GREATER OSAKA BEGINS A NEW CENTURY OF BIOSCIENCE

The Greater Osaka metropolitan area is home to the world’s leading research facilities. In addition to the renowned academic institutions like Osaka University and Kyoto University, there is the Saito Bio-Medical Cluster in northern Osaka, which aspires to be Japan’s leading hub for drug discovery. To the west is SPring-8, the world’s most powerful synchrotron radiation facility. The Kobe Medical Industry City hopes to become the future center for regenerative medicine. In the Kansai Science City and many other locations, key national projects in the field of bioscience are underway.

In Osaka Prefecture, the heart of the Greater Osaka, is found a significant cluster of Japanese pharmaceutical companies, which trace their history back for four centuries. Their research facilities are flanked by other research institutions including Osaka University and the National Cardiovascular Center. Based in Osaka are over 2000 scientists, the world authority in immunology, Dr. Tadamitsu Kishimoto, among them, all engaging actively in their fields of research. The National Institute of Biomedical Innovation recently started up as the core facility in pharmaceutical and biomedical research to conduct work in advanced areas of science and technology such as genome science. Private enterprise and academic institutions are in partnership in many forms, generating numerous bio-ventures. Several devices are in place to promote such ventures.

The Biotechnology Business Competition JAPAN, the country’s leading biotechnology competition, is held in Osaka. The Saito Bio Incubator was set up by the public sector but is run by the private sector. The Saito Liaison Office was established to propel links between industry and academia in the biotechnology sector. Osaka is rich in innovative and ingenious ideas that lead the way forward for the rest of Japan. By way of illustration, AnGes MG, Inc. is a bio-venture company that has grown successfully to be publicly listed, the first to do so as a venture that originated from university research. There are many other university-seeded bio-ventures with extremely original ideas. Osaka is the birthplace and nursing bed for the growth of such biotechnological innovation, and thus one of the foremost biotech clusters in Asia.

In September next year, Osaka will host BioJapan 2006, one of the most esteemed biotechnology events in Japan, attracting Japanese and international researchers working in the field of bioscience, alongside representatives of private enterprises and bio-clusters. The world’s leading-edge bioscience topics will unfold in full array.

Osaka promises you new and exciting encounters in bioscience.

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I look forward to welcoming as many visitors to osaka as possible. Let us talk about bioscience!

Governor of Osaka prefecture
Fusae Ohta

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North Osaka, rich in potential, Home to a growing world-class biotech cluster

North Osaka - the hub of drug companies, academic and research institutions

North Osaka is home to Osaka University, the National Cardiovascular Center and numerous other academic and research institutions conducting world-class research. The surrounding areas of Kyoto, Kobe and Nara also have research bodies and industries of the biotech sector.

Worthy of special note is Doshomachi, an area in central Osaka City. Osaka has long been a leading center of commerce in Japan, where rice and many other commodities were gathered and then distributed to other parts of the country. It was highly prosperous in the Edo era and Doshomachi attracted manufacturers and wholesalers of drugs. To this day, the area is a hub of major pharmaceutical companies on a scale rarely found in the world. It plays no small part in the economic vitality of Osaka.

Capitalizing on such potential, a plan to create a world-class bio-cluster in North Osaka galvanized into action at the start of the 21st century. The OCCI set up the Bioindustry Promotion Committee as a vehicle for realizing the plan, adopting promotion strategies, campaigning with central government, organizing platforms for bio-industry promotion and much more.

Tanabe Seiyaku Co., Ltd a key Doshomachi company

Tanabe Seiyaku Co., Ltd. was the first company in Japan that engaged in the manufacture and selling of drugs.

Tanabeya Matazaemon, a business tycoon, obtained a trade license from the Shogun in 1604 and started trading drugs and other products with parts of Asia. In 1678, his descendant, Tanabeya Gohei, started making and selling a herbal composite in Tosabori (near Doshomachi). This is how Tanabe Seiyaku began. It has one of the longest histories among pharmaceutical companies in the world. Today, it plays a key role in Doshomachi and together with Takeda Pharmaceutical Company Limited has been a keen and full supporter of the North Osaka Bio-cluster Project since its inception.

Tanabe Seiyaku is well known as the originator of Diltiazem. It is now directing its energy into the marketing of Remicade, a remedy for Crohn’s disease and rheumatoid arthritis. Among drugs under developed are Roflumilast (now in its final clinical study phase), a therapeutic agent for asthma and COPD, and highly innovative drugs with unique mechanism of action for diabetes and polliakuria. In research, extensive alliances with Japanese and foreign companies and institutes have been formed in the pursuit of leading-edge drug development research.

Deeply rooted in Osaka, Tanabe Seiyaku is helping to create the North Osaka Bio-cluster, so as to provide new and excellent products to the world.

North Osaka Bio-cluster

High hopes from pharmaceutical companies

It is becoming increasingly difficult for an individual pharmaceutical company to develop a new drug due to the difficulty in finding “seeds” or due to limited funds. In order to reduce the risks of development and to ensure a higher success rate of new drug candidates, good liaison is essential among industrial, academic and government sectors.

The North Osaka Bio-cluster, exemplary in this respect, has raised great hopes of innovative drug development. The OCCI has taken on the role of coordinator, providing support by offering various platforms.

The North Osaka Bio-cluster hopes that pharmaceutical companies and other bio-clusters, irrespective of Japanese and foreign, will form partnerships that will lead to the creation of new drugs, in turn generating opportunities for widening the vision of Osaka researchers.

OCCI, leading the way in North Osaka Bio-cluster formation

OCCI Activities

Bio-industry promotion strategy - Bio Information Highway Plan Phase II in progress

In 2001, as a North Osaka Bio-cluster promotion strategy, the Bio Information Highway Plan Phase I was initiated. Together with Osaka Prefectural Government and Osaka University, OCCI successfully attracted 23 billion yen worth of national projects and facilities including the BioGrid Center Project and drug discovery projects of the National Institute of Biomedical Innovation, the Knowledge cluster initiative and the Saito Bio Incubator. In the wake of this success, Phase II was begun in March 2004. The platform activities listed below are among the 25 projects now in progress.

Many platform activities

An excellent platform has been provided for the promotion of joint development through three-sector collaboration, especially in medical device, R&D support equipment, functional foods, and nanobiotechnology, and for the creation of bio-ventures originating from university research seeds.

