."

To support the sales of these functional foods and supplements, Kosuna is leading a drive to overhaul Japan's ingredient reporting laws. As it stands, health products, as opposed to medical products, are not required to display their functionality or how they should be consumed on the label, and unlike

normal food products do not even have to display a list of ingredients. The association has pressed the Japanese government to amend this law, which could soon be on the cards. "This will allow consumers to buy health products with peace of mind in the near future," says Kosuna.



北海道バイオ工業会

Hokkaido Association for Bio-Business
N21, W12, Kita-ku, Sapporo,
Hokkaido 001-0021, Japan
Tel: +81-(0)11-299-8878
www.hokkaido-bio.jp/e/

HOKKAIDO MITSUI CHEMICALS

It's part of the culture

Hokkaido Mitsui Chemicals (HMC) is one of the few companies in the world that possesses a plant cell culture technology that can produce a steady and highly productive yield of components useful for cosmetics and functional foods. As natural disasters and over-harvesting make the procurement of certain plants increasingly difficult, many companies are looking to HMC to help support their product development.

When Mitsui Chemicals, one of Japan's biggest chemical companies, opened a plant close to central Hokkaido 70 years ago, it was taking a big step in a major new direction for the development of chemical components—one that turned out to be a major success. HMC has since been developing its plant cell culture technology to produce high-value chemical compounds that are used in a range of industries. "Companies are attracted by the fact that we can produce components quickly and with high yield," says Homare Tabata, director of HMC's Phytochemical Research Center.

Over the years, many cosmetic companies have approached HMC for the company's ability to mass-produce compounds that are difficult to find naturally. The first compound that HMC cultured using

their plant cell culture technology was shikonin, which has the ability to heal scars. A major Japanese cosmetic manufacturer used this to manufacture a 'bio-lipstick' that turned out to be a best-selling product for many years.

One of the major advantages of the plant cell culture process is that it produces high yields in a short time. In the case of *Lithospermum erythrorhizon* cultured cells, approximately 20% shikonin can be produced on a dry weight basis within 14 days, far surpassing the speed and yield of natural cultivation, which can take up to three years and give only 2% of the product by dry mass. Similarly favourable results are observed for a range of other components.

Over the years, HMC has developed a subculture library consisting of more than 40 plant cell lines that the company uses when it is asked to develop custom-made components. According to Tabata, the company expects to see a substantial expansion of its order book over the next few years. "Companies eventually come to us when they find out that we can provide a steady, highly productive yield of the components they are looking for," he says.



Mitsui Chemicals Group

Hokkaido Mitsui Chemicals
1 Toyonuma, Sunagawa-shi,
Hokkaido 073-0138, Japan
Tel: +81-(0)125-54-3131
support.prc@hmci.co.jp



AMINO UP CHEMICAL

Functional food backed by science

Armed with a portfolio of popular-selling functional food products, Amino Up has gained a worldwide reputation for products with scientifically proven effects—the result of years of investment in research and the establishment of an international network of institutions with which it conducts collaborative research. The company is now expanding to previously unexplored countries to pursue its mission of giving back to society.

Established in 1977 in a leafy suburb on the outskirts of the city of Sapporo, Amino Up has taken advantage of the abundance of agricultural produce found on the island of Hokkaido. Using Hokkaido produce, the company develops value-added food products and supplements with physiological activity, including food containing mushroom-derived immunostimulators, low molecularized polyphenol, antiallergic agents, antioxidants and plant-growth regulators.

One of the company's most well-known supplements, called active hexose correlated compound or AHCC, is made from the mycelia of shiitake mushrooms and is reported to activate immunocytes, which can help in alleviating the side-effects of anticancer drugs and even help in the treatment of infectious diseases such as hepatitis. Oligonol, another of the company's products, is the world's first low molecularized polyphenol which, unlike conventional polyphenols, is readily absorbed by the body, maximizing its potential health benefits.

The chairman of Amino Up, Ken-ichi Kosuna, is confident that the company's range of attractive products will allow it to achieve its ambitious sales targets. "We are focusing all our energy on expanding into overseas markets, which currently make up 20% of our total sales—a figure that we aim to raise to 50% within three years," he says.

