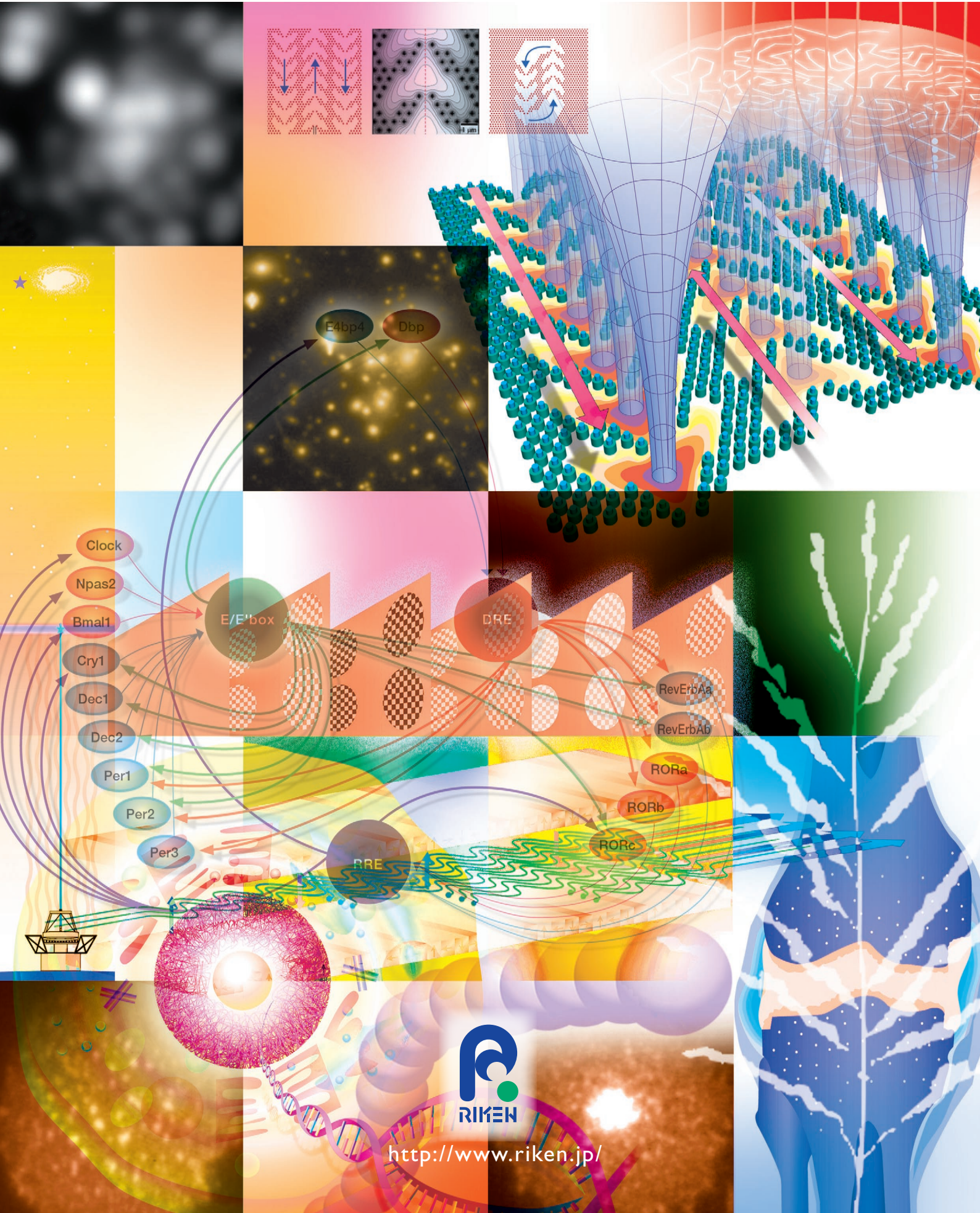


# RIKEN 2005-6

## ANNUAL REPORT



<http://www.riken.jp/>

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# RIKEN, Working for the World

I wish to remind the reader that those carrying out scientific research at RIKEN are “human beings” with abundant intellect and sensitive emotions and feelings. Therefore, I feel that reading about our cutting-edge research results together with the profiles of the researchers who produced them as presented in this Report will be a means for the reader to gain a better understanding of the activities at RIKEN.

Society changes rapidly over time. RIKEN must respond flexibly to the demands of the rapidly changing society. For this purpose RIKEN at the beginning of the 21st century has the following four missions.

1. Producing research results which are “Only One” or “Number One” in the world.
2. Developing and constructing high-level and reliable research infrastructures for domestic and foreign research institutions and researchers, and making them widely and readily available for their use.
3. Returning the research achievements to society in a variety of ways.
4. Developing new research systems ahead of other institutions in order to lead scientific research in Japan.

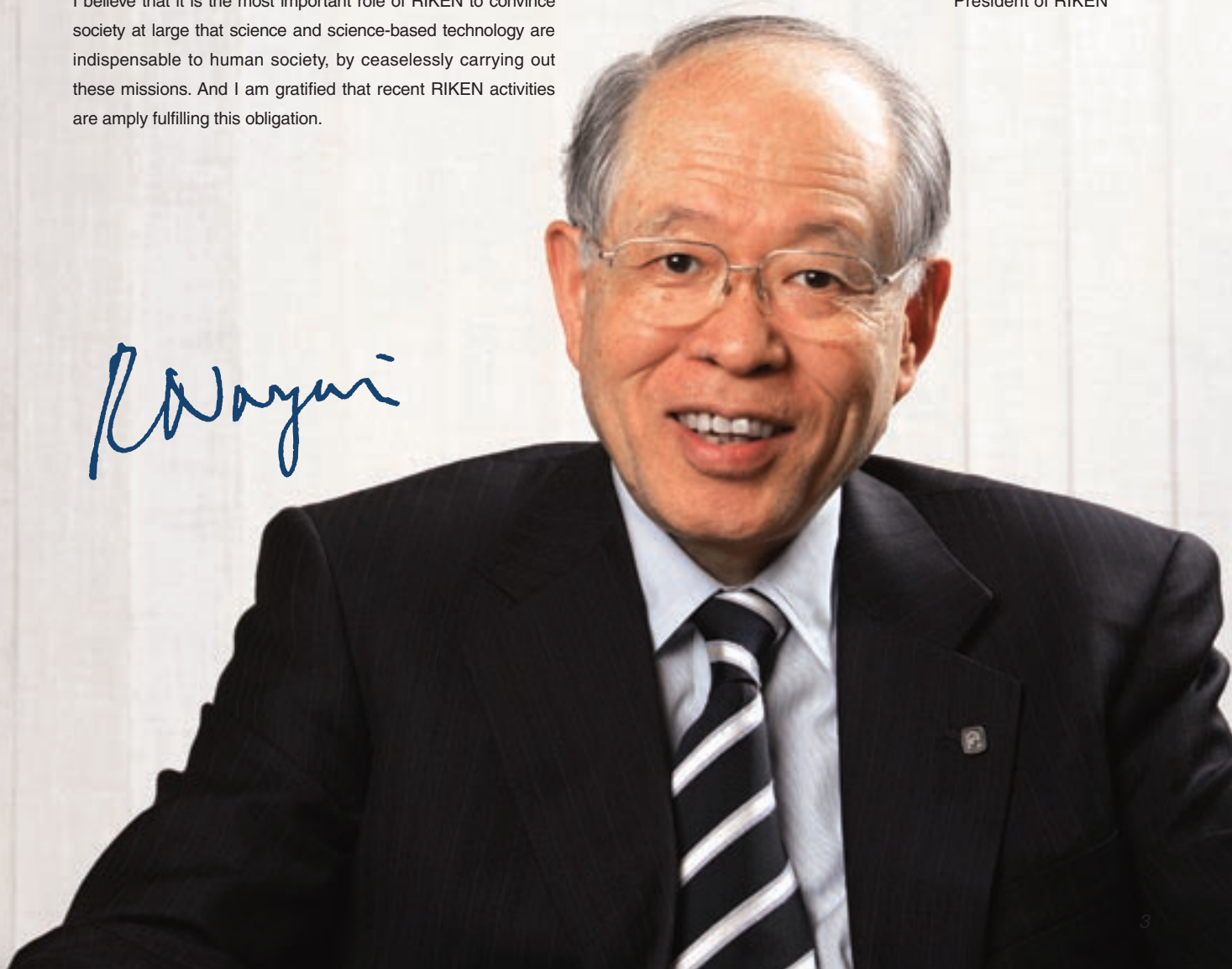
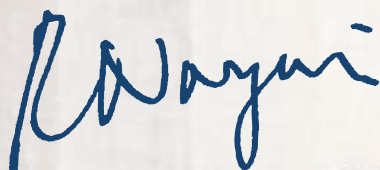
I believe that it is the most important role of RIKEN to convince society at large that science and science-based technology are indispensable to human society, by ceaselessly carrying out these missions. And I am gratified that recent RIKEN activities are amply fulfilling this obligation.

The world is now in transition from the “age of competition” to the “age of collaboration.” Even now RIKEN is actively promoting collaboration with universities and research institutions inside and outside Japan. From now on, I think that we must further promote the globalization of our activities. In order for RIKEN to be a world-class institution, it is necessary for our researchers to plunge themselves into the flow of a group of first-class researchers who move from place to place all over the world, in North America, Europe and Asia. I would like to send out RIKEN researchers to many countries in order to further develop science. And I would like to find the best possible young people from all over the world, recruit them to RIKEN and nurture them. This is because exchange of researchers with different cultural backgrounds will greatly contribute to enhancing the quality of researchers and to developing a healthy research community. And now that almost all economic activities are related to science-based technology, it has become important to collaborate with the industrial sector.

I sincerely hope that through this Annual Report, many people in society at large will gain an understanding of RIKEN's activities and will give their unwavering support for them.

June 2006

Ryoji Noyori (D. Eng.)  
President of RIKEN



# Profile of RIKEN

## An unrivaled research system

### Japan's only comprehensive approach to investigating the natural sciences

With more than 80 years of research in the natural sciences, RIKEN is unique in Japan. It has conducted cutting-edge research covering a diverse range of fields that include physics, chemistry, engineering, biology and medical science. Research has spanned everything from basic investigations to practical applications. RIKEN actively disseminates its scientific and technological findings, encourages research collaborations between research institutes, and facilitates the transfer of technology into industry.

**Objective:** To conduct thorough research investigations that extend and elevate the boundaries of science and technology (excluding only human and social sciences).

**Mission:** To produce internationally recognized results that fully exploit all the benefits of RIKEN's research environment and to maximize the social benefits of those results. This will be possible by pioneering new fields for research and undertaking research in important areas based on social need.

**Expectations:** For 88 years, RIKEN has sought to extract tangible and intangible goods from its research results. It is expected to sustain its success through continuous self-improvement that maintains RIKEN's leading role and drives scientific and technological innovations. Our tactics include efforts to recruit young, outstanding researchers from across the globe to work in a highly charged, competitive, international and fluid environment that is designed to encourage active research. Increasing collaborations with universities and research institutes within Japan and internationally as well as deepening ties with our local communities will also inspire advanced investigations. Finally, a superior evaluation system of research activities will guide researchers and ensure that their efforts exceed expectations.

**History:** RIKEN was established in 1917 as a private research foundation in the northwest area of Tokyo. After World War II, it was restructured and renamed the Science Research Institute Ltd., or KAKEN, which became a public corporation, RIKEN, in 1958 when the main headquarters moved out of Tokyo to its current location in Wako so that it could expand its research activities. With continued expansion of its research activities, other facilities were established in Tsukuba, Harima, Yokohama, Kobe, Sendai, Nagoya, the United Kingdom, and the United States. In the fall of 2003, RIKEN underwent another administrative restructuring. It now operates as an independent administrative institution.



**Hantaro Nagaoka**

**Physicist**

With his Saturnian model of an atom, Nagaoka said that atoms look like the planet with rings of electrons circling a positively charged core. He was also the architect of Japan's platform for physical sciences and the Director of the Physics Division for the RIKEN Foundation.



**Kohtaro Honda**

**Magnetic physicist**

His investigations in metallurgy and magnetism contributed to raising the international status of Japanese work in these areas through his invention and study of K.S. magnet steel, the world's strongest permanent magnet.



**Umetaro Suzuki**

**Agricultural chemist**

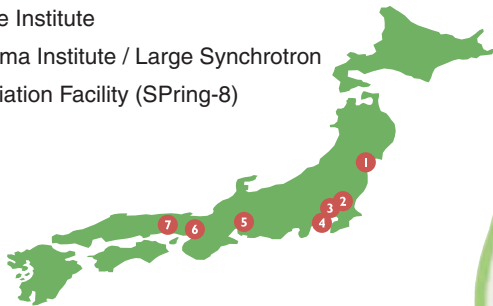
The founder of vitamin research in Japan, Suzuki successfully isolated vitamin B1 from rice bran, calling it oryzanin, this was effective in preventing and treating the related vitamin deficiency disease, beriberi. He was also instrumental in inventing and developing other products that were marketed under RIKEN Vitamin, which financed much of RIKEN's activities as the RIKEN Foundation.



Wako Institute and RIKEN Headquarters

## RIKEN spans Japan

- 1 Terahertz Lights Research Program (Sendai)
- 2 Tsukuba Institute
- 3 Wako Institute, RIKEN Headquarters
- 4 Yokohama Institute
- 5 Bio-Mimetic Control Research Center (Nagoya)
- 6 Kobe Institute
- 7 Harima Institute / Large Synchrotron Radiation Facility (SPRING-8)



Yokohama Institute

Harima Institute  
Large Synchrotron Radiation Facility (SPRING-8)



Kobe Institute



**Masatoshi Okochi**

### Scientist and executive

While promoting original, atypical basic research, Okochi sought ways to nurture emerging results into industries, founding the RIKEN Industrial Group (RIKEN Konzern) in the process. He is credited with creating RIKEN's unique environment as a researcher's haven during his term as the RIKEN Foundation's third director.



**Yoshio Nishina**

### Physicist

His Klein-Nishina formula, derived together with Oskar Klein, opened the way to a new physics, and his laboratory in RIKEN inspired many scientists by emphasizing researcher interaction. His tenure as the president of the Scientific Research Institute Ltd. (KAKEN) was marked by particle physics investigations. The Nishina crater in the moon is named after him.



**Shin-ichiro Tomonaga**

### Theoretical physicist

Tomonaga's RIKEN career started when he joined Nishina's laboratory in 1932; there he determined how a group of the same type of particles interacted. He shared the Nobel Prize in Physics with Richard Feynman and Julian Schwinger for their quantum electrodynamics theory.



**Hideki Yukawa**

### Theoretical physicist

Another alumnus of Nishina's laboratory, Yukawa joined that laboratory in 1940 and later became a RIKEN chief scientist from 1961-5, working on the properties of elementary particles. His prediction of meson particle existence earned him the Nobel Prize in 1949, making him the first Japanese national to be so decorated.

# 2005–6 Highlights

The RIKEN Annual report provides an overview of RIKEN's activities in 2005 by highlighting its research output and its organizational structures as well as key operational data.

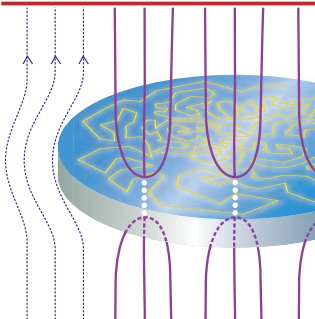
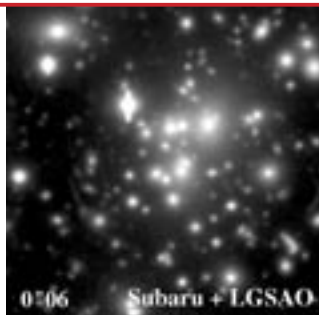
## Research

*Research is, of course, the most important of RIKEN's activities. In the past twelve months, RIKEN's researchers have been highly prolific. Just nine of the most exciting findings are highlighted here; these are described at length by the researchers later in this report.*

**1** → page 10

### Artificial Stars

RIKEN researchers shot a laser into the Earth's sodium atmospheric level (100 km high). This created an artificial star that guides observations from the Subaru Telescope and increases its precision.



**2** → page 12

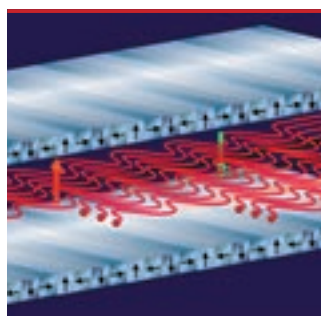
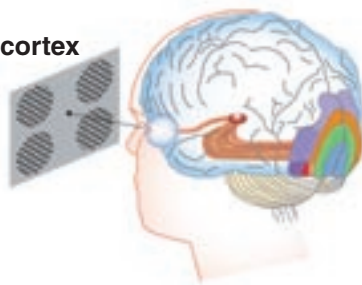
### Direct observation of superconducting flux quanta under motion control

Using an electron microscope, RIKEN researchers were the first to observe directly the motion of individual quantum particles trapped in a superconductor.

**3** → page 14

### For efficiency, the visual cortex self-adjusts to changes in the environment

The region of the brain that enables object differentiation, or contrast adaptation, in visual perception was identified.



**4** → page 16

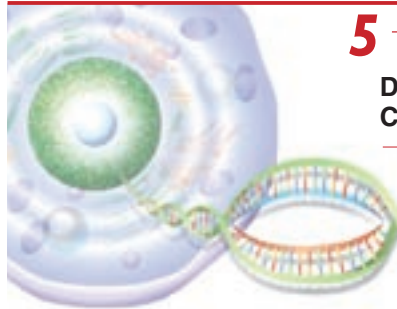
### Next generation light source for all scientists

SPring-8 researchers are building an X-ray free electron laser that is a billion times more intense than the X-rays at SPring-8.

**5** → page 18

### Discovering a new RNA Continent

Researchers identified a novel structure of RNA that challenges major assumptions about the roles and functions of this vital participant in life.



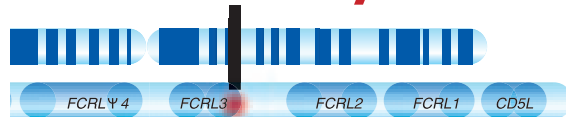
**6** → page 20

### Genetic determination in rice yields

Ever wondered why some rice plants produce more grains than others? Researchers at RIKEN have found a gene that determines grain output and uses this knowledge to produce a new strain that is harder and yields 20% more rice.



**7** → page 22



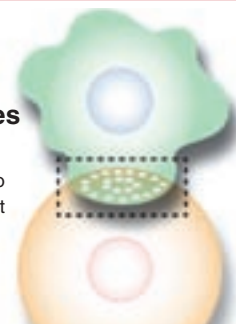
### Slight genetic differences may cause autoimmune diseases

In studying a causal gene for rheumatoid arthritis, RIKEN researchers found that disease onset is triggered by only slight differences in the genes.

**8** → page 24

### Molecular microclusters trigger immune responses

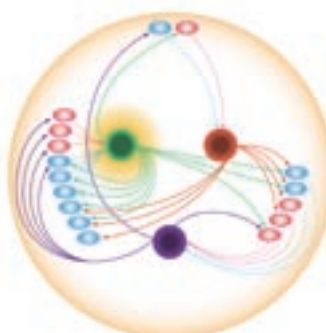
In order to respond to hostile threats to the body, a set of molecules must first clump together into a "microcluster".



**9** → page 26

### Revealing the genetic processes controlling circadian rhythm

A series of experiments conducted by RIKEN researchers revealed a DNA switch that can tell the time.



# Organization

**RIKEN recognizes that research requires flexible organization within its permanent facilities and strives to create that flexibility. Therefore, it strives to give each of its institutes and research organizations the freedom to collaborate as needed without sacrificing the uniqueness of individual research projects. The institutes are highlighted here.**

## Wako Institute → page 36

The Wako Institute is home to several different research centers, including the Discovery Research Institute (DRI), Frontier Research System (FRS), and Brain Science Institute (BSI), as well as Initiative Research Units and Sponsored Laboratories. DRI launched a new research project in 2005 that seeks to create new forms of light. FRS has been restructured in response to a shift in priorities, and now promotes integrated and collaborative research; as a result several new projects started as others ended. By participating in the International Neuroinformatics Coordinating Facility as the Japanese representative, BSI continues to promote international research collaborations. Finally, the Center for Intellectual Property Strategies (CIPS) began developing ways to efficiently transition research achievements into practical industrial applications that ultimately benefit society.



## Tsukuba Institute → page 44

The Tsukuba Institute's BioResource Center, which celebrated its fifth anniversary in 2005, collects, stores, and distributes biological resources and the associated technologies for research. It continues to be highly evaluated inside and outside of Japan and has been honored by the promotion of the Center's director to vice-chair of a new international organization to manage mouse resources around the world.



## Harima Institute → page 46

The RIKEN SPring-8 Center (RSC) was launched at Harima Institute in 2005. The Center seeks to use radiant light at the large-scale synchrotron radiation facility (SPring-8) and develop the next-generation radiant light source. Using the X-ray Free Electron Laser (XFEL), a testing laser, the Center successfully generated undulatory light. A full-scale accelerator construction starts in 2006. The Center continues to exploit SPring-8 to produce research achievements across many disciplines.



## Yokohama Institute → page 48

In 2005, the Center of Research Network for Infectious Diseases (CRNID) was added to the four other centers currently included at the Yokohama Institute. These are the Genomic Science Center (GSC), Plant Science Center (PSC), SNP Research Center (SRC), and Research Center for Allergy and Immunology (RCAI), and they continue to produce important research output. The CRNID is the base for an extensive research program on new and reemerging infectious diseases and the center is committed to strengthening the network of collaboration and promoting joint studies domestically and internationally. Educational activities on new and reemerging infectious diseases for the public are also planned.



## Kobe Institute → page 54

The Center for Development Biology (CDB) at the Kobe Institute seeks to understand how diseases are contracted and may reemerge, as well as to develop a course towards practical regenerative medicine. Embarking on its second term, the Center successfully broadened its output in 2005 and also made remarkable inroads in international collaboration. The Kobe Institute initiated the Asia and Pacific Development Biology Network (APDBN), and the Network's secretary was set up in the Publicity and Internationalization Office of CDB.



# Data & Information

*RIKEN became an independent administrative institution in October 2003, a change that also transformed its management system. Below, RIKEN's management and key data are provided to give a snapshot of the current state of its activities,*

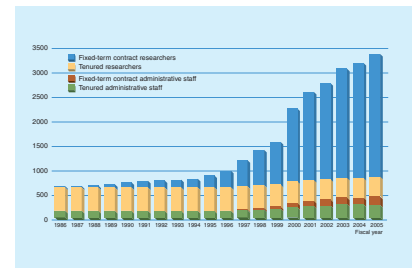
## The transformation into an Independent Administrative Institution → page 58

As part of RIKEN's transformation, RIKEN's new President, Ryoji Noyori, issued the Noyori Initiative shortly after he took the office. This Initiative outlines RIKEN's strategy for pushing its research institutes to even greater levels of success.



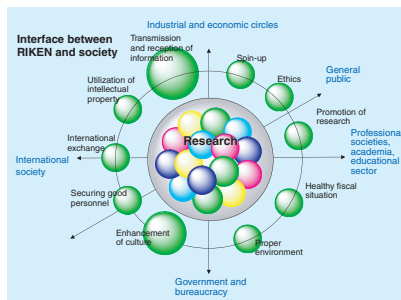
## Personnel → page 64

In FY 2005, RIKEN introduced two new systems for its researchers that are designed to facilitate researcher mobility: a retirement benefit system and a performance-based annual salary system.



## Evaluation → page 60

RIKEN actively works to develop compliance measures that improves its scientific governance.



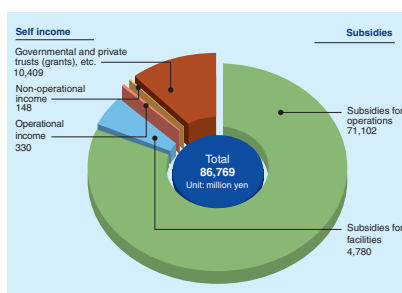
## Promoting public understanding → page 66

RIKEN offered 205 seminars and 40 symposiums in FY 2005 for increased communication between scientists throughout Japan. In addition, RIKEN's annual Open Day events attracted over 13,000 visitors to its facilities.



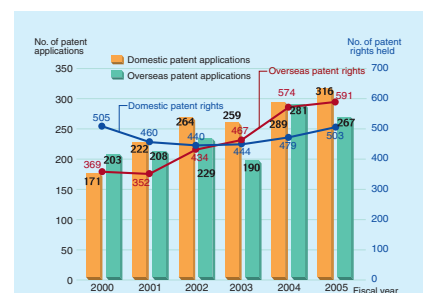
## Budget → page 62

While the government remains RIKEN's primary financial supporter, RIKEN is also developing other sources of funding and has successfully acquired significant amounts of external funding.



## Technology transfer, collaborative research, making RIKEN's research results available to society → page 68

The Center for Intellectual Property Strategies facilitates the translation of research achievements into RIKEN intellectual property. Each year, the number of patents granted to RIKEN increases.





## Nine major achievements in 2005–6

# Research

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Direct observation of superconducting flux quanta under motion control .....	12
For efficiency, the visual cortex self-adjusts to changes in the environment .....	14
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Discovering a new RNA Continent .....	18
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# Artificial Stars

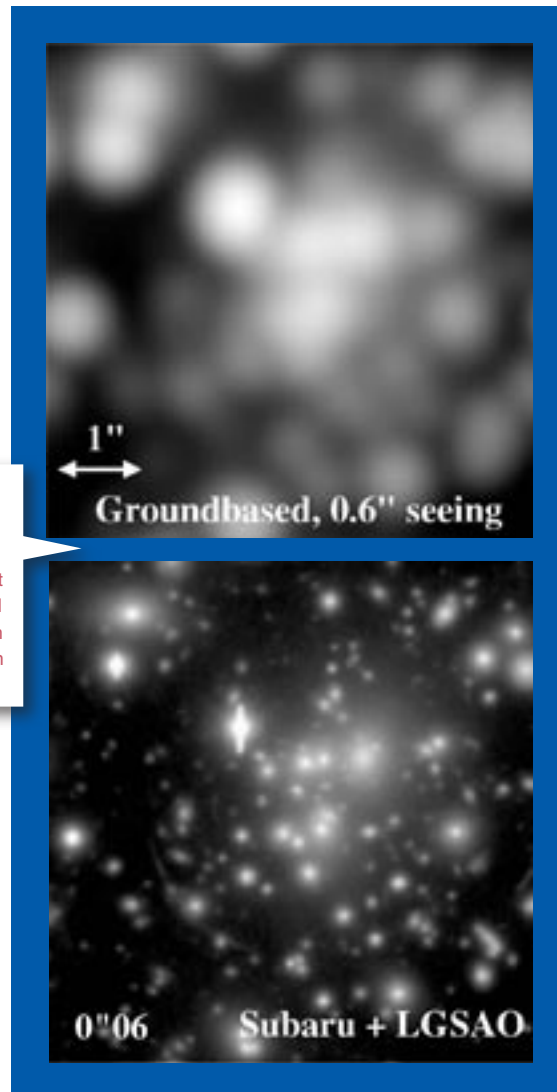
Researchers in the Solid-State Optical Science Research Unit have developed a laser that can enhance the performance of the Subaru telescope by using a guide star artificially created one hundred kilometers above the Earth.

## KEY CONCEPTS

- 1 Earth's atmosphere hinders astronomical observation
- 2 Laser-generated guide star in sodium layer of Earth's atmosphere
- 3 Combined two laser beams to produce the star using sum frequency generation
- 4 Increased spatial resolution is two times that of the Hubble Space Telescope

### Adaptive optics improves spatial resolution

Above: Image taken without using an adaptive optical system. Below: Image taken with an adaptive optical system using a laser guide star.



## In the words of the researchers

### Satoshi Wada

Discovery Research Institute  
Solid-State Optical Science  
Research Unit



## Passionately pursuing new materials to illuminate the way for science

Current efforts to build solid-state lasers are an outgrowth of materials science. I am an expert in non-linear optics research, but to develop new wavelength conversion technology, it was necessary to expand into laser technology research. In the end, my quest to develop new materials and methods for solid-state measurements produced an oscillating solid-state laser and non-linear optical crystals.

At that point, I shifted my attention to my current project: to develop a laser that generates a two-micron wavelength. If we are successful, such a laser will be able to measure carbon dioxide concentrations. It could be installed on a satellite that Japan plans to launch and used to monitor environmental conditions on earth.

Science and engineering are complimentary processes—advances in one invariably lead to changes in the other. With our new laser developments, the history of space may well be revealed, thus changing the course of astronomical studies.

## The planet's atmosphere hinders astronomical observation

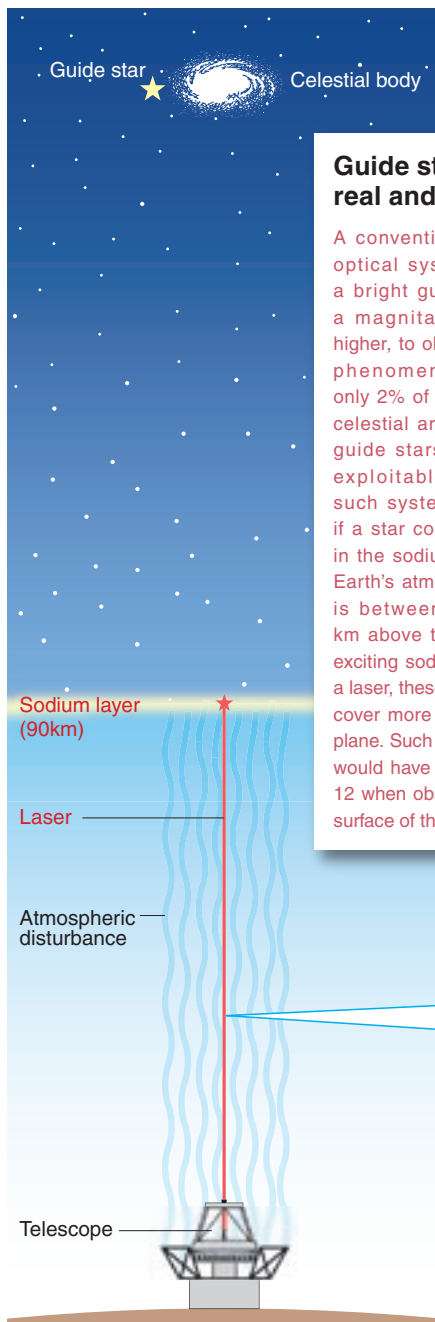
Atmospheric turbulence degrades images of space captured from observatories on Earth. Even for telescopes placed at the highest possible elevations where the atmosphere is thin, the effects cannot be fully eliminated. This is why the Subaru telescope, built by the National Astronomical Observatory of Japan on the summit of Mauna Kea (4200 meters above sea level), can produce only blurred images.

There are currently two approaches to reducing the effects of atmospheric interference. One is to put telescopes in orbit around the earth, beyond the reach of that interference. The Hubble telescope, launched by the United States in 1990, was the result of

that approach. The other approach is to design methods to eliminate the atmospheric effects by compensating for the wave front around the telescope.

## The Subaru's adaptive optics

To compensate for atmospheric turbulence, the Subaru telescope has an adaptive optical system. This system measures the turbulence effect and rapidly adjusts the surface of the variable mirror within the telescope up to one hundred times a second. However for this system to be effective, a bright star is needed, to guide the observation of the targeted celestial body. This star needs a magnitude of 15 or higher so that the telescope can use this star's light as a light source. However, only 2% of the observable celestial area has guide stars, severely limiting the scope



Guide star  Celestial body 

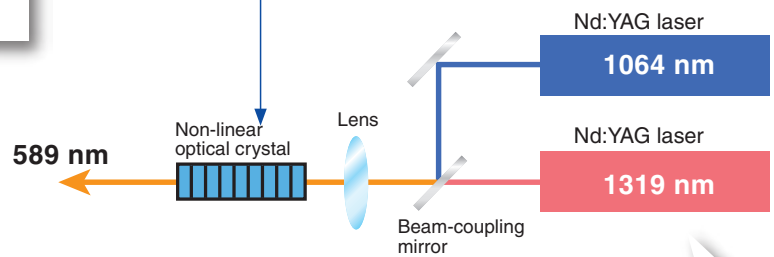
### Guide stars: real and artificial

A conventional adaptive optical system requires a bright guide star, with a magnitude of 15 or higher, to observe celestial phenomena. However, only 2% of the observable celestial area has usable guide stars, limiting the exploitable benefits of such systems. However, if a star could be created in the sodium layer of the Earth's atmosphere, which is between 80 and 100 km above the surface, by exciting sodium atoms with a laser, these systems could cover more of the celestial plane. Such an artificial star would have a magnitude of 12 when observed from the surface of the Earth.