1. Japan Bio-technology Business Competition

OCCI holds this competition in association with the Osaka Prefectural Government, aiming at venture-company creation and technology transfer. 28 bio-ventures have already started up, 15 technology transfers, 49 joint research and private business subsidized projects, 30 investment and loans, and 30 successful research funding bids are all to its credit.
2. Forum for Industrialization of Next Generation Medical System

Joint development of medical device is undertaken by indicating clinical needs and offering development seeds to private enterprise direct. Over 100 companies take part and over 25 universities and medical institutions across Japan make proposals. 43 proposals are being discussed with a view to joint development. 14 proposals have already seen commercialization.

3. Study Group on Development of Functional Food

Utilizing the latest information on functions and safety of foods, the Group develops new products and verification methods.

4. Internet marketing of new drug discovery seeds

Dormant drug discovery seeds and technologies are listed on the Internet so they can be commercialized. Under trial operation.

5. Bio Business School supported by NPO Bio Business Station

Bio Business Station, an NPO set up to support bio-ventures, is supporting the School help create and foster venture companies.

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Osaka University’s origin
Schools set up by citizens

Osaka University has its roots in Kaitokudo and Tekijuku, schools set up by citizens in the Edo period.

Kaitokudo was founded in 1724. A place of learning for the people of Osaka, it flourished for 150 years and is the forebear of the arts faculties of the University.

Tekijuku was founded in 1838 by Ogata Koan. It had a school and a medical clinic, which later gave rise to the University’s medical school. Ogata had studied medicine and Rangaku (Western learning through Dutch) in Nagasaki, the only window open to the outside in isolationist Japan. Through Tekijuku, he introduced smallpox vaccination and cholera treatment while educating a total of over 1000 students. Students became dynamic forces in the shaping of modern Japan, including Tsunetami Sano, founder of the Japan Red Cross Society and Sensai Nagayo, the pioneering scholar of hygiene in Japan.

In 1931, the Osaka Imperial University was inaugurated, backed by citizens’ support and help in funding. The building of the university hospital was partly funded by public donations. Productive liaison between industrial, academic and government sectors is greatly desired today. Osaka University’s history is a real embodiment of the concept.

Herein lies the baseline of our motto, Live Locally, Grow Globally.

Free of preconceptions,
Eagerness to face new challenges

Kaitokudo believed that education was the most important legacy of its age. Even during recession, it taught philosophy, shunning utilitarian subjects such as accounting. Tekijuku did not confine its learning to medicine and Rangaku but included the humanities in its curriculum. Osaka University is proud of such heritage and values both basic and applied research in the natural sciences as well as cultural sciences.

Our breadth of vision is reflected well in our organization and research topics.

The School of Human Sciences teaches students to scrutinize the very essence of human beings. The School of Engineering Science is based on an interdisciplinary approach to teaching and research in science and engineering. The University’s medical and engineering faculties have joined forces to create successful new disciplines such as Bioinformatics and Business Engineering, a fusion of marketing and technology.

The Faculty of Medicine has long pursued the now-popular research combining brain functionality and proteins. In the fields of sugar chain and immunology research, the University is a world leader. In association with other institutions, the University this year will start a new project on children’s mental health.

Our breadth of vision engenders the eagerness to face new challenges free of preconceptions a precious gene that the University will pass on to posterity.

New campus in Nakanoshima
Stronger contribution to the community

Under a new system of independent administration since 2004, Osaka University’s free and liberal spirit has been strengthened.

Each year, 200–300 patents are granted to the University and more than 50 venture companies have sprung up, ranking the University among the top in Japan on this score.

Last spring, the Nakanoshima Center was established, a third campus site located in the heart of Osaka City. Consultancy and seminars on technology and management topics for private business as well as public lectures/courses are on offer.

In the vicinity of Osaka University are located the National Cardiovascular Center, the National Institute of Biomedical Innovation, the National Museum of Ethnology and many other educational and research institutions. Personnel interaction with these will be further promoted so that together we may serve the community and develop our network with the world.

Rooted in the local community but spreading wings globally, such are the human resources and research results that Osaka University aims to foster: Live Locally, Grow Globally the encapsulation of our aspiration.

http://www.osaka-u.ac.jp
Back to the basics

An immunologist turned clinical scientist turned administrative innovator, Tadamitsu Kishimoto now has a chance to return to his first love—basic science

In the 1970s and 1980s Tadamitsu Kishimoto made a name for himself by pursuing abstract scientific questions about how the immune system regulates itself. From the late 1980s he enhanced his prestige by translating his findings—notably the discovery of interleukin-6 (IL-6) and its receptor—into clinical treatment for autoimmune diseases. From the late 1990s, as the president of Osaka University, he helped establish a research framework that promises to support innovation at the forefront of research for years to come.

A man of many hats, Kishimoto is once again donning the one that is most comfortable for him—that of basic scientist. With support of the five-year US$5 million grant from Chugai Pharmaceutical Co. Ltd, he will head back to the laboratory to address a basic science question that still nags at him.

Kishimoto’s first major success came in 1986 with the discovery and cloning of interleukin-6, a gene first identified as giving rise to B-cells. [Hirano T, et al. Nature 324; 73-76.] It was a time when many scientists were proposing different names for factors known, but not yet isolated and identified, to stimulate B cell production. “Faxes were flying back and forth,” he recalls. “It was a very exciting time.”

Kishimoto says his medical training was of little use in these early stages when his team was struggling with the molecular techniques necessary for pulling the molecular needle out of the haystack. But his tenaciousness paid off. After much struggle, his team succeeded in isolating cDNA for what would be known as IL-6.

And when the cDNA threw up a surprise—being present in benign heart tumors that induced autoimmune disease symptoms such as fever, joint pains and anemia—Kishimoto’s medical instincts kicked in. Following the pathway of IL-6, he identified its receptor unit—and one part of this unit was found to be involved in the signal-receptor process of a whole class of proteins that regulate the immune system. The discovery changed the way people thought. [Taga, T et al, Cell 58; 573-581]

In 2003, at age 64—an age when most Japanese researchers are told to retire—he returned to the laboratory with the help of the Chugai’s grant. He is happy to be back addressing basic scientific problems.

He realizes that the question he laid before himself will be a tough nut to crack. “We know that IL-6 therapy has a dramatic effect. But we don’t know what changes before and after the treatment,” he says. He will begin by analyzing gene and protein expression profiles. “This could tell us what causes diseases like rheumatoid arthritis,” he says. Not satisfied with a partial understanding of IL-6’s connection to disease development, he seeks the underlying basic principles. “I’m almost finished,” he says.

To ensure the international competitiveness of his university he created new graduate schools that have opened the doors for unique interdisciplinary research. “For the next step in research, the fusion of biology and nanotechnology will be very important,” he says.