International collaboration

Amino Up plans to implement its international sales strategy by building upon the connections it has established with overseas institutions over

its years of research and development (R&D). The company is currently carrying out collaborative research with 35 institutions abroad, ranging from universities to research laboratories and medical institutions. "We have maintained very strong relationships with research institutions in the US for over ten years," says Hajime Fujii, executive director of Amino Up's R&D division. The company has also received many enquiries from institutions in Europe who are interested in its products.



Ken-ichi Kosuna, chairman of Amino Up

Collaborative research, however, would not be possible without the right staff. A wide range of researchers are employed at Amino Up, including experts in medicine, pharmacology, chemistry, agricultural chemistry, microbiology and environmental science, who carry out cutting-edge research with overseas institutions in areas such as bioactive substances, structural analyses of active constituents and clarification of action mechanisms.

"Many institutions want to carry out human clinical studies and animal experiments to examine the mechanism and functions of the chemical ingredients that make up AHCC and Oligonol," says Fujii. One of the unforeseen outcomes of this international network of collaborators is that they will sometimes make suggestions to Amino Up for research themes—even to the extent of carrying out research free of charge. "Our collaborative research may not immediately lead to direct sales, but since it gives our products a deeper scientific

grounding, this eventually leads to more sales," says Fujii. Amino Up invests 15% of its revenue into research, considerably more than the industry average. Fujii believes that Amino Up's approach of conducting in-depth research in a narrow field will help the company achieve its goals.

Product demand from overseas is expected to grow strongly over the next few years, and Amino Up plans to be ready. The company has from the very start worked towards satisfying the demands of overseas companies, which tend to have much stricter requirements than Amino Up's domestic customers. With this in mind, the level of its research and standard of its facilities have always fulfilled global standards, not just Japanese ones. "We have obtained ISO 9001 for our quality management systems and ISO 22000 for the food safety standards on all our food products," says Fujii. It is company policy that any experiment carried out at Amino Up has to be of a standard acceptable abroad.

The international reach of the company is also evident closer to home. Each year, Amino Up supports an international symposium in Sapporo in its role as the headquarters of the AHCC Research Association. Now in its 19th year, the symposium is the longest-running international symposium to be held in Sapporo. The first AHCC gathering started in relative anonymity with just nine researchers in attendance. As Amino Up's international presence grew, so did the attendance, which last year reached 350 including 100 researchers from



AHCC products



International Congress on Nutrition and Integrative Medicine in Sapporo

15 countries who came to discuss among other things the most recent results of research conducted on functional foods. As a sign of the symposium's significance on the international stage, last year's keynote speech was made by John Milner, an eminent researcher from the National Cancer Institute in the US. The AHCC Research Association also carries out symposia in the US and China. The association's extensive global network includes 200 overseas-based members and 1,100 Japan-based members.

The science behind the products

AHCC has long been known to help defend against infection and fight cancer by stimulating the immune system to increase the body's natural defence mechanisms. The numbers tell the story of a clearly popular product: used for more than 20 years in over 20 countries, researched by more than 70 leading institutions worldwide with results confirming its safety and lack of side effects, and the subject of over 60 international scientific publications.

Recent research, however, has revealed a new function of AHCC that is particularly timely considering Japan's current situation. A working group consisting of several Japanese universities and research institutes has published a paper based on three years of research into the effect of radiation on the body for astronauts in space. The report

shows that AHCC is effective in suppressing radiation-induced leukaemia and congenital anomalies. "The Japanese government has expressed an interest in using AHCC on people affected by the recent nuclear accident in Japan," says Kosuna. "I would like to see it used for victims of such accidents all over the world." Recent clinical tests in the US have also shown that AHCC provides a significant boost to the immune system in combination with influenza vaccination.

Another of Amino Up's top-selling products, Oligonol, is a unique product made from lychee fruit that provides several well-documented benefits with a daily dose of just 100 milligrams. The results of a clinical study in the US and Japan have shown that taking Oligonol over a period of several weeks reduces the appearance of skin blemishes and wrinkles. It is also able to inhibit the absorption of lipid molecules as well as stimulate fat metabolism. Additional beneficial effects of Oligonol in cardiovascular health, fatigue and pain reduction have also been indicated in clinical studies.