### Crystals

Sum-frequency production of the laser needed a non-linear optical crystal. Our investigations of several crystals revealed a solid-state crystal that would suit our needs.

- ① BaMgF<sub>4</sub> ② Nd:GdVO<sub>4</sub>
- ③ Nd:GdVO<sub>4</sub> ④ AgGaInS<sub>2</sub>, Ce:KTP, Cr:MgSiO<sub>4</sub>, Ti:sapphire
- ⑤ Nd:LuVO<sub>4</sub>, Nd:YVO<sub>4</sub> ⑥ Nd:GdVO<sub>4</sub> ⑦ Cr:GSGG



### Diagram of the sum-frequency 589nm beam

To generate a high-output coherent light that can produce a bright orange beam of 589 nm (the Sodium D line used in many sodium lamps), the team mixed two laser beams (with frequencies of 1064 and 1319) using a non-linear optical crystal. The target frequency emerges from the following sum-frequency:  $1/1319 + 1/1064 = 1/589$ .

of studies that exploit the optical system of this telescope.

## Generating an artificial guide star

To make this optical system more efficient, we decided to create a guide star artificially. Working with the National Astronomical Observatory of Japan, members of our research unit looked at the sodium layer of the atmosphere, which is about one hundred kilometers above the surface of the planet. Would it be possible to create a star in this layer that could serve as a guide star by exciting a point in this layer with a laser (excitation light emission)? To do this we would have to construct a high-powered laser that could emit 589 nm photons, the output needed to

excite sodium atoms in the atmospheric layer sufficiently to produce light.

## Sum frequency generation with two lasers

Currently, there is no laser that can generate a solid-state laser at 589 nm and that could stimulate sodium atoms to emit a steady light that would not be subject to changes in temperature. Such a laser needs to produce a spectrally pure beam, reliably, easily, and with high power.

Therefore, the collaborative team focused on two laser lights generated by an Nd:YAG lasers that have wavelengths of 1064 and 1319 nm. Using a method called sum frequency generation that used a non-linear crystal to combine these light beams, we produced a

bright orange coherent light. ("Coherent light" is light whose peaks and valleys all occur at the same time.) When fired into the sodium layer, the beam produced a guide star with a 50-centimeter diameter.

## Anticipating a five-fold upgrade in image resolution

Using this man-made star, the Subaru telescope will be able to take finer detailed photographs of celestial phenomena regardless of their location. Using this system, Subaru's images should demonstrate a five-fold improvement in spatial resolution, an increase over the current three-fold improvement gained by the Hubble telescope. Testing in 2006 of the whole system should generate even better resolution results.

# Direct observation of superconducting flux quanta under motion control

Control of the motion of flux quanta constitutes a key technique in the application of superconductivity. The Quantum Phenomena Observation Technology Laboratory of the Single Quantum Dynamics Research Group has succeeded, by using an electron microscope, in becoming the first laboratory in the world to observe how motions of individual flux quanta are controlled.

## KEY CONCEPTS

- 1 Magnetic flux lines in a superconductor
- 2 Observing flux quanta through an electron microscope
- 3 Moving flux quanta with a ratchet channel
- 4 Controlling quanta motion in any direction



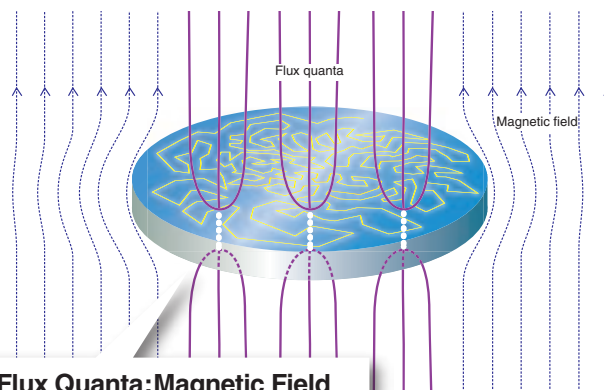
## In the words of the researchers

### Yoshihiko Togawa

Frontier Research System  
Single Quantum Dynamics Research Group  
Quantum Phenomena Observation Technology  
Laboratory

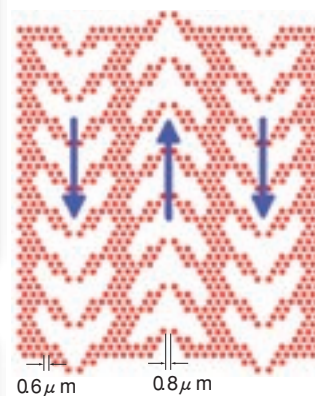
## Potential for further applications

Although the study is in its initial stages, results appear to indicate that we can develop a ratchet-based tool such as pincettes capable of moving target flux quanta in a desired direction. This tool can be used in a variety of applications. Superconductor-based high-sensitive magnetic field sensors on MRI, for instance, may be deprived of their intended sensitivity by noises generated from the movements of flux quanta. If, in such cases, obstructive flux quanta can be removed from the device by using pincettes, we will be able to develop more sensitive sensors. The motion of flux quanta generates voltage in its vertical direction. This indicates the possibility of, for instance, developing a ratchet-based tiny electric generator as well as a live body-simulated device that is capable of moving itself utilizing fluctuations in heat.



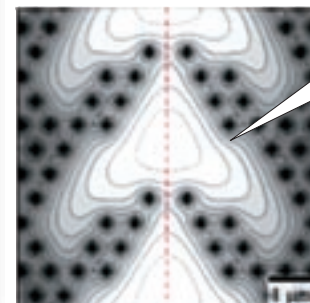
## 1 Flux Quanta: Magnetic Field Lines in a Superconductor

If a magnetic field is applied to a type II superconductor, such as widely used niobium titanium (NbTi), magnetic flux lines turn into very fine filaments in a superconductor (dotted line in the figure). These magnetic flux lines in a superconductor take a specific value ( $2.07 \times 10^{-15}$  Wb) and are quantized, resulting in their being named "flux quanta".



## 2 Structure in Test Sample

We have prepared a test sample having a distribution with a spatially asymmetric pinning center by irradiating a gallium ion beam to a niobium superconductor. We have pinned flux quanta in this distribution to enclose unpinned (free to move) flux quanta within the regions being formed by spatially asymmetric potential (the wedge-shaped region in the figure to the right). Then we generated a 1-dimensional channel by connecting these wedge-shaped regions.



## What are Flux Quanta ?

The superconducting state, which emerges in ultra-low temperatures, conducts electrical current without electrical resistance. This condition, therefore, allows for the transmission of large currents and the creation of a strong electromagnet without being accompanying with heat or energy losses. Superconductivity is also a physical phenomenon, whose application to ultra high-sensitive magnetic field sensors and super-fast switching devices is being studied. The flux quanta being observed in our study and the superconducting state are closely connected. Since the superconducting state excludes

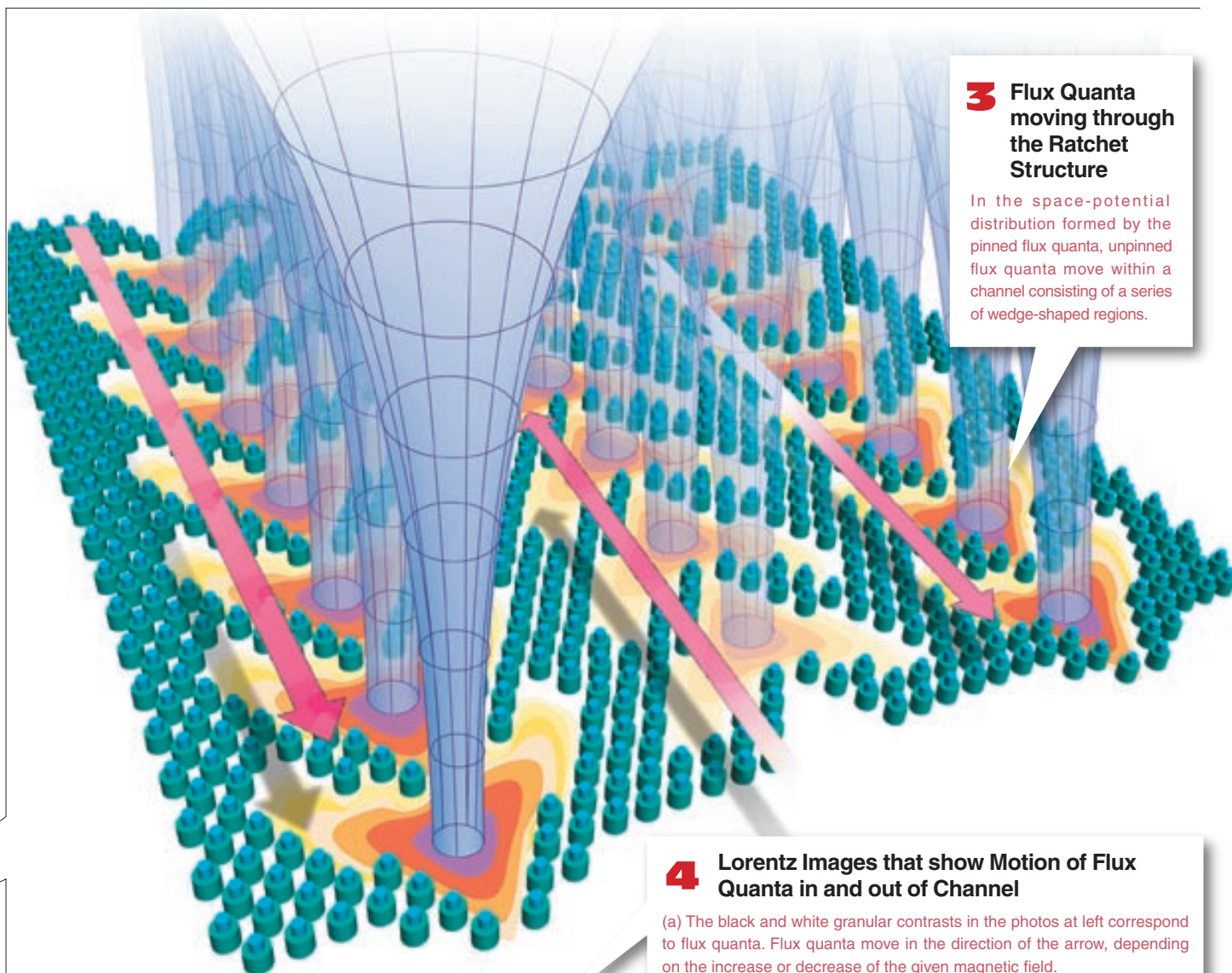
magnetic field, however, one cannot exist in a superconductor. But if strong magnetic field is applied externally, a superconductor can allow magnetic field lines to penetrate it, and it will yield to the pressure of the magnetic field. Magnetic field lines in this state become bunches of specific volume, which are called flux quanta.

## Controlling Motion of Flux Quanta

Electric current applied to a superconductor gives force to flux quanta and, as flux quanta move using this force, electrical resistance is generated and the superconducting state is lost due to the resulting heat generation. In

### 3 Flux Quanta moving through the Ratchet Structure

In the space-potential distribution formed by the pinned flux quanta, unpinned flux quanta move within a channel consisting of a series of wedge-shaped regions.

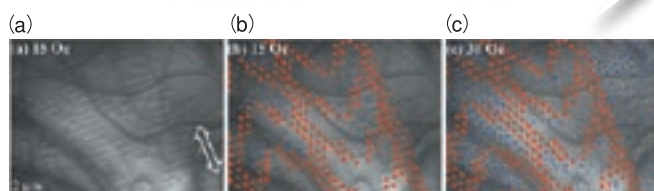


### 4 Lorentz Images that show Motion of Flux Quanta in and out of Channel

(a) The black and white granular contrasts in the photos at left correspond to flux quanta. Flux quanta move in the direction of the arrow, depending on the increase or decrease of the given magnetic field.

(b) Motion of flux quanta when a downward force is applied. In the same photo as (a), red dots represent pinned flux quanta and blue dots represent unpinned freely movable flux quanta. In the upward channel, flux quanta are caught in the pocket of the wedge-shaped regions.

(c) Motion of flux quanta when an upward force is applied. A large number of flux quanta move in the forward direction of the upward channel. As the result of (b) and (c), motion of flux quanta is rectified upward.



superconducting devices, too, the motion of flux quanta generates noise and thus prevents technical enhancement of the devices. This is what triggered the study for controlling the motion of flux quanta.

A major controlling method employed so far was “pinning”, in which flux quanta are artificially fixed and immobilized. In this approach, flux quanta are caught and immobilized in defects prepared on a superconductor. In recent years, studies for direct motion control of the flux quanta were initiated in addition to pinning them in a superconductor. These studies determined that a mechanism called “ratchet” offers an efficient way of controlling the motion of the

flux quanta by allowing them to move to a certain degree but not in opposite directions.

### Observing the Motion Control

The team then conducted an experiment to observe how the individual quantum behaves when its motion is controlled. Using microfabrication technology, the team created a channel in the thin film of a single crystal niobium superconductor. This channel, made up of a series of wedge-shaped regions, is designed to allow movement of flux quanta. This channel has a forward flow direction (easier to flow) and a reverse flow direction (difficult to flow) for flux quanta that are expected to work as a feed check valve. In the experiment, an external

magnetic field was applied in such a way that the force for both the forward and reverse directions is exerted to flux quanta. The electron microscope observation of the individual flux quantum motion in the channel revealed that the wedge-shaped channel functions as a ratchet. The team also found that the channel shape enables flux quanta to move not only in the one-dimensional direction but in the two-dimensional direction as well. We believe this controlling approach will lead the way to the development of new superconducting devices, such as noise-suppressed superconducting devices, and logical circuits on which the flux quanta themselves are used for signal transmission.

# For efficiency, the visual cortex self-adjusts to changes in the environment

Humans discriminate objects with high fidelity, irrespective of changes in the environment such as brightness. Using fMRI experiments on the human visual cortex, the Brain Science Institute's Laboratory for Cognitive Brain Mapping has uncovered the mechanism of "contrast adaptation" for discriminating objects based on contrasts in brightness.

## KEY CONCEPTS

- 1 The human visual system has a contrast adaptation system
- 2 Visual cortex controls contrast adaptation in the brain
- 3 The laboratory successfully quantified the effects of contrast adaptation for neurons in different visual areas
- 4 Area V4 plays a role in "monitoring" changes in the environment

## In the words of the researchers

### Kang Cheng

Brain Science Institute  
Cognitive Brain Science Group  
Laboratory for Cognitive Brain  
Mapping



## Designing experiments from fresh perspectives

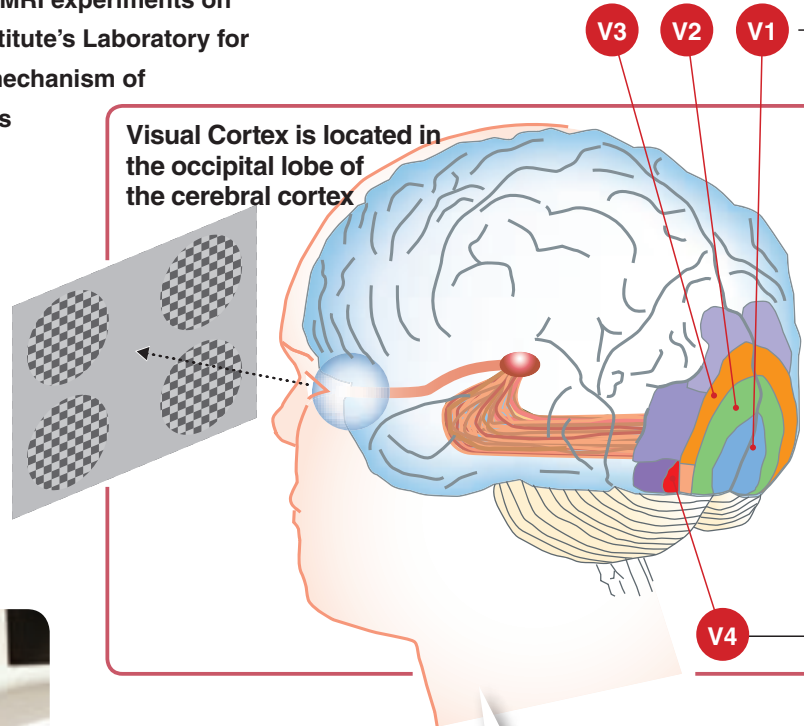
A series of experiments using fMRI confirmed the existence of contrast adaptation in human visual system. Originally we were only interested in area V1, but the fMRI provides the opportunity to simultaneously observe the behaviors of other visual areas, from area V2 to area V4, and therefore we had this unexpected finding in area V4.

Area V4 does not respond to the absolute amount of contrast changes, but to the changes themselves. This discovery, we believe, has important social implications.

We began the experiment with the hypothesis that "there must be a mechanism in the visual system capable of accurately capturing contrast changes in different environments." Using fMRI, we confirmed this hypothesis in areas V1 to V3. Based on some initial observations in area V4, we also designed a set of new experiments, and eventually uncovered some unusual properties of area V4. Thus, it is important to have a general objective and to design experiments based on that objective, and yet be able to change that experiment based on other novel observations.

In the future, we want to investigate the possibility of similar contrast-adaptation and change-detection mechanisms in other sensory systems, including the auditory and gustatory systems.

Visual Cortex is located in the occipital lobe of the cerebral cortex



## Mechanism of Vision

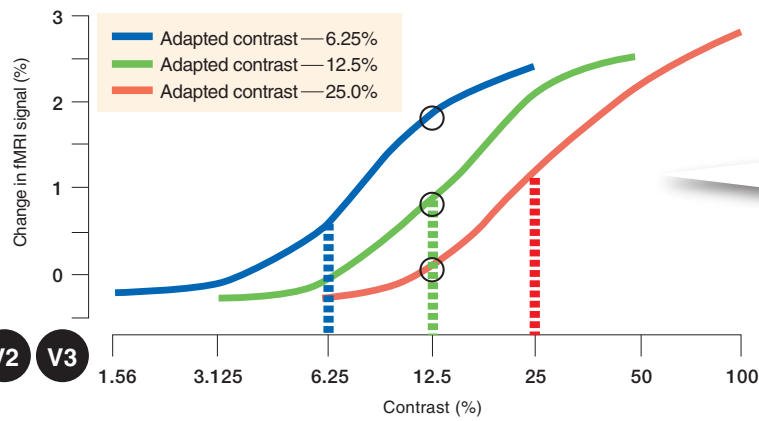
Electric signals from the retina are first sent to the primary visual cortex (area V1) of the occipital lobe located in the posterior part of the cerebral neocortex, and then to the visual association cortex through higher order visual areas (areas V2–V4) for object recognition.

## The mechanism of contrast discrimination in the visual cortex

If you leave a dark room and go out into the sun or vice versa, you will not be able to see things clearly for a short time. However, as your eyes adjust to the new environment, things become clear again. The phenomena are called "light adaptation" and "dark adaptation" respectively. A similar phenomenon is observed if the contrast changes. When, for instance, it is necessary to discriminate ambiguous contrasting states, such as the contour of a mountain in the mist, the visual system detects minute differences between lightness and darkness. The visual cortex is thought to regulate these phenomenon.

## A new hypothesis that explains contrast adaptation validated

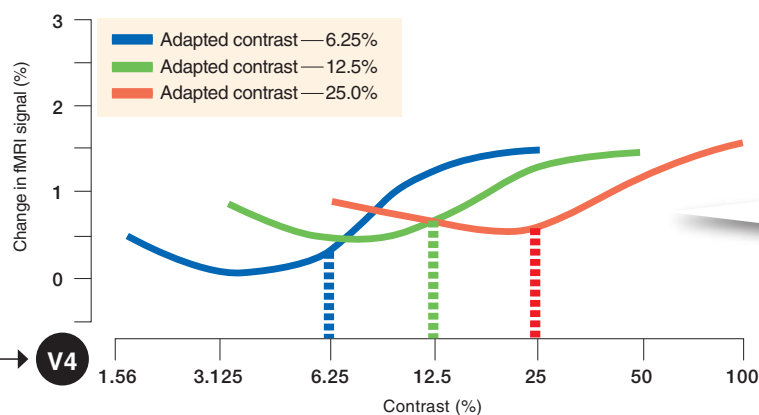
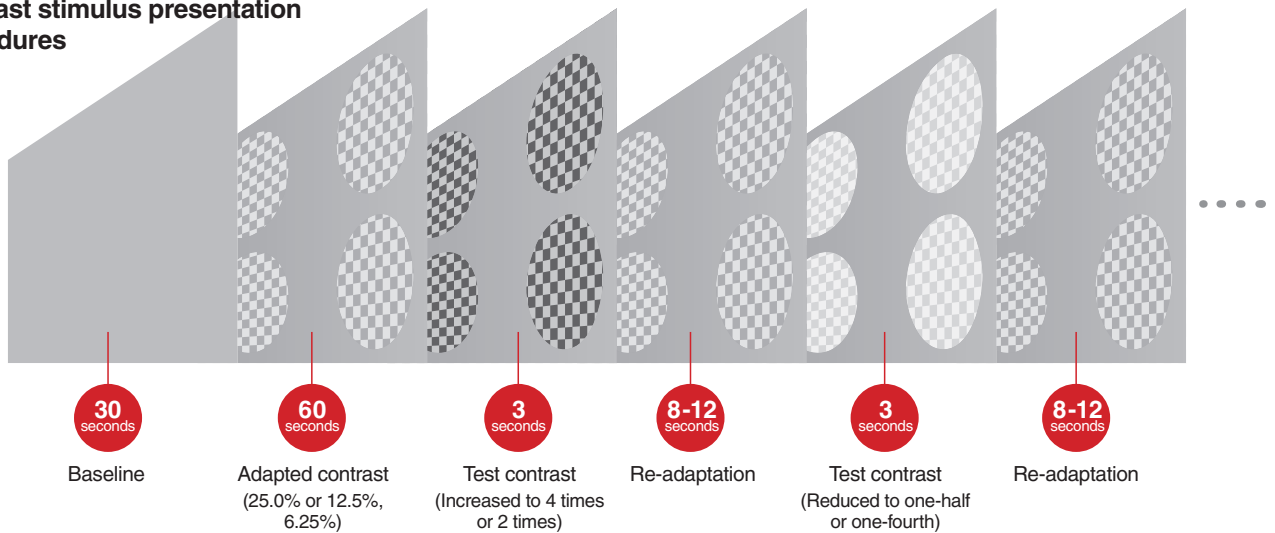
The laboratory assumed that there must be a mechanism in the brain that changes the detectable contrast range according to the mean of contrasts in a given environment in order for the eyes to discern contrasts resulting from changes in that environment. With such a contrast mechanism, the visual system would always be able to discriminate objects efficiently and with high sensitivity. Our experiments confirmed this hypothesis. Moreover, we found that a higher-order visual cortex, V4, monitors changes in contrast through a more complex mechanism.



### Contrast response in areas V1 to V3

As a consequence of the change in contrast, the contrast response function shifts horizontally. Depending on the current contrast value to which the subject is adapted, the magnitude of the response to the same contrast (black circles) varies greatly.

### Contrast stimulus presentation procedures



### Contrast response function in area V4

Unlike in areas V1–V3, the contrast response function in area V4 area is U-shaped. The responses are always positive, regardless of test contrast condition.

### Monitoring of environmental changes by higher-order visual cortices

In the experiments, visual patterns of different levels of contrast were consecutively presented to subjects and the activities of populations of neurons in visual cortices (areas V1–V4) were measured with functional magnetic resonance imaging (fMRI).

The results confirmed, as we hypothesized, that the contrast range to which neurons respond with high sensitivity shifts in areas V1, V2, and V3. In these areas, neuronal response increases or decreases in response to incremental shifts in contrast.

However, in area V4 neuronal activity increased not only when contrast increased but also when contrast was decreased. This suggests that contrast adaptation enables precise discrimination of contrast over wider ranges in areas V1 to V3, while area V4 responds to the actual contrast changes.

Area V4 seems to be sensitive to salient changes in the environment, that is it can not only detect the extent of changes but also the corresponding weaknesses in the immediate surroundings. This feature of area V4 most likely enables the area to serve as a monitor of changes in the ambient environment.

### Expected Application to Aging Society

Aging leads to slower responses in various aspects of daily life. For example, older drivers have slower reactions to changes in traffic lights or when a pedestrian steps unexpectedly onto the road. If we can determine the relationship between the ability to respond to changes in scenery and how the visual system monitors those changes, then results like these may help improve our social lives.

# Next generation light source for all scientists

The X-ray free electron laser (XFEL) will make great contributions to the new frontiers of science. It is a new type of light that is a billion times more intense than the X-rays at SPring-8. With this new light it will be possible to see the smallest known parts of the world, things that are 0.1 nanometers or smaller—opening up new methods for studying biological and physical phenomena.

## KEY CONCEPTS

- 1 Short, atom-sized wavelengths
- 2 Coherent light waves with aligned, regular peaks and valleys
- 3 Light a billion times more intense than conventional light
- 4 New light exposes new directions in science

## In the words of the researchers

### Tetsuya Ishikawa

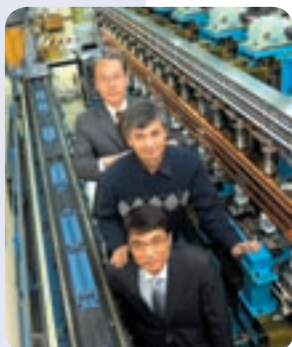
(at the front)  
RIKEN SPring-8 Center  
Coherent X-ray Optics Laboratory

### Hideo Kitamura

(in the middle)  
RIKEN SPring-8 Center  
Coherent Synchrotron Light Source  
Physics Laboratory

### Tsumoru Shintake

(at the back)  
RIKEN SPring-8 Center  
Advanced Electron Beam Physics  
Laboratory



## Hitherto unseen phenomena exposed with a new laser

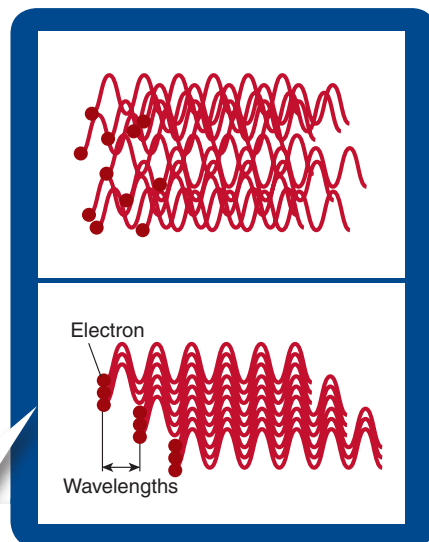
When this plan was first proposed at a symposium fifteen years ago, it was dismissed as technically infeasible. However, four technological developments that contributed to the development of SPring-8 made this project suddenly feasible. These are a low-emittance electron gun and high-gradient field C-band accelerator (both proposed by Shintake), an In-Vacuum Undulator by Kitamura, and Ishikawa's beamline technology. When combined they created a facility on the SPring-8 compound that could generate intense and stable X-rays with wavelengths of 0.1 nanometers or shorter. This facility is smaller than its foreign counterparts. We then constructed a 60-meter test accelerator in 2005. Once our plan was designed as "a key technology of national importance", the construction of a fully-fledged accelerator in 2006 started making it possible to produce a light never before seen by humans.

## Conventional X-rays reveal only 20–30% of all protein

A worldwide effort to analyze the structures of proteins is underway to determine the basic mechanisms at work in living beings. Getting X-ray diffraction images of proteins is one way to do this, however the protein must first be crystallized before it can be irradiated to get an image. This is unavoidable, even at the largest synchrotron radiation facility, SPring-8. Since only 20–30% of proteins can be crystallized, this means that most proteins cannot be analyzed. Developing a more intense X-ray that can analyze non-crystallized proteins would make it possible to study more.

## Next generation light—the X-ray free electron laser (XFEL)

X-ray radiation facilities, including SPring-8, generate ordinary X-rays by feeding electrons to an undulator. An undulator controls the motion of electrons with magnets. When electrons excited into a high-energy state pass through the undulator, their orbits are twisted by the magnetic field. They generate X-rays, but their positions are irregular and not aligned. If these unbound electrons could be aligned before they can release X-rays, they might generate more intense X-rays. The X-ray free electron laser (XFEL) is created by aligning the electrons before X-rays are produced.



## Natural light (top) and coherent light (bottom)

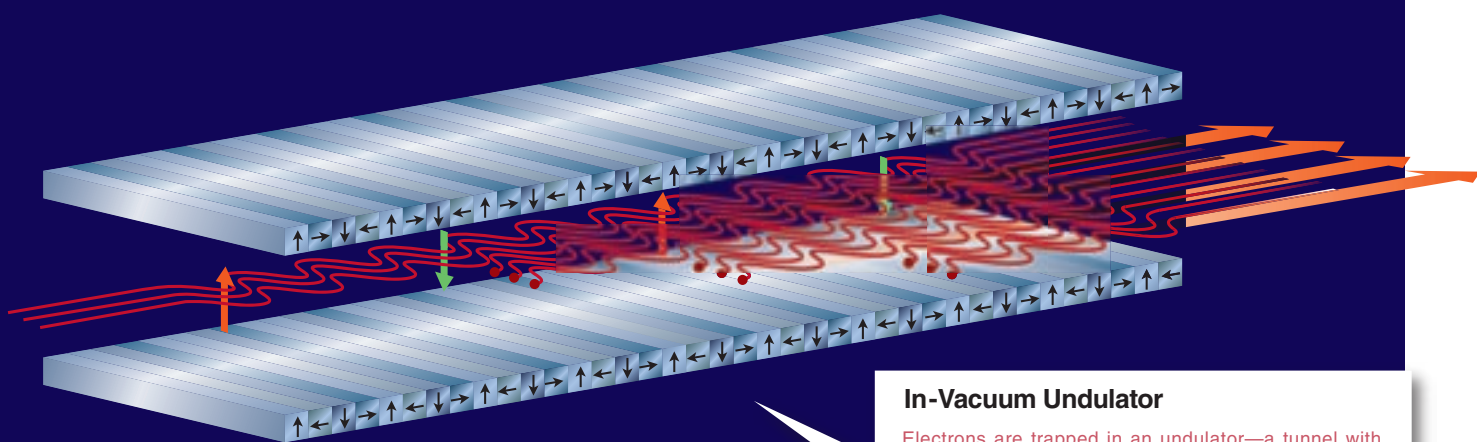
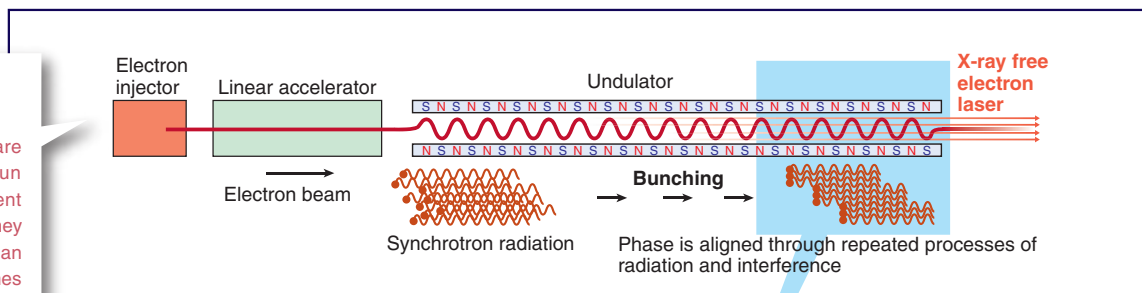
Ordinary, or natural, light generates wave frequencies with disorder peaks and valleys that can cancel each other out and thereby weaken the intensity of the light. When, however, the positions of electrons that generate these highs and lows are aligned so that each wave's peaks and valleys is synchronized to the peaks and valleys of all the other waves, light becomes more intense. This uniform procession generates coherent light. Laser light is coherent light. The XFEL project team is working on creating a coherent X-ray laser that is one billion times brighter than SPring-8's X-ray by forcing the electrons into a synchronized procession.





### How does XFEL work?

Highly parallel electrons are shot from the electron gun into C-band a high-gradient linear accelerator where they gain speed and generate an electron beam that becomes an X-ray free electron laser (XFEL) as the beam travels through this new, elongated undulator.



### In-Vacuum Undulator

Electrons are trapped in an undulator—a tunnel with double-layered magnets aligning all along the tunnel that alternates north and south poles. The magnets force the electrons down the tunnel to generate intense synchrotron radiation. An In-Vacuum undulator has magnets placed within a vacuum container to narrow the space between magnets. Micron precision magnet positioning generates the free electron laser.