The institutes have allowed Toshio Yanagida, an engineer by training, to pursue his instinctual grasp of the molecular processes. He can follow his fancy—and single molecules—around the cells to understand how they do their physical work in changing the cells’ structures. Keiichi Namba was able to use electron cryomicroscopy to unravel the nanoscale machine-like properties of the helical flagellar filament. [Nature, 424: 643-650 (2003)]

In the early 1990s Kishimoto began investigating clinical applications of his findings in autoimmune diseases such as rheumatoid arthritis and Castleman’s disease, a rare disorder in the lymphatic system that causes benign tumors. Working with Chugai, they found that blocking IL-6 improves anemia and serum levels of the C-reactive protein in Castleman’s disease patients. An antibody for this orphan disease went on the market in June 2005 in Japan. Chugai will apply to use the antibody for treatment of rheumatoid arthritis patients in 2006 in Japan, where clinical trials concluded this year, and is developing an arthritis treatment with Roche in Europe and the United States where clinical trials are underway and an application will be submitted in 2007.

Since 1997, Kishimoto says he was continually distracted from the excitement of discovery by his concern for the future of Osaka University, where he became president in 1997.
SPOTLIGHT ON OSAKA

Osaka University, 21st Century COE Program

Research Candidates for the Future Advanced Medicine

Promotion of Translational Research: Verification of the Potential

Center for Integrated Cell and Tissue Regulation

Osaka Univ.
CONTRIBUTION TO INFECTIOUS DISEASE PREVENTION AND CONTROL
ESTABLISHMENT OF JAPAN-THAILAND RESEARCH COLLABORATION CENTER
(RCC) On Emerging And Re-emerging Infections By The Research Institute For Microbial Diseases, Osaka University

THE RESEARCH INSTITUTE FOR MICROBIAL DISEASES

The Research Institute for Microbial Diseases at Osaka University stands as the central research organization for the research of infectious diseases in Japan. Scientists are researching a broad range of topics from basic study of microbiology to human immunology and clinical application of new vaccines utilizing the most advanced laboratory equipment available.

Throughout its history, the institute has achieved many significant research results, including the discovery of Vibrio parahaemolyticus and other pathogenic organisms and the development of vaccines, and contributed the results to society via the Research Foundation for Microbial Diseases of Osaka University, a vaccine manufacturer.

Currently, our world is being attacked by new emerging infectious diseases such as avian influenza, severe acute respiratory syndrome (SARS), and bovine spongiform encephalopathy (BSE), and the social and economical damage by such is immense. It is therefore essential to develop and integrate international research networks in order to contain these infectious diseases.

The Research Institute for Microbial Diseases, Osaka University, established the Japan-Thailand Research Collaboration Center (RCC) on Emerging and Re-emerging Infections in September 2005 with the purpose of extending its research network to other areas in Asia.

This project is part of the “Research Center Establishment Program for Containment of Emerging and Re-emerging Infectious Diseases” funded by the Ministry of Education, Culture, Sports, Science and Technology of Japan and in addition to the Research Institute for Microbial Diseases of Osaka University, the Institute of Medical Science, University of Tokyo and the Institute of Tropical Medicine, Nagasaki University, also participate in the program and are going to establish research centers and construct international research networks in China and Vietnam, respectively, for collaborative research and information dissemination in Asia.

http://www.biken.osaka-u.ac.jp/e/
INTERNATIONAL FUNCTION FOR PROTEIN DATABASE

The three-dimensional (3-D) structure of proteins and other biological macromolecules stored in the Protein Data Bank (PDB) are essential for life sciences. IPR (PDBj) is contributing to the construction and dissemination of a protein 3-D structure database, in cooperation with centers in the United States (Research Collaboratory Structural Bioinformatics) and Europe (European Bioinformatics Institute). IPR (PDBj) has also established the Osaka branch of BioMagResBank (BMRB) for world-wide biological NMR database in collaboration with University of Wisconsin. Visit the website to deposit your data and search for what you want.

URL: http://www.pdbj.org/

PDBj (one of wwPDB members for Protein structure database)
BMRB Osaka Center for Biological NMR database

INTERNATIONAL JOINT-USE INSTITUTE

The Division of International Collaboration Research, led by a foreign principal investigator, was established this year as a key station for international scientific collaboration.

Foreign visiting professors and international collaborative researchers are joining the research at IPR with financial support.

Support is provided to enable researchers from overseas to make use of facilities such as MS, NMR (solution & solid), and the SPring-8 beamline, which was designed for biological macromolecular assemblies, in their research. Participation is elicited every year (visit IPR website)

http://www.protein.osaka-u.ac.jp/
SPOTLIGHT ON OSAKA

NATIONAL INSTITUTE OF BIOMEDICAL INNOVATION (NIBIO)

Established in April 2005 as a core center for fundamental technology of drug development
The first research organization established by the Ministry of Health, Labour, and Welfare to support and assist the development of novel drugs, etc
Active promotion of interaction and support among pharmaceutical companies, universities/research institutes, and national research organizations

NIBIO conducts the following activities through its pharmaceutical industry-government-academia collaboration:

| I. RESEARCH FOR BIOMEDICAL INNOVATION | Development of new technologies for standard use in the development of novel drugs, etc. |
|--------------------------------------|--------------------------------------------------------------------------------------|
| 1. Toxicogenomic research for drug safety evaluation |
| 2. Protein analysis research on human diseases using human biological materials |
| 3. Basis technology development for effective utilization of human disease-related proteins |
| 4. Basic research for new generation vaccine and antiviral agent development |
| 5. Basic research for new generation antibody production |
| 6. Development and application of gene transfer technologies |

| II. RESEARCH FOR BIORESOURCES | Research on bioresources for use in experiments and studies of drugs, etc. |
|-------------------------------|--------------------------------------------------------------------------|
| 1. Gene bank (JCRB: Japanese Collection of Research Bioresources) |
| 2. Cell bank (JCRB) |
| 3. Experimental animal models (JCRB) |
| 4. Research Center for Medicinal Plant Resources |
| 5. Tsukuba Primate Research Center |

| III. RESEARCH AND DEVELOPMENT PROMOTION | Research consignment for the development of novel drugs, etc. Promotion of orphan drug development |
|----------------------------------------|---------------------------------------------------------------------------------------------|
| 1. Programs for basic research promotion |
| 2. Programs for commercialization support (Bayh-Dole consignment to venture companies) |
| 3. Programs for research and development promotion of orphan drugs, etc. |

Director general: Dr. Koichi Yamanishi
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A considerable amount of research is also being carried out on natriuretic peptides. Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) have already been developed for clinical use in diagnosis and therapeutic drugs for heart failure. Research is also underway on the use of C-type natriuretic peptide (CNP) to prevent restenosis after percutaneous transluminal coronary angioplasty (PTCA) for ischemic heart disease and to reduce cardiac hypertrophy and fibrosis after myocardial infarction.