Amino Up is continuously looking for new products to add to its product portfolio. A substance derived from agricultural products in Hokkaido is currently of particular interest. Another compound that is now undergoing clinical testing and is scheduled for a product launch next year is a supplement that has the ability to alleviate the symptoms of physical and mental stress, and to induce sleep. "This compound has the potential to help people who have suffered from the recent disaster in Japan," says Kosuna.

Giving back

With their fundamentally scientific approach to the development of health products and an increasing number of effective products already on the market and in clinical testing, Amino Up is well on the way to fulfilling its goal of giving back to society. This community-oriented ethos is something that Kosuna believes in strongly and it is a mindset that he continuously tries to instil in the company's staff. In a particularly unusual measure for a Japanese company, all the employees at Amino Up are



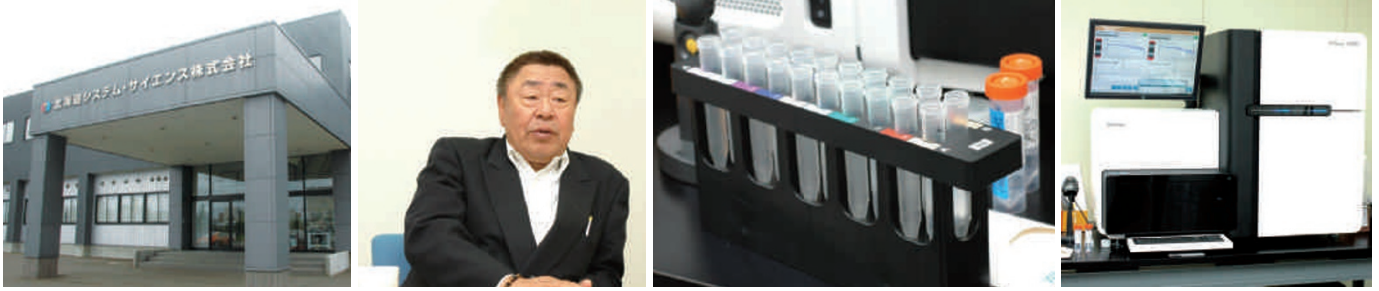
Oligonol products

required to perform volunteer duties that range from donating blood to helping take care of people in retirement homes. Every six months, each employee writes a report on the kind of volunteer work they have carried out, which forms part of their performance evaluation. "It is not enough for a company simply to say that it gives back to the community—every employee should accept that responsibility," says Kosuna.

From the moment people enter Amino Up's newly built headquarters, they are left in little wonder about the corporate message that the company is trying to project. Located in the middle of the spacious lobby next to the entrance of the main building is a bench on which sits a life-sized mannequin of the twentieth-century film and fashion icon Audrey Hepburn. "I chose to set the mannequin there because it is well-known that Audrey was a strong advocate of giving back to society, which I believe is a true representation of Amino Up's corporate spirit," says Kosuna.

**Amino Up
Chemical**

Amino Up Chemical
363-32 Shin-ei, Kiyota, Sapporo,
Hokkaido 004-0839, Japan
Tel: +81-(0)11-889-2277
www.aminoup.co.jp/e/



HOKKAIDO SYSTEM SCIENCE

Japan's one-stop DNA solution provider

Over the past two decades, researchers in Japan have turned time and again to one company to meet their DNA and RNA synthesis and analysis needs—Hokkaido System Science (HSS). Unlike the vast majority of their competitors, HSS can provide fast, cost-effective and precise analysis of micro-organisms using its next-generation DNA sequencing facilities. It also holds an exclusive licence for a vector-capping technology that allows HSS to create full-length complementary DNA libraries from RNA samples. Having earned a steadfast reputation domestically, HSS this year has for the first time made its technology available to researchers anywhere in the world.

Hokkaido System Science was one of the first companies in Japan to provide commercial DNA analyses in the early '90s, and from that pioneering start has continued to develop its range of services using the latest in DNA technology. The company is now Japan's premier one-stop shop for DNA solutions, offering services from custom DNA synthesis to DNA sequencing and DNA microarray analysis to name a few. Now, after focusing on Japan's domestic market for many years, HSS CEO Yukio Mizutani is looking to make his company's services available internationally. "This year we have decided to make the push abroad," he says.