### X-rays cast no reflections in mirrors

Most modern FEL are infrared light, and generated by mirrors at both ends of the undulator that cause electrons to bounce back and forth. In this way the infrared light passes repeatedly through the undulator and, through those oscillations, the phases of infrared light are aligned and amplified. However, mirrors cannot reflect X-ray light, so another method was used to amplify the light. Instead of a single undulator, X-ray light passed through several undulators, where each aligns the phase and amplifies laser light intensity as the electrons move from one undulator to the

next. The electrons travel about 1 km in the XFEL device—a testament to the successful, interdisciplinary collaboration between engineers and researchers from a legion of disciplines.

### XFEL exposed new worlds

This new light will have significant impact on our future. DVDs are the offspring of basic research on ruby lasers made public in 1960. Discovering optical technology makes visible matter that once eluded us—it exposes us to new possibilities. Decades from now, we will be creating new materials by modify the temperature or pressure of materials, techniques that defy conventional

approaches. Successful construction of an XFEL will mean that we can expose the world to light that is one billion times brighter than the X-ray generated at SPring-8. Analytical operations, which take several hours with SPring-8, will be completed in a second. XFEL produces a wavelength with cycles measuring about the diameter of an electron (approximately 0.1 nanometers), giving it the power to analyze materials at the atomic level. Just as infrared lasers greatly changed contemporary physics 40 years ago, XFEL will dynamically influence the course of natural sciences in the coming decades.

## Discovering a new RNA Continent

The view of the mammalian genome and its content changed drastically when RNA transcripts became the subject of extensive investigation. The Genome Exploration Research Group in the Genomic Science Center has discovered a previously overlooked transcription continent, whose existence is hard to reconcile with the conventional concepts of gene expression.

### KEY CONCEPTS

- 1 The “junk” sequences have gained in value
- 2 The number of non-coding RNAs equals the number of protein-coding transcripts
- 3 Regions of DNA can be transcribed in both directions, giving functional products that may interact
- 4 The concept of gene expression needs to be revised



### In the words of the researchers

**Yoshihide Hayashizaki**

Genomic Sciences Center  
Genome Exploration Research Group

### Remodeling the basics of life science by rewriting concepts of gene expression

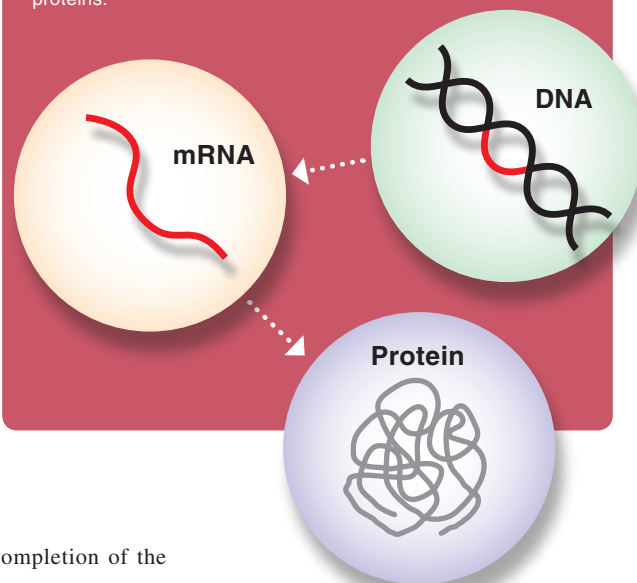
Genomic science emerged in the 1980s, and Japanese researchers quickly recognized the value of large-scale automated gene sequencing. But, while the U.S. announced that sequencing of the human genome would be completed by 2003, Japan could not secure the budget to undertake these projects.

To avoid competing with the U.S., I pursued new technologies that led to work on cDNA just when the functional merits of those technologies could be best appreciated. I was overcome with joy. I am proud to be an architect of the platform on which new life sciences will be built.

Sequencing all the transcriptomes is one of my remaining goals: I want to be a pioneer in this exciting new field and learn how to control the effects of non-coding RNA.

### The role of RNA in the classical concept of gene expression

Parts of DNA (genes) are “read” by specific enzymes, producing single stranded RNA transcripts, called mRNA transcripts. These transcripts are processed by cutting out parts of the transcript—a process called splicing which results in mature mRNA transcripts. Once mRNA transcripts are transported out of the nucleus, other enzymes translate them into proteins—the workhorses of the cell. Traditionally, the stretch of DNA coding for a protein was named gene, implicitly assuming that there were no transcripts not corresponding to proteins.

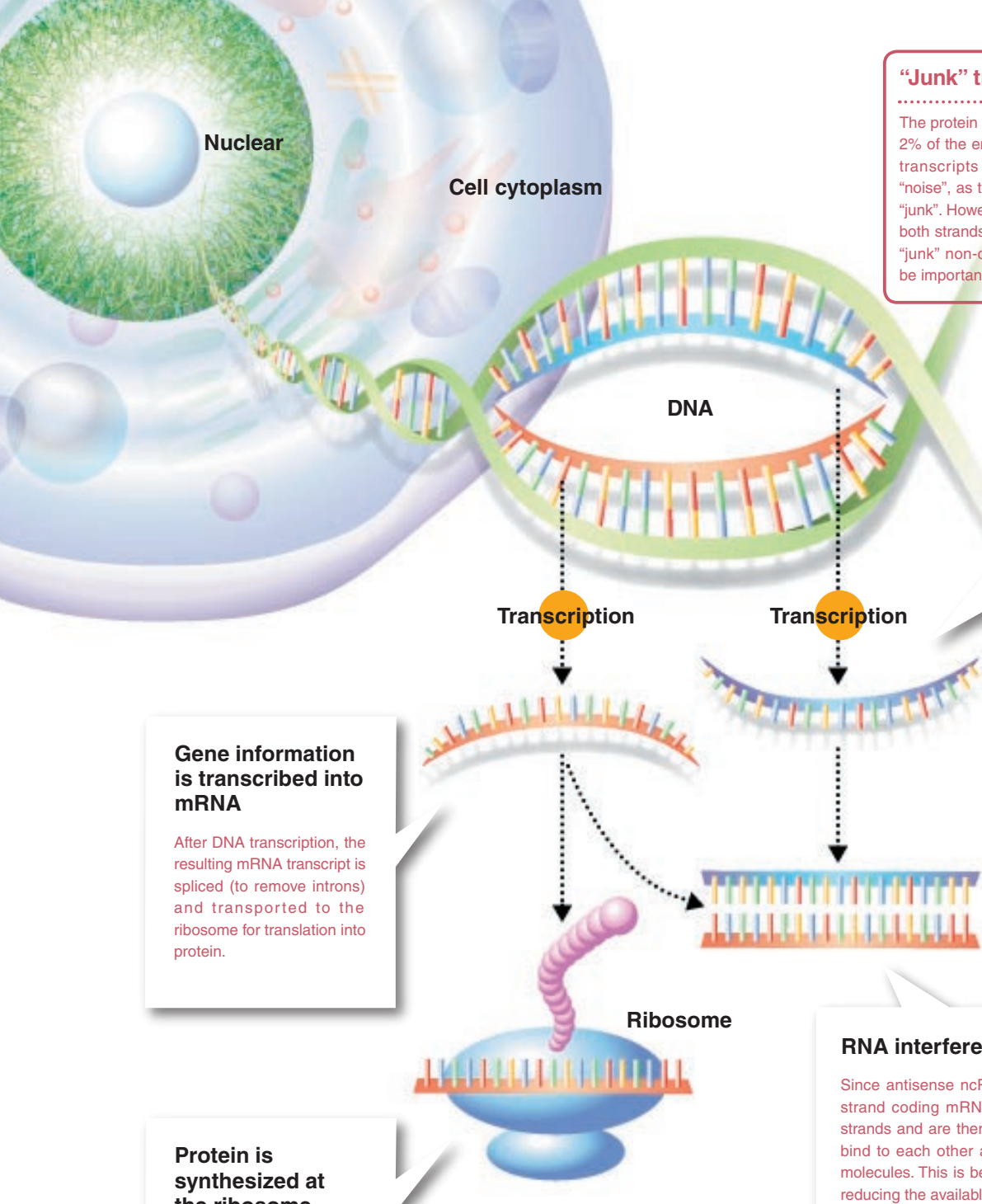


### From junk to gold

In April 2003, when the completion of the Human Genome Project was announced, humans were thought to have roughly 22,000 genes. What remained, most people believed, was the task of uncovering the functions of the proteins corresponding to those genes. The Genome Exploration Research Group of the Genomic Science Center proved this to be a premature conclusion. The human genome has around three billion base pairs, and only 2% codes for proteins. The remaining 98% was considered “junk” DNA, meaningless material. However, this junk holds a gold mine of information.

### The number of non-coding RNA equals the number of coding RNA

The researchers collected all transcribed mRNAs in the mouse to study the transcriptome. They found that 70% of the total genome is both transcribed and spliced. Interestingly, half of all these transcripts (23,318 of 44,147), turned out to have no corresponding protein—non-protein coding



**“Junk” transcripts**

The protein coding transcripts are only about 2% of the entire genome’s transcripts. Other transcripts were traditionally considered “noise”, as the rest of DNA was regarded as “junk”. However, evidence for transcription of both strands of the DNA was found, and the “junk” non-coding transcripts turned out to be important gene expression regulators.

**Sense versus Antisense**

The strands are named sense and antisense according to the transcriptional direction of the transcript of interest, irrespective of the coding potential. The same region on both strands can be either coding on the sense strand while non-coding on the antisense strand or coding, respectively non-coding, on both strands at the same time. This is due to the fact that the gene of interest is by convention said to be located on the sense strand. The transcript on the other strand then becomes antisense by default, regardless of the actual transcript’s coding potential.

**Gene information is transcribed into mRNA**

After DNA transcription, the resulting mRNA transcript is spliced (to remove introns) and transported to the ribosome for translation into protein.

**RNA interference**

Since antisense ncRNA is complimentary to sense strand coding mRNA (they are copies of opposite strands and are therefore complementary), they can bind to each other and form double stranded RNA molecules. This is believed to regulate translation by reducing the available amount of mRNA transcripts.

**Protein is synthesized at the ribosome**

When the mRNA transcript arrives at the ribosome, the information in the mature mRNA is translated into an amino acid sequence. When the amino acid sequence is finished, it folds into a protein.

transcripts (ncRNA). The large majority of these transcript has unknown functions. This vast array of transcripts was named the “RNA continent”, a large realm within the world of the genome. We are sure we will find a similar “RNA continent” in the human genome.

**On the Other Strand ...**

DNA has two strands, named “sense” and “antisense” according to transcription direction. It was generally assumed that a region of DNA could only be “read” in one direction. It was therefore surprising when our researchers found that as much as 72% of all known genes also have transcripts on the other strand, called antisense transcripts. These may bind to the coding transcript to block splicing and translation, thereby regulating gene expression.

**Full-length cDNA Technology**

These studies used full-length complementary DNA (cDNA) technology developed by this laboratory. Unlike DNA, RNA is fragile and quickly decomposes. In order to have a stable molecule with the same information content, the RNA transcripts are reversely transcribed into cDNA. However, this technique yielded only short cDNA fragments for a long time. With the full-length cDNA technique, researchers are now able to capture entire sequences. This technology was an absolute requisite for the results described here.

# Genetic determination in rice yields

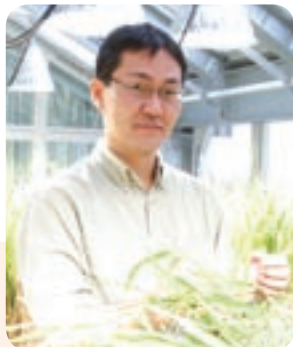
As the world's population continues to grow, food production remains stable.

Increasing crop yields with increasing land demands is one way to avoid possible food shortages.

The Biodynamics Research Team at the Plant Science Center in Yokohama exploited the now fully sequenced rice genome to find the gene that determines the number of grains of rice each stalk produces and create a new strain of Koshihikari that is hardier and produces 20% more rice.

## KEY CONCEPTS

- 1 Identified key gene in determining rice yield
- 2 Created a new, short, hardy rice plant that produces 20% more rice
- 3 Using traditional crossbreeding techniques instead of genetic modification.
- 4 Contributed to the green revolution by promising large increases in rice production



### In the words of the researchers

#### Hitoshi Sakakibara

Plant Science Center  
Plant Productivity Systems Research Group  
Biodynamics Research Team

### Developing a new rice strain with traditional breeding methods, safely

It used to take twelve years to create better strains of plants using traditional approaches to cross-breeding simply because we could not easily identify the genes that were associated with desirable characteristics. However, with the full sequencing of the rice genome in 2002, it became possible to develop new methods of research that exploit this genomic information.

The same methods used to discover the yield-determining gene of rice can easily be used with other grains such as corn and wheat to help increase their productions.

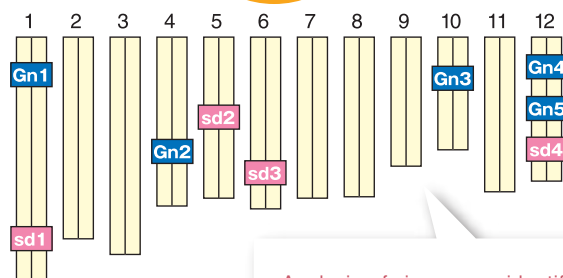
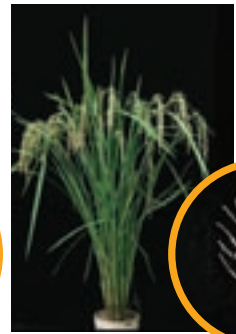
In the future, we would like to study cytokinin, a phytohormone discovered some 50 years ago, in the hope that our findings can be applied to efforts to increase the biomass of trees and other organisms and thereby further enhance plant productivity.

### Height and grain output comparisons of Koshihikari and Habataki

#### Koshihikari



#### Habataki



Analysis of rice genes identified [Gn] gene region as the region associated with grain output. Most influential of those genes was a gene in the Gn1 region. In addition, genes [sd] related to the height of rice were located at the sd1 area in the p1 region.

### Inspired by the Rice Genome

The contributions by Japanese researchers to deciphering the rice genome were significant, especially in today's global setting where countries are competing to create high-yield varieties of rice plants that are also resistant to diseases, insects and climate. While the over-production of rice in Japan is now raising concern, there are many countries in the world suffering food shortages. Increasing the production of stable grains, therefore, is a mid- to long-term priority for the world, especially since its population is expected to reach nine billion by 2050.

Working with researchers at Nagoya University and Honda Research Institute Japan, Hitoshi Sakakibara, the leader of

the Biodynamics Research Team, crossed Koshihikari, the preferred rice in Japan, with Habataki, a rice popular in India and other countries. The strain was selected to have characteristics from both parent plants so that it would be possible to determine which gene contributes to those traits in the parent plants.

### Cytokinin, a phytohormone, is the crucial factor

The gene that determines grain output was located following extensive analysis in the

**Introducing useful genes efficiently with crossbreeding**

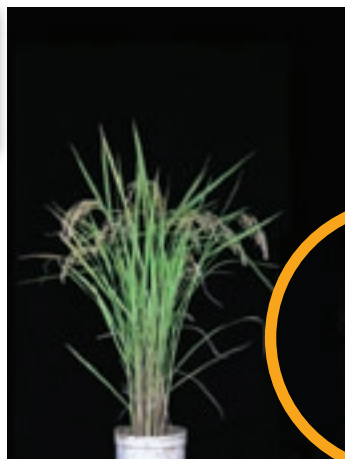
**1 Koshihikari**



Koshihikari is tasty, but its height makes it vulnerable to strong winds



**2 Koshihikari + sd1**



Habataki-derived sd1 is introduced into Koshihikari. Offspring were shorter, but grain production remained the same.



**+sd1**

**3 Koshihikari + Gn1**

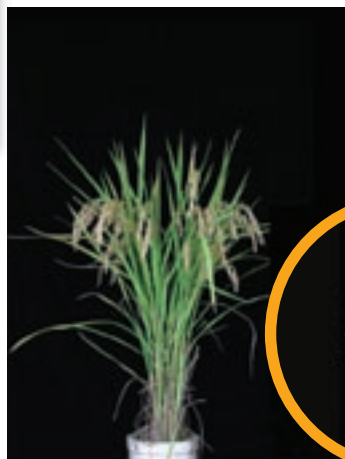


Habataki-derived Gn1 is introduced into Koshihikari. Offspring were as tall as Koshihikari and yielded an increased number of grains. However, each ear of rice is too heavy for the plant to support it, so the plant falls over easily.



**+Gn1**

**4 Koshihikari + sd1 + Gn1**



sd1 and Gn1 are introduced into Koshihikari. The resulting strain of Koshihikari has limited height but an increased rice grain output after five repeated crossings that introduced Habataki genes to Koshihikari.



**+sd1**  
**+Gn1**

[Gn1] area of the brachial on chromosome 1 of rice. Further studies showed that this gene regulates the degradation of cytokinin, a phytohormone.

Cytokinin has several physiologically active functions, including the promotion of cell division and preventing aging. In our studies, the OsCKX2 gene is less active and cytokinin degradation is restricted, and cytokinin content is able to accumulate in the flower bud and produce more flowers. A corresponding increase in grains of rice follows. This presence of this gene in Habataki explains why it is more productive than Koshihikari.

In a parallel study aimed at identifying the height-determining gene of rice, we

identified a gene in the Ph1 region of the lower arm of chromosome 1 that plays a key role in producing shorter rice plants that are less susceptible to strong winds and rains.

**Second Green Revolution with Molecular Breeding**

To introduce Habataki-derived genes that would increase yield and reduce height, the researchers used traditional crossbreeding techniques in combination with molecular breeding that used data from genetic screenings of two varieties is used in parallel. Genetic modification techniques, which are controversial, were not used. After several successful crossings, the researchers produced a

strain of Koshihikari that is approximately 18% shorter and with approximately 20% more grains per stalk than other variations of Koshihikari.

In the 1960s, the International Rice Research Institute in the Philippines started the “Green Revolution” when they produced a high-yield variety of rice. They indirectly increased yields by reducing the height of rice and, thus, making it more robust in harsh weather. RIKEN’s researchers did not merely try to prevent rice plants from falling—they also tried to increase grain yield. They were successful, and with this new technological method now proven, may trigger the Second Green Revolution and help avoid future food shortages.

Reference: Ashikari, M., Sakakibara, H., Lin, S.-Y., Yamamoto, T., Takashi, T., Nishimura, A., Angeles, E. R., Qian, Q., Kitano, H. and Matsuoka, M. Cytokinin oxidase regulates rice grain production. Science 309:741–745 (2005).

# Slight genetic differences may cause autoimmune diseases

Inflammation of the tissue surrounding the joint leads to rheumatoid arthritis, a painful autoimmune disease that many believe has genetic risk factors.

This year researchers of the Laboratory for Rheumatic Diseases at the RIKEN SNP Research Center compared genetic sequences between rheumatoid arthritis patients and non-patients and identified one of the causal genes of rheumatoid arthritis: FCRL3.

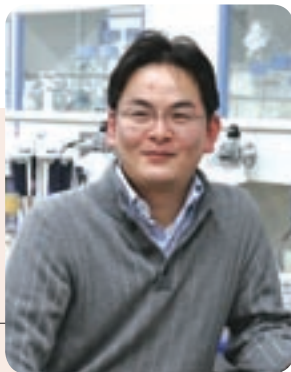
## KEY CONCEPTS

- 1 Variations of FCRL3 may be a cause factor in rheumatoid arthritis
- 2 FCRL3 is expressed in lymph cells
- 3 One form of FCRL3 leads to more antibodies production than other forms
- 4 A treatment for autoimmune diseases may soon be possible

## In the words of the researchers

### Yuta Kochi

SNP Research Center  
Laboratory for Rheumatic Diseases



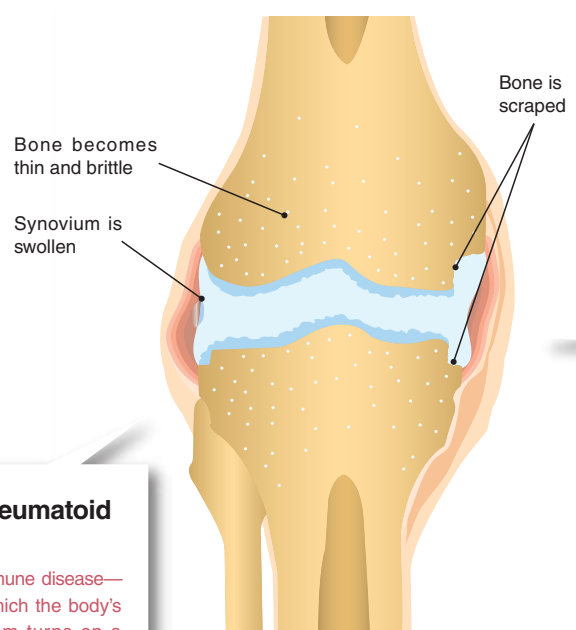
## Small genetic differences make new treatments possible

As an internal clinician treating patients suffering from rheumatism, I have wondered why we could see such variation in the course of the disease and in response to treatment. I suspected that differences in genes might just provide the answer.

It is commonly said that less than 0.1% of the human genes are different from person to person, and it is these slight differences that determine the overall health and susceptibility of any individual to disease. Now, thanks to significant advances in technology, it is now possible to detect individual genetic variations and identify those variations that might increase one's risk for certain diseases. Such investigations will influence not just how diseases may be cured or treated, but also how to address differences in disease progression in response to treatment. This revolutionary approach will not just impact medicine and immunology, but will also make it possible to develop customised treatments based on the genetic composition of the patient.

## What is rheumatoid arthritis?

It is an autoimmune disease—a disease in which the body's immune system turns on a specific part of itself – that is triggered sudden inflammation of the tissue lining the joints between bones, a tissue called synovium.

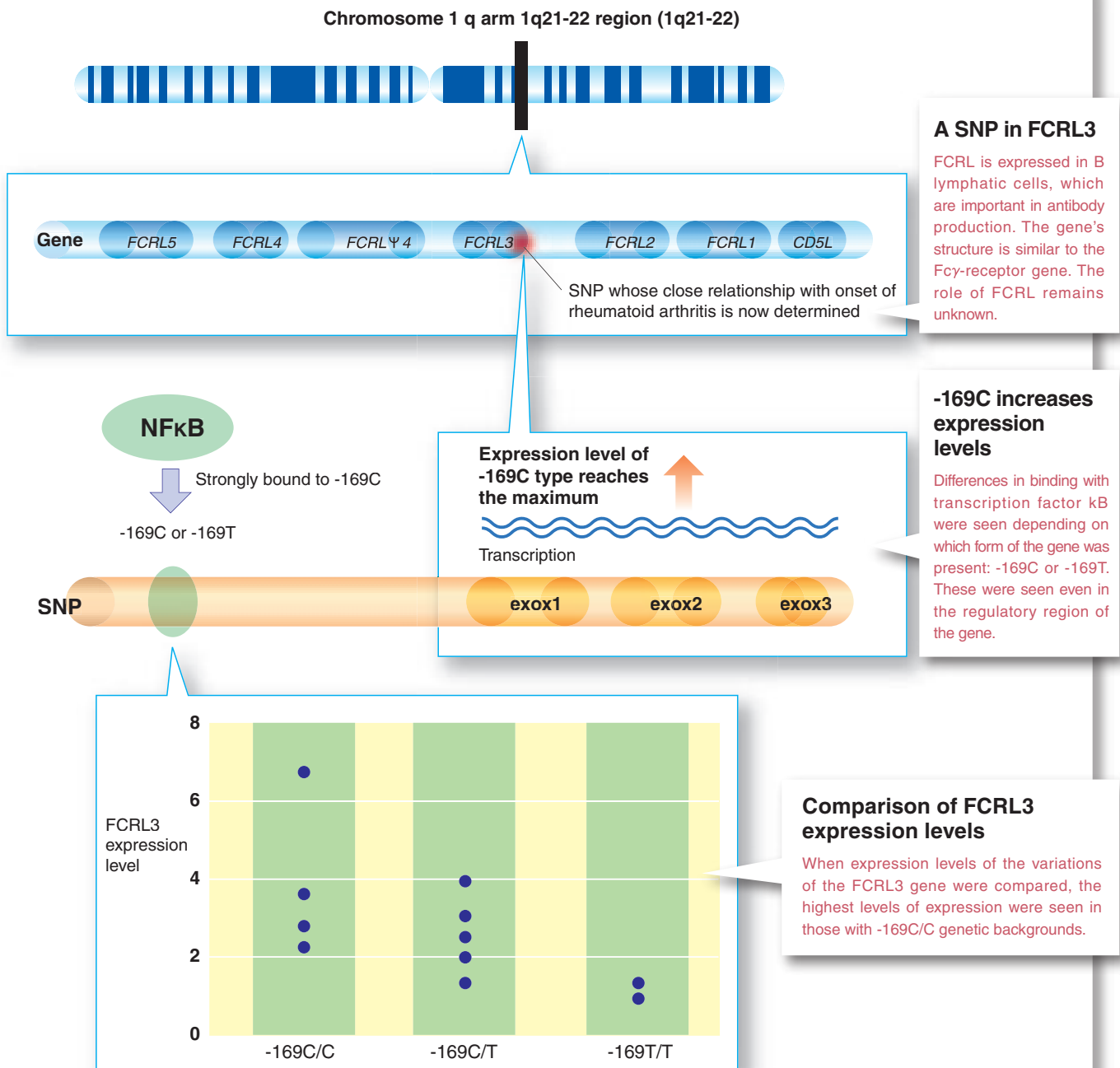


## Identified: a causal gene for rheumatoid arthritis

More than 5% of the people in Japan have some form of autoimmune disease or allergy in which the body's immune system turns on the body in one way or another. These diseases have complex pathological processes that complicate efforts to development reliable therapies. One common autoimmune disease is rheumatoid arthritis, which causes pain and immobility as joints to swell and deform. The process begins when the

tissue that lines and cushions the joint, the synovium, swells.

Yuta Kochi and his team focused on single nucleotide polymorphisms (or SNPs) to find clues to the genetic roots of rheumatoid arthritis. A SNP is a tiny difference in DNA, just one letter, that can account for much of the variations seen in people. Analyses of gene sequences between patients with arthritis and normal subjects revealed a polymorphism, a naturally occurring variation of a gene, in FCRL3 that is closely related to the onset of this disease.



## FCRL3 controls B-cells

Looking at the full genomes of patients with rheumatoid arthritis, the researchers identified how transcription factors bound more strongly to SNP that controls FCRL3 expression, thereby increasing that gene's expression levels. Those patients who have a certain form of FCRL3 with high expression also had higher levels of autoantibodies in the blood—a sign associated with the onset of arthritis.

While the function of FCRL3 is not yet known, its expression is also seen in B-cells in the spleen

and the tonsils. B-cells are a type of lymph cell that participates in immunity. FCRL3 appears to increase B-cell activity, which increases the number of autoantibodies in the body.

## Anticipating cures for autoimmune diseases

Collaborative research conducted at the SNP Research Center and at various research institutes inside Japan and overseas, including the University of Tokyo, International Medical Center of Japan, University of Oklahoma (U.S.A), Hanyang University (S. Korea), and

Sankyo Co. Ltd. Together, they found that carriers of this polymorphism were also more susceptible to lupus, Graves' disease, and chronic thyroiditis. The rate at which carriers of this form of the gene report some form of autoimmune disease is two times higher than those with a different form. About 35% of Japanese carry this form of the gene.

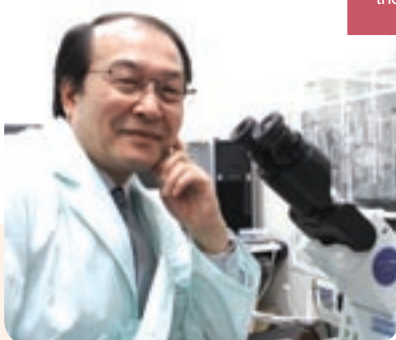
If the role of FCRL3 in immunity and in autoantibody production can be determined, new methods for treating and even preventing rheumatoid arthritis and other autoimmune disorders will soon be possible.

# Molecular microclusters trigger immune responses

How does the immune system start and sustain its response to biological threats? The Laboratory for Cell Signaling, at the Research Center for Allergy and Immunology, discovered that immune responses start and continue at a site called a “microcluster”, which is formed by receptors and signaling molecules.

## KEY CONCEPTS

- 1 Immune responses start at microclusters
- 2 Microclusters are generated at the interface between T cells and antigen-presenting cells
- 3 Microclusters also maintain T cell activation
- 4 New types of immune-modulating drugs may emerge as a result of this study



### In the words of the researchers

#### Takashi Saito

Research Center for Allergy  
and Immunology  
Laboratory for Cell Signaling

### An immune suppressor on the horizon

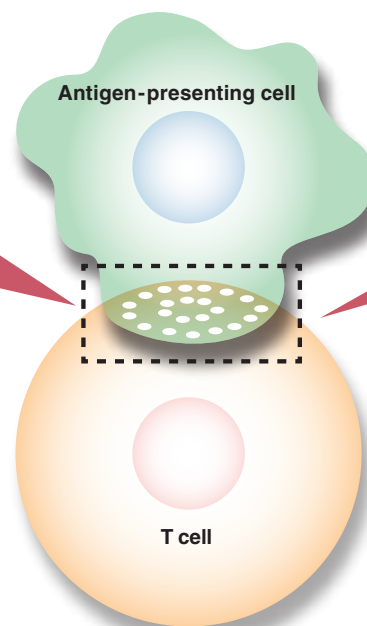
RCAI has already developed a microscope that makes it possible to observe the movement of a single molecule. Our work exploits real-time nano-level analyses made possible by this microscope to observe and understand the complex molecular activity of the immune system. Observations of the dynamic behavior at the site of the immune synapse revealed that immune response begins at a microcluster.

For treatment and resolution for allergies, autoimmune diseases and rejections after organ transplantation, it is crucial to regulate immune responses. The drugs that have been used for this purpose were designed to suppress the T cell function. This finding is expected to pave the way for the development of more advanced drugs that may specifically modulate activation of T cells.

### Microcluster

Upon contact between a T cell and an APC, hundreds of microclusters were formed where activation signals are transduced and maintained. We have found that this formation of microclusters is the start of the immune response.

The moment at which a T cell comes into contact with an antigen-presenting cell and recognizes an antigen, and induces activation signals



### Immune Responses start at Microclusters

The immune system is indispensable for protecting our body from foreign agents. Immune responses start as antigen-presenting cells (APCs), which take in and decompose foreign substances (antigens) such as viruses and pollens, and give information about antigens to T cells, one of the lymphocytes, so that the T cells can recognize antigens.

However, researchers have previously been unable to pinpoint correctly where that information exchange takes place so as to understand how the immunological reactions begin. As immune responses start, receptors and signaling molecules in cells gather to form a unique structure, called an immunological synapse, at the interface between T cells and APCs. It was believed that this was the

starting point of immune responses.

Utilizing bio-molecular imaging techniques, Group Director Takashi Saito of the Laboratory for Cell Signaling, and a researcher in his group, Tadashi Yokosuka, have succeeded in observing dynamic movements of molecules at the interfaces between T cells and APCs through the high-sensitivity laser microscope (the Single-Molecule Microscope). This observation was achieved in collaboration with Unit Leader Makio Tokunaga and senior researcher Kumiko Sogawa of the Laboratory for Single Molecule Immunoinaging. Together, the team was able to see that conventional beliefs about the immune synapse's role in immunological behavior were wrong. It was not the synapse but a microcluster that triggered the immune response. The microclusters form about ten minutes before the immune synapse, also

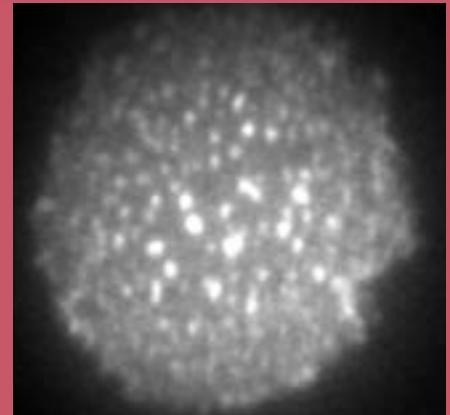
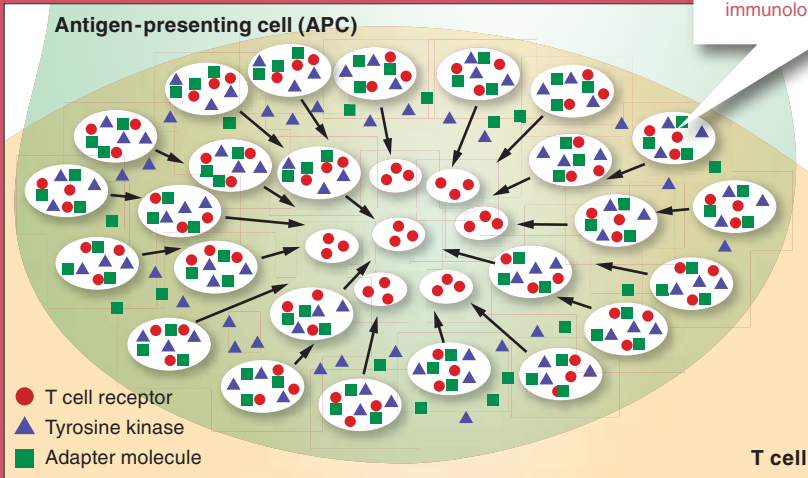


**Microclusters are involved in starting and sustaining immune responses**

**Moving microclusters**

A microcluster, a complex of activation molecules consisting of T cell receptors (TCR) and signaling molecules, moves to the center and forms c-SMAC. Antigen receptors gather at the center of immunological synapses.