Noritoshi Nagaya
Director, Department of Regenerative Medicine and Tissue Engineering:
Progress in Application of Myocardial and Vascular Regeneration Using Cells and Peptides

Dr. Noritoshi Nagaya, Director of the Department of Regenerative Medicine and Tissue Engineering at the Advanced Medical Engineering Center, is engaged in research which ranges broadly from basic research to clinical applications, such as transplantation of bone marrow-derived mesenchymal stem cells and allogeneic and xenogenic organ replacement. Therapy for dilated and ischemic cardiomyopathy, in which myocardial and vascular regeneration is brought about with transplantation of bone marrow-derived mesenchymal stem cells, has been developed in collaboration with the Departments of Cardiovascular Medicine and Cardiovascular Surgery, and is already being used in clinical practice. Regulatory peptides have also been used in the development of therapies for intractable heart diseases. Ghrelin has been tried in the therapy of heart failure and adrenomedullin has been applied in translational research on the vascular regeneration in myocardial infarction, pulmonary hypertension, and peripheral artery obstruction.

Other topics of interest include the creation of genetic experimental models such as mini-pigs with stable SLA genes and a known genetic background, tailor-made tissue transplantation in which patients’ cells are incorporated into allogeneic or xenogenic decellularized tissues, optimal methods for isolating and preserving donor organs in heart or lung transplantation, and immunosuppressive therapy for organ transplants.

Shigeo Wakabayashi
Director, Department of Molecular Physiology:
Challenge from Basic Science for Overcoming Cardiovascular Diseases: Elucidation of Structure, Function and Pathogenic Significance of Ion Transport Proteins

Cardiovascular diseases are closely linked to abnormal regulation of ion concentrations such as Ca++, Na+, and H+ in cardiac and vascular cells. Dr. Shigeo Wakabayashi, Director of the Department of Molecular Physiology, and his colleagues have elucidated the molecular structures, detailed functions, and pathogenic significance of Na+/H+ and Na+/Ca++ exchangers which regulate myocardial ion metabolism. They are also trying to elucidate the regulatory mechanism which involves various factors (such as CHP), myocardial and vascular regeneration in myocardial infarction, pulmonary hypertension, and peripheral artery obstruction.

Research is also being conducted on the molecular mechanisms involved in, for example, how abnormalities of cytoskeletal proteins lead to muscle degeneration as well as cell death in intractable cardiomyopathy and
muscular dystrophy. It was recently found that the stretch-activated Ca\(^{2+}\)-permeable channel (TRPV\(^{\text{h}}\)) is activated in the muscle-cell membranes of model animals and patients having such degenerative diseases, and that excess Ca\(^{2+}\)-influx mediated by this activation is a dominant factor resulting in muscle degeneration. The development of new drugs capable of specifically targeting such Ca\(^{2+}\)-permeable channels is another important research topic.

**Naoki Mochizuki**
Director, Department of Structural Analysis:
Bioimaging for the Visualization of Cardiovascular Cellular Mechanisms of Contraction and Motility, and Cell-cell Adhesion

Bioimaging, which shows in images how and where proteins function in living cells, is at the cutting edge of molecular biology. Dr. Naoki Mochizuki, Director of the Department of Structural Analysis, and colleagues have been using bioimaging in their research on cardiomyocyte, vascular smooth-muscle cell, and vascular endothelial cell mechanisms of contraction and motility and cell-cell adhesion. Some research results obtained through the movement of Fer tyrosine kinase localized to microtubules and of FBPI\(^{\text{h}}\) involved in endocytosis have been posted on their web site.

They have also developed an intracellular molecular imaging technique based on FRET (Fluorescent Resonance Energy Transfer) to visualize molecular on/off switching of molecular weight GTP-binding proteins. Through further integration of protein structural imaging and bioimaging, they are taking aim at functional analysis of the target molecules which would be employed in the next generation medical methods, and drug development.

**Hidehiro Iida**
The Advanced Medical Engineering Center Director, Department of Investigative Radiology:
Progress in Imaging Technology for Diagnostic Imaging Devices, and Potential for Use of Imaging in Early Diagnosis and New Drug Development

At the Advanced Medical Engineering Center, Department of Investigative Radiology, Director Dr. Hidehiro Iida and colleagues are evolving imaging technologies for cutting-edge diagnostic imaging equipment (including PET, MRI, SPECT, and X-ray CT) that are indispensable for the diagnosis of cardiovascular disease. A new PET system that compensates for patient movement, requires less time, and is less stressful for patients is currently being introduced into clinical applications.

The Center is also working toward the construction of an integrated diagnostic imaging system using molecular imaging, that will combine diagnostic imaging with the use of tracers (ligand/nanoparticle-peptide etc.) For new drug development, this system can be used in preclinical and clinical trials. In the future, it is hoped that diagnostic imaging and tracers can be applied not only in the area of cardiovascular disease, but also to the early diagnosis of cancer and degenerative diseases such as Parkinson’s disease, and to the target selection for new drug development.

**NANOMEDICINE**

**Hidezo Mori**
Director, Department of Cardiac Physiology:
Nano-Level Imaging Technologies for Structural and Functional Analysis of Disease-Related Proteins and New Microangiography for Clinical Use

Dr. Hidezo Mori, Director of the Department of Cardiac Physiology, and his colleagues are engaged in research aimed at next generation therapy based on the two fields of basic research and translational research.
To ensure long, energetic and healthy life in a sustainable industrial society

R & D in medical engineering to sustain and boost human health: Working in Kansai, the hub of public, private and academic sector activities in life science

The National Institute of Advanced Industrial Science and Technology (AIST) is a public research organization formed from the 15 research laboratories of the former Agency of Industrial Science and Technology and acquiring independent administrative institution status in 2001. Research activities have been ongoing in many fields but the unifying aim is to improve standards in industrial technology. President Hiroyuki Yoshikawa believes, “Improving Japan’s industrial technology standards is necessary not only as a means of honing our country’s international competitiveness but also as a means of creating a sustainable society, a task now facing all mankind. We can expedite the realization of a stable world order.”

President Yoshikawa explains: “Life science and biotechnology are expected to make important contributions to overcoming these problems that we face.”

AIST Kansai is AIST’s research center in the Kansai area. Its development effort focuses on medical engineering that would assist in maintaining and boosting health in an aging society. President Yoshikawa adds, “Kansai is home to a large number of public, private and academic sector bodies in the life science and medical engineering sectors. We are conducting our activities in close liaison with them.”