Hokkaido System Science was established in 1988 in a period that saw rapid growth in bio-related businesses in Japan. Its original business model, however, was radically different from today, focusing instead on the supply of equipment for physical and chemical research. Three years later, the company changed direction and devoted itself to services based around DNA synthesis, an emerging technology at the time.

Only one other Japanese company was offering DNA synthesis back in those days, and Mizutani saw the opportunity to help Japanese research. "It was my dream to support researchers in their work, which is why we started to offer

custom DNA sequencing as well as DNA microarray analyses," he says.

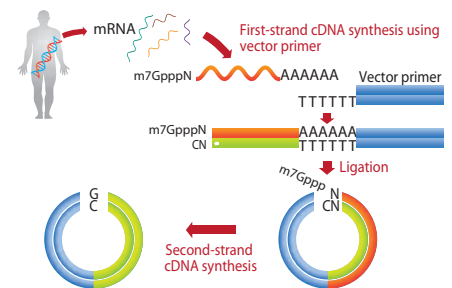
Many of HSS's early competitors have since disappeared, a fate met by many other bio-related companies in Japan during the country's tough economic winter of the past two decades. Hokkaido System Science has not only survived, it has expanded and flourished, emerging as one of Japan's leading providers of DNA solutions. "Unlike our competitors, we were able to stay in business because we avoided unnecessary risks and remained committed to our goal of providing premium DNA-related solutions," says Mizutani.

Hokkaido System Science stands out from its competition in many ways, but perhaps most important is its cutting-edge technology and facilities. Although the latest in DNA sequencing and other technologies come at a price, Mizutani believes that the financial cost to the company is not only worth it, but absolutely vital to the company's success. "Our DNA synthesizer is special because it can produce DNA material on a gram level, while our competitors' synthesizers can only produce micrograms or nanograms of DNA," he says.

In Japan, many researchers, particularly in the field of agriculture, turn to HSS when they need a large amount of precise genetic information on soil micro-organisms in a short time. One of the two next-generation DNA sequencers that the company has imported from overseas is able to produce up to 1 million reads at a time, with each read consisting of 350 to 400 sequences.

The services offered by HSS go far beyond synthesis and sequencing, however. Unlike government institutions that own similar equipment, HSS goes a step further by conducting analyses on sequencing data. The company also provides after-care service by visiting or calling customers a month after delivery to ensure that the results have met expectations and whether they have been useful in the research being carried out.

Another of HSS's unique offerings is a technology that allows for the efficient and accurate construction of full-length libraries of complementary



The HSS's vector-capping technology

DNA, which are essential for research on identifying genes and determining their promoter regions. The technology was invented by Seishi Kato, a researcher at the National Rehabilitation Center for Persons with Disabilities, and now HSS holds the exclusive rights to the technology. "In contrast to the other methods that are available, my vector-capping technology involves very few steps and provides highly accurate data," says Kato. The small number of steps considerably reduces the complexity of the process, and also allows results in a full complement of unbroken messenger RNA. Another important advantage of the vector-capping technology is that it can be carried out on a sample one hundred times smaller than is normally required. This is particularly useful in cases where analysis is to be carried out on rare plant or animal species that are difficult to procure.

"We are confident that our extensive experience in providing comprehensive support to researchers in Japan will help us to provide researchers abroad with the DNA solution that they are looking for," says Mizutani.

 **HSS**
Hokkaido System Science Co., Ltd.

Hokkaido System Science
2-1, Shinkawa Nishi 2-1, Kita-ku,
Sapporo, Hokkaido 001-0932, Japan
Tel: +81-(0)11-768-5901
www.hssnet.co.jp/index_e.htm



OBIIHRO UNIVERSITY OF AGRICULTURE AND VETERINARY MEDICINE, TOKACHI REGIONAL PROMOTION FOUNDATION

Preserving food safety in Hokkaido's heartland

The Tokachi district of Hokkaido on the island's southeastern Pacific Coast contributes 250 billion yen each year in upland and livestock production to the regional economy. In a region where food production is the heart and soul of the economy and society, the district's only university, the Obihiro University of Agriculture and Veterinary Medicine, has set itself apart by establishing as one of its core principles the preservation of food safety.