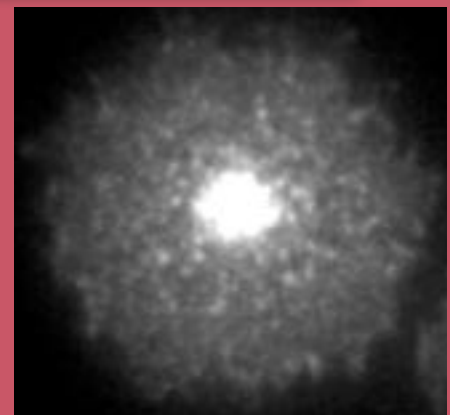
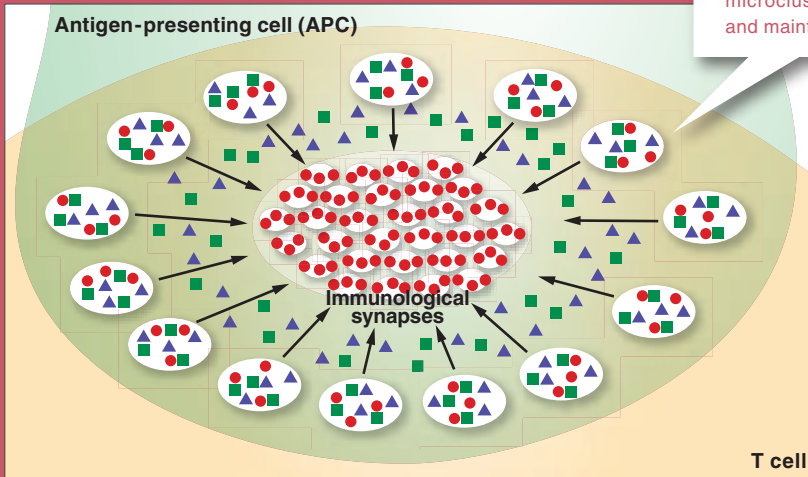
**Microclusters immediately after contact between the T cell and the APC**



**Microclusters after immunological synapses have been formed**

**Maintenance of activation at the peripheral microclusters**

Even after the immunological synapses form, microclusters are still continuously generated and maintain the activation.



suggesting that immune responses start immediately after the entry of antigens, and harmful antigens are detected more quickly than has been believed.

**Microclusters maintain immune responses, too**

A microcluster is a small chunk of 50–200 molecules that gather on the surface of a T cell. A microcluster is comprised of receptors that recognize antigens, and signaling molecules that transfer information.

After being generated, microclusters migrate toward the center of the interface and form the central part of an immunological synapse. Protein phosphorylation and

other molecular processes are completed before the microcluster reaches the center. Once the immune synapse is formed, other microclusters continue to emerge along the periphery of the contact surface.

From these observations, we could see that immune response activation does not occur at the immunological synapse but at the peripheral microclusters. This mechanism is responsible not only for starting but also for sustaining immune responses.

**Controlling T cell activation medically**

Many people suffer from allergies and autoimmune diseases such as rheumatism and

nephritis. These diseases are caused by over-activated immune systems.

In organ transplants, immuno-suppressors are needed to prevent rejection. On the other hand, the role of adjuvant, immune activators, boosting the immune system, has been drawing the attention of doctors in cancer treatment and health promotion for elderly people.

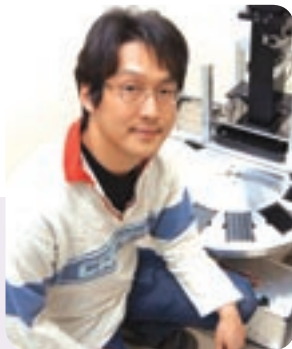
The specific enzymes that work in cell signaling systems have been regarded as the keys to control the immune system. Now microclusters have been shown to trigger and sustain T cell activation and have become a target for research on artificial regulation of the immune response.

# Revealing the genetic processes controlling circadian rhythm

Circadian clocks regulate several biological processes in many types of organisms, including mammals, in which these clocks control sleep/wake cycles, blood pressure, body temperature and hormone secretion. Now researchers in the Laboratory for Systems Biology have identified the DNA sequence that switches the morning switch on, thereby regulating the whole circadian process.

## KEY CONCEPTS

- 1 Developed technology that accurately measures circadian rhythm at the cellular level
- 2 Developed technology to manipulate protein function molecularly
- 3 Proved that the role of the on/off switch in the circadian clock is associated with the morning sequence
- 4 Opens the door to developing new treatments for biorhythm disorders



### In the words of the researchers

**Hiroki Ueda**

Center for Developmental Biology  
Laboratory for Systems Biology

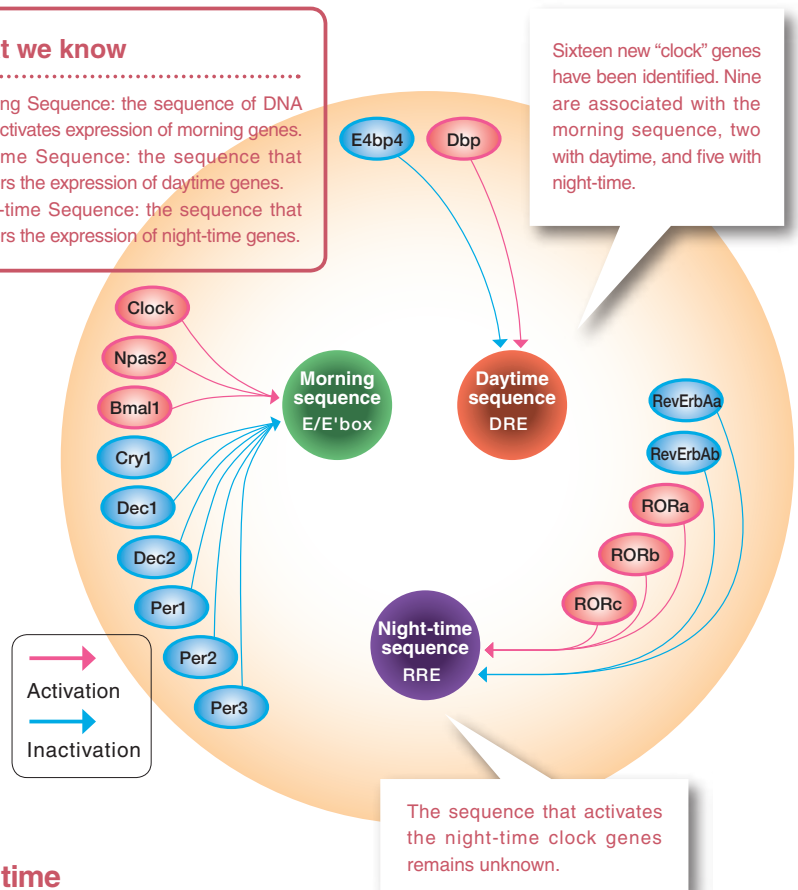
## Quantitative analysis of huge data sets reveal clock genes

I was in my third year of university when the draft genome sequences of *E. coli* and yeast were published. Even those simple organisms have thousands of genes, and the equipment at the time meant it was so time and labor intensive just to decode a single gene that I believed unlocking the secrets of life would be impossible without the aid of robots and computers. Undaunted, I set my undergraduate mind to find ways to effectively handle massive amounts of data and testing.

I chose to study circadian rhythm because the phenomenon needs to be studied in time and that time, more than any other factor, is key to its actions. Having nearly cracked that, I want expand my study to include the role of space. I hope to understand how life itself emerges from processes like differentiation and regeneration.

### What we know

- Morning Sequence: the sequence of DNA that activates expression of morning genes.
- Daytime Sequence: the sequence that triggers the expression of daytime genes.
- Night-time Sequence: the sequence that triggers the expression of night-time genes.



## Circadian time

In the 18th century, Carolus Linneaus, a Swedish botanist, created a flower clock garden that kept time by noting the different opening and closing times of the various flowering plants. While not perfect, the timepiece took advantage of a well known fact about plants and animals—most living organisms have a cyclical sense of time, a circadian clock. While empirical evidence for circadian phenomena in flowers, bacteria, flies, mice and humans exists, the mechanism that regulates this activity at the genetic level was elusive.

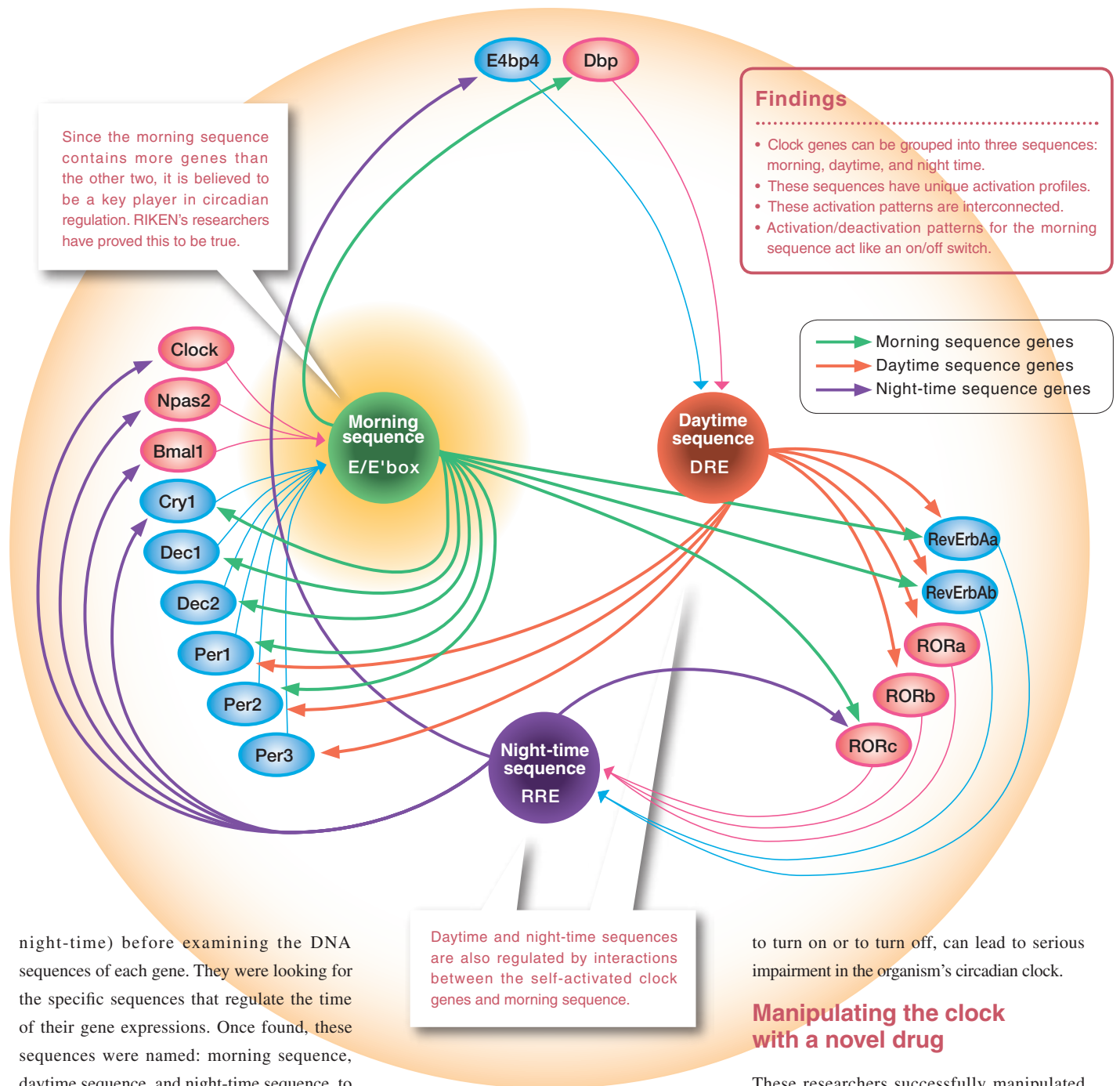
That is, until the Laboratory for Systems Biology in the Center for Developmental Biology at RIKEN Kobe Institute found the genetic on/off switch. This switch is a DNA

sequence, the morning sequence, that activates the morning genes, those genes that rise with the sun. This DNA switch has a critical role in regulating that bio-function.

## How does the morning sequence regulate circadian rhythm?

To date, sixteen genes that keep track of time have been identified. Each of these “clock genes” is expressed for a specific duration of time during the day, but to observe this the researchers first needed to developed special experimental tools.

Tools in hand, the researchers classified the genes into three groups (morning, daytime,



Since the morning sequence contains more genes than the other two, it is believed to be a key player in circadian regulation. RIKEN's researchers have proved this to be true.

### Findings

- Clock genes can be grouped into three sequences: morning, daytime, and night time.
- These sequences have unique activation profiles.
- These activation patterns are interconnected.
- Activation/deactivation patterns for the morning sequence act like an on/off switch.

- Morning sequence genes
- Daytime sequence genes
- Night-time sequence genes

Daytime and night-time sequences are also regulated by interactions between the self-activated clock genes and morning sequence.

night-time) before examining the DNA sequences of each gene. They were looking for the specific sequences that regulate the time of their gene expressions. Once found, these sequences were named: morning sequence, daytime sequence, and night-time sequence, to correspond to each category.

The next step was to determine what each of these sequences did. When they overexpressed genes that inhibit morning sequence activity (E-box/E'-box), the expression levels of all the clock genes fell, not just the morning sequence. By contrast, inhibition of daytime (D-box) and night-time sequences (RPE) affected only the gene expression in each sequences associated gene group.

What would happen if the opposite process was performed? If the genes in the morning sequence were dominantly activated to sustain activity throughout the day, what would happen? To do this, the team inserted mutations on two genes: Bmal1 and Clock, that prevent morning gene inactivation. Of the 6,000 mutations only seven are found

to prevent inactivation: three Clock and four Bmal1 mutants. These mutants were introduced into cultured mouse cells and the cell responses were monitored. Various combinations were used to determine the phenotype of each mutation. In this way, they found that the mutants, which are insensitive to repressors that turn off activation, disrupt the biological rhythm.

Therefore, impairing either the activation (turning on) or inhibition (turning off) of gene expression for genes in the morning sequence affects the cell's sense of time. The circadian rhythm becomes disordered. Clearly an on/off switch in the morning sequence is important in maintaining an appropriate circadian rhythm. Inappropriate activity on either side, i.e. failure

to turn on or to turn off, can lead to serious impairment in the organism's circadian clock.

### Manipulating the clock with a novel drug

These researchers successfully manipulated the functions of these genes in mammalian cells, a feat that many feared to difficult. They used a method called function genomics that employs computational approaches to the analysis of huge amount of data to determine patterns of activation that might indication gene function. Systems biologists attempt to take these data and analyses and fit them into a complete picture of genetic function and structure within larger interactive networks of activity.

Looking forward, the finding will help a more detailed unfolding of the mechanisms of circadian rhythm. This may one day produce diagnostic and therapeutic processes to alleviate and prevent related disorders, including insomnia, depression, and withdrawal.

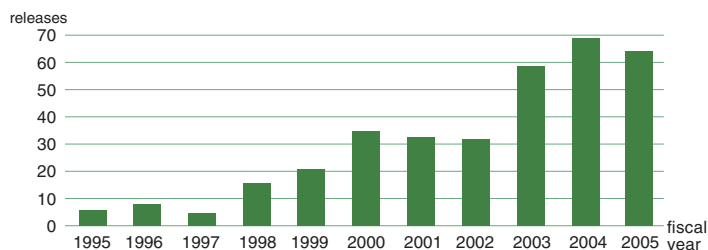
RIKEN issued sixty-four press releases to call attention to the research output of its various laboratories in FY 2005. The following table provides the pertinent details of those releases, including release date and title, institute, laboratory, researcher(s), and bibliographical data.

# 2005

Release Date	Title	Institute	Laboratory(ies)	Researcher(s)	Publication Information
Apr. 15	FCRL3: A possible genetic link for rheumatoid arthritis	SRC	For Rheumatic Diseases	Kazuhiko YAMAMOTO Ryou YAMADA Yuta KOCHI	Nature Genetics 37, 478–485 (2005)
26	Call for applications for Integrated Collaborative Research with Industry for fiscal year 2005	CIPS	Center for Intellectual Property Strategies (CIPS)		
27	New annual salary system for RIKEN Chief Scientists	Headquarters	Personnel Division		
27	Understanding slippage: genetic variations and lumbar disc problems	SRC	Laboratory for Bone and Joint Diseases	Siro IKEGAWA	Nature Genetics 37, 607–612 (2005)
28	DNA repair processes start with protein tags	DRI	Cellular Physiology Laboratory	Fumio HANAOKA	Cell 121, 387–400 (2005)
May. 10	Realization of an Artificial Atom with Carbon Nanotubes	DRI	Advanced Device Laboratory	Koji ISHIBASHI	Phys. Rev. Lett. 94, 186806 (2005)
13	Call for companies to participate in collaborative research on SNP analysis	SRC	SRC and Yokohama Research Promotion Division		
17	Merits of cellular stress during muscle development	DRI	Bioarchitect Research Group	Nobuhiro MORISHIMA	J. Cell Biol. 169, 555–560 (2005)
24	RIKEN–US jointly developed special computer now operational	DRI	RIKEN BNL Research Center	Hideto EN'YO	
24	Need new antibodies: More mutations, faster	DRI	Genetic Dynamics Research Unit	Kunihiro OTA	Nature Biotechnology, published online 29 May 2005
26	Discovery of the Cubical Expansion of Solid Oxygen by 1% in a Magnetic Field	Harima Institute	Quantum Magnetic Materials Research Team	Koichi KATSUMATA	J. Phys.: Condens. Matter 17, L235–L239 (2005)
Jun. 2	Release of the DNA Book® database	GSC	Genome Exploration Research Group	Yoshihide HAYASHIZAKI	
9	Elucidation of the Mechanism for the Switch from Proliferation to Differentiation of Retina Stem Cells	IRU	Masai Initiative Research Unit	Ichiro MASAI	Development 132, 3027–3043 (2005)
10	The database and search system for patent information are open to the public free of charge	CIPS	Center for Intellectual Property Strategies (CIPS)		
17	Discovery of a Protein Essential for Growth of Glial Cells which in turn Support Neurons	BSI	Laboratory for Neural Cell Polarity	Mineko KENGAKU Mototsugu EIRAKU	Nature Neuroscience 8, 873–880 (2005)
20	Call for themes for genetic research on diseases under the BioBank Japan Project	SRC	SRC Yokohama Research Promotion Division		
30	A new methodology for elucidation of unknown gene structures based on both tiling arrays and genome data	GSC	Rhename Informatics Team	Tetsuro TOYODA	The Plant Journal 43, 611–621 (2005)
Jul. 1	Establishment of the Center of Research Network for Infectious Diseases	Yokohama Institute	Yokohama Research Promotion Division		
1	Agrobacterium hijacks chloroplast metabolism	PSC	Biodynamics Research Team	Hitoshi SAKAKIBARA	PNAS published July 5, 2005
6	Solid State Laser for Subaru Laser Guide Star Adaptive Optics	DRI	Solid-State Optical Science Research Unit	Satoshi WADA	
19	Mechanism of proteins to obtain functions from small structural changes now explained	Harima Institute	Oligomeric Protein Crystallography Team	Naoki KUNISHIMA	Journal of Molecular Biology available online 20 July 2005
20	Elucidation of the New Infection Mechanism of Pseudomonas aeruginosa	DRI	Environmental Molecular Biology Laboratory	Toshiaki KUDO	J. Bacteriol 187, 5242–5248 (2005)
28	Elucidation of the Molecular Mechanism of the Initiation of Mitosis	DRI	Antibiotics Labaoratory	Hiroyuki OSADA	PNAS 102, 11663–11668 (2005)
29	Let there be light-sensing cells	CDB	Laboratory for Organogenesis and Neurogenesis	Yoshiki SASAI	PNAS 102, 11331–11336 (2005)
Aug. 5	Motion control of superconducting flux quantum	FRS	Quantum Phenomena Observation Technology Lab.	Yoshihiko TOGAWA	Phys. Rev. Lett. 95, 87002 (2005)
8	Structural analysis of the protein complex involved in the maintenance of plasmid DNA	DRI	Cellular Physiology Laboratory	Katsuhiko KAMATA Fumio HANAOKA	Molecular Cell 19, 497–509 (2005)
9	Great progress toward solution of the human visual structure	BSI	Laboratory For Cognitive Brain Mapping	Keiji TANAKA	Neuron 47, 607–620 (2005)

DRI..... Discovery Research Institute  
 FRS..... Frontier Research System  
 BSI..... Brain Science Institute  
 IRU..... Initiative Research Unit  
 CIPS..... BioResource Center  
 RSC..... RIKEN SPing-8 Center  
 GSC..... Genomic Sciences Center  
 PSC..... Plant Science Center  
 SRC..... SNP Research Center  
 RCAI..... Research Center for Allergy and Immunology  
 CDB..... Center for Developmental Biology

### Annual Press Releases



Release Date	Title	Institute	Laboratory(ies)	Researcher(s)	Publication Information
Aug. 10	Identification of the master genes directly associated with xylem cell differentiation	PSC	Morphoregulation Research Team	Taku DEMURA	Genes & Dev 19, 1855–1860 (2005)
19	Signs of quantum phase transition in a spin-ladder material have been observed for the first time	Harima Institute	Quantum Magnetic Materials Research Team	Koichi KATSUMATA	Phys. Rev. Lett. 95, 087204 (2005)
26	The discovery of a novel RNA Continent through comprehensive analyses of mammalian transcriptomes	GSC	Genome Exploration Research Group	Yoshihide HAYASHIZAKI	Science 309, 1564–1566 (2005) Science 309, 1559–1563 (2005)
Sep. 6	Development of High-performance Polymerization Catalysts Capable of Precisely Controlling the Polymer Structure	DRI	Organometallic Chemistry Laboratory	Zhaomin HOU	Speech in Japanese, at the Society of Polymer Science, Japan
16	Memorandum of Understanding on General Collaboration on life sciences and biotechnology between RIKEN and the Agency for Science, Technology and Research, Singapore	Headquarters	Policy Planning Division		
26	Promising new treatment for diabetes	RCAI	Laboratory for Immune Regulation	Masaru TANIGUCHI	JEM 202, 913–918 (2005)
27	Development of a Full-automatic Single Nucleotide Polymorphisms Analysis System	SRC		Yusuke NAKAMURA	
Oct. 4	First Determination of the Location of Short Gamma-Ray Bursts	DRI	Cosmic Radiation Laboratory	Kazuo MAKISHIMA	Nature 437, 845–850 (2005)
19	A joint statement with the Ministry of Agriculture, Forestry and Fisheries on the Rice Full-Length cDNA Encyclopedia DNABook®	GSC	Genome Exploration Research Group	Yoshihide HAYASHIZAKI	
21	Success in Design and Tertiary Structure Determination of an Artificial Protein	RSC	Biometal Science Laboratory	Yoshitsugu SHIRO	Journal of Molecular Biology online
24	International Consortium Completes Map of Human Genetic Variation	SRC		Yusuke NAKAMURA	Nature 437, 1299–1320 (2005)
Nov. 2	World's First Realization of Interconnected Nanowires	DRI	Surface Chemistry Laboratory	Maki KAWAI	Journal of the American Chemical Society 127,15030–15031 (2005)
7	Identification of the starting point of immune response: -- T cell receptor microclusters initiate and sustain T cell activation --	RCAI	Laboratory for Cell Signaling	Takashi SAITO	Nature Immunology 6, 1253–1262 (2005)
11	Establishment of the RIKEN Honorary Fellow program, and award of fellowship to Dr. Leo Esaki	Headquarters	General Affairs Section		
19	Elucidation of the Docking Mechanism of Hormone Granules to the Plasma Membrane	IRU	Fukuda Initiative Research Unit	Mitsunori FUKUDA	J. Biol. Chem. 280, 39175–39184 (2005)
21	A New Discovery in the Brain Mechanism Visually Recognizing "Objects"	BSI	Laboratory for Cognitive Brain Mapping	Keiji TANAKA	Nature Neuroscience 8, 1768–1775 (2005)
29	Powerful supercomputer environment formulation system for protein analysis come to completion: protein analysis become easier without expert knowledge	GSC	BioKnowledge Federation Research Team	Fumikazu KONISHI	
Dec. 1	Discovery of mechanistic basis of nascent T cell receptors Self-oligomerization by electrostatic interaction confers autonomous signaling	RCAI	Laboratory for Cell Signaling	Takashi SAITO	Nature Immunology 7, 67–75 (2005)
2	The development of a nano-coating material to improve the precision of nanofabrication by RIKEN and Tokyo Ohka Kogyo Co., Ltd.	CIPS	Innovative Nanopatterning Laboratory, CIPS Collaborator: Tokyo Ohka Kogyo Co., Ltd.	Shigenori FUJIKAWA	
7	Direct Observation of Electrons Movement of Molecular Crystals	RSC	Soft X-ray Spectroscopy Laboratory Condensed Molecular Materials Laboratory	Shik SHIN Reizo KATO	Phys. Rev. Lett. 95, 246402 (2005)
13	Discovery of a New Material That Contracts on Heating	DRI	Magnetic Materials Laboratory	Koji TAKENAKA	Appl. Phys. Lett. 87, 261902 (2005)
21	Fullerene doubles durability of photocatalyst coating material	DRI	Nanophotonics Laboratory	Satoshi KAWATA	Phys. Rev. Lett. 95, 267407 (2005)
26	Endurance of photocatalyst coating materials goes up twice using fullerene	CIPS	Integrated Materials Research Laboratory	Yusuke TAJIMA	

# 2006

Release Date	Title	Institute	Laboratory(ies)	Researcher(s)	Publication Information
Jan. 18	Development of a new manufacturing method for organic single-crystal devices	DRI	Condensed Molecular Materials Laboratory	Reizo KATO Hiroshi YAMAMOTO	Journal of the American Chemical Society
20	Public Release of Database of the predicted three-dimensional structures of influenza viral neuraminidase	GSC	Protein Research Group	Shigeyuki YOKOYAMA Hideaki UMEYAMA	
23	Establishment of basic policies regarding research misconduct	Headquarters	Auditing and Compliance Office	Fumikazu KABE Shin OHKOUCHI Yoshiharu DOI	
30	Discovery of a New Inactivation Mechanism of a Plant Growth-Promoting Hormone, "Gibberellin"	PSC	Cellular Growth and Development Research Team	Shinjiro YAMAGUCHI Takahito NOMURA	Plant Cell 18, 442–456 (2006)
Feb. 2	Telencephalin, a Molecule Necessary to Keep the Brain Pliable	BSI	Laboratory for Neurobiology of Synapse	Yoshihiro YOSHIHARA Hitomi MATSUNO	The Journal of Neuroscience 26, 1776–1786 (2006)
9	Reaction Mechanism of "Dioxygenase" Elucidated, after 50 Years from Its Discovery	RSC	Biometal Science Laboratory	Yoshitsugu SHIRO Hiroshi SUGIMOTO	PNAS 103, 2611–2616 (2006)
27	Features of Protein Folding Dynamics Have Been Demonstrated Theoretically	RSC	Structural Biochemistry Laboratory	Yuichiro MAEDA Tetsuro FUJISAWA	Implication of the Scaling Relationship for the Submillisecond Intermediates of Protein Folding Journal of Molecular Biology
Mar. 3	Reveromycin A, a "Magic Bullet" That Zeroes in on Osteoclasts	DRI	Antibiotics Laboratory	Hiroyuki OSADA	PNAS 103, 4729–4734 (2006)
10	Elucidating How a Firefly Emits Light	RSC	Kinetic Crystallography Research Team	Hiroaki KATO	Nature 440, 372–376 (2006)
13	Research and Development of "RI-MAN," a Robot That Can Hold a Person in Its Arms Using Tactile Sensors	FRS	Environment Adaptive Robotic Systems Laboratory Biologically Integrative Sensors Laboratory	Zhi-Wei LUO Toshiharu MUKAI	
14	Elucidation of a New Function of "BANK", an Adaptor Molecule	RCAI	Laboratory for Lymphocyte Differentiation	Tomohiro KUROSAKI	Immunity 24, 259–268 (2006)
22	Initial Gene Catalog of the Highly Disease-Related Human Chromosome 11 Has Been Completed	GSC	Genome Annotation and Comparative Analysis Team	Todd TAYLOR	Nature 440, 497–500 (2006)
24	Fast X-Ray Stroboscopy Reveals Intracrystalline Deformation Caused by Laser Irradiation	RSC	Coherent X-ray Optics Laboratory	Tetsuya ISHIKAWA	Physical Review Letters 96, 115505 (2006)
27	Identification of a Common Immune Regulator in Both Innate and Adaptive Immune Responses - The innate immune signaling molecule regulates acquired immune system through T cell activation. -	RCAI	Research Center for Allergy and Immunology Laboratory for Cell Signaling	Takashi SAITO Nobutaka SUZUKI	Science 311, 1927–1932 (2006)

## Breakdown

Category	RIKEN Press Releases	Press Releases issued jointly but initiated by another institute	References
Research Results	55	4	6
Other	9	5	12
<b>Total</b>	<b>64</b>	<b>9</b>	<b>18</b>

Organization	RIKEN Press Releases	Press Releases issued jointly but initiated by another institute	References
Discovery Research Institute (DRI)	17		3
Frontier Research System (FRS)	2		1
Brain Science Institute (BSI)	4	1	2
Initiative Research Unit (IRU)	1		
Center for Intellectual Property Strategies (CIPS)	4		
BioResource Center (BRC)			1
RIKEN SPring-8 Center (RSC)	9	2	1
Genomic Sciences Center (GSC)	7	2	1
Plant Science Center (PSC)	3	1	
SNP Research Center (SRC)	6		
Research Center for Allergy and Immunology (RCAI)	5	1	1
Yokohama Institute and Center of Research Network for Infectious Diseases (CRNID)	1	1	
Center for Developmental Biology (CDB)	1		
Other	4	1	7
<b>Total</b>	<b>64</b>	<b>9</b>	<b>18</b>

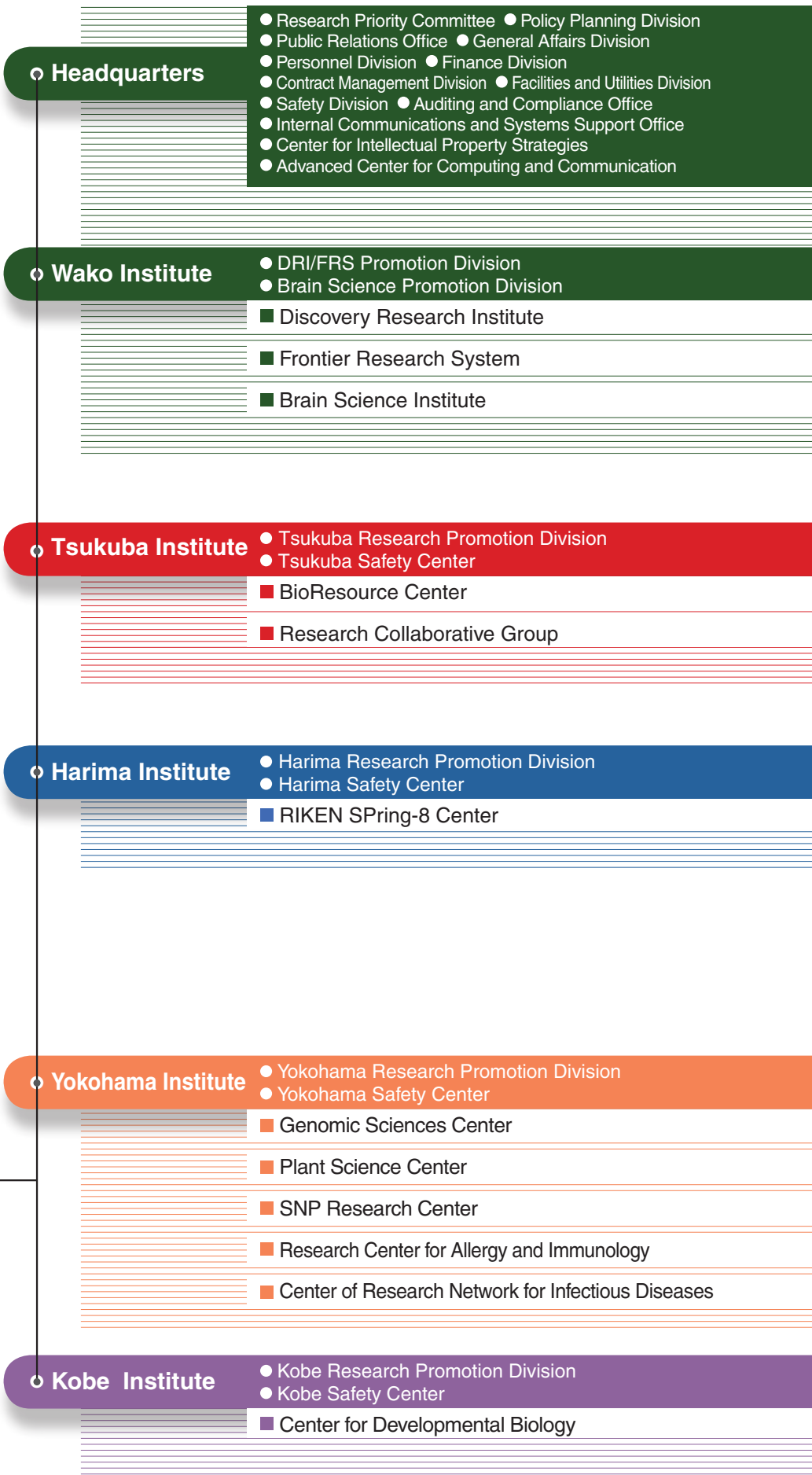
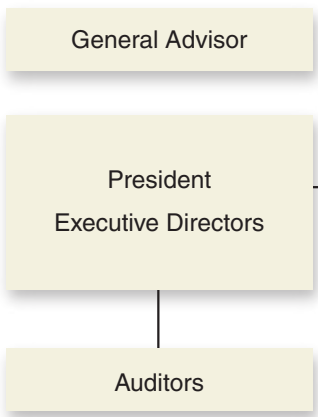
## Research institutes and centers

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# RIKEN's extensive studies at their nationwide facilities

RIKEN manages its distributed network of institutes and research centers throughout Japan from its headquarters in the Wako Institute. These centers are mutually interactive and collaborative, in part through strong ties to its management core.