Discovering treatments for stress-related diseases by developing identification and measuring methods of stress markers

We live in an age full of stress. Anxiety, anger and sorrow resulting from human relationships, fatigue from work, noise, toxic chemical substances, viruses, bacteria, ultraviolet radiation and other natural threats – the sources of stress around us are countless. Stress is not only threatening our physical bodies but also our mental health.

AIST’s Human Stress Signal Research Center (HSSRC) interprets stress broadly as stimuli and signals to living organisms. HSSRC is researching the interrelationship of stress with the human body and health with the primary aim of identifying stress markers. Director Etsuo Niki remarks, “We have already succeeded in the identification of several types of stress markers. At present, we are verifying their effectiveness.” Development in tandem is underway on devices that would speedily make quantitative measurement of these stress markers. A lab-on-a-chip for stress marker measurement has already been created.

“Our ultimate aim is to develop new diagnostic, prevention and treatment methods of stress-induced diseases, which would in turn create and successfully develop a comprehensive health industry that improves quality of life for all,” says Director Niki of his ambition.

**Human Stress Signal Research Center**

[http://unit.aist.go.jp/hss-center/index_e.html](http://unit.aist.go.jp/hss-center/index_e.html)

Contributing to regenerative medicine through new technologies for measuring and manipulating cell function and for cell and tissue utilization

One of the central issues in the post-genome era is to move toward manifesting functions equivalent to or better than those of natural cells by understanding the movement of biological molecules and the flow of information transmission in living cells, and by manipulating living cells. However, Director Noboru Yumoto of the AIST’s Research Institute for Cell Engineering (RICE) states, “We have already reached the limits of conventional cell engineering and genetic manipulation technologies, and breakthroughs based on fusing these with other technologies are being sought around the globe.”

The RICE has developed technologies that regenerate and replace on the cellular and tissue level bodily functions lost by disease or accident. Director Yumoto says, “One of these technologies regenerates tissues such as bone, cartilage, cardiac muscle and blood vessels using three-dimensional cell culture technology, and is able to make tissues and cells with notably superior biocompatibility.”

Moreover, cell chips that make possible a comprehensive analysis of genes that carry out cell functions, and a “bioluminescent molecular probe” that is useful in visualizing the molecular events in living cells have also been developed. According to Director Yumoto, “We are conducting further research targeting the development of technologies that can manipulate cells based on the cell information obtained by these technologies.”

**Research Institute for Cell Engineering**

[http://unit.aist.go.jp/rice/english/index_e.html](http://unit.aist.go.jp/rice/english/index_e.html)
COLLABORATIVE RESEARCH FACILITY IS OPENED TO BIOVENTURE BUSINESSES

A biotechnology-related collaborative research facility has been established at AIST Kansai. To activate the R&D potential and technological seeds that AIST has, occupancy and use of laboratories and research rooms is being offered to businesses and researchers aiming to create venture businesses and new industries. Advanced measuring instruments such as electron microscopes can be utilized and collaborative research with AIST can be efficiently conducted.

SUCCESSFUL IDENTIFICATION AND STRUCTURAL DETERMINATION OF OXIDATIVE STRESS MARKERS

HSSRC recently succeeded in identifying new oxidative stress markers (Biochem. Biophys. Res. Commun. (2005) 336, 1-9). The method of structural determination and analysis of oxides of such lipids as linoleic ester and cholesterol, and of oxides of such proteins as peroxiredoxin (Prx) and DJ-1 has been established, and it has been confirmed that the blood concentrations of these oxides correlate with a variety of diseases. “In the future we aim to use these markers for diagnosing bodily health, for the early detection of disease, as well as for evaluating the efficacy of foods, supplements and drugs.” (Director Niki)

DEVELOPMENT OF THE WORLD’S FIRST ENZYME CHIP THAT ANALYZES THE INTERACTION OF NEW DRUG CANDIDATE SUBSTANCES AND TARGET PROTEINS USING MULTIPLE SAMPLES

A new type of enzyme chip has been developed by RICE (Nature Biotechnol. (2005) 23, 622-627). If, for example, multiple types of enzymes are fixed to a chip and allowed to react with a new drug candidate substance, the specificity and the strength of the interaction of the compound with multiple enzymes can be quickly analyzed. Jun Miyake, Leader of TERC, explains, “The development of new drugs until now often had to be discontinued due to adverse reactions in the later stages of the development. However, if use of this chip allows simultaneous and efficient analysis of efficacy and safety on the level of molecular interactions, then the pharmacological efficacy and adverse reactions of compounds can be grasped at an early stage prior to pre-clinical studies.”

A TECHNOLOGY TO COMPENSATE FOR DISABILITIES BASED ON NEUROIMAGING RESEARCH IS UNDER DEVELOPMENT

The Living Informatics Group, Institute for Human Science and Biomedical Engineering has been conducting unique collaborative research at AIST Kansai involving universities, hospitals and businesses in the Kansai region.

Non-invasive methods such as the measurement of brain magnetic fields and electroencephalogram have been used to research human sensory and language systems, and specifically, early practical applications are expected to address:

1. Development of algorithms to measure and analyze brain functions with high temporal and spatial precision, and use of these algorithms to clarify higher order visual cognition processes and the neurological basis of language function disorders; and
2. Development of technologies to compensate auditory function based on understanding the cerebral mechanisms of bone-conducted ultrasound perception.

Stress-marker for oxidatively modified proteins (Biochem. Biophys. Res. Commun. (2004) 317, 722-728)
Research and development has remarkably been progressed in the field of life science. Aiming to promote innovative research in advanced field of life science, it was strongly anticipated to establish facilities to support research and development for international, interdisciplinary and cross-industrial projects. Based on the concept of Northern Osaka, to be a franchise in life science research, said by Dr. Yuichi Yamamura of ex President of Osaka University, Senri Life Science Center Co. Ltd and Senri Life Science Foundation were established in March 1988 and July 1990, respectively.

The Foundation is implementing public programs promoting life science through supporting knowledge-based cluster creation project, and organizing scientific forum and technical workshop as a program to bring up man of ability, as well as continuous alliance with universities and research institutes. The knowledge-based cluster creation project is aiming to produce innovative drugs in Northern Osaka area and has facilitated research for molecular targeted drug and therapy to immunity-infection diseases, leading to active fruits.

The Foundation will keep in mind of clear vision on creating bio-medical cluster fostering industry with global competitiveness.