Surrounded by dairy farms and fields of potatoes and buckwheat, the Obihiro University of Agriculture and Veterinary Medicine is situated in the heart of the Tokachi Plain where it is well placed to integrate veterinary medicine and agricultural and livestock studies into a single school system. "It is the only institution like it in Japan and one that offers an optimal environment for learning these subjects," says Hideyuki Nagasawa, president of the university. The subjects taught at the university are well matched with the regional industries, giving students and faculty the opportunity to work hand-in-hand with local communities in the fields just outside its doors.

"Our university established the single-school system in 1949 when Japan suffered the outbreak of mad cow disease," says Nagasawa. "The issue triggered food safety concerns among consumers, and we had to convince them not only with scientific veterinary evidence but also with proof in terms of our livestock and agriculture, and also socioeconomic factors." To tackle such issues as proving the origin of feed and cattle, the university adopted the principle of the preservation of food safety to ensure the development of human resources in all areas involved in safety, including international matters. The adoption of this principle has been significant for farmers and food producers in the Tokachi area. "From an academic point of view, our mission is to contribute to local communities and international societies," says Nagasawa.

The commitment to food safety enshrined by the Obihiro University of Agriculture and

Veterinary Medicine also forms part of a regional innovation project established in 2005 with the support of the Japanese government's Regional Innovation Strategic Support Program. The Tokachi Agriculture, Bioscience Project, known as the Tokachi ABC Project, contributes to the preservation of food safety by promoting the development of new, simple inspection systems that allow hazardous bacterial contaminants in food to be detected faster and more accurately. These systems help guarantee the safety of agricultural and livestock products and processed foods exported from the Tokachi district.

The other main focus of the Tokachi ABC project is research on functional foods with the aim of identifying and isolating functional components from agricultural and livestock items and by-products of food processing in the region and commercializing the research outcomes. An inspection laboratory to support the project's research is currently being set up at the university with the help of the Tokachi Regional Promotion Foundation. "The laboratory will inspect food materials harvested and produced in the region, continue the development of a new inspection system, and analyze the functionality of food materials," says Shigeru Ito, special duty professor at Obihiro University. "We expect the inspection laboratory to play a vital role in creating a regional biology cluster for food and agriculture. The cluster framework will also be expanded to include food development and regional innovation in the future."

Through the Tokachi ABC Project, Ito hopes to commercialize locally produced food components such as chicory inulin, a possible sugar replacement, and high-polyphenol azuki beans, a potential antioxidant-based health protective. "We want to use the physical, scientific and wellness functionalities of such food components and residues from food processing to make functional foods that support the health of people with conditions like metabolic syndrome," says Ito, "and we want the health benefits of those foods to be guaranteed through our work at the inspection laboratory."

Obihiro University's food safety program has allowed it to establish Asia's first World Organisation for Animal Health (OIE) Collaborating Centre for the Surveillance and Control of Animal Protozoan Disease. The National Research Center for Protozoan Diseases (NRCPD) provides OIE-certified laboratories for research on diseases and promotes the development of expertise and industry standardization. In 2007 the centre became the world's only OIE Reference Laboratory for bovine babesiosis and equine piroplasmiasis, and the second OIE Reference Laboratory for animal trypanosomiasis. The OIE Reference laboratories develop, preserve and share reagents and compounds used in the diagnosis and control of animal disease, develop and implement new diagnosis and control methods, and collect, analyze and disclose epidemiological information.

The OIE is the world's only international veterinary organization and is recognized by 178 member countries. The activities of the OIE include collecting and providing information on animal infectious diseases and zoonoses—diseases that can be transmitted between humans and animals—and drawing up international codes for the import and export of animals and animal-derived products. "It is also responsible for compiling international standards on animal disease diagnosis and animal vaccines," says Ikuo Igarashi, an OIE expert and a professor of the NRCPD. "On trade issues, the World Trade Organization complies with the OIE's international codes, which are worked out using scientific evidence obtained through collaboration among experts from its reference laboratories and collaborating centres."