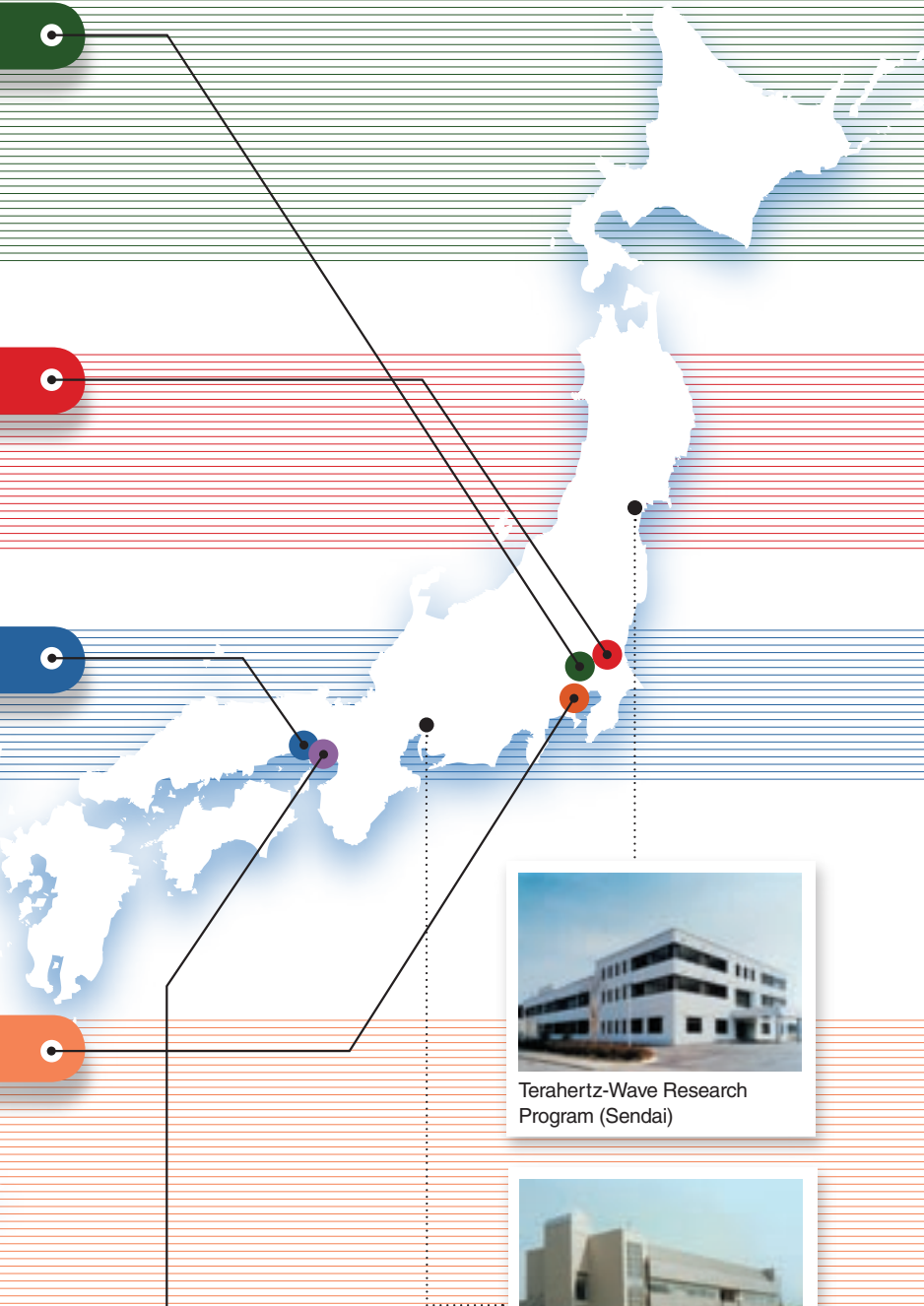
Large Synchrotron Radiation Facility (SPring-8)



Terahertz-Wave Research Program (Sendai)



Bio-Mimetic Control Research Center (Nagoya)



## Two new centers started

### Headquarters

### Center for Intellectual Property Strategies

## Returning the fruits of research to society

The Center for Intellectual Property Strategies (CIPS) was founded on April 1, 2005 to implement President Noyori's "RIKEN that is useful to the World". Specifically, the Center is aimed at effectively creating top-caliber research results (intellectual property) and returning them to society through cooperation with the business community.

CIPS is comprised of the Intellectual Property Management Group, the VCAD System Research Program, the Integrated Collaborative Research Program with Industry, and the Sponsored Laboratories. The Intellectual Property Management Group is engaged in creating intellectual property utilizing research results from the whole of RIKEN Center and promoting cooperation with the industrial community through licensing of intellectual property. At the same time, this group is responsible for raising research funds externally, including competitive funds. The VCAD System Research Program, with development of the volume CAD (VCAD) system as its key

project, makes innovations in information and manufacturing technologies in the manufacturing industry. In the Integrated Collaborative Research Program with Industry, RIKEN and enterprises are promoting development and research in an integrated manner in various fields. The Sponsored Laboratories invite researchers with outstanding credentials to promote research on selected special themes.

CIPS also extends support to RIKEN Venture Businesses that are established based on the core competencies of RIKEN.

### CIPS in FY 2005

From June 2005, patent information owned by RIKEN has public on a website called R-BIGIN : RIKEN Business Information for Global IP Network, the RIKEN patent disclosure database and search system. This website allows anyone to search RIKEN's patent information at any time without charge.

We held the RIKEN Techno Conference 2005 in November 2005 as a new form of cooperation with the industrial community. In this conference, unlike other conventional lecture meetings and exhibitions, RIKEN researchers introduce, in a personal presentation format, RIKEN patents not yet revealed to the public as well as the latest research results to personnel in business who are responsible for incorporating technology. We have had a lot of participants at the conference from many companies.

The Integrated Collaborative Research Program with Industry, which was started in 2004, created two major research achievements this year. Collaborative research with Tokyo Ohka Kogyo Co., Ltd. succeeded in developing nano-materials, which are expected to enhance nano-engineering. A joint study with Toray Industries Inc. succeeded in doubling the life of photocatalytic coating materials used in fullerene. Commercialization and manufacturing of these products are expected in the future.

### MESSAGE

## Looking back on the past year

### Eiichi Maruyama

Director  
Center for Intellectual Property Strategy



This center has carried out diversified activities in the past year to return our distinguished research achievements, which have been enabled through cooperation with the industrial community, to society. Patent liaison staff at this center hold seminars about filing patent applications for researchers working in the various RIKEN institutes. These seminars offer the above information taking into consideration the characteristics of respective institutes and are succeeding in arousing researchers' interest in making patent applications. Our commercial viability coordinators make timely visits to business enterprises to discuss the practical application of research achievements. They are also engaged in certification and follow-up consultation of the venture corporations under the RIKEN venture system.

In the RIKEN Techno Conference 2005 held in November, we have publicized RIKEN's technical information to 21 firms that participated in the conference and exchanged substantial arguments on the publicized information in the individual business meetings.

In addition, we have constructed a system called R-BIGIN on our website. Anyone can visit the site to find RIKEN's patent information. Researchers working with

business firms are cordially invited to use the Researchers' Database on the website.

In the Integrated Collaborative Research Program with Industry, started in 2004, two out of the seven teams held press conferences in October 2004 about the achievements of their collaborative development. We were able to release the results to the press within one year of the start thanks to the very efficient cooperative framework.

One of the center's plans in 2006 is to start up a bio-related business through cooperation with a pharmaceutical company utilizing the latest RIKEN research developments in this field. The first term of the five-year "Integrated Volume-CAD System Research Program" of the VCAD System was completed this March. In the second term, the project started from this April as the new "VCAD System Research Program." The research techniques and processes will be more sophisticated than ever so that the research results may be commercialized and used in the industrial community.

## CRNID fights emerging and reemerging infectious diseases

From the mid-1970s to the early 1980s, we mistakenly believed we had triumphed over infectious diseases. As a result, research into these diseases lost prominence and the number of researchers declined significantly. Today, we are once again keenly aware that infectious disease remains a pressing medical issue.

Recognizing this need, MEXT decided to substantially increase funding for and development of research that could one day prevent, diagnose, and treat infectious diseases. They established the Center of Research Network for Infectious Diseases (CRNID) as part of its Program of Founding Research Centers for Emerging and Reemerging Infectious Diseases. Over the next five years, CRNID will focus on

establishing a cooperative network in Japan and overseas for furthering knowledge and training young researchers. The center will also gather useful information and research results, and help develop an infrastructure that can rapidly respond to domestic or overseas outbreaks of emerging or reemerging infectious diseases.

Among CRNID's goals are (1) developing both a domestic and international cooperative structure for joint research and mutual use of research facilities and ensuring the effective use of research resources and information, (2) determining the practical operation issues involved in supporting such a cooperative structure and suggesting effective solutions, and (3) working to increase public knowledge

about emerging and reemerging infectious diseases.

### CRNID in FY 2005

The CRNID office opened in July 2005. Staff began investigating the establishment of overseas bases, including looking into issues such as income taxation for dispatched researchers and laws and procedures regarding tax exemptions for equipment. To broadcast the center's work, CRNID held a symposium, launched a newsletter, and initiated efforts to promote better understanding of emerging and reemerging infectious disease among the general public.

### MESSAGE

## Inauguration of the Center and its Credo

**Yoshiyuki Nagai**

Director

Center of Research Network for Infectious Diseases



Infectious diseases demand global-scale collaborative research. The purpose of this program is to install research bases in countries and regions where outbreaks of new and re-emerging infectious diseases are observed in order to enable joint research with local researchers by sharing samples and information about the causal organisms. Also included in the purpose is the development of young researchers through the above processes. Research bases were offered for public subscription in May 2005. In July, the following three pairs and the Hokkaido University were selected as research bases. They were Nagasaki University and the National Institute of Hygiene and Epidemiology in Vietnam, Osaka University and the National Institute of Health in Thailand, and the University of Tokyo and the Chinese Academy of Sciences. However, setting up overseas collaboration bases and maintaining them over long periods is not always easy and may involve various difficulties. CRNID's primary role is to coordinate activities that alleviate this problem while enabling projects to develop and grow. RIKEN was selected to house this center in part because its location is convenient for all partners in the network and in part because it is an impartial player in this research. It can make sound choices for projects

and resource allocations.

In addition, with the center being part of RIKEN, opportunities for collaborations with RIKEN researchers are possible that exploit the accumulated knowledge and technological prowess of RIKEN's institutes. Taken together, these provide CRNID with a solid foundation on which to prevent infections that threaten lives and social order.

It is essential that on-going research into infectious diseases maintain and build on international networks of foreign researchers. In just one hundred years, for instance, the Pasteur Institute has established dozens of research centers, and Oxford University, fourteen that span the globe. Whether their researchers are working in Asia, Africa, or South America, they have consistently achieved success in understanding malaria, typhoid fever, and more recently in developing rapid responses to prevent a serious outbreak of bird flu. Their research output is a foundation for future efforts to develop countermeasures to infectious diseases.

CRNID supports long term projects, rather than short term goals, under the far-reaching MEXT policy that created it.

## The facilities in Wako contain cutting edge technologies

The campus also houses the RIKEN Headquarters and the Wako Institute, which incorporates the Discovery Research Institute, the Frontier Research System, the Brain Science Institute, the Initiative Research Units, and the Sponsored Laboratories.



### BSI Central Building

Biological, engineering, and information scientists are among those gathered here to investigate brain function.

### RI Beam Factory

From hydrogen to uranium, the RI (radioisotope) Beam Factory can provide the most intense RI beams for all known elements, surpassing world standards.

### BSI East Building

Functional magnetic resonance imaging (fMRI) and magnetoencephalogram (MEG) equipment are housed here.

### Frontier Research Laboratories

These labs foster new research into new scientific fields and technologies.

### Information Science Building

Site of one of the fastest super-computers in the world, the RIKEN Super Combined Cluster.

### Main Research Building

Has been home to research since Wako's establishment in 1966.

## History of Wako Institute

### Chemistry and Material Physics Building

Material science leading to new materials, such as bio-degradable plastic materials, is conducted here.

### Nanoscience Joint Laboratories

To facilitate research at the nanoscale, advanced experimentation rooms that provide suitably clean and cold environments were built.



### Bioscience Building

Complete studies of biological life are conducted at the molecular, cellular, system, and organism levels within these walls.



The Wako Institute (as of October 2005)



**1917** RIKEN Foundation established in Tokyo. Komagome Building No.1 is shown here.



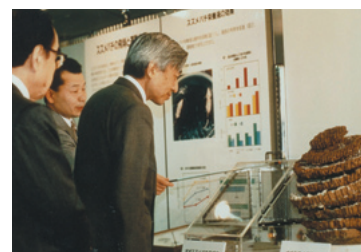
**1938** 60-inch cyclotron completed.



**1967** Yamato Laboratory opened on the Wako Campus.



**1987** Ring cyclotron completed.



**1992** Japan's Emperor visited the Wako Institute.

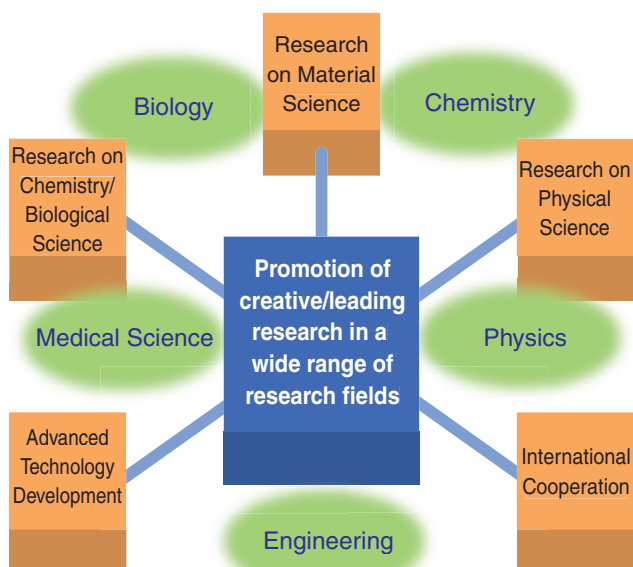


**2005** RI Beam Factory being built.

## The historical roots of RIKEN's research system

The Discovery Research Institute (DRI) operates on a flexible, cross-disciplinary platform that supports its Chief Scientists and their laboratories as they produce creative, ground-breaking findings.

In a competition-based system, Chief Scientists are free to pursue projects that chart new territories of knowledge. DRI also has created a structure that facilitates collaboration between labs that encourages interdisciplinary research that ties the work of its laboratories together—fertilizing new areas of research, synthesizes others, and seeds possible commercialization. Nanoscience at DRI is one example of how the newest fields in basic science are contributing to our understanding of physical phenomena, but there are several others, including molecular investigations that may help protect the environment and studies on systems of spontaneous evolution to gain insight into the origins of life by charting



the life cycle of a star. Finally, optical imaging technologies are being pursued collaboratively within RIKEN and with other research organizations to push the use of laser technology in basic science beyond its current limits.

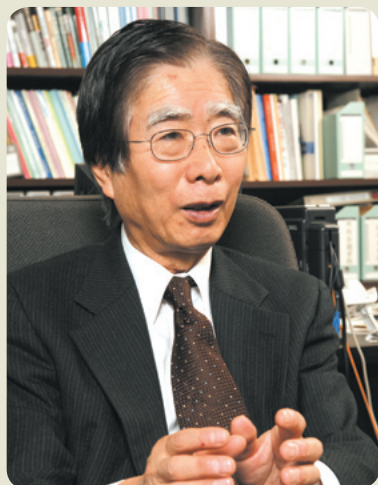
Basic research is supported by RIKEN's Advanced Development Support Center, which develops new research tools and provides technical and analytic support for those new technologies for our researchers.

### MESSAGE

## Achievements in diverse fields and the future perspective

### Koji Kaya

Director  
Discovery Research Institute



The Discovery Research Institute was busy last year. The pinnacle event was the creation of the Extreme Photonics Project under the leadership of Katsumi Midorikawa of the Midorikawa Laser Technology Laboratory. Midorikawa received international attention when his team developed a highly accurate, soft X-ray laser. The project links several facilities in Japan to RIKEN, including the Institute for Molecular Science (in Okazaki) and the National Institute of Natural Sciences, to develop a wide range of innovative laser-based technologies.

In addition, Chief Scientist Maki Kawai's team has learned how to measure a single molecule by developing technology that bombards a trapped molecule with electrons having different energy levels. This process makes it possible to observe the molecule's electrons.

RIKEN researchers led by Hiroyuki Osada developed a chemical library that houses hundreds of thousands of tiny microchips. This process successfully enables molecular bonding without disrupting molecular functions. And Akihiko Nakano's group recently announced a new breakthrough in how molecules in living organisms communicate. These studies clearly

demonstrate the importance of biochemical studies and in RIKEN.

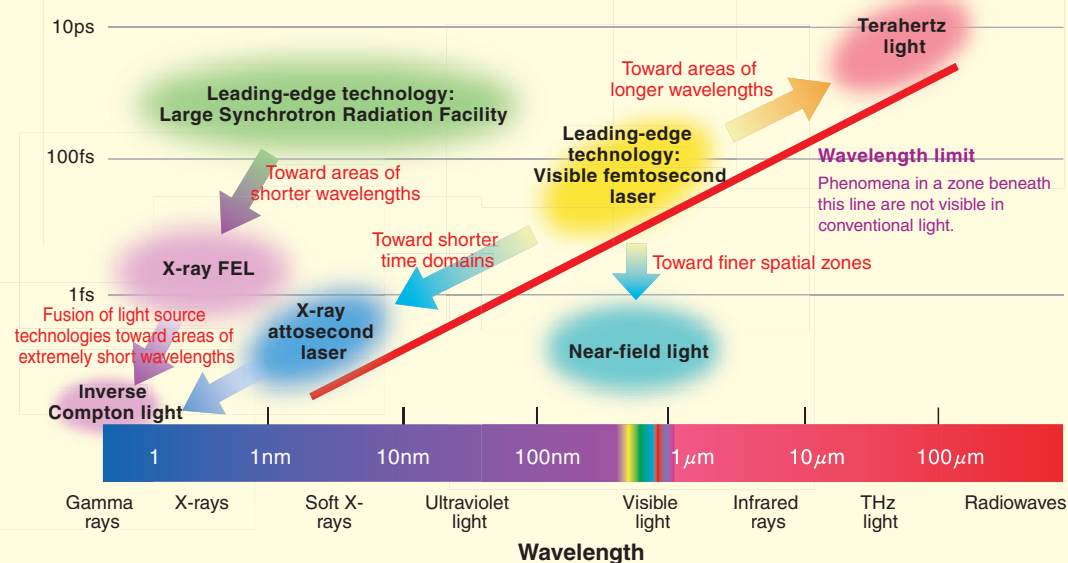
In 2006, nanoscientific investigations of the chemistry of liquids—in the Chemical Dynamics laboratory headed by Toshinori Suzuki—are expected to be quite promising.

From the management side, RIKEN introduced a new personnel management system designed to attract young, highly motivated scientists called the Associate Chief Scientist system. This system will give young researchers the opportunity to pursue independent research and develop leadership skills. This system will be also used at the new Nishina Center for Accelerator-Based Science and at the SPring-8 Center.

The RI Beam Factory (RIBF), formerly a part of the Discovery Research Institute, transforms into the Nishina Center in 2006. With this transition, DRI made some organizational changes including affiliation changes for former DRI laboratories, and the two associated overseas RIKEN centers (RIKEN Brookhaven National Laboratory Research Center (RBRC) in the United States and RIKEN Facility Office at the Rutherford Appleton Laboratory (RIKEN RAL) in the United Kingdom) will also join

## Innovating light

### Pulse width



### Novel lights help create novel science and technology

Building on RIKEN's optical prowess, our laboratories will attempt to create new forms of light that can drive new scientific and industrial pursuits.

## FY 2005 Evaluation committee

2006

2/26-28 ILAC2006 (Institute Laboratories Advisory Council)

## Major symposiums in FY 2005

Date	Title	Main Lecturer(s)	Host Laboratory
2005/4/1	New Development of Vanadate Laser	Satoshi WADA and five others	Solid-State Optical Science Research Unit
2005/4/28	Extreme Photonics Research	Katsumi MIDORIKAWA and thirteen others	Laser Technology Laboratory
2005/5/27	Open Symposium Vol.16 Trends and Advances in Micro-Fabrication Techniques and Research Activities—Latest Micro-Fabrication Research Projects	Hitoshi OHMORI and five others	Materials Fabrication Laboratory
2005/10/27	The 4th Nanophotonics Symposium	Satoshi KAWATA and six others	Nanophotonics Laboratory
2005/11/09	The Third Chemical Biology Symposium —New Dimension of Chemical Biology Studies	Hiroyuki OSADA and ten others	Chemical Biology Research Group
2005/11/28-29	Molecular Ensemble 2005	Shik SHIN and sixteen others	Condensed Molecular Materials Laboratory
2006/1/27	The 9th Symposium on Biomolecular Chemistry	Shinya HAGIHARA and six others	Synthetic Cellular Chemistry Laboratory
2006/2/18	Complex Electron Systems Research	Hidenori TAKAGI and 21 others	Magnetic Materials Laboratory
2006/3/7	Simulation Research on Biodynamic	Ryutaro Himeno and 46 others	Computational Biomechanics Unit
2006/3/16	The Third Environmental Molecular Science Symposium	Toshiaki KUDO and 18 others	Ecomolecular Science Research Group

the new center. RBRC and RIKEN RAL are well established centers with impressive achievements. RBRC should continue to expand on those successes for the next five years. RIKEN RAL, which hosts a number of Japanese physicists, focuses on muon studies that maintain Japan's leading role in material investigations.

Even though J-PARC, in Tokaimura, will be completed in two years and will house a new muon facility, RIKEN RAL's activities will continue.

I wholeheartedly support the new direction of the Nishina Center for Accelerator-Based Science.

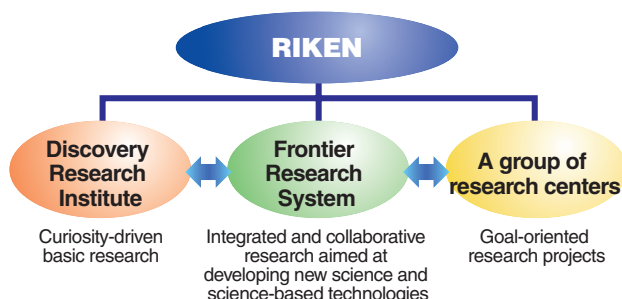
## Exploring New Fields through Project-Based Research

The Frontier Research System, FRS, originally inaugurated in October 1986 as the International Frontier Research Program, is a groundbreaking project-based research organization that recruits, worldwide, competent research talent in a wide range of fields, organizing cutting-edge research projects on a fixed-term basis with time-limited contract researchers. FRS was established on the basis of a new concept of dealing with the fast-moving world of modern science with a more flexible, agile organizational style.

In 1997, one of the FRS's most successful research groups was spun off as an independent institute, the Brain Science Institute. Since then, other project-oriented research programs have been established both within RIKEN and without. This is testament to the success of FRS's organizational style and the attention it has drawn. In addition, FRS takes advantage of

regional research capabilities, linking these with the research potential of RIKEN as a whole. It was the incorporation of research activities in Sendai and Nagoya in 1997 that brought about the creation of the FRS as it exists today.

Another recently launched effort is the Integrated Collaborative Research Program with Industry, inaugurated in 2004, which was followed by the Integrated Volume-CAD System Research Program and the Nanoscience Research Program, all intended to ramp up integration and collaboration with research and industry outside of RIKEN. The former two were spun off in 2005 into a separate research center,



the Center for Intellectual Property Strategy, in line with advice from both the Frontier Research Advisory Council and the RIKEN Advisory Council suggesting that the mission of the FRS be reexamined. As a result, this mission has been more clearly defined as (a) integrative and collaborative research toward the development of new fields in science and technology and (b) incubating projects dealing in new fields of research with the aim of spinning them off into independent centers.

### MESSAGE

## Energizing RIKEN by Breaking New Ground to Create the Future of Science and Technology

**Kohei Tamao**

Director  
Frontier Research System



The Frontier Research System has this year taken on a new credo, "the fountainhead of RIKEN's vitality," in light of its two main missions: integrated, collaborative research for the development of new scientific and technological fields, and the incubation of new research projects that possess the potential of becoming new research centers. The entirety of FRS, as its very name implies, is dedicated to the continued revitalization of RIKEN as a whole through cutting-edge developments in science and technology.

Tasked with such a mission, the selection of what research projects to take up becomes critically important. Having been advised in February 2006 by its Frontier Research Advisory Committee, an outside panel of experts that evaluate and advise the FRS on a regular basis, to increase the transparency of its project selection process, the FRS has been reviewing the procedures by which it selects new projects. FRS will further take the issue up in RIKEN's Research Priority Council, in order to view the issue more broadly from a RIKEN-wide standpoint.

Constantly reinventing itself, the FRS has undergone a few interesting changes over just

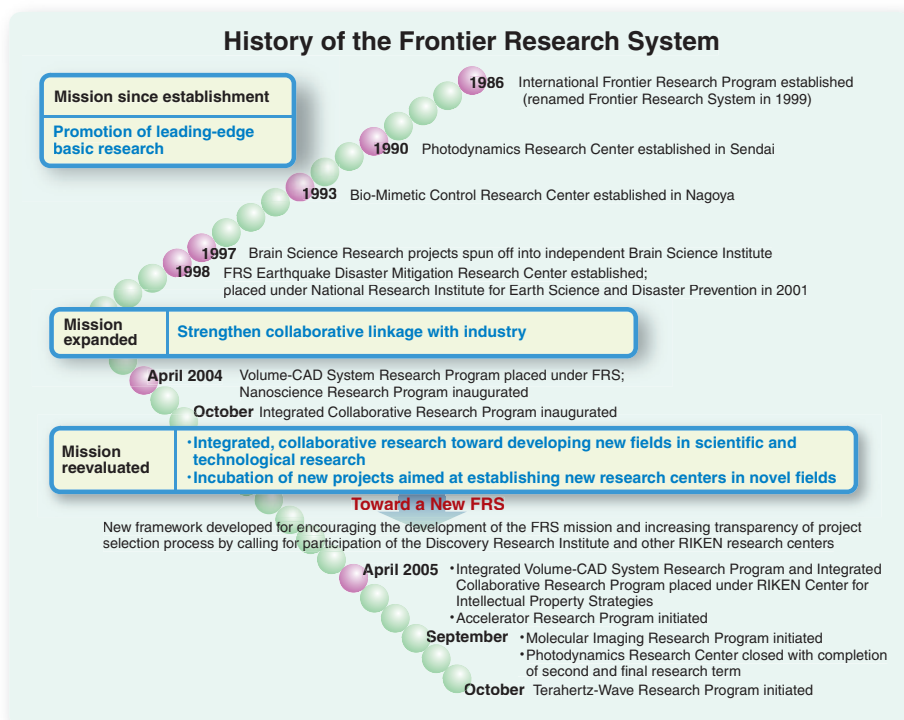
the past two years or so. The Photodynamics Research Center in Sendai wound up a 15-year project in September 2005. Over its first and second halves, terms I and II, the Center produced many remarkable achievements, one result of which was the selection of one project for continuation, the Terahertz-Wave Research Program, which was inaugurated in October, 2005. FRS's Bio-Mimetic Control Research Center and Single Quantum Dynamics Research Group underwent mid-term evaluations during 2005, receiving high acclaim. The Bio-Mimetic Control Research Center seeks to learn more about information processing in living animals and to fabricate robots, while the Single Quantum Dynamics Research Group is advancing scientific knowledge in a number of fields, including leading-edge work on the practical realization of a quantum computer.

Another project, the Molecular Imaging Research Program, was inaugurated in September 2005. Utilizing molecular imaging techniques and positron emission tomography, this Program seeks to advance the development and design of new drugs by exploring novel candidate substances. A new facility is currently under construction in the Kobe Medical Industry



There are other recent developments. RIKEN's Accelerator Research Program was in 2005 placed under FRS prior to being relaunched in April 2006 as an independent center, the Nishina Center for Accelerator-Based Research, and a totally new research program, the Molecular Imaging Research Program, breaking ground in a new field, was launched in September. The second and final term of FRS's Photodynamics Research Center in Sendai was also completed in September, one group of which continues today as the Terahertz-Wave Research Program. In April 2006 another new program was initiated, the Functional RNA Research Program, and RIKEN's Initiative Research Program was placed under FRS.

Clearly, the Frontier Research System is a vital force in RIKEN, keeping it on the forefront of scientific research and technology.



Development Project in Hyogo Prefecture, which will go into full-time operation in October 2006. This project is currently being conducted on a five-year basis with an eye to spinning it off as an independent center within RIKEN. Another program was launched in 2006, the Functional RNA Research Program, which seeks to increase our understanding of RNA-regulated gene expression and the creation of a functional RNA database.

Another important effort, RIKEN's Accelerator Research Program, was placed under FRS in 2005, and spun off in 2006 as the Nishina Center for Accelerator-Based Science. RIKEN's Initiative Research Unit system, first inaugurated in 2001, was placed under FRS in 2005 and renamed the Initiative Research Program. It allows young scientists with creative ideas to set up a small laboratory of several researchers and explore new fields.

The FRS celebrates its 20th anniversary in 2006, and a number of events are planned, culminating in an FRS Symposium at which a number of FRS researchers selected for the excellence of their work will explain their projects and progress, and an award ceremony held to recognize them. The aims of the seminar are to make FRS research

## Activities of the Frontier Research System

### 2005

- |          |  |
|----------|--|
| 4/1      | Accelerator Research Program established   |
| 8/10-11  | Mid-term review of Bio-Mimetic Control Center, Nagoya                              |
| 9/1      | Molecular Imaging Research Program inaugurated                                     |
| 9/30     | Photodynamics Research Center closed after end of second and final term            |
| 10/1     | The Terahertz-wave Research Program inaugurated from Photodynamics Research Center |
| 11/14-15 | Mid-term review of Single Quantum Dynamics Research Group                          |

### 2006

- |         |   |
|---------|---|
| 2/20-21 | 4th Frontier Research System Advisory Council held  |
| 3/31    | FRS Accelerator Research Program spun off as the Nishina Center for Accelerator-Based Science |

more transparent, provide a venue for the exchange of ideas among FRS researchers, and encourage increased collaboration.