Senri Life Science Center is the facility where the Senri Life Science Foundation bases its activities. The Center is located in the green hills of northern Osaka, but is accessible in only 15 minutes from both Osaka International Airport and Shin Osaka (Bullet Train) Station. From downtown Osaka, it takes 20 minutes by subway. The Senri Life Science Center is surrounded by several research institutes including those of Osaka University.

A convenient transport system and strong alliances with research facilities near the Center make it an ideal place for international conferences. The center has two halls, one exhibition room and 14 seminar rooms. A simultaneous interpretation system and PC connection facilities for presentation accommodation are available. On site accommodation provides a perfect atmosphere for interaction. Hotel accommodation is also available within walking distance.

Senri Life Science Foundation
Senri Life Science Center Co. Ltd
Senri Life Science Project
Detailed information should be requested to Senri Life Science Center, Co. Ltd.
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TEL +81 6 6873 2010 (reservation) FAX +81 6 6873 2011
Building a Drug Development Value Chain That Ensures Promotion of Efficient Collaboration between BioResearchers and the BioIndustries in Japan and Acceleration of New Drug Development

The NPO BioGrid Center Kansai was established in 2004 under the auspices of the “BioGrid Project” which was begun with research consignment by the Ministry of Education, Culture, Sports, Science and Technology for new drug development. The BioGrid Project is conducting genetic analysis and protein structure prediction and developing software necessary for the in silico screening of promising drugs and the simulation of biological responses to proteins. This project has established what may be called a huge virtual laboratory, where Osaka University, related research institutions, and the industries are connected by high-speed, high-volume, and secure communications lines.

The objectives of the NPO BioGrid Center Kansai are to support the operation of this information infrastructure network and to ensure prompt technical transfer of research findings to the industry. The institute is also undertaking intellectual property management and exploitation, marketing, nurturing of research-oriented enterprises, support of venture companies, and the like. One of the significant achievements of the institute is the establishment of a drug development value chain. The expertise of academia, bioventures, and major IT corporations is incorporated in the value chain to optimize its workflows and in silico drug development is conducted. Also, in combination with the chemical synthesis of compounds, lead compounds are created through the value chain. The institute utilizes some of the most advanced technology in the world, such as “SPring-8,” a large-scale synchrotron radiation facility, for protein crystallographic research and a supercomputer system known as the “Earth Simulator” for optimization of in silico screening and lead compound creation.

The value chain comprises a system capable of responding to the expectations of global pharmaceutical industries, beginning with the discovery of the protein causing a disease, to the efficient and continuous creation of lead compounds.

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Osaka has been historically known as the “city of merchants” and the spirit of entrepreneurship lives on today. “Go and do something different and interesting,” people would say.

In Saito, you will find this vitality of Osaka embodied in its research network and business network key facilities including Osaka University, the National Cardiovascular Center, and the National Institute of Biomedical Innovation, life science sector companies, bio-ventures, venture supporters, economic organizations, local governments. We all await you with a very warm welcome.

The Saito Bioscience Seminar is a twice-a-month event when researchers, private enterprise, venture managers and business supporters working in Saito come together.

Each Seminar is given by a guest lecturer who is an expert in leading-edge research or business. New human networks and collaboration result from these sessions.

**Collaboration through Liaison between Industrial, Academic and Government Sectors**

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**Incubation Facilities at Saito Bio Incubator**

In order to commercialize seeds that research bodies in Osaka possess, an entrepreneur incubator facility has been in operation since July 2004, the Saito Bio Incubator.

This Incubator was built by government funding but is leased out to Bio Sight Capital Co., Ltd., a venture capital firm. This is the first attempt at a government-built privately-operated system, aimed at harnessing private-sector know-how in order to provide a broad range of incubation support.

Currently, over 20 bio-venture and other companies are tenants at the Incubator, which is now fully occupied. In the adjoining Saito Bio Hills Center (see photo on left), some ten rental lab spaces are planned to be made available as an extension to the Incubator.
SPOTLIGHT ON OSAKA

Saito Life Science Park Promotion Council
Address: NS-bldg. 8F, Tanimachi 2-2-22, Chuo-ku, Osaka City, 540-0012 E-mail: info@saito-kokubun.co.jp URL: http://www.saito-kokubun.co.jp/eng/

Saito Bio Hills Center, support for all researchers - opening in the spring of 2006

- Purchasing Reagents, Equipments, etc.
- Library More than 2,000 collections of medical journals etc.
- Meeting Café and space (200 people)
- Rental wet labs (69 m²/room)
- Tennis Court also available for futsal, basketball etc.

Saito Bio Hills Center (next to “Saito Bio Incubator”)

O-BIC

PROMOTING AND FACILITATING FOREIGN DIRECT INVESTMENT IN OSAKA, JAPAN

Located in Osaka, the heart of Japan’s Kansai region, the Osaka Business & Investment Center (O-BIC) was established in April, 2001, through the joint efforts of the Osaka Prefectural Government, Osaka Municipal Government, and the Osaka Chamber of Commerce and Industry (OCCI). Functioning as a one-stop support center, O-BIC promotes foreign direct investment in Osaka and other areas of the Japanese market by offering in-depth assistance and expert advice specifically tailored to the individual requirements of each organization.

Friendly, experienced O-BIC staff members are available to furnish foreign companies with prompt replies to inquiries. All services are available at no charge and strict confidentiality is always maintained.

- Osaka Business Market
- Potential Business Partners & Customers
- Incentives
- Offices, Plants, and Residences
- Human Resources
- Professionals and Supporting Companies
- Information of Foreign Companies in Osaka
- Osaka Facts and Figures
- Information and Support for Business Permits and Approvals

Osaka Business & Investment Center (O-BIC)
c/o Osaka Chamber of Commerce & Industry (OCCI), International Division
2-8 Hommachibashi, Chuo-ku, Osaka 540-0029, Japan
Tel: +81-6-6944-6298 fax: +81-6-6944-6293
e-mail: o-bic@osaka.cci.or.jp
URL: www.o-bic.net

THE 6TH JAPAN BIO BUSINESS COMPETITION CALL FOR APPLICATIONS

First prize: ￥5 million (2 winners)
Second prize: ￥1 million (5 winners)
Other prizes

The Japan Bio Business Competition is the first competition of new ideas of bio-business in Japan jointly supported by the government, academia, and industry in Osaka.

Biomedicine: Drugs, medical devices, medical instruments/analytical systems, regenerative medicine, etc.

Bioscience: Genes, proteins, bio-informatics, etc.

Environmental Bio: Production utilizing biological processes and environment protection utilizing biotechnology

Agricultural Biology: Microorganisms, genetically-modified agricultural products, functional foods, etc.

Nano Biology: Biochips, drug delivery systems, biologically compatible materials and products, medical micromachines, etc.