Obihiro University of Agriculture and Veterinary Medicine
Inada-cho, Obihiro,
Hokkaido 080-8555, Japan
Tel: +81-(0)155-49-5216
www.obihro.ac.jp/english



Tokachi Regional Promotion Foundation
23-9, W22, N2, Obihiro,
Hokkaido 080-2462, Japan
Tel: +81-(0)155-38-8808
t_zaidan@tokachi-zaidan.jp



ASAHIKAWA MEDICAL UNIVERSITY

Making the world a smaller place

Innovative telemedicine technology developed by Asahikawa Medical University (AMU) in Hokkaido has revolutionized the delivery of medical care. For almost 20 years, AMU's pioneering technology has allowed its medical expertise to be sent to hospitals in isolated parts of Japan's most northern island, and beyond—the university has established telemedicine links with medical institutions in the US, Singapore and Thailand, and the AMU technology is soon to be adopted as an official medical support infrastructure in China.

Twenty years ago, before the internet and modern computer networks, researchers at AMU in central Hokkaido developed telemedicine technology that allowed for the remote sharing of medical information using an interactive audiovisual media platform to assist in remote medical procedures, examinations and consultations. "The basic philosophy for our telemedicine technology from the very beginning was to transport information, not doctors or patients," says Akitoshi Yoshida, president of AMU. Now, after 20 years of improvements, the university can now offer a telemedicine system that supports real-time telemedicine transmission in a three-dimensional high-definition format. The crystal-clear images produced using AMU's technology has already impressed many research and medical institutions in Asia, and China is currently implementing its own telemedicine network based on the technology with the help of AMU.

Asahikawa Medical University's telemedicine technology was very much born out of necessity. In contrast to the densely urbanized metropolises to the south, Hokkaido is only sparsely populated, accounting for almost a quarter of the country's land area but just 5% of its population. The relatively long distances between major centres in the prefecture can mean that patients could have to travel for many hours to reach the nearest well-equipped medical facility, a hindrance made all the more severe by the sub-zero temperatures and deep snowcover of the Hokkaido winter. This means that

the advanced medical facilities of an institution like AMU remain essentially inaccessible to a large proportion of the prefecture's residents.

Rather than requiring patients to visit the medical facility, or sending equipment and specialists to remote clinics, researchers at AMU turned to the potential of telemedicine technology to distribute the university's medical expertise in order to assist with patient treatment remotely, providing patients with the opportunity to have virtual consultations with specialist doctors. The benefits of this system are manifold: patients are relieved of the trouble and cost of travelling to a distant hospital, they can leave hospital earlier because their illness has been dealt with by a specialist at an earlier stage, and it allows rural hospitals to increase their income. Telemedicine also plays a particularly important role in providing expert diagnoses using visual media such as X-rays, computed tomography and magnetic resonance imaging scans, which AMU specialists can process and return to the originating clinic within just two hours. Between 2009 and 2010, the AMU used their telemedicine system in 5,797 patient cases.

A survey by the Japanese government has revealed a very positive response to the telemedicine technology. Of the 218 patients surveyed in five hospitals, 60% responded that they would prefer to speak with doctors at AMU via telemedicine rather than visit the university for treatment in person, irrespective of the specialist area of consulting doctor.

The very first telemedicine transmissions at AMU took place in October 1994. Even though the original system pales in comparison with the cutting-edge technology employed today, the real-time visuals achieved back then were very crisp for their time. That first transmission was made over a link between AMU and the Yoichi Society Hospital 190 kilometres away. Using an analogue optical fibre connection, expert ophthalmologists at AMU guided doctors at the rural hospital during an eye examination using transmitted images. Financial support from the Japanese government saw this telemedicine technology develop further, resulting in the successful expansion of the telemedicine



A breakthrough in medical care: The first AMU telemedicine transmission in 1994

network across the Tsugaru Strait to the main island of Honshu and into Fukushima Prefecture.

The first international telemedicine transmissions took place just two years later, in December 1996, when an eye operation conducted at AMU was relayed in real-time in 30-frame-a-second video to one of the largest eye research institutes in the US, the Schepens Eye Research Institute, which is affiliated with the Harvard Medical School. The eye operation was watched by the institute's founder, Schepens, who remarked on the first-class quality of the audio and video.