It is an exciting time for the Frontier Research System, and we look forward to continuing to push forward the frontiers of scientific and technological achievement at an ever-accelerating pace.

## To know what it means to be human, you must first ask how their brains work?

The human brain is a giant network of networked neurons. As information moves between neurons and their networks, physical and mental processes are triggered that produce behaviors in the world. Through evolution, human brains enable social interactions, too. How does that organ accomplish these feats? More, what is the mind that is capable of understanding them? Finding answers to these questions is why the Brain Science Institute was established in October 1997.

Among the unique features of BSI is its commitment to maintaining an agile research system. Four strategically targeted research areas have been created to ensure we meet our goals within a twenty-year time frame. These areas are:

- Understanding the brain,
- Protecting the brain,
- Creating the brain, and

- Nurturing the brain.

BSI is also interdisciplinary and integrative. Neuroscience is necessarily interdisciplinary, and draws on methods and approaches from biology, information science, and social science. These disciplines reveal the brain's secrets at the molecular, cellular, network, systems, and whole organism level, the same way that behavior studies do. Each finding must be linked to others at every level of research if a systematic understanding of the brain is to emerge.

As the core brain science institute in Japan, BSI is focused on developing a strong international presence by interacting and cooperating with institutes through the world. BSI has built a strong partnership with the Massachusetts Institute of Technology (MIT) and with institutes in North America, France, Sweden, the United Kingdom, China, South Korea, India and Australia. In these alliances,

BSI represents all of Japan's brain science activity. Furthermore, BSI ensures innovative research output by recruiting highly skilled researchers from around the globe. To date, one-fifth of its research staff and its laboratory heads and unit leaders are non-Japanese.

Being large, BSI has attained a critical mass of people, knowledge and technology to support novel research. Its researchers can leverage their primary expertise in working with other researchers from different fields. Ideas and skills are shared. With this critical mass attained, every day brings fresh discoveries.

In this dynamic, charged environment, the involvement of young researchers is essential to fully take advantage of BSI's unique offerings. BSI's researchers are typically in their mid-thirties, hired under a fixed-term system, and are dedicated to solving the mysteries of the human brain.

### MESSAGE

## The last year at BSI: deepening international and social ties

**Shun-ichi Amari**

Director, Brain Science Institute



The BSI Advisory Council met after a two-year hiatus in 2005. Between these meetings, BSI concentrated its efforts on improving the research center and these efforts were highly evaluated.

Brain science at BSI is interdisciplinary and collaborative. BSI's researchers have gathered together to draw from various approaches and research fields available at the institute to answer their questions about the brain. For example, recent advances in brain science require more human and animal studies that can then be integrated with theoretical brain studies to deepen our understanding. This fusion is encouraged at BSI by the BSI Director's Fund. This fund, established last year, will support cross-disciplinary, collaborative projects that exploits new technologies and fuses methodologies from experimental and theoretical studies.

BSI also stepped up its efforts to educate young neuroscientists with a twenty-lecture Tutorial Series. Some of BSI's leading researchers reviewed the methods and trends in their fields to BSI and non-BSI researchers. In addition, colloquia centered on specific themes brought researchers from different research fields together to explore ideas. Finally,

taking advantage of BSI's dominant position in cerebellum research, BSI organized ten focused colloquia on the cerebellum.

Deepening international links, BSI established a framework for cooperation with foreign universities and institutes. Of particular note is a new collaboration between the University of Newcastle-upon-Tyne and BSI. BSI is also in negotiations with the Karolinska Institute in Sweden to finalize an agreement that would foster even closer interactions between neuroscientists and students via a RIKEN-wide research agreement. Another collaborative agreement between the National Neuroscience Facility in Australia and BSI was also finalized this year.

When the International Neuroinformatics Coordinating Facility (INCF) was established in July 2005 to promote international neuroinformatics partnerships, Japan, through BSI, joined. Each participating country must also create a domestic coordinating organization, and the Japanese node for the INCF is housed in BSI. The Japanese node's activities began in April 2006.

A symposium held in January 2006 to commemorate the opening of Germany's Bernstein

## BSI in FY 2005

Two major events top BSI's list of achievements in 2005. The first is the location of the Neuroinformatics Japan Center (NIJC), platform for Japanese neuroinformatics\*, in BSI. NIJC is Japan's representative in the International Neuroinformatics Coordinating Facility (INCF). As the Japanese node of INCF, the NIJC plays a role in the promotion of Neuroinformatics. The other is that BSI Group Director Takao Hensch received the Society for Neuroscience's Young Scientist Award at the 2005 annual meeting in the United States. He is the first non-U.S.-based researcher to be presented this honour, given to a remarkable young scientist with an impressive record of achievements in

his or her first 10 years as a researcher. Dr. Hensch's achievements are testaments to the interdisciplinary and integrated research environment of BSI.

In the January 2006 meeting of the Brain Science Advisory Council, BSI's research management and future plans were well evaluated and good recommendations were made. To promote neuroscientific research cooperation, BSI entered into research agreements with the National Neuroscience Facility in Australia in September 2005, and the University of Newcastle-upon-Tyne in the United Kingdom in October 2005. Under these partnerships, BSI agrees to expand personnel exchange, hold joint seminars, and promote collaborative research.

BSI's notable research results in 2005 include the discovery that DNER protein is required for neuroglial cell metabolism. Another lab revealed that eye and brain

function are coordinated to locate a specific "object" in space and recognize it. Yet others found a novel excretory function for intracellular calcium channels, developed a road map to study brain learning, development and memory, and identified a new protein, called the "telencephalon" protein, that seems to keep the brain pliable.

\* Neuroinformatics: a new field that links brain and information sciences by establishing innovative ways to store, integrate, share, and analyze accumulating experimental data through information technology.

Center for Computational Neuroscience was organized by BSI. Finally, BSI's longstanding partnership with MIT has expanded to include several international exchanges, including ones that foster exchange between younger researchers at MIT and BSI as well as other institutes.

In the future, BSI will contribute to society with proposals that are based on its research output. It currently cooperates with educators and education policy makers by making research results available. Moreover, BSI researchers are getting closer to developing true brain-to-machine interfaces as well as improving robotic and social engineering based on their activities. Strategic research is also underway that will fundamentally support preventive and medical treatments for dementia and other neurological diseases. These activities are designed to find viable solutions to real social and ethical concerns—concerns BSI will monitor to ensure that brain science maintains its close connections with society.

## The year's key events

### 2005

5/24–12/20 BSI Tutorial Series (once a week)

6/27–8/27 BSI Summer Program Internship Course

7/12–7/22 BSI Summer Program Lecture Course

10/31–11/2 BSI Retreat

### 2006

1/24–1/26 BSI Advisory Council (VSAC) meeting

2/2–2/4 Japan-Germany Symposium on Computational Neuroscience

2/27 INCF Japan Node Establishment Forum

3/18 Worldwide Brain Awareness Week 2006

3/24 Meeting on nurturing children's social and intellectual development

3/26–28 The Fifth Piconer–RIKEN BSI Symposium on Neuroscience

### No Resources, No Research

The Tsukuba Institute started as the Tsukuba Life Science Research Center in 1984, and has been involved in pioneering research on genes. It was renamed the RIKEN Tsukuba Institute in April 2000 and RIKEN established the BioResource Center within the Tsukuba Institute in January 2001 to collect, preserve, and distribute biological resources for life science research, as well as develop new technologies that exploit these resources. Additionally, in order to advance the projects undertaken by the BioResource Center, three laboratories that belong to other research institutes/centers of RIKEN were established as collaborative research groups that are aligned with activities of the BioResource Center at the Tsukuba campus.

#### BioResource Center

Biological resources, or bioresources, like experimental animals and plants, cell lines of

human and animal origin, genetic materials (DNA) and microbes, are indispensable intellectual foundations for life science investigations. They are also invaluable intellectual assets.

Since its founding, BRC has operated under the three principles of “Trust”, “Sustainability” and “Leadership”. These guide how BRC makes its contributions to science. Unlike other resource facilities in the world, BRC is comprehensive. All resources provided by the Center are RIKEN BRC branded resources. Working closely with domestic and overseas organizations, we are:

1. Collecting, preserving, and distributing mouse, Arabidopsis, human and animal cells, genetic materials, microbes, and related information,
2. Developing novel resources and innovative methods for maintaining quality and analyzing resources.
3. Providing training for the use and applications of bioresources.

This Center is the core facilities for five resources selected by the National BioResource Project, launched by Ministry of Education, Culture, Sports, Science and Technology (MEXT) in FY 2002. In this capacity, BRC plays a central role in establishing a solid infrastructure in Japan.

#### BRC in FY 2005

This was the fifth year of BRC’s operation. It marks a turning point that coincided with the retirement of the Center’s founding director, Dr. Kazuo Moriwaki. Dr. Yuichi Obata succeeded to this position, but even after the change of directorship, the basic three principles have been maintained. In today’s world, where science and society are going through drastic changes, even the continuous existence of the BioResource Center would be challenged if the Center failed to respond to the demands from the social and scientific communities properly.

#### MESSAGE

### As an International Core Center for Biological Resource

**Yuichi Obata**

Director  
BioResource Center



Since I took the office of the BRC Director in April 2005, a year has passed. Working under the principles of “Trust”, “Sustainability” and “Leadership” that BRC inherited from Dr. Moriwaki, the former and founding Director, the Center continues to contribute to life science through bioresources for research materials.

BRC has been conducting projects to collect, preserve and distribute bioresources. In FY 2005, BRC became the second largest repository for mice in the world. For plant, cell and genetic resources, the Center is now one of the three major resources centers in the world. Furthermore, the number of registrations of newly identified species of microbes in the BRC was the second largest in the world. Currently, 2400 Japanese and over 1200 overseas organizations use BRC. Clearly the center is evolving into an international core for bioresources.

BRC plays a key role in the dissemination of the research achievements of the researchers. Researchers can obtain bioresources needed for their research through BRC. Meanwhile, depositing bioresources into BRC reduces the burden of maintaining and distributing resources for the researchers, freeing researchers to focus

on their own work.

Since 2004, the Center has been giving training courses for effective use of its bioresources, courses. For-profit organizations are welcome to send their staff for training, just as academic organizations are. We plan to accept participants from Asian countries in the future.

As for strategy, BRC needs to form policies from the viewpoint of national interest as it is Japan’s core institute. In that context, we should have unique resources developed in Japan and promote research in priority research areas of the nation. It is also important to cooperate with other nations to build an international network of cooperation.

FIMRe (Federation of International Mouse Resources), established in 2004, is an organization composed of 17 mouse resource centers around the world. FIMRe has established a mouse strain database through cooperation among its members. BRC is one of the founding members and hosted the Fourth conference at the Tsukuba Campus in May 2006.

2006 marked the fifth anniversary of the Center. We are currently developing a road-map toward where we should be at the end of the second five-year stage and furthermore

Foresight and flexibility will become more important.

To become one of the world's finest bioresource centers, BRC must increase the number and variety of its stock of resources. Its efforts are starting to receive recognition. The Experimental Plant Division received a special prize at the 2005 Convention of the Botanical Society of Japan for its contributions to plant sciences.

One of BRC's important roles is to improve the quality of resources to ensure that experimental results can be reproduced and excellent results are consistently achieved. To improve the quality of bioresources, each laboratory at the Center has initiated surveys on achievements by users with the resources offered. The survey results will become information accompanying resources to promote further use of bioresources.

In order to help users to make better achievements, this Center has been providing training courses on resource utilization since 2004. As they have been highly appreciated, we have extended the training courses to recombinant adenoviral vector handling and microbes in 2005.

ten years from now. Our vision is to facilitate unique resources and to conduct strong research and development in BRC while observing the social and scientific development to ensure the sustainability of the Center.

In order to conduct projects through consultation with researchers at home and abroad, BRC has the RIKEN Advisory Council, the BioResource Center Advisory Council and six resource committees responsible for each of the types of resource at BRC, including bioresource information. Furthermore the Research Ethics Committee, the Recombinant DNA Experiment Committee and the Animal Experiments Committee involve external researchers and citizen representation in order to maintain transparency of the operation. Minutes of these committees are open to the public.

In the future, we hope to establish the RIKEN BRC as a brand of the highest quality of bioresources and to earn trust, appreciation and admiration from the scientific community.

These were added to courses on mouse embryo cryopreservation and cultured plant cells. Training courses are open to many communities, including industry. We plan to further develop the training courses and to extend invitations to overseas users.

Science is an international endeavor, and bioresources are therefore in demand from countries all around the world. In this post-genomic era, the number and variety of bioresources is rapidly increasing. Therefore it is essential that all key resource centers cooperate among themselves to preserve and distribute needed bioresources. In light of this, BRC joined with 17 organizations around the world to establish the Federation of International Mouse Resources in 2005. Dr. Obata has served as the vice chair of the Federation since its inception.

Additionally, we are working to encourage more cooperation among Asian countries to promote a networking of resource centers. Such systems typically lag behind European and North American efforts. In 2005, we signed memoranda of understanding for collaboration with Singaporean and Taiwanese research organizations. These activities will continue in the hopes of developing an Asian network.

We will also increase the promotion of BRC activities with researchers. By publicizing these activities, access to the BRC will increase, and this then will generate more excellent results, consequently creating a spiral of mutual benefit. To this end, BRC organized many symposia and exhibitions at conferences of academic societies.

## Main activities in FY 2005

2005	
4/20, 23	Open Campus
4/21-23	Participation at the 2nd Mouse Resource Centers Roundtable Meeting for the establishment of the Federation of International Mouse Resources. (Rome, Italy)
8/1	Signed an MoU with National Applied Research Laboratories in Taiwan
8/24-26	Gene Engineering Division – Training course on recombinant adenoviral vector
8/29-30	Microbe Division – Training course on culturing and preservation method for anaerobic microbe
9/22	Experimental Plant Division – Received the Botanical Society of Japan Special Award at the 69th Convention
9/29	National BioResource Project “Cell” Symposium organized by the BRC Cell Engineering Division
10/9-10	Participation at the 3rd Federation of International Mouse Resource Meeting (Bethesda, MD)
10/11-14	Bioresource Engineering Division – Training course on cryopreservation of mouse embryos and sperms
10/21	The 25th Anniversary Ceremony and Symposium RIKEN-JCM (Microbe Division)
10/25-26	Participation at the 8th task force meeting of the OECD/WPB/BRC (Paris, France)
11/7-9	Experimental Plant Division – Training course on culturing method for plant cell lines
12/7-10	The 28th Annual Meeting of the Molecular Biology Society of Japan: Symposium and Panel display
12/13-15	Microbe Division – Training course on Terminal RFLP method for analysis of intestine bacteria
2006	
3/9	NBRP Symposium “Frontlines of Bioresources in Life Science” symposium and panel display
3/14-15, 23	Life Science Joint Symposium in 2006: Panel display

### Creating new light to observe imperceptible things

The Harima Institute was established in 1997 to promote frontier research using the world's largest third-generation synchrotron radiation facility, "SPring-8". The construction of SPring-8 began in 1991 by RIKEN in collaboration with the Japan Atomic Energy Research Institute (now integrated into the Japan Atomic Energy Agency) at the Harima Science Garden City in Nishi Harima, Hyogo Prefecture, and was completed in 1997. SPring-8 began to operate as a fully operational public facility open to the world. Presently the facility is utilized by about 10,000 scientists per year to conduct the most-advanced research for the 21st century. The management and operation of SPring-8 as well as support for public users have been entrusted to the Japan Synchrotron Radiation Research Institute (JASRI).

Synchrotron Radiation (SR) is made up of very intense X-rays generated from electrons traveling at close to the speed of light when its direction is altered by a magnetic field. SR has been utilized in a great variation of

research fields, such as life science, materials science, nanotechnology, environmental science, earth science, and industrial applications.

#### The RIKEN SPring-8 Center

The RIKEN SPring-8 Center (RSC) was established in October 2005 with a mission to make substantial contributions to the further advancement and development of science and technology at SPring-8. The RSC conducts advanced research to upgrade SPring-8 to maintain its leading position among the world's SR facilities. The RSC frontier research is actively conducted by using the outstanding SR of SPring-8. In the fields of Structural Biology, for instance, three-dimensional (3-D) structures are determined to further understand the mechanisms of biological catalysts at the atomic level. Combinations of various methods with SR are being studied in the fields of Material Science

as well. RIKEN will begin the 5-year Project of the X-ray Free Electron Laser (XFEL) at SPring-8 in FY 2006, which draws world attention as a new light source for the next generation of the SR facility.

#### RSC in FY 2005

In the RSC, diverse research is being conducted in nine institute laboratories and four research groups, with the support from the Division of Synchrotron Radiation Instrumentation. A wide range of results has been achieved in fiscal year 2005.

In physics research, we, the scientists at the RSC, have completed the construction of the XFEL prototype, an accelerator with a total length of 60m, and successfully generated the first undulator beam. Applying this experience and acquired skills, we will start building the XFEL in the fiscal year of 2006. The prototype will be used as a public facility in the future. In May 2005, the "XFEL symposium" held

#### MESSAGE

### SPring-8 — a center of excellence for optical science

**Hiroyoshi Suematsu**

Director  
Harima Institute



A dramatic change occurred in October 2005 in the situation surrounding the Harima Institute. The Japan Atomic Energy Research Institute (currently the Japan Atomic Energy Agency), which has jointly participated in the construction and installation of SPring-8 with RIKEN, withdrew from its management in September. For the future operation of SPring-8, RIKEN will reinforce cooperation with the Japan Synchrotron Radiation Research Institute (JASRI) to ensure the optimal utilization of this joint facility, the largest of its kind in Japan. It was decided to transfer the RIKEN-unique synchrotron radiation science and biological and physical studies, as well as the refinement of SPring-8 and development of the next generation light source, to the RIKEN SPring-8 Center (RSC) that is to be newly established.

One of our recent major research achievements is the successful determination of structures of diversified proteins by use of synchrotron radiation available from SPring-8. We have played an ever-greater role as a key research base in the "Protein 3000 Project" through the

above achievement as well as in the elucidation of many of the so far unknown reactions and response mechanisms of biological materials.

After our study on X-ray free electron laser (XFEL) has been authorized as an essential national technology, our biggest task in 2006 is to ensure a successful start for the construction of the facility for this study in the SPring-8 facility compound. XFEL, which has been left unexploited so far, is a far more intense light than the radiant light available from SPring-8, and promises to be a major development in the future as an ultimate source of X-rays. This facility will be completed during 2010. A prototype of the XFEL device was completed in 2005, and it is currently used for adjustment of the device functions as well as for R&D purposes.

The large SPring-8 synchrotron radiation facility is used by a total of 10,000 Japanese and foreign researchers for a year. This facility is widely used by a variety of disciplines, including the life sciences for protein conformation analysis, material science, typically represented by nanotechnology, earth science, and

at University of Tokyo drew great attention from the participants with lively and constructive discussions.

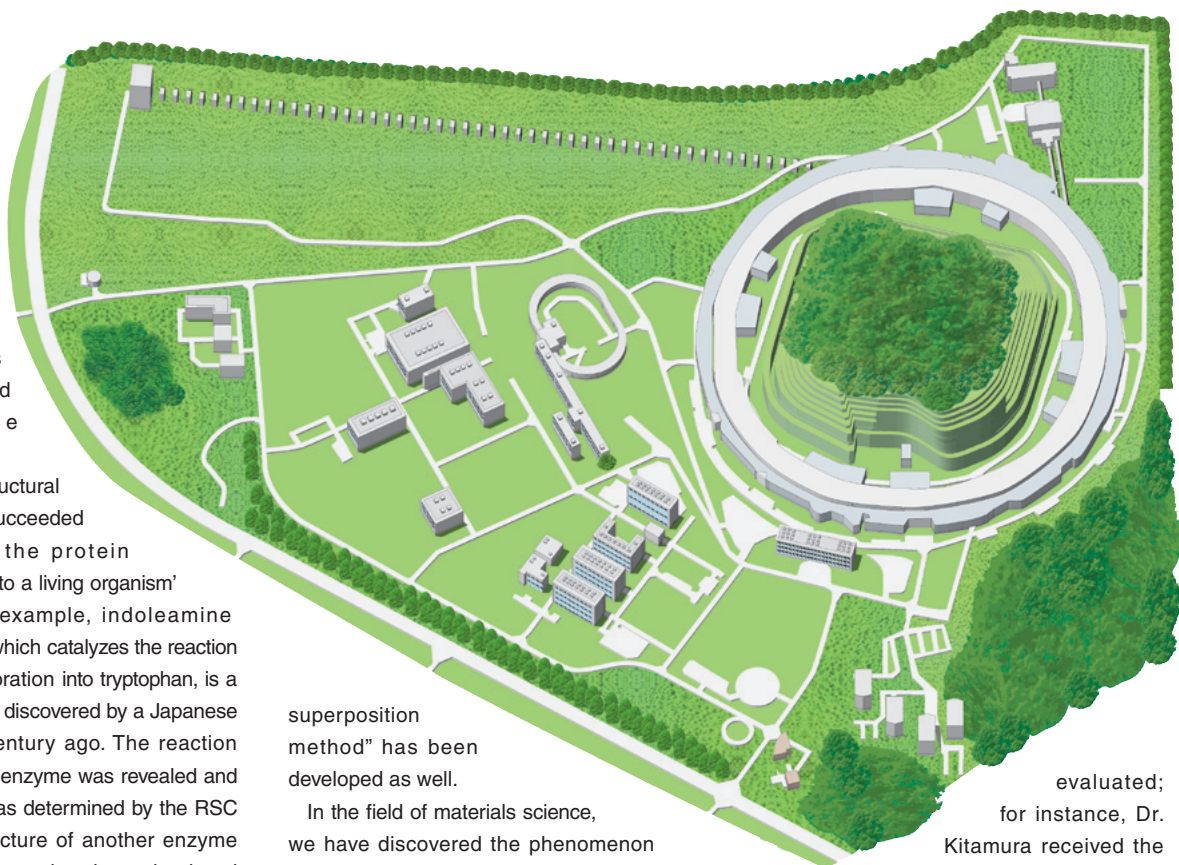
In the field of structural biology, we have succeeded in determining the protein structures related to a living organism's functions. For example, indoleamine 2,3-dioxygenase, which catalyzes the reaction for oxygen incorporation into tryptophan, is a well-known enzyme discovered by a Japanese scientist half a century ago. The reaction mechanism of this enzyme was revealed and its 3-D structure was determined by the RSC scientist. The structure of another enzyme called luciferase was also determined and the detailed mechanism of bioluminescence for the Japanese firefly was elucidated. A new method to detect the slight changing of the protein structure named "multiple

superposition method" has been developed as well.

In the field of materials science, we have discovered the phenomenon that solid oxygen expands greatly in an intense magnetic field below minus 272 degrees Celsius.

In the remarkable year of 2005, the research activities of the RSC were highly

evaluated; for instance, Dr. Kitamura received the Science and Technology award from the minister from Ministry of Education, Culture, Sports, Science and Technology (MEXT).



archaeology. A noticeable trend these days is a rapid increase of usage by corporations for commercial purposes. Our campus contains bases of research for many institutes including Osaka University, the University of Hyogo, Japan Atomic Energy Agency, Taiwanese institutes and consortiums of companies, forming an important center of excellence.

As a key research base, the Harima Institute and SPring-8 will contribute actively to realize the concept "To increase contributions to society and humankind", which is one of the five precepts of the Noyori Initiative.

## Major activities in FY 2005 in the fields of international exchange, publicity and workshops

### 2005

4/23	SPring-8 / RIKEN Harima Institute Open day
5/19	Symposium on X-ray Free Electron Laser
6/10-11	First semester meeting on Study of Quantum Materials—collaborative research into the use of synchrotron radiation.
8/5-7	The Fourth Annual Meeting of Structural-Biological Whole Cell Project
9/7	Meeting on Structure and Electron State in Molecular System
10/1	RIKEN SPring-8 Center launched
11/25-26	Kansai Thin Film and Surface Physics Seminar / RIKEN Quantum Materials Research Seminar
12/5	Workshop on Tasks and Future Prospects for Radiation Detectors and Electronic Circuits

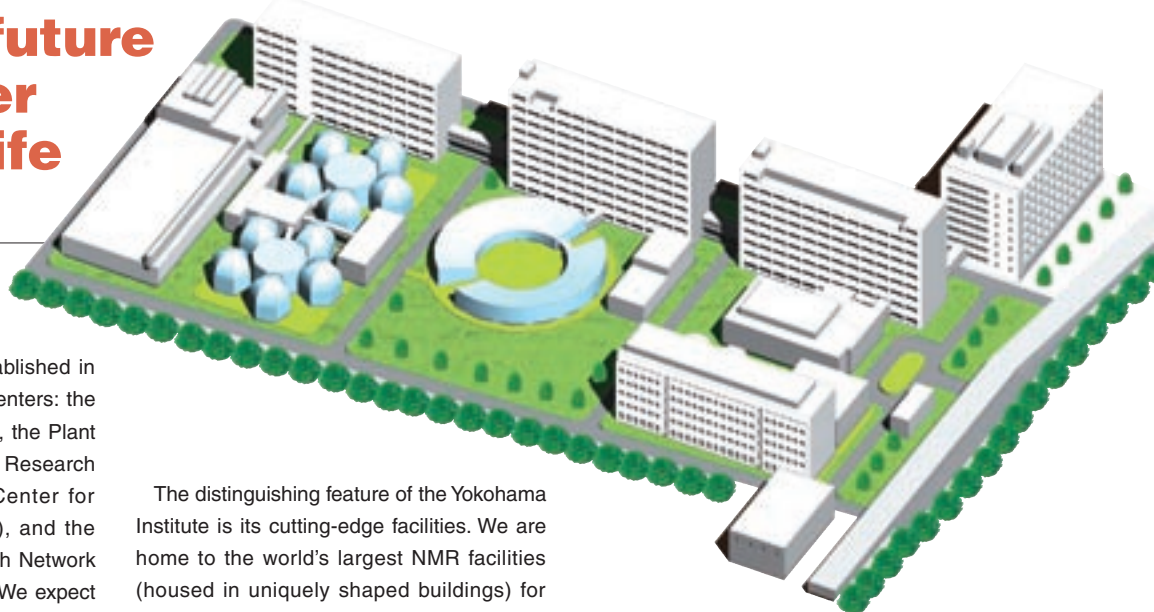
### 2006

2/1-3	RIKEN SPring-8 Center Advisory Council
3/7-8	The Fourth International Workshop on X-ray Damage to Biological Crystalline Samples

## Yokohama

### Yokohama Institute

# Life science research for a brighter future and a better quality of life



The Yokohama Institute was established in April 2000 and consists of five centers: the Genomic Sciences Center (GSC), the Plant Science Center (PSC), the SNP Research Center (SRC), the Research Center for Allergy and Immunology (RCAI), and the newly opened Center of Research Network for Infectious Diseases (CRNID). We expect that the institute's research achievements, in addition to their scholarly significance, will serve as a technological platform for the development of new drugs, personalized medicine, improved agricultural production, and an overall better quality of life.

The distinguishing feature of the Yokohama Institute is its cutting-edge facilities. We are home to the world's largest NMR facilities (housed in uniquely shaped buildings) for determining the three-dimensional structure of proteins. We also have the world's most accurate SNP typing system, as well as high-speed DNA sequencing facilities, experimental greenhouses and animal research (mouse) facilities.

## MESSAGE

### Yearly activities of Yokohama Institute and our hopes for FY 2006

#### Tomoya Ogawa

Director  
Yokohama Institute



In FY 2005, the Plant Science Center and the SNP Research Center started their second phase with new directors. Director Shinozaki heads the former to take over the strategy from the first phase and is now developing it even further. Director Nakamura heads the latter to develop the research results obtained so far and promotes a broad range of research on genes related to diseases and disorders.

In July 2005, a new facility, the Center of Research Network for Infectious Diseases, was launched. The major mission of the Center is to provide support for building a network of research centers in the field of infectious diseases.

In June 2006, a meeting of the RIKEN Advisory Council (RAC) was held. Its recommendations will be publicized on our website. Additionally, RIKEN will be evaluated at Ministry of Education, Culture, Sports, Science and Technology (MEXT) evaluation meeting in July, and will be comprehensively evaluated by the Council for Science and Technology Policy. FY 2006 is the halfway point of the first phase of the mid-term plan for RIKEN as an independent administrative corporation. The Yokohama Institute also needs

to consider the above recommendations and evaluation and to have them reflected in the next mid-term plan.

In drawing up the next mid-term plan, we should fully consider the social circumstances surrounding RIKEN and the Yokohama Institute as well as our vision. From the viewpoint of the international strategy in particular, it will be important to develop cooperation with Asian research institutes and universities besides cooperation with those in the U.S.A. and the E.U. We will need to provide an amicable contribution to human resource development and research activities in Asia.

In addition to outgoing activities, it is also important to vitalize interactions within RIKEN. For example, the Yokohama Institute holds a Science Talk every month for cross-disciplinary communication among researchers. In FY 2005, we held the Science Salon twice. For the first one, we had President Noyori's talk, "Research Evaluation," and for the second one, Dr. Takeshi Yoro gave a talk entitled "Life Science and Society." In the face of the recent rapid expansion of research areas and further specialization, our perspective tends to be too narrow to grasp the entire picture. However,



## Yokohama Institute in FY 2005

### 1 PSC and SRC enter their second phase

The second phase for each center began with the appointment of new center directors: Kazuo Shinozaki at PSC and Yusuke Nakamura at SRC. Each center will build on its previous research achievements with translational research in the areas of medicine and agricultural production.

### 2 Yokohama Institute Open Day (June)

More than 1,600 visitors from the general public learned about leading-edge life science research through researcher presentations, interactive experiments and panel exhibits.

### 3 Center of Research Network for Infectious Diseases opens (July)

CRNID was established as part of the Japanese government's Program of Founding Research Centers for Emerging and Reemerging Infectious Diseases. The center will coordinate the government

program, establish a domestic and international research network for infectious disease, distribute timely and useful information, and support the creation and operation of cooperative research facilities.

### 4 Exhibition space opens (June)

A special exhibition space was opened on the first floor of the Main Office Building. The space includes an explanation of basic life science concepts, introduces the institute's research activities, and offers several interactive games to test visitors' life science knowledge.

### 5 Student tours, experiment classes and teacher courses

A total of 924 persons came to the institute in 2005 for study tours. Visitors included government and public officials, business representatives, academic societies, schools, and other individuals and groups. Special experiment classes (e.g. DNA extraction) were held for science-oriented high-school students and science instructors.

### 6 Comprehensive agreement with Yokohama City University (November)

The Yokohama Institute and Yokohama City University reached a basic agreement that formalizes an already close relationship with the university's Graduate School for Supramolecular Biology, which is adjacent to the institute. The agreement aims for comprehensive cooperation in such areas as collaborative research and the training of personnel.

### 7 Science Salon talks

The institute has been hosting lectures by prominent scientific figures at its Science Salons since September 2005, to help stimulate researchers' imaginations and promote interaction with the local community. The first two speakers were Nobel Prize winner and RIKEN President Dr. Ryoji Noyori, and anatomist and best-selling author Dr. Takeshi Yoro. The institute also initiated a Science Talk series for professional development and the Salon Concert series for entertainment. Such events provide social exchange and relaxation opportunities for researchers and staff.

we researchers should always try to raise fresh interest in how our research activities are positioned as cultural activities, and where they are heading for. Launched in 2004 as a musical activity, the Salon Concert has had its 19th event already. Its audience now includes people from companies in the surrounding areas in addition to personnel from the Yokohama Institute. It is my wish that this event may grow as a happy forum for exchange.

The extension work on the Main Office Building will be completed at the end of 2006. In addition to expansion of the cafeteria space, the new section will include an exhibition space and a cafe. Under consideration is a day-care facility for children, like Kids Wako, that can help women personnel, if only a little, as they try to return to the workplace after childbirth. From a long-term view, I would like to increase the ratio of personnel from overseas to 20–30 percent of all personnel at Yokohama Institute. In order to build a truly international research institute, I am determined to carefully take the necessary measures while obtaining cooperation from the local governments of Kanagawa Prefecture and the City of Yokohama.