Application fee: None
Application deadline: Tuesday, November 15, 2005
Applications from overseas are eligible only when the applicants will start up a venture carrying out research activities in Japan.

http://mic.e-osaka.ne.jp/biocompe/
E-mail: biocompe@mic.e-osaka.ne.jp
Limited Six Month Grace Period

It is not widely known but Japan does have a six month grace period. If a researcher publishes a paper before a patent application was filed, Japanese patent rights will not be lost if the researcher files a direct Japanese grace period patent application within six months from that publication date. The grace period claim must be made at the time of filing and certain other conditions are applicable.

Japan’s six month grace period is only applicable where the “person having the right to obtain a patent” has (1) conducted an experiment, (2) made a presentation in an online or printed publication, or (3) made a presentation in writing at a Japanese Patent Office (JPO) designated study meeting.

The direct Japanese grace period application can ONLY be filed as a (i) PCT application designating Japan OR (ii) direct JPO filing within six months from said publication date. Japan’s grace period cannot be claimed by filing a regular or provisional US application first, and then file a Japanese case within one year from the initial US filing date. The grace period filing can only be achieved by (i) or (ii) as described earlier.

Infringement Immunity for Research

Japan’s experimental use provision, section 69(1), provides that “the effects of a patent right shall not extend to the working of the patent right for the purposes of experiment or research.” If the purpose of the research is economical or commercial, said acts will be patent infringement.

The accepted meaning of the phrase “experiment or research” in the Japanese patent law section 69(1) is “experiment or research in order to improve technologies”, and not “experiment or research in order to produce or assign the product covered by the patent”. Experiments conducted to test the commercial viability is not “experimental use”.

Industry commissioned research conducted by academics in Japan will be infringing since they are for commercial purposes. “Experimental use” is determined as an experiment conducted to test only a technical effect of the patented invention for non-commercial purposes.

The Supreme Court of Japan had decided that conducting clinical trials for Japanese regulatory approval is not patent infringement under section 69(1) so long as the acts done before the expiry of the patent are for the purpose of securing health regulatory approval to sell the drug after the expiry of the patent, Ono Pharmaceutical v. Kyoto Pharmaceutical (1999). The scope of this decision is applicable to the clinical trials of pharmaceutical products (generic, new chemical entity or biologic) that requires regulatory approval under Japan’s Pharmaceutical Affairs Law.

Stringent Data Requirements for Therapeutic Inventions

For inventions that claim a pharmacological or therapeutic effect, data describing such an effect MUST be included in the specification as filed. The JPO does not have the USPTO patent practice where an applicant can provide additional post-filing data to support therapeutic assertions made in the specification.

If data demonstrating such therapeutic effect was not found in the specification as filed, the application will be rejected as not enabled and/or not completed. Said pharmacological or therapeutic activity cannot be predicted or inferred, unless it was common general knowledge, and data confirming such activity has to be in application as filed.

While our Firm does not agree with this hardline Japanese position, this position has been endorsed by several Japanese High Court rulings. In recent years, there is an emerging US judicial trend invalidating some pioneering biotechnology patents on the lack of written description and/or enablement grounds. These developments are unfortunate for science and industry as a whole.

Many researchers use the US provisional patent system for a “cheap and quick” patent filing date but the wisdom and value of such cases in Japan are questionable if they do not contain therapeutic data supporting the invention as claimed. So it is advisable to perform more experiments and include as much demonstrative data or working examples in the patent application to have a broader and stronger Japanese and US patent.
AnGes MG, a gene therapy developer, is one of the few Japanese biotech start-ups that fancy investors. Since it was founded in 1999, the spin-off from Osaka University has been on a steady growth path, and now it's about to beat competitors in completing a clinical trial of a key drug candidate. That will pave the way for commercializing genetic medicine, a type of medicine that no one has marketed yet in developed countries.

The most important of three projects in AnGes’s pipeline is developing a drug based on HGF (Hepatocyte Growth Factor) gene. HGF was originally discovered in mid-1980s as a protein that helps hepatic cells multiply. But in 1995, Ryuichi Morishita, Osaka University professor and later founder of AnGes, developed a method to regenerate blood vessels just by injecting HGF genes into muscles.

That discovery has opened the door for curing fatal maladies caused by clogged vessels, such as ischemic heart diseases and peripheral arterial diseases. “There was no fundamental medicine for those diseases. We want to make our medicine available as soon as possible,” says Ei Yamada, President & CEO at AnGes.

Peripheral arterial diseases are often triggered as diabetes progresses, which could lead to deteriorating blood circulations and necrotizing lower limbs. In the U.S., about 100,000 people lose their legs in amputations due to the disease every year. While current treatments cannot ensure a sufficient recovery, HGF genetic medicine could become an easier, safer and more effective treatment. AnGes says HGF genetic medicine has a stronger capability to regenerate vessels and induce less side effects than rival drug candidates.

So far, development looks to be going promptly. AnGes hopes to complete Phase III clinical trial in Japan for HGF genetic medicine for use in peripheral arterial diseases. It also wants to tap the much bigger U.S. and European markets, aiming to end Phase II testing in the U.S. swiftly. And the company has recently found that HGF could be also applied to treat Parkinson’s disease.

In the fledgling biotech industry in Japan, AnGes has always been on the leading edge. One reason, Yamada says, is that HGF gene itself has a huge potential. In addition, AnGes’s able management and strong passion to save patients have led to a number of strategic partnerships. In 2001, AnGes cut a deal with Daiichi Pharmaceutical, which agreed to shoulder hefty expenditure to develop HGF genetic medicine in return for marketing licenses. That alliance enabled AnGes to become the first university start-up to go public in 2002.

In recent moves, AnGes joined hands with Japan’s Alfresa Pharma to develop a drug candidate for atopic dermatitis therapy, which is based on a synthetic gene that inhibits NFkB. It has recently entered Phase I testing in Japan. What’s more, AnGes is developing an effective and safe vector, which helps carry genes into a cell, by using membranes of a virus called Hamagglutinating Virus of Japan (HVJ).

Despite its small size, the 85-employee company sets ambitious goals: to put HGF genetic medicine on market, and to grow out of being a venture company in the near future. “While making efforts to get stronger, we aim to take the next steps towards becoming a comprehensive pharmaceutical company,” Yamada says.
Combating Cancer and Other Severe Diseases Using Novel Innovative Drugs Derived from Hepatocyte Growth Factor (HGF)

**PRODUCT CANDIDATES**

1. **NK4**, a bifunctional molecule as HGF-antagonist and angiogenesis inhibitor, for treatment of cancers.