Building on this success, AMU continued to improve its technology and expand its network, and in 1999 constructed a two-storey telemedicine centre. It was from this control centre, where the latest telemedicine diagnosis technology for all of the operating rooms at the university had been brought together, that the AMU revealed the next generation of its telemedicine technology to the world. With two decades of hard work, AMU researchers have since extended the hospital-to-hospital telemedicine network to include 49 hospitals throughout Japan as well as medical facilities in China, Singapore, Thailand and the US.

"Asahikawa Medical University has developed a world-leading technology, and we believe that it is only a matter of time before it takes off worldwide because no-one that discovers it can fail to be impressed — seeing is truly believing," says Yoshida.



ASAHIKAWA MEDICAL UNIVERSITY



Bringing Asia together

In 2006, the world witnessed the first three-dimensional (3D) stereoscopic high-definition transmission of a medical procedure, an eye operation at Asahikawa Medical University (AMU) that was watched by surgeons at the Singapore National Eye Center. This breakthrough telemedicine technology developed by researchers at AMU is now destined for a much larger role as a key medical care infrastructure in the world's most populous nation — China.

In the winter of 2006 in an operating theatre at AMU in central Hokkaido, Akitoshi Yoshida, a highly experienced ophthalmologist, was performing routine but highly technical microsurgery to remove a cataract and haemorrhaging from the eye of a 73-year-old Japanese man. What was far from routine, however, was the fact that the procedure was being watched in real-time and in high-definition 3D by eye surgeons thousands of kilometres away at the Singapore National Eye Center and Chulalongkorn University Hospital in Thailand. Transmitting over the Asia Broadband Network, which at the time supported a high-speed 75 meg-



Another world first: Eye surgery transmitted to Thailand using AMU's 3D telemedicine technology

abit-per-second research link between Singapore and Japan, the high-definition 3D telemedicine link was a groundbreaking advance that impressed many in Asia and around the world. "It was the first time we had seen a surgical operation exactly as it is in real life, with the same depth and realism that

the surgeon sees," said Ang Chong Lye, director of the Singapore National Eye Centre.

In the eye operation, Yoshida, who is president of AMU and chairman of the university's Department of Ophthalmology, removed the cataract and later used a cutter to cut away the haemorrhaging. The surgery was, of course, a success, but the patient was not the only one to benefit from the procedure. The telemedicine link used to share the operation marked a huge leap forward in the training of the medical community in southeast Asia. The 3D high-definition images allowed the audience of 25 surgeons at the Singapore National Eye Center to watch actual surgery in unprecedented detail, something that they do not always have the opportunity to do. "This is one more barrier removed in training and research; it is really a brave new frontier for medicine," says Lye. Building on the 2D video telemedicine platform developed many years earlier by AMU researchers, the 3D format allowed the surgeons in Singapore to observe the finer details of the microsurgery that were not visible before.

Far from being simply an opportunity for Yoshida to demonstrate his high-level surgical skills, however, the main purpose of the event was to break down the disparities in the level of surgical techniques that exist among countries. "I think the surgical level should be the same all over the world," he says. The development of the 3D telemedicine technology and establishing the high-capacity data link for exclusive research use between Singapore and Japan also proved to be a bridge-building exercise. In the end, the data link was implemented with the support of the Singaporean government and the Japanese government's National Institute of Information and Communication Technology.

Asahikawa Medical University's demonstration of its 3D telemedicine technology left a strong impression with Chinese officials. After multiple visits by Chinese Ministry of Health officials to AMU since 2009, the Chinese government has now signed an agreement with the university to roll out the technology in China. Under the accord, AMU will install a telemedicine system at the China-Japan Friend-



Expanding into China: AMU signs an agreement with two major Chinese hospitals for the roll-out of AMU's 3D telemedicine technology

ship Hospital in Beijing and the Ruijin Hospital in Shanghai, which will allow surgeons at AMU to provide real-time medical support to doctors in those Chinese hospitals. The Beijing and Shanghai hospitals will also use their telemedicine facilities to provide remote medical advice to doctors in two rural hospitals in order to assist with surgical procedures and patient consultations. As a training medium the system works the other way too: when a patient from a rural area visits one of the major hospitals for a complex procedure, doctors back in the rural hospital will be able to observe the operation in 3D. When the patient returns home, the rural doctor will then be able to work closely with the city hospital doctor to make sure that the patient gets the most appropriate medical care.