## 2005 award-winners at a glance

Genomic Sciences Center	
Haraaki SEKI	FY 2005 Botanical Society of Japan Promotion Award (September 2005)
Yusuke NISHIYAMA	Best Poster Award First International Symposium, Research Center for Environment Friendly Polymers (October 2005)
Hiroshi HIROTA	Award for Excellence to Authors Publishing in Bioscience, Biotechnology, and Biochemistry in 2004 (March 2005)
Yoshihide HAYASHIZAKI	Remarkable contribution to science and technology in 2005 (December 2005)
Plant Science Center	
Shigeo YOSHIDA	FY 2005 Japan Agriculture Prize, 42nd Yomiuri Prize of Agricultural Science (April 2005)
Hideki TAKAHASHI	Promotion Award, Japanese Society of Plant Physiologists (April 2005)
Masami HIRAI	Promotion Award, Japanese Society of Plant Cell and Molecular Biology (August 2005)
Taku DEMURA	Promotion Award, Botanical Society of Japan (September 2005)
Takahito NOMURA	Promotion Award, Japanese Society of Chemical Regulation of Plants (November 2005)
SNP Research Center	
Toshihiro TANAKA	Young Scientist Award from MEXT (April 2005)
Research Center for Allergy and Immunology	
Toshio HIRANO	Medical Award, Japan Medical Association (November 2005)
Michio HIROSHIMA	Young Scientist Award, Biophysical Society of Japan (November 2005)
Sidonia FAGARASAN	Young Scientist Award from MEXT (April 2005)

## Benefiting society by unraveling the successful life strategies acquired over more than four billion years of evolution

DNA (genes, genomes) and proteins are the basis of life processes.

Systematic and focused research into the structure and function of DNA and proteins is providing an international initiative for life science research to produce technological breakthroughs in medicine, environmental safeguarding and food production that can be applied in various industries.

Since its establishment in 1998, the Genomic Sciences Center (GSC) has produced world-acclaimed gene, genome and protein research achievements. GSC has been located at the Yokohama Institute since 2000.

GSC research currently focuses on (1) unraveling of the strategies of life, (2) the development and application of advanced research technologies, (3) the development of model animals for various

human diseases and (4) focused analysis of genome functional information.

GSC is also a major player in national initiatives such as the Protein 3000 Project (identification of the structure and function of 3,000 proteins), the National BioResource Project (development of research mice) and the Genome Network Project (elucidation of the gene networks related to life processes and disease).

### GSC in FY 2005

Major research publications at GSC in 2005 included the discovery of an RNA Continent and the sequencing of the chimpanzee Y chromosome.

For the RNA Continent, GSC researchers have demonstrated that 70 percent of the

entire genome in mice is transcribed to both mRNA (which codes for proteins) and non-coding RNA (ncRNA). The findings imply that ncRNA transcribes such non-coding regions, once thought to be "junk" sequences, and such ncRNAs may regulate when, where and how much gene should function. The higher the organism, the more ncRNA it contains, and increasing evidence points to ncRNA as having a role in maintaining the complexity of life processes. These findings challenge a basic precept of genetic science and were covered widely in the media.

As for the chimpanzee Y chromosome, GSC led a joint team of researchers in Japan and Korea whose efforts have resulted in important clues in the elucidation of the evolutionary paths taken by humans and chimpanzees.

### MESSAGE

## Thinking back over 2005

### Yoshiyuki Sakaki

Director  
Genomic Sciences Center



So far, the Genomic Sciences Center has been undertaking comprehensive, systematic and profound analysis of elements that support life phenomena, including genomes, genes and proteins.

The discovery of so-called non-coding RNA (ncRNA), on which we published a paper this year, is a result of in-depth analysis of these elements. This report has had a significant impact around the world while overriding the previously shared perception concerning the regulation of gene expression by uncovering the presence of numerous RNAs that do not produce proteins. This achievement is expected to contribute greatly to the development of the Genome Network Project launched the year before last.

In the comparative genome study focusing on the human species and primates, Y chromosome (sex chromosome) comparison was conducted between humans and chimpanzees. As a result, it was proven that Y chromosomes evolve at a higher rate than autosomal chromosomes. Furthermore, it is now possible to plot ancestor-type Y chromosome, enabling insight into the change of the genomic structure in the process of the evolution toward the human species.

Launched in FY 2002, the Protein 3000 Project is another program that has brought about

steady advances, including the determination of the structures of a large number of proteins and the development of a new structural analysis method.

The center has set out the theme of its second phase as "From unraveling of elements to unraveling of the system." In order to lead activities under this theme, the center started acting as the stronghold of the RTK Consortium, aiming to conduct analysis of the signal transduction channels based on system biology. A Japan-China-Korea cooperation program for analysis of mutant mice is also among the activities it has started.

While the center's current genome analysis capability is at the world's top level, it introduced a very fast DNA sequencer called 454 for the first time in Japan. We would like to conduct genome analysis on bacterial flora inside the human intestines using this sequencer. Our plan is to probe the relationship between the bacterial flora and our health and diseases.

# Improving agricultural production and crop quality for a healthy, sustainable society and environmental well-being

The Plant Science Center (PSC) was established in 2000 to contribute to the UN's Millennium Project, and is Japan's only plant research center focusing on global-level issues and solutions for food supply and environmental problems. In its first five years, PSC produced a significant number of research results under the motto "Learning from Plants, Utilize Plants".

The center began its second five-year phase in 2005, focusing on plant metabolic systems with the aim of improving production volumes and the quality of food crops.

Working in cooperation with partners such as domestic universities and their affiliated research centers, industry, and foreign research organizations, PSC aims to contribute to the creation of a sustainable society through tangible research results and contributions to efforts to augment food

production, improve health and ensure the well-being of the environment.

## PSC in FY 2005

PSC's former research achievements include genome analysis in model plants (transcriptomes, proteomes, metabolomes) and functional analysis of plant metabolites. Based on these, at the start of its second phase PSC began to clarify plant metabolic systems by understanding control mechanisms such as growth restriction, morphogenesis, photosynthesis, metabolism and environmental response as a whole system. Our aim is to improve agricultural production volumes and food crop quality through the use of restriction genes, metabolism genes and novel metabolites.



Particular efforts in 2005 included improving the PSC metabolome analysis infrastructure to accommodate the analysis of a diversity of plant metabolites, and the undertaking of a significant number of joint research projects.

Two especially notable research results included the identification of an important gene, *OsCKX2*, involved in determining grain numbers, which researchers used to increase grain yields by 20 percent; and the discovery of a master transcription factor for plant woodiness.

## MESSAGE

### Aiming to unravel the metabolic system

**Kazuo Shinozaki**

Director  
Plant Science Center



The second phase of PSC started in FY 2005. Based on the results of our research in plant science in the first phase, we wish to carry out research that can contribute to society by improving plant productivity through research on genome functions, such as metabolomes.

The global population is expected to reach nine billion in 2050. In order to accommodate this explosive population increase and the accompanying food problem, we are carrying out new projects for contributing to the realization of a sustainable society through improvement of plant productivity, creation of novel crops and bio-materials and the achievement of environmental well-being.

Among these projects, the research of the metabolic network related to plant functionality is the backbone of the research carried out at PSC. Metabolic products from plants include a large number of secondary metabolic products useful for our health along with primary metabolic products such as sugars, amino acids and fat. In the second phase, we will focus our effort on the development of metabolome analysis technology for extensive probing of these metabolic products. Based on research into the genome function of model plants, we will unravel their metabolic network (or metabolic system), and develop research for improving plant productivity by utilizing results of the research.

Research carried over from the first phase have delivered great results, as represented by the Sakakibara team's discovery of a gene that increases the yield of rice by 20 percent by phytohormone regulation, as well as the Demura team's identification of the critical control factor for producing the woody cells of a tree.

Some research groups have been launched anew in the second phase, including the Saito group, which has succeeded in developing a technology for enabling greater deposits of anthocyanins as observed in blueberries, and the Shirasu group, which is promoting leading-edge research concerning plant disease resistance. As for my group, we will continue to study important controlling genes involved with resistance to dryness stress.

FY 2005 has also been a year of active cooperation with universities and other research institutes. For example, we have started joint research with a rice plant genome study group under the Ministry of Agriculture, Fisheries and Forestry, the Institute for Advanced Biosciences at Keio University, the Kihara Institute for Biological Research at Yokohama City University, and Nagoya University, among other institutes. We wish to link the basic research results to their applications through cooperation with external institutes and enterprises so that research can deliver accomplishments useful for the real world.

## Working to establish personalized medicine by determining the genetic information related to lifestyle diseases and medicinal effects

Genetic polymorphisms are the slight variations in genetic information among individuals, responsible for individual differences in physical constitution. Systematic mapping of the link between genetic polymorphisms and lifestyle diseases or drug responsiveness can help identify the genes related to disorders and clarify the effect genetic polymorphisms have on gene function. Such systematic mapping is expected to contribute to the realization of personalized medicine.

Among the various types of genetic polymorphisms, the SNP Research Center (SRC) has targeted single nucleotide polymorphisms (SNPs) for analyzing and identifying disorder-causing genes. SRC has developed its own high-speed, high-precision SNP analysis method to generate the necessary SNP data.

Genetic polymorphism research is a crucial step in developing personalized

medical treatments that minimize physical harm. SRC is home to the world's fastest analytical instrument for determining the sequence of bases in test subjects in certain areas of the genes responsible for genotype differences in individuals.

SRC also has research teams investigating and analyzing genes related to cardiovascular disease, rheumatism, bone and joint disease, diabetes, allergic diseases and obesity, with the aim of developing effective treatments.

### SRC in FY 2005

SRC was the largest contributor to the International HapMap Project (which came to a close in 2005), providing 24.3 percent of the project's data. The HapMap project was a cooperative international effort among research institutes to create an

SNP database from the DNA of subjects of Asian, African and Caucasian descent.

SRC, in cooperation with Toppan Printing and Shimadzu Corporation, succeeded in developing a new instrument capable of analyzing a drop of blood for gene sequence differences in 90 minutes. The center also developed a prediction system for associating SNP genotype with sensitivity to warfarin, the most commonly used oral anticoagulant medicine. This system will allow for advance estimation of warfarin dose requirements, making personalized warfarin treatment possible.

SRC's research achievements in 2005 are a step forward in making personalized medicine a practical reality.

### MESSAGE

## Next-generation medical care envisioned from FY 2005 research results

**Yusuke Nakamura**

Director  
SNP Research Center



The greatest topic in FY 2005 for SRC was its considerable contribution to the International HapMap Project. In this project, international research institutes cooperated to create a database of all chromosomes found among Asians, Africans and Caucasians. SRC has contributed as much as 24.3 percent of all data analysis, which is the highest figure among the research institutes participating in this research project.

As a result of the accomplishments of the project, a global SNP research foundation has been built. In the future, we can expect that this foundation will be utilized in SNP-based research into diseases as well as in research on the side effects of drugs, leading to rapid advancement in those fields. For example, it is safe to say that this database will help the realization of personalized medication through studies on relationships between differences of genetic coding and the manifestation of side effects of drugs.

Also, joint research with Shimadzu Corporation and Toppan Printing succeeded in developing equipment that can judge in 90 minutes differences in the genetic coding from just one drop of blood. In FY 2006, we plan to

test this equipment at about 20 hospitals. Should there be no problem, it will be commercialized in FY 2007 in order to realize personalized medicine.

We have two future plans. First, we will continue to undertake analysis of 47 target diseases, carrying on our previous year's mission. We will also promote joint research with Asian research groups. While we are the top runner in the world in the field of SNP analysis, it is still necessary for us to cooperate with Asian countries. I hope the cooperative community in Asia will grow step by step through our cooperation on research into diseases peculiar to Asia and infectious diseases.

To date, SRC has discovered and reported genes related to incidences of cardiac infarction, rheumatoid arthritis, osteoarthritis, Crohn's disease, disk herniation, asthma, and so on. We are determined to continue our contribution to new medicine development and the establishment of personalized medicine through SNP analysis to identify yet-hidden causes of diseases.

# Comprehensive immunological research, from elucidation of the immune system to the development of novel therapeutic approaches for immunological and allergic diseases

Immunity is a highly complex defense system that protects the body against illness. Allergies, autoimmune diseases, cancer and the rejection of implanted cells and organs are directly related to this intricate protective system. Elucidating the mechanisms of the immune system and developing new therapeutic approaches will be an important challenge for immunological research in the coming decades.

The Research Center for Allergy and Immunology (RCAI) was established in 2001 with the intention of creating a central base for comprehensive immunological research in Japan and to accelerate the transfer of new findings to clinical applications. The center's research teams moved into centralized and permanent facilities at the Yokohama Institute in 2004. RCAI research activities span virtually all areas of immunobiology yet share a common interest in the study of regulatory mechanisms of the

immune system, which are directly relevant to clinical applications. It is the explicit goal of RCAI to contribute to the development and evaluation of novel treatment regimes for immunological disorders. To this end, RCAI has created a Strategic Research Program, made up of three units that specialize in allergy, autoimmune diseases and cell therapy.

## RCAI in FY 2005

In the second year since the center's inauguration, some 170 researchers and technicians moved forward with their basic and comprehensive research of immunological and allergic diseases.

The number of people suffering from allergic disorders such as asthma or allergic dermatitis, or immunological disorders such as rheumatoid arthritis, is on the rise. It is believed that more than 30 percent of the

Japanese population suffers from an allergic disorder, yet current treatments only address symptoms. RCAI continued with its efforts to develop a vaccine for allergy to cedar pollen, which has shown highly promising results in animal tests. Following the road map which the Council for Science and Technology Policy set out for cedar pollinosis research, we moved forward with plans for studies on safety and effectiveness in collaboration with external institutions.

The center made several important contributions in FY 2005. Dr. Masaru Taniguchi (RCAI director and head of the Laboratory for Immune Regulation) and his colleagues were the first to elucidate the mechanisms behind early graft loss in transplanted pancreatic islets and successfully controlled this loss, while Dr. Takashi Saito and his colleagues at the Laboratory for Cell Signaling identified T cell receptor microclusters as the starting point of immune response.

## MESSAGE

### RCAI's missions and the progress this year

#### Masaru Taniguchi

Director  
Research Center for Allergy and Immunology



An international symposium held in June 2005 under the joint auspices of RCAI and the Japanese Society for Immunology was attended by 550 people from various countries, and contributed to building an international foundation. We will hold the symposium every year from now on, so it will be important to build a reputation that being invited to the symposium will be considered an honor. We have also started the "RCAI International Research Collaboration Awards Program," under which selected foreign researchers are invited to build a semi-independent research group within the laboratory of their collaboration partner at the Center. At present, 12 projects are in progress. We believe it is also one of RIKEN's missions to foster young research leaders whose achievements are well-recognized in the world.

At present, approximately 30 percent of Japanese have some allergies, and the importance of research on allergy is growing. The symposium on pollinosis, held under the joint auspices of Ministry of Education, Culture, Sports, Science and Technology, was attended by the general public, and I believe we were able to introduce RCAI's research activities to a wide range of people.

The "ENU Mutagenesis Project", which is being carried out together with the Genomic Sciences Center (GSC), aims at developing a mouse that has atopic dermatitis and specifying its causative genes, within a few years.

One of the study results in 2005 is the successful development of an artificial lymph node for the first time in the world. Transplanting an artificial lymph node can prevent infectious diseases, and we are awaiting its use on aged people and patients with serious infectious diseases and cancer.

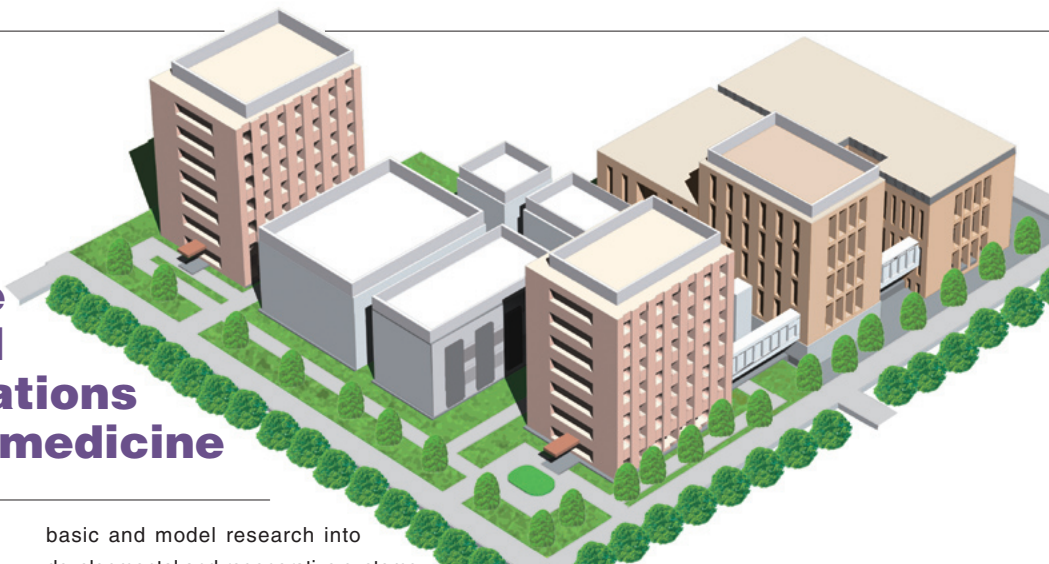
Furthermore, we have succeeded in controlling transplant rejection of insulin-producing islet cells in the liver by regulating the activities of Natural Killer T cells, a subset of lymphocytes. We have also developed a new optical microscope allowing observation of single molecules in living immune cells. By using this microscope, Group Director Takashi Saito has discovered the start point of immunological responses.

We hope to continue developing unique techniques and equipments that will lead to breakthroughs in basic concepts in immunology.

## Kobe

### Kobe Institute

# Investigating developmental and regenerative mechanisms and laying the foundations for regenerative medicine



The Kobe Institute is home of the Center for Developmental Biology (CDB), which aims to promote basic research into developmental biology, as well as to conduct basic and model research in cell therapy and organ regeneration for use in medical applications. The Institute serves as one of the keystone institutes, along with the Institute for Biomedical Research and Innovation, in Kobe's industry-government-academic research cluster, which seeks to develop new advances in medicine for the 21st century.

### Center for Developmental Biology

The Center for Development Biology (CDB) was launched in April 2000 to conduct

basic and model research into developmental and regenerative systems in animals, and to investigate possible applications in regenerative medicine.

The CDB conducts research not only into areas of basic developmental biology, such as classical embryology, molecular cell biology, neurogenesis, evolutionary biology, functional genomics and bioinformatics, but also into fields of medical research, such as regenerative medicine and stem cell research.

To enable the CDB to conduct such a wide range of research activities, the Center employs a number of talented researchers both from Japan and from overseas, placing great emphasis on originality and independence and respecting the

independence of each research team. One of the key features of the Center is that innovative work in both fundamental research and biomedical science can be carried out in the same institute. It is hoped that the opportunity for close trans-disciplinary interaction will help both to advance the fields of development and regeneration and to yield innovative contributions to life science in the 21st century.

### CDB in FY 2005

Although the sequencing of genomes has been advancing rapidly, knowledge of the

## MESSAGE

### Toward the secondary state of the CDB

#### Masatoshi Takeichi

Director  
Center for Developmental Biology



In 2005, the CDB entered its second five-year term, after a very successful first, and continued to build on that success. The Laboratory for Genomic Reprogramming, headed by Teruhiko Wakayama, reported on the identification of an agent that increases the success rate of attempts to clone mice from somatic cells to as much as three times that of other methods, a result that may have only been possible in the Wakayama lab, given its expertise in nuclear transfer.

In a study with significant implications for the field of regenerative medicine, the Laboratory for Organogenesis and Neurogenesis headed by Yoshiki Sasai succeeded in inducing the differentiation of retinal precursor cells (from which retinal neurons arise) from ES cells in culture. This achievement was made possible by modifying a method for inducing mouse ES cells to differentiate into cortical precursors that was first reported by the Sasai lab last year. Also in 2005, the Laboratory for Cell Lineage Modulation led by Toru Kondo

launched a new program that aims at the transdifferentiation neural stem cells, which may one day lead to advances in regenerative medicine.

The CDB is also making a strong effort toward international cooperation, particularly in the Asia-Oceania region. It continues to support the Asia-Pacific Developmental Biology Network (APDBN), which was established to promote scientific exchange and communication regarding developmental biology and related fields in Asia and Oceania. The APDBN was launched under the auspices of the International Society of Developmental Biologists, an organization which I now serve as president, with administrative support from the CDB Office for Science Communications and International Affairs. In June 2006, we will hold a symposium sponsored by the APDBN at the annual meeting of the Japanese Society of Developmental Biologists, and plan to take a leading role in the holding of symposia across the Asia-Pacific region, in places such as India and Singapore.



means by which an individual cell (the fertilized egg) is able to give rise to a wide variety of differentiated cell types remains imperfect. Similarly, the function of any given gene has so far only been revealed in a limited number of model organisms.

The approximately 30 research teams in CDB are divided into three distinct types: the Core Research Program, the Creative Research Promoting Program, and Supporting Laboratories, all of which work toward elucidating aspects of development and regeneration. Translational research, which seeks to apply basic research results to human clinical needs after satisfying rigorous safety and ethical standards, is also a goal of the Center's work.

In 2005, we achieved results with great promise of application in regenerative medicine; for example, a CDB lab achieved a world-first by inducing the differentiation of neural retina precursors and photoreceptor cells from ES cells. Other successes have deep implications for animal development and improving our understanding of

regeneration; for example, CDB researchers established technology to improve the efficiency of mouse cloning, and identified the gene that acts as the first determinant of the fate of germline cells. Other labs are conducting research that may one day lead to the discovery of new pharmaceuticals, such as the discovery by one CDB research program that genes active in morning hours play a central role in controlling the body's 24-hour biological clock in mice.

As in previous years, CDB scientists received numerous awards in 2005. In April, CDB Director Masatoshi Takeichi was honored with the Japan Prize, and Team Leader Hiroki R. Ueda received a Tokyo Techno Forum 21 Gold Medal Prize, which is awarded to promising young researchers. In September, the CDB 2004 Annual Report created by the Office for Science Communications and International Affairs won a Japan Graphic Services Industry Association prize awarded by the



by Japanese Ministry of Health, Labor and Welfare.

The CDB is strongly committed to scientific communications, outreach and public understanding of science, and conducts a variety of programs, including the CDB symposium, attended by both domestic and foreign researchers; numerous scientific seminars; the annual open house, which allows members of the public to explore the CDB; an intensive lecture program in the summer as part of the the Graduate School Affiliates Program with neighboring universities; an exhibition in Osaka Science and Technology Center Exhibition Hall; and the creation of various communication, educational and promotional tools.

CDB holds its annual symposium every spring, and we hope to continue to promote and improve this already successful series of scientific meetings. We have enjoyed increased international recognition of and attendance to these meetings in each successive year, with approximately 20 percent of the total attendance coming from abroad last year. This success on the international is a wonderful achievement. The international character of our research and activities is of great importance to all of us at the CDB, and we will work to continue to develop our annual symposium series reach a truly global level, so that an invitation to speak at a CDB Symposium will be perceived as an honor.

## Main activities in FY 2005

### 2005

- 4/1 Graduate school affiliation started in cooperation with Osaka University Graduate School of Medicine.
- 4/20 Director Takeichi awarded 2005 Japan Prize
- 4/11-13 2005 (fourth) CDB symposium
- 4/28 Team Leader Hiroki R. Ueda awarded the Gold Medal Prize.
- 5/9-10 CDB-DRI-BSI-RCAI Joint Retreat
- 5/21 Open House
- 7/1 CDB entered into institutional collaborative agreement with GSF (Germany)
- 8/24-25 Affiliated Graduate Schools Intensive Lecture Program
- 10/11 RIKEN Art & Science Exhibition in Kobe
- 11/3-7 Second Asia Reproductive Biotechnology Society meeting in Bangkok, Thailand
- 11/28-29 2005 CDB Retreat

### 2006

- 2/12-15 Fourth meeting of CDB Advisory Council

# Two new research systems expand the breadth of research

## Sponsored Laboratories

To build stronger bonds between RIKEN and industry, RIKEN created the Sponsored Laboratory Program, whereby an invited scientist can establish a laboratory at RIKEN using only corporate and other private funds. As of 1 April 2006 there was one Sponsored Laboratory in operation: the Abe Laboratory.

Dr. Takashi Abe finds, extracts, and analyses the bioactive compounds from hornets to reveal their functional mechanisms.

## Initiative Research Units

RIKEN started the Initiative Research Unit System to provide young (under 40) researchers with the opportunity to take on creative and novel research at RIKEN. Successful candidates, Ph.D.s with a few years post-doctoral research in the natural sciences, are invited to establish and manage an independent laboratory. Nine Initiative Research Units are active in March 2006.

- Kawai Initiative Research Unit: to develop a terahertz imaging system
- Masai Initiative Research Unit: investigating the mechanisms underlying neuronal differentiation and circuit development in the vertebrate retina
- Imakubo Initiative Research Unit: to create organic conductors that have supramolecular structures and multiple functions
- Fukuda Initiative Research Unit: examining the role of synaptotagmin-like proteins in intracellular membrane trafficking
- Kishi Initiative Research Unit: investigating ubiquitin regulation of the cell cycle
- Nishii Initiative Research Unit: performing molecular and genetic analysis of embryo morphogenesis in *Volvox*
- Iwawaki Initiative Research Unit: investigating ER stress and its roles *in vivo*

- Nakagawa Initiative Research Unit: examining the molecular mechanisms that control cell behaviour in the central nervous system
- Manabe Initiative Research Unit: developing a new catalytic system for novel organic synthesis



## Trends at RIKEN

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## The transformation into an Independent Administrative Institution

### Setting mid-term objectives and drafting mid-term and annual plans

In October 2003, RIKEN's status changed to Independent Administrative Institution (IAI). The Japanese government established mid-term objectives for the new IAIs to meet within three to five years, and it now oversees their efforts towards achieving these objectives. IAIs were required to

draft mid-term plans describing how they would achieve their objectives, and to get these approved by the ministry in charge, which in RIKEN's case is the Ministry of Education, Culture, Sports, Science and Technology (MEXT). RIKEN also has to submit a plan to MEXT each fiscal year.

Committees appointed by the government conduct evaluations of IAIs each year and at the end of the terms for their mid-term objectives. Based on the outcomes of its evaluations, RIKEN makes changes as necessary.



#### Summary of mid-term plan

Category	Target
<p><b>1. Improvement of operations</b></p> <p>1) Publication and utilization of research results</p> <ul style="list-style-type: none"> <li>• Publish original results</li> <li>• Publish in journals that are highly regarded in the relevant fields</li> <li>• Register intellectual property</li> <li>• License patents</li> <li>• Issue press releases</li> <li>• Publish <i>RIKEN News</i></li> </ul> <p>2) Training and development of researchers and technical staff</p> <ul style="list-style-type: none"> <li>• Special Postdoctoral Researchers</li> <li>• Initiative Research Scientists</li> <li>• Junior Research Associates (JRA)</li> </ul>	<p><b>1. Improvement of operations</b></p> <p>1) Publication and utilization of research results</p> <ul style="list-style-type: none"> <li>• 1,800 or more papers annually</li> <li>• 50% or more of 1,800 papers</li> <li>• 600 applications in fiscal year 2007</li> <li>• 12%</li> <li>• 40 a year</li> <li>• 12 a year</li> </ul> <p>2) Training and development of researchers and technical staff</p> <ul style="list-style-type: none"> <li>• Maintain constant level of 200 researchers</li> <li>• 10 researchers by fiscal year 2007</li> <li>• Maintain constant level of 140 JRAs</li> </ul>
<p><b>2. Improvement of operational and managerial efficiency</b></p> <ul style="list-style-type: none"> <li>• Increase operational efficiency</li> <li>• Increase procurement efficiency</li> <li>• Increase managerial efficiency</li> </ul>	<p><b>2. Improvement of operational and managerial efficiency</b></p> <ul style="list-style-type: none"> <li>• Reduce expenditure by 1% annually</li> <li>• Reduce expenditure by 2% annually</li> <li>• Reduce administrative costs by 15% (before taxes)</li> </ul>

## The Noyori Initiative

On becoming the first President of RIKEN as an Independent Administrative Institution, Ryoji Noyori issued the "Noyori Initiative" for the future of the institute.

Through the Noyori Initiative, RIKEN is putting into practice its mid-term plan and continuing to pursue scientific research at the very highest levels.



## Research Priority Committee

Consisting of both RIKEN employees and outside members, the Research Priority Committee advises the President on the management of the whole of RIKEN, and discusses what direction future research should take and what areas of research should be prioritized. It works by deciding on issues that need to be addressed and then discussing them at monthly meetings through the year.

The Research Priority Committee also manages the Strategic Programs for R&D (President's Discretionary Fund). This fund promotes strategic research, in particular collaborative projects that span different research fields or are carried out by two or more of the centers and institutes within RIKEN. Applications are accepted twice a year, and the committee makes its selections through strict academic evaluation. Projects then receive funding for two years.



### 1 Visibility of RIKEN

- Improve and strengthen RIKEN's public image
- RIKEN staff should be committed to informing the public of the importance of science

### 2 Maintaining RIKEN's outstanding history of achievement in science and technology

- Sustain and deepen RIKEN's research spirit
- Emphasize RIKEN's consistently high level of research output
- Increase intellectual property activities, and provide scientific knowledge and achievements to industry and society

### 3 RIKEN that motivates researchers

- Promote research driven by curiosity
- Seek unique, risky projects
- Develop talent

### 4 RIKEN that is useful to the world

- Find and foster ties with industry and society
- Produce science and technology that will support science in a more fundamental way than simply working with industry

### 5 RIKEN that contributes to culture

- Increase RIKEN's cultural level
- Provide information to the humanities and social sciences

## RIKEN Science Council

The RIKEN Science Council is concerned with the broad and long-term issues of what fields RIKEN should research, and with formulating a vision for researchers at RIKEN. It responds to inquiries from the President, and reports its findings to the President. The council has approximately thirty members, including Directors, Chief Scientists, and Group Directors, and always has lively debates. In 2005 it produced a report called, "The need for a petaflops computer (the so-called post-Earth Simulator) and measures for its research and development."



# Strengthening scientific governance

## Recommendations from the RIKEN Advisory Council and RIKEN's responses

The RIKEN Advisory Council (RAC) serves as an external advisor and evaluates the scientific and administrative activities for the RIKEN President. RAC is made up of highly influential and successful people from outside RIKEN.

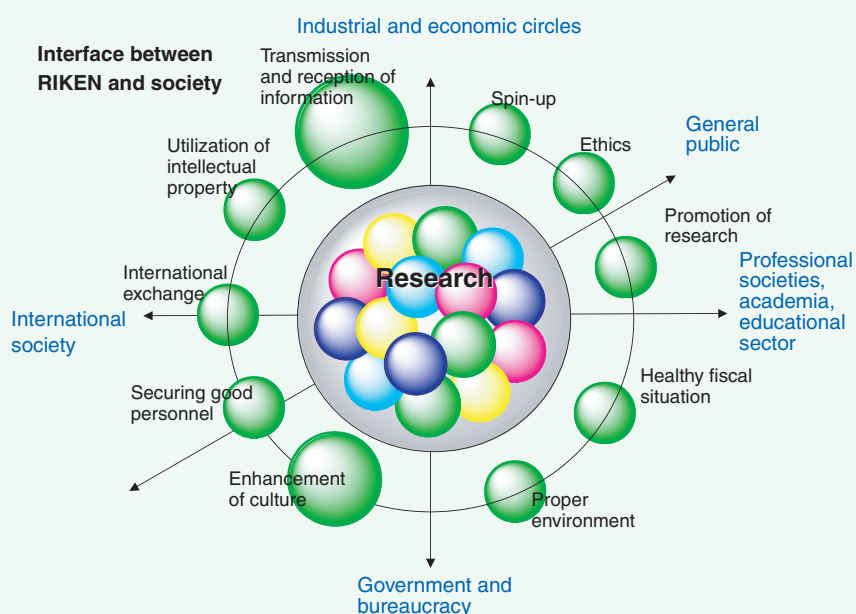
The first RAC following RIKEN's transition

to an Independent Administrative Institution was in June 2004. The report of that session is available on the RIKEN website at <http://www.riken.jp/r-world/info/release/press/2004/040819/index.html>. RAC highly praised RIKEN's operational policies, research activities, and the Noyori Initiative.

It recommended unifying the organization according to the anticipated directions of science, to make it stronger, and its strengthening its scientific governance.

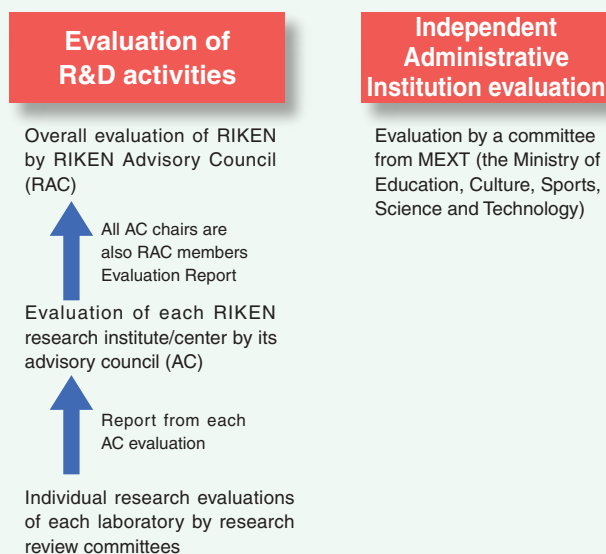
RIKEN quickly developed concrete measures that address those concerns. It outlined "Ten Important Managerial Items" and created study groups to investigate ways to tackle them as well as implement the Noyori Initiative and develop appropriate governance of scientific activities. These groups, staffed mainly by junior members of RIKEN, have affected the way resources are allocated and thereby strengthened RIKEN's role in generating science in line with its stated objectives.

Fig. 1 ● Ten Important Managerial Items



The Transmission and Reception of Information study group visiting a facility outside RIKEN

Fig. 2 ● Evaluation at RIKEN



### Overall evaluation of RIKEN

Established in 1993, the RIKEN Advisory Council (RAC) is an advisory body for the whole of RIKEN. The council is made up of distinguished members of national and international scientific and academic communities. RAC conducts thorough reviews of RIKEN's research and management activities, and provides advice to the RIKEN President.

### Evaluation of the research institutes and centers within RIKEN

Each institute and center within RIKEN has its own advisory council (AC) that observes and assesses its research activities. International experts in the relevant areas of research are invited to sit on these councils.

### Evaluation of research at laboratory level

Research groups and laboratories receive independent assessments by panels of external experts.

### Governmental evaluation

After the term of its mid-term plan, a MEXT committee will evaluate the extent to which RIKEN met its mid-term objectives.

## Compliance

### What is compliance?

Compliance refers to adherence to the laws, rules of ethics, and procedures that are at work within a society.

### Compliance at RIKEN

In the last few years, some RIKEN employees have not always observed established rules and standards. There have been incidences of harassment, false or inaccurate travel expense claims, and falsification of scientific data. RIKEN is Japan's biggest and most comprehensive research institute for natural sciences and receives large amounts of public funding. As such, in addition to producing top-quality scientific achievements, it must set a proper example by maintaining and improving its research promotion systems. Therefore, compliance is an extremely important management issue. In April 2005 RIKEN established an Auditing and Compliance Office to establish systems that avoid problems before they

happen and effectively handle problems as they arise.

### Objectives and policies

Compliance is not just an issue for researchers. It affects everyone who works at RIKEN, including the technicians and administrative staff who provide support for the scientific research. The Auditing and Compliance Office aims to change people's ways of thinking, raise awareness of compliance among all employees, and create an atmosphere that discourages inaccurate or illicit practices in research and official duties. RIKEN should be a place where people are motivated and proud to work, and that produces excellent achievements that are useful to society.

### Achievements in fiscal year 2005

- Established an internal Legal Advice Office, staffed by lawyers

- Drew up Basic Policies Regarding Research Misconduct
- Started compliance training for new employees
- Began training counselors for sexual harassment
- Investigated reports of sexual harassment, abuse of power, and research misconduct



Seminar on prevention of research misconduct

## Focus 1

### Legal advice

The Legal Advice Office provides everyone at RIKEN with free consultation. All employees can receive legal advice and guidance, from a lawyer, about matters relating to their work at

RIKEN including things that may be unfair.

Employees may also talk about problems or concerns related to their work with designated counselors. These people are selected from

male and female employees at all the RIKEN campuses and have received training.

## Focus 2

### Dealing with research misconduct

In December 2004, RIKEN admitted that three scientific papers published by its researchers had contained falsified data. To prevent future events like these, it is essential to instill high moral standards in our researchers. In cases where research misconduct is suspected, RIKEN

must act properly and impartially. If misconduct is confirmed, RIKEN must not conceal the incident. It must be made public and RIKEN must explain what has happened.

On December 22, 2005, RIKEN set out its Basic Policies Regarding Research Misconduct,

for dealing with research misconduct within the institute. Before this, the RIKEN Science Council, which consists of researchers at RIKEN, had already published a "Statement on Scientific Misconduct and its Prevention," on November 2, 2004.

# Endeavoring to diversify funding

## The government remains RIKEN's primary financial supporter

Like other Independent Administrative Institutions, RIKEN is responsible for determining how to distribute the funds it receives from the government. Yet, while the government does not impose

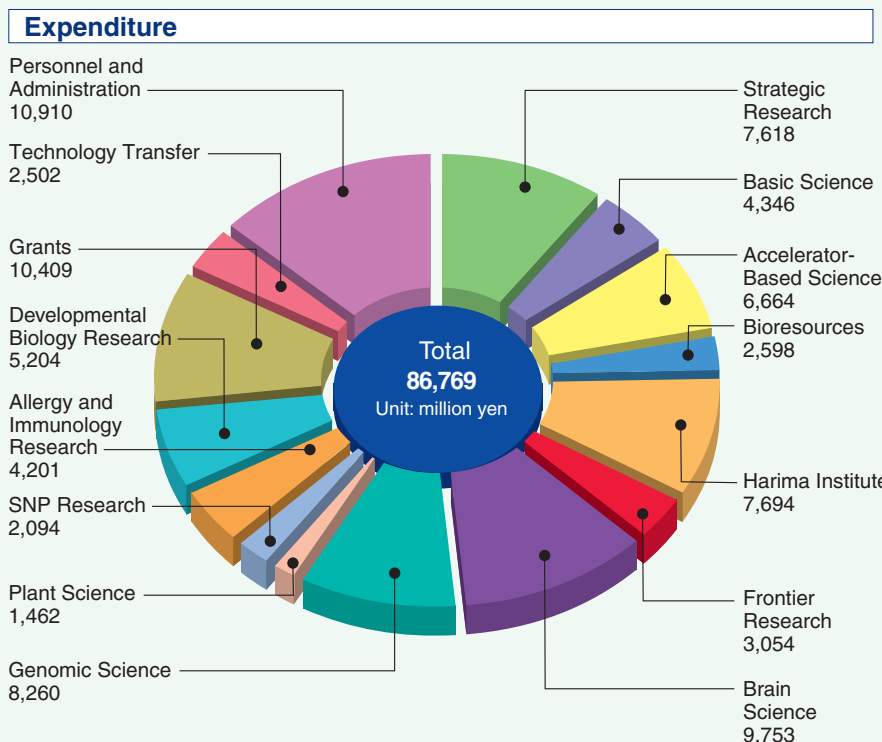
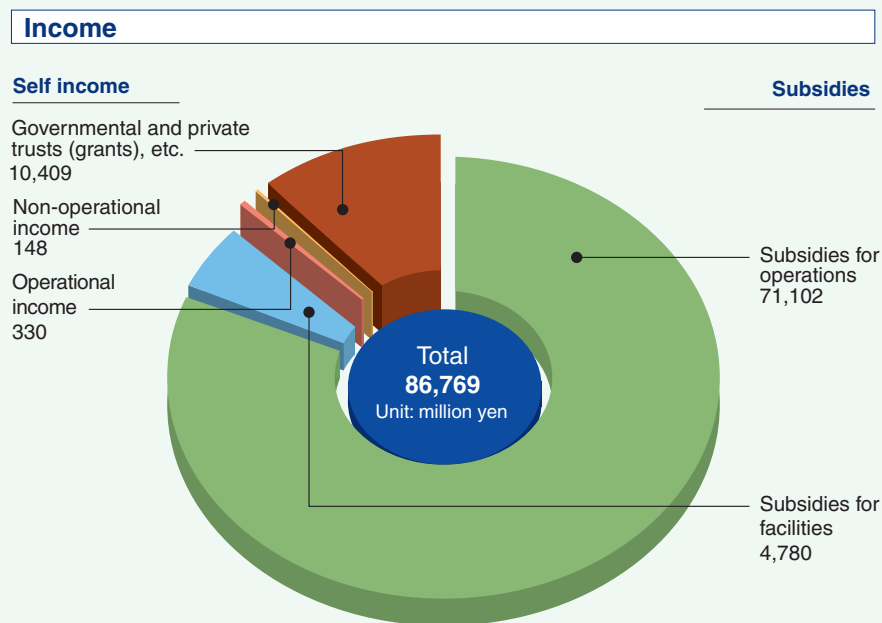
requirements on how its funds are used at RIKEN, it does monitor and evaluate management spending activities closely.

RIKEN also develops other sources of funding to reduce its dependency on

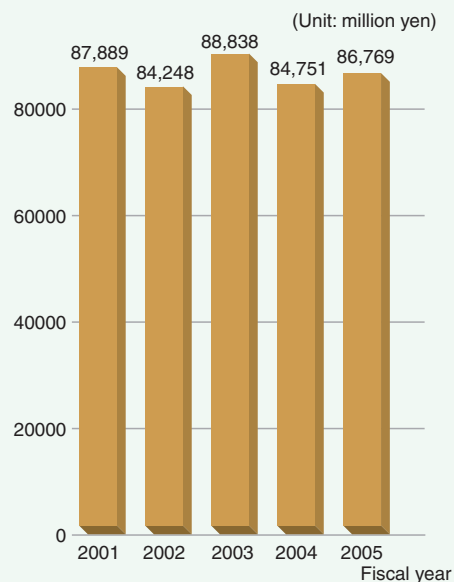
government subsidies. These include:

- ① Operational income earned through licensing, patent royalties, or through the distribution of research materials
- ② Non-operational income from real estate, rental income and earned interest
- ③ Governmental and private trusts (grants)

**Fig. 1** ● Projected 2005 Budget



**Fig. 2** ● Recent budgets



## External funds

RIKEN also acquired funds from various government bodies, including MEXT (the Ministry of Education, Culture, Sports, Science and Technology), as well as public and private organizations, in fiscal year 2005.

**Table 1 ● Acquisition of external funds**

Category	Description	FY2002		FY2003		FY2004		FY2005		
		thousand yen	cases	thousand yen	cases	thousand yen	cases	thousand yen	cases	
1. Competitive Funds	Grants-in-aid for Scientific Research	1,837,863	338	1,966,905	367	2,457,819	426	2,537,702	484	
	Grants-in-aid for Scientific Research (Ministry of Health, Labour and Welfare, and Ministry of Environment)	122,250	4	113,180	4	60,828	2	132,770	4	
	Special Coordination Funds for the promoting of Science and Technology	1,038,847	27	712,442	16	534,383	10	417,196	8	
	Projects Sponsored by Organs Promoting Science and Technology	1,150,782	56	1,212,054	63	1,457,174	70	1,318,038	64	
	Basic Research Programs (Japan Science and Technology Agency)	0	0	0	0	0	0	555,857	2	
	Other Publicly Supported Projects	188,408	9	196,874	12	208,099	8	277,428	14	
<b>Sub-total</b>		<b>4,338,150</b>	<b>434</b>	<b>4,201,455</b>	<b>462</b>	<b>4,718,303</b>	<b>516</b>	<b>5,238,991</b>	<b>576</b>	
2. Uncompetitive Funds	Commission	Government commissioned research	12,005,981	16	26,282,726	35	8,278,807	25	9,488,341	27
		Government-related commissioned research	1,010,093	15	1,040,228	25	148,179	25	263,316	28
	Subsidy	Government subsidy	102,320	39	127,533	33	97,880	31	75,584	13
		Private grant	61,321	29	66,696	33	60,750	46	51,343	36
	Collaborative Research	Defrayment	23,450	3	78,743	10	114,366	14	127,033	20
<b>Sub-total</b>		<b>13,203,165</b>	<b>102</b>	<b>27,595,926</b>	<b>136</b>	<b>8,699,982</b>	<b>141</b>	<b>10,005,617</b>	<b>124</b>	
<b>Total</b>		<b>17,541,315</b>	<b>536</b>	<b>31,797,381</b>	<b>598</b>	<b>13,418,285</b>	<b>657</b>	<b>15,244,608</b>	<b>700</b>	

The above has been rearranged since the previous year in line with changes made in selection criteria that went into effect in 2006.

**Table 2 ● Acquisition of external funds, grouped by center**

Institute		FY2002		FY2003		FY2004		FY2005	
		cases	thousand yen	cases	thousand yen	cases	thousand yen	cases	thousand yen
Wako Institute	Discovery Research Institute	221	2,426,813	237	3,747,840	238	2,241,103	245	2,302,283
	Frontier Research System	34	208,400	44	435,395	52	198,067	48	703,247
	Brain Science Institute	116	701,134	108	736,577	108	816,774	122	578,572
	Center for Intellectual Property Strategies	0	0	0	0	0	0	7	25,364
	Others	11	37,171	18	351,394	13	187,834	23	242,539
	<b>Sub-total</b>		<b>382</b>	<b>3,373,518</b>	<b>407</b>	<b>5,271,206</b>	<b>411</b>	<b>3,443,778</b>	<b>445</b>
Tsukuba Institute	BioResource Center	18	1,514,407	18	1,570,676	26	126,100	28	131,450
Harima Institute	RIKEN SPring-8 Center	23	155,349	14	288,026	19	462,761	17	378,820
	Cooperation research using SPring-8	6	860,388	4	909,330	3	809,761	8	1,663,736
	<b>Sub-total</b>	<b>29</b>	<b>1,015,737</b>	<b>18</b>	<b>1,197,356</b>	<b>22</b>	<b>1,272,522</b>	<b>25</b>	<b>2,042,556</b>
Yokohama Institute	Genomic Sciences Center	28	9,442,410	37	12,711,837	36	5,626,659	35	5,791,594
	Plant Science Center	8	19,900	21	390,843	20	97,743	27	200,210
	SNP Research Center	4	1,424,265	7	6,732,818	8	1,239,500	12	1,730,406
	Research Center for Allergy and Immunology	11	158,711	23	187,817	68	496,433	65	487,897
	Center of Research Network for Infectious Diseases	0	0	0	0	0	0	1	169,546
	<b>Sub-total</b>	<b>51</b>	<b>11,045,286</b>	<b>88</b>	<b>20,023,315</b>	<b>132</b>	<b>7,460,335</b>	<b>140</b>	<b>8,379,653</b>
Kobe Institute	Center for Developmental Biology	56	592,367	67	3,734,828	66	1,115,550	62	838,944
<b>Total</b>		<b>536</b>	<b>17,541,315</b>	<b>598</b>	<b>31,797,381</b>	<b>657</b>	<b>13,418,285</b>	<b>700</b>	<b>15,244,608</b>

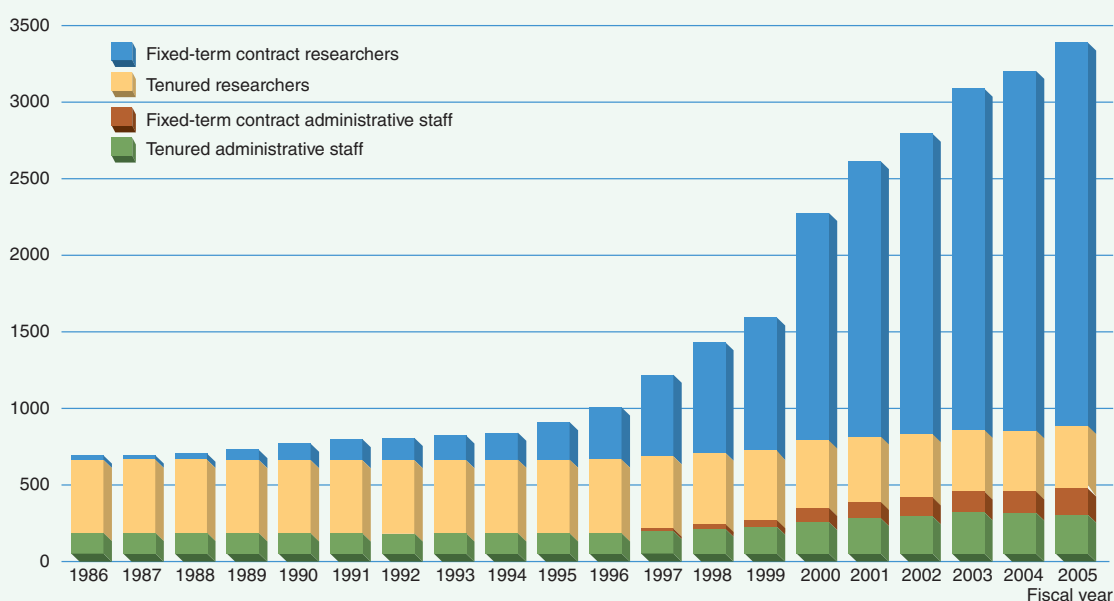
# Enabling the best people to achieve the best results

RIKEN uses a two-tiered employment system. One is a tenured system with a mandatory retirement age. The core scientists of the Institute Laboratories, which are headed by Chief Scientists, are tenured RIKEN employees. The other is a fixed-contract system with the option for annual

renewal. Scientists working exclusively on fixed-term projects are usually fixed-term contract employees. To promote mobility and to stimulate innovative research, an annual salary system was introduced in April 2005 for Chief Scientists. In this and other ways, RIKEN is working to forge employment

policies that will encourage scientists in their endeavors. In addition, RIKEN is making an active effort to increase its hire of foreign scientists with the goal of making RIKEN an international center of excellence.

**Fig. 1 ● RIKEN Personnel**



## Tenured employees

Tenured employees are primarily located in Institute Laboratories and administrative divisions.

**Table 1 ● Tenured employees**

Category	Fiscal year					
	2000	2001	2002	2003	2004	2005
Research	441	430	426	413	413	413
Administrative	204	225	237	272	272	271
<b>Total</b>	<b>645</b>	<b>655</b>	<b>663</b>	<b>685</b>	<b>685</b>	<b>684</b>

## Fixed-term Contract Employees

Employment of fixed-term contract scientists began with the establishment of the Frontier Research System in 1986. There are now fixed-term employees in all of RIKEN's centers and institutes.

**Table 2 ● Fixed-term contract employees**

Category	Fiscal year					
	2000	2001	2002	2003	2004	2005
Frontier Research System	140	145	191	137	156	126
Brain Science Institute	426	459	499	527	532	532
BioResource Center	—	17	17	17	17	17
Genomic Sciences Center	250	335	276	214	226	261
Plant Science Center	64	97	100	100	100	98
SNP Research Center	50	74	81	81	81	81
Research Center for Allergy and Immunology	—	105	153	153	153	170
Center for Developmental Biology	203	243	243	243	243	248
Center for Intellectual Property Strategies	—	—	—	—	—	36
Other	—	—	16	24	49	57



## New salary system

RIKEN believes that in order to foster the high level of scientific inquiry and methodology that is essential for Japanese science and technology to advance, an appropriate degree of mobility is necessary so that scientists can acquire experience at a wide range of facilities. RIKEN also believes that appropriate remuneration for outstanding achievements is one way to motivate and encourage young people to aspire to careers in the sciences.

With these objectives in mind, a new annual salary system, with a retirement package designed to encourage mobility and incentive bonuses to be awarded for outstanding achievements, was introduced in fiscal 2005 for Chief Scientists.

It is hoped that as this system is more widely applied within RIKEN and at other organizations, it will stimulate greater mobility among Japanese scientists, making them more internationally competitive and raising the standard of science and technology in Japan.

## Fostering the development of young researchers

### Special Postdoctoral Researcher Program

RIKEN's program for Special Postdoctoral Researchers was instituted in fiscal 1989 to provide young and creative scientists the opportunity to be involved in autonomous and independent research. Candidates must be under the age of 35 and must have a doctorate degree in the natural sciences or equivalent research capability, and must independently and responsibly pursue a research topic of their own choosing at RIKEN. The Special Postdoctoral Researcher contract is for one year, renewable upon evaluation each year, up to a maximum of three years.

In fiscal 2005, RIKEN accepted a total of 206 Special Postdoctoral Researchers.

### Junior Research Associate Program

The JRA program employs young doctoral candidates to work at RIKEN laboratories as part-time staff. The intent of the program

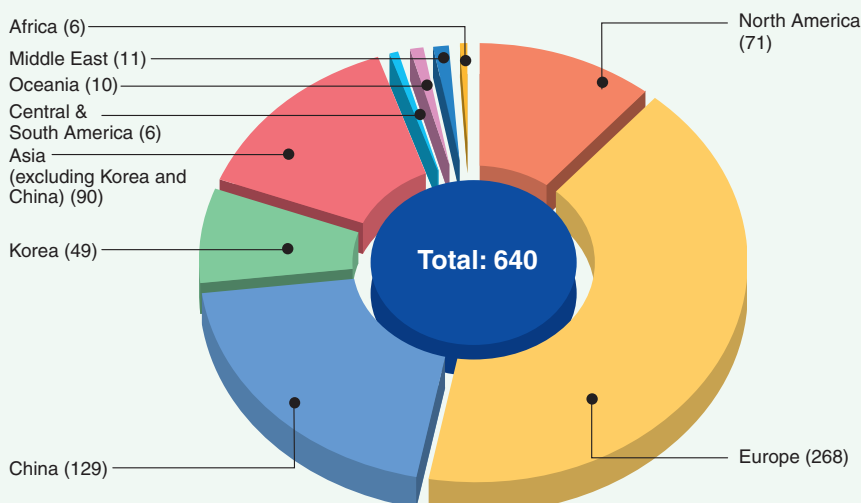
is to foster the development of the next generation of researchers. The Junior Research Associate contract is for one year, renewable upon evaluation each year, up to a maximum of three years, and the JRA is expected to complete his or doctoral degree within this time.

In fiscal 2005, RIKEN accepted a total of 142 Junior Research Associates.

## International Diversity

Acknowledging the value of international cooperation, RIKEN recruits researchers from around the world. Various services are provided to help these researchers and their families adjust to life and work in Japan. There are publications such as a booklet called *Life in RIKEN* and *ICO News*, a newsletter, and ICO Room, where staff are ready and waiting to assist with a wide range of everyday needs. In addition, the RIKEN centers and institutes each have their own Help Desks and international public relations offices to further support the foreign researcher.

**Fig. 2** ● Countries of origin of foreign researchers at RIKEN in FY 2005



**Fig. 3** ● Foreign researchers by center/institute

Discovery Research Institute	180
Frontier Research System	75
Brain Science Institute	193
BioResource Center	10
SPring-8 Center	26
Genomic Sciences Center	57
Plant Science Center	6
SNP Research Center	6
Research Center for Allergy and Immunology	16
Center for Developmental Biology	42
Center for Intellectual Property Strategies	9
Center for Advanced Technology Development	3
Units and Initiative Research Units	10
Administration	7

## Communicating with the scientific community and the general public

The publication of papers and oral presentations are important ways of conveying RIKEN's activities to the international scientific community. For particularly noteworthy achievements, RIKEN will hold press conferences to get the news to as wide an audience as possible. RIKEN Symposiums provide a forum for research activities that are of special interest in academic and industrial circles, and give RIKEN scientists the opportunity to discuss

their work with as many people as possible. The Research Ethics Committee meets with well-informed members of the community to solicit opinions and exchange ideas on the advancement of science in general. RIKEN also opens up its campuses to the general public on the RIKEN Open Day, and hosts a variety of scientific lectures and other activities to encourage greater understanding of its science and technology.



RIKEN Gallery, Wako

**Table 1 ● Published original papers**

		Fiscal year			
		2002	2003	2004	2005
Discovery Research Institute	European languages	636	697	639	647
	Japanese	22	40	41	27
Frontier Research System	European languages	200	202	279	244
	Japanese	57	65	80	62
Brain Science Institute	European languages	266	253	334	290
	Japanese	20	20	24	30
BioResource Center	European languages	32	36	87	72
	Japanese	3	1	4	4
Harima Institute (SPRING-8 Center)	European languages	166	122	191	224
	Japanese	7	0	3	9
Genomic Sciences Center	European languages	105	135	102	63
	Japanese	9	3	2	2
Plant Science Center	European languages	61	43	63	56
	Japanese	0	0	1	2
SNP Research Center	European languages	33	5	40	32
	Japanese	4	0	1	1
Research Center for Allergy and Immunology	European languages	58	67	94	102
	Japanese	2	1	4	4
Center for Developmental Biology	European languages	48	76	85	89
	Japanese	0	0	4	4
Center for Intellectual Property Strategies	European languages	0	0	0	25
	Japanese	0	0	0	10
Others	European languages	59	66	32	44
	Japanese	12	18	13	19
Total	European languages	1,664	1,702	1,946	1,888
	Japanese	136	148	177	174

The above figures are based on primary author submissions for each center and institute. The figures for the Discovery Research Institute include submissions from the Advanced Development and Supporting Center, research units, and the RIKEN BNL Research Center. "Others" includes Initiative Research Unites and special laboratories.

**Table 3 ● Comparison of total number of citations, number of citations per paper, and number of citations per paper within Japan of published RIKEN papers**

	Total number of citations	Number of citations per paper	Number of citations per paper within Japan
Biology and biochemistry	37,091	17.54	12.73
Physics	33,828	8.23	7.12
Molecular biology and genetics	30,911	24.81	19.96
Chemistry	19,384	9.52	8.33
Neuroscience and behavior	17,951	21.86	12.24
Plant and animal science	13,904	18.92	5.71
Clinical medicine	7,446	13.23	8.76
Immunology	5,026	31.81	18.30
Microbiology	4,842	10.83	10.35
Engineering	4,489	4.20	2.94
Materials science	1,777	4.99	4.67

(Source: Thomson ISI Essential Science Indicators™)

**Table 2 ● Oral presentations**

		Fiscal year			
		2002	2003	2004	2005
Discovery Research Institute	Overseas	532	767	797	681
	Domestic	1,068	1,429	1,489	1,446
Frontier Research System	Overseas	232	290	346	267
	Domestic	268	302	417	338
Brain Science Institute	Overseas	288	268	394	328
	Domestic	445	360	473	512
BioResource Center	Overseas	26	19	42	56
	Domestic	100	95	117	168
Harima Institute (SPRING-8 Center)	Overseas	159	130	214	192
	Domestic	293	308	330	364
Genomic Sciences Center	Overseas	197	156	167	109
	Domestic	365	276	239	251
Plant Science Center	Overseas	66	88	87	79
	Domestic	150	101	140	170
SNP Research Center	Overseas	6	6	28	13
	Domestic	11	21	48	45
Research Center for Allergy and Immunology	Overseas	56	40	92	74
	Domestic	124	121	209	201
Center for Developmental Biology	Overseas	51	52	50	102
	Domestic	100	75	47	115
Center for Intellectual Property Strategies	Overseas	0	0	0	26
	Domestic	0	0	0	130
Others	Overseas	62	60	50	54
	Domestic	166	117	117	75
Total	Overseas	1,675	1,876	2,267	1,981
	Domestic	3,090	3,205	3,586	3,815

**Table 4 ● RIKEN seminars and symposiums**

	Fiscal year			
	2002	2003	2004	2005
RIKEN Seminars	142	179	205	205
RIKEN Symposiums	37	39	40	40

## Press releases

In fiscal 2005, there were 55 research-related press releases (including ones for RIKEN-initiated joint research with other organizations) and nine press releases regarding other matters. Additionally, there were nine press releases related to joint research initiated by other organizations, and 18 distributed reference materials.



## Enhancing RIKEN's public image

### RIKEN Open Day visitors

		Fiscal year		
		2005	2004	
Wako Institute		April 23	7,103	5,843
Tsukuba Institute	General Open Day	April 20	551	655
	Special Open Day	April 23	381	395
	Total		932	1,050
Harima Institute		April 23	2,506	3,391
Yokohama Institute		June 25	1,663	1,589
Kobe Institute		May 21	1,401	1,626
Photodynamics Research Center		Not held this year		90
Bio-Mimetic Control Research Center		September 23	645	255



## RIKEN Science Lecture 2005

### The October 11, 2005, RIKEN Science Lecture was held in Kobe and titled "Present, Past and Future Linked by Light"

Participants: 216

Lectures: "The Dream Light: The X-ray Free Electron Laser (XFEL)"

Hideo Kitamura, Chief Scientist, Coherent Synchrotron Light Source Physics Laboratory, RIKEN Harima Institute

"Using SPring-8 for archeological research: Ancient mirrors"

Takayasu Higuchi, Professor Emeritus, Kyoto University  
Director, Sen-Oku Hakukokan, Sumitomo Collection

"Generative cells: The mechanisms for regenerating and passing on the genetic code"

Mitunori Saitou, Team Leader, Mammalian Germ Cell Biology, Center for Developmental Biology, RIKEN Kobe Institute

"Advances in positron medicine and molecular imaging"

Yasuyoshi Watanabe, Molecular Imaging Research Program, Frontier Research System, RIKEN Wako Institute



## Research Ethics Committee Hearings

Advances in the life sciences have brought science and society closer together than ever before. Research activity involving human subjects requires the understanding and full cooperation of the people who provide samples and undergo tests. RIKEN has six research ethics committees on its four campuses. These committees include outside authorities and are charged with overseeing all human-related research at RIKEN. The research ethics committees review the scientific and ethical aspects of all human-related research that is undertaken at RIKEN at the start of every project and whenever a project is changed.

### Wako Institute

First Research Ethics Committee:

Research on the human genome and gene analysis

■ Convened: 5 times in fiscal 2005

■ Reviewed: 9 research plans

■ Results: Approved 7; conditional approval for 1; and 1 pending

Second Research Ethics Committee:

Research on human subjects using fMRI (Functional Magnetic Resource Imaging)

■ Convened: 0 times in fiscal 2005

■ Reviewed: 0 research plans

Third Research Ethics Committee:

Research on human subjects and research using samples of human origin (other than areas covered by first two committees)

■ Convened: 13 times in fiscal 2005

■ Reviewed: 72 research plans

■ Results: Approved 66; conditional approval for 6

### Tsukuba Institute

Research Ethics Committee

■ Convened: 3 times in fiscal 2005

■ Reviewed: 16 research plans

■ Results: Approved 13; conditional approval for 3

### Yokohama Institute

Research Ethics Committee

■ Convened: 14 times in fiscal 2005

■ Reviewed: 60 research plans

■ Results: Approved 48; conditional approval for 11; and 1 pending

### Kobe Institute

Research Ethics Committee

■ Convened: 3 times in fiscal 2005

■ Reviewed: 4 research plans

■ Results: Approved 2 cases; conditional approval for 2

# The Center for Intellectual Property Strategies: bridging the gap between the laboratory and industry

On April 1, 2005, the Center for Intellectual Property Strategies (CIPS) was established for the purpose of making RIKEN's research results, its intellectual property, more readily available to industry and society as a whole, in line with RIKEN President Noyori's call to make this institute more useful in the

world in which we live. The Center not only provides administrative support to efforts encouraging the licensing of intellectual property produced through research activities and the acquisition of external and competitive funding, but serves as an umbrella for special research programs such

as the VCAD System Research Program and the Integrated Collaborative Research Program with Industry, with the aim of strategically promoting the availability and actual utilization of their research results.

## 1 Acquiring patents

RIKEN works with its researchers to identify patentable intellectual property and provides consultation toward the patenting of inventions. It also holds patent seminars and provides instruction on inventions and intellectual property tailored to specific fields of science and technology and projects being conducted at RIKEN. These efforts have been rewarded by an increased awareness

of both intellectual property issues and the patent application process, and the number of patent applications being made from all RIKEN campuses has risen. The possibilities of applying in other nations for inventions for which domestic application has already been completed are also thoroughly investigated.

The licensability of patent rights possessed by RIKEN or its scientists or collaborators

are also regularly checked and verified to efficiently maintain them as necessary.

● In 2005:  
583 patent applications were filed, one application was made for utility model registration, and two trademark applications filed (in 2004, 570 patent applications and one trademark application were filed).

Table/Fig. 1 ● Patent Applications and Registrations

	Fiscal year							
	1998	1999	2000	2001	2002	2003	2004	2005
Domestic applications	123	141	171	222	264	259	289	316
Overseas applications	135	111	203	208	229	190	281	267
Domestic registrations	635	651	505	460	440	444	479	503
Overseas registrations	337	345	369	352	434	467	574	591
New domestic patents						80	102	75
New overseas patents						108	140	88

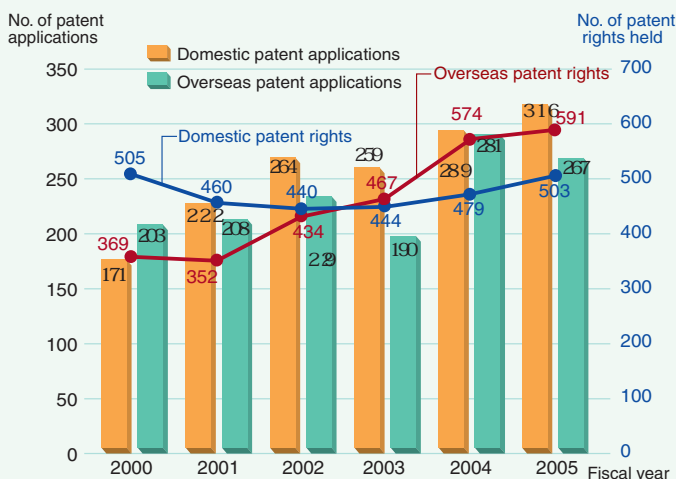