2. **HGF** for treatment of diseases such as renal failure, hepatic failure, cutaneous ulcer, etc.

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**HGF AS REGENERATIVE MEDICINE**

- HGF plays roles in tissue repair and protection
  - Liver
  - Kidney
  - Lung
  - Blood vessels
  - Heart
  - Nervous system
  - Gastrointestinal
  - Skin

**NK4 PROVIDES “FREEZE & DORMANCY” THERAPY OF CANCER**

- Malignant tumor
- Angiogenesis allows tumor growth
- Proteolysis of basement membrane
- Invasion
- Metastasis
- Inhibition of metastasis
- Inhibition of invasion
- Growth inhibition by anti-angiogenesis
- NK4-treatment

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Kringle Pharma, Inc.
info@kringle-pharma.com
http://www.kringle-pharma.com/en/index.html
Strex, Inc. was established in October of 2003 as the first venture company by Nagoya University. The company was founded by Associate Prof. Keiji Naruse of the Department of Physiology (Cell Biophysics) at Nagoya University Graduate School of Medicine (currently Prof. at the Department of Cardiovascular Physiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences).

The company supplies devices that make use of mechanical stress and soft lithography, which are Prof. Naruse’s areas of interest, in bioresearch and clinical applications.

Prof. Naruse was fortunate in this start up. He encountered Norio Ishida, CEO of an instrument manufacturing company and current CEO of Strex, Inc., and Hiroyuki Masumoto, CEO of B-Bridge International, Inc., who primarily handles sales of bioresearch reagents in Silicon Valley in the US. At, Strex, Inc., the roles are divided up, where Prof. Naruse proposes ideas based on the results of his research, Mr. Ishida develops the products, and Mr. Masumoto handles overseas business and negotiations.

**SOFT LITHOGRAPHY IS EMPLOYED TO EXPOSE CELLS TO STRETCH STRESS.**

**Stretch System**

The stretch system is a system in which, out of the various types of mechanical stress formed in living organisms, uniaxial stretch stress is applied to tissues and cells with high precision and reproducibility. For example, the movement of the vascular wall in association with cardiac output-induced changes in blood pressure and vascular pulse can be simulated using cultured vascular endothelial cells, so that the stretch system can be used in the analysis and elucidation of cell morphology, intracellular signaling mechanisms, and vasoactive substance-releasing mechanisms in response to stress. The stretch system can be applied to various types of cells, such as myocardial, fibroblast, and chondrocyte cells. A stretch system mounted on a microscope capable of measuring intracellular calcium dynamics and a stretch system for biochemical analysis are also available in the company’s line up. In addition, there are a biaxial system, in which the stretch system is independently stretched along the X-Y axes, and a stretch system equipped with a CO2 incubator. It is feasible to stretch three-dimensional cultured cells and tissues on the system. The system should be a promising tool in the future regenerative medicine.

**MICROSCALE SPERM SORTER EMPLOYING MICROFLUIDICS**

Today, 1 in 10 couples is infertile. Infertility therapy is a serious social issue in every country. One of the keys to successful infertility therapy is the harvesting of sperm with good motility. Unlike conventional methods, the sperm sorter which makes use of the microfluidics developed by Prof. Shuichi Takayama and Prof. Gary Smith at the University of Michigan, allows sperm with good motility to be easily separated in a few minutes. In collaboration with Nagoya University, Strex Inc. conducted clinical studies on the sperm sorter for in vitro fertilization (IVF), with great success. A single-chip fertilization system is currently being developed. The advantages of single-chip innovations will be fully exploited, and excellent results can also be expected for risk management in the clinical setting. The sperm sorter is also being developed for artificial insemination (AIH) which could be useful in general gynecology.
Osaka, Hokkaido and Beyond

Osaka's biotech prowess draws plenty of collaborations with other biotech clusters, and the northern island of Hokkaido is one of the most productive. It has been strengthening ties with Osaka-based universities and companies through joint research, capital alliances and sponsorships for college lectures.

But few people outside the region may notice that the remote, spacious island, which resembles Denmark in economic size and activities, is quietly trying to make itself a massive research and business centre for biotechnology. Beset by the sluggish economy that relies on agriculture and small businesses, Hokkaido is betting on biotech as a pillar of the future growth engine.

In fact, the biotech industry in Hokkaido has been growing steadily. The number of biotech companies totaled 75 in 2004, up from 34 in 1999. “Unlike Osaka, which is strong in drug development, Hokkaido takes advantage of ample natural resources,” says Ikkei Matsuda, president of Hokkaido Venture Capital, which invests in a dozen biotech companies in Hokkaido, Osaka and the U.S. Many of Hokkaido's biotech firms focus on nutraceuticals and food products.

For example, industry experts say Amino Up Chemical, which mainly produces a nutritional supplement made from mycelia of shiitake mushroom, is flourishing. The compound, called Active Hexose Correlated Compound (AHCC), can activate immunocytes, alleviating side-effects of anticancer drugs and helping to cure infectious diseases like hepatitis. “We want to entrench the concept of complementary and alternative medicine,” says president Kenichi Kosuna.

The 50-employee company's success lies largely in solid management and cutting-edge technology to culture mycelia. More notably, thorough clinical research at more than 60 universities and hospitals around the globe has established its credibility. So, doctors are increasingly using AHCC products, which are now selling in 15 countries. Also, Amino Up has recently developed a novel technology to extract polyphenol from plants and break polymers into smaller particles, which can boost polyphenol's systemic absorption and its antioxidant effect.

Primary Cell, a university start-up armed with nine employees, is also looking to explore new business areas. The company produces custom-made primary culture cells from bone, liver and other organs of lab animals for use in screening drug candidates. Last year, it developed the world's first system to culture primary cells of visceral adipocyte. President Toshio Taira says there is great demand for means of screening drug candidates for diabetes and other metabolic syndromes. The company is also developing primary culture cells of gastrointestinal tracts, as demand is rising from food makers to examine specifically how nutrition is absorbed or discharged.

Meanwhile, the prestigious Hokkaido University, together with government and industry, is trying to establish a large research and business park around its campus. The area houses various state-of-the-art facilities including the Frontier Research Center for Post-Genomic Science and Technology, whose mainstream research areas include glycol and lipid engineering.

The university is eager to improve efficiency. It has recently established an organization called Creative Research Initiative “Sousei” to break down barriers among faculties, support technology transfer from academic to industry and encourage human interaction. Already, a few large manufacturers have set up labs there, but the university hopes its renewed efforts will lure more private investment. “We believe companies can easily envisage a business model from science to the market by joining hands with Hokkaido University,” says Hiroshi Takahashi, director of Sousei.

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