Due to the sheer vastness of China coupled with often undeveloped infrastructure and huge income-related disparities in the level of health care available in the country, the 'shortening' of the vast distances between city and rural hospitals provided by the AMU's telemedicine technology promises to take medical care in China to a completely new level. The Chinese government eventually plans to expand its telemedicine network. "We are very grateful to receive support from Asahikawa Medical University for telemedicine, which is an area of medicine that we are putting a lot of emphasis on," says Ma Xiaowei, the Chinese government's deputy minister of health.



ASAHIKAWA MEDICAL UNIVERSITY

Medical information at your fingertips

As the medical care industry begins to embrace the potential of preventative medicine to reduce patient numbers and improve public health, systems for the centralized management of an individual's medical status and history have become more important than ever before. Medical record technology developed by Asahikawa Medical University (AMU) not only gives doctors access to the most up-to-date medical information on a patient no matter where they happen to be, it also gives the patients themselves the tools to manage and understand their own health risks.

With the medical systems in countries around the world searching for ways to deal with the seemingly ever-increasing burden of patient numbers, the medical industry itself has begun to turn to preventative medicine to help stem the tide. "Ultimately, people should be responsible for their own health—even if they are healthy," says Akitoshi Yoshida, president of AMU.

According to Yoshida, that personal responsibility starts with a proper understanding of one's own medical status. In Japan, some medical institutions have started distributing portable-sized paper medical records to patients so that individuals can essentially take ownership of their own health status and develop a better understanding

of their personal health risk factors. The US, too, has recently embarked on a similar scheme whereby people are advised to carry around a memory stick or 'MedicTag' carrying each person's vital healthcare information to help with emergency treatment in the case of an accident. Asahikawa Medical University has taken this concept a step further. "We have developed a medical record management system called Medical Record Link that patients themselves can manage," says Yoshida.

The Medical Record Link system, referred to at the AMU as a 'hotline for doctors,' works by having individuals input their medical information into an online system hosted on AMU's server, which was developed with the support of the Japanese government. The system is aimed primarily at giving doctors access to the patient information they need to develop the most appropriate treatment plan for a given patient, even if they have never seen that patient before. Information such as blood type or whether a patient has a pacemaker or an allergy to certain medicines, for example, can have profound consequences for treatment options.

The Medical Record Link allows patients to give a doctor access to their personal medical information stored on the system using their mobile phone. Entering their private security code brings up vital up-to-date health information that can help the doctor decide on a course of treatment. Patients can also grant doctors access to their record, giving clinicians the ability to access and update patient information. A number of organizations in Japan have expressed interest in adopting the system for their patients. "The National Cancer Center in Japan, for example, would like to make this system available to people with cancer," says Yoshida.

An added benefit of the Medical Record Link that came to the fore in 2011 derives from its implementation on dedicated servers at AMU—a fact that will allow it to remain operable during national disasters even when other network services have been knocked out or rendered



Medical Record Link: Using mobile phones to give individuals more control over their health

inaccessible due to high call volumes. In fact, the university recently conducted an experiment using mobile phones in Kesennuma, one of the areas in northern Japan hardest hit by the recent major earthquake that rocked the area. Using the system, psychiatrists at AMU were able to monitor the mental health of evacuees remotely by mobile phone.

The Medical Record Link, like AMU's telemedicine technology, exemplifies the community-focused medical research being conducted by the university. Established in 1973, Asahikawa Medical University has become Hokkaido's core medical university, training physicians that work closely with the local community. That community spirit now extends worldwide, with medical technologies that are already starting to make a difference in people's lives and contribute to the equitable delivery of medical care.



Asahikawa Medical University
 2-1-1 Midorigaoka-Higashi, Asahikawa,
 Hokkaido 078-8510, Japan
 Tel: +81-(0)166-65-2111
www.asahikawa-med.ac.jp/english/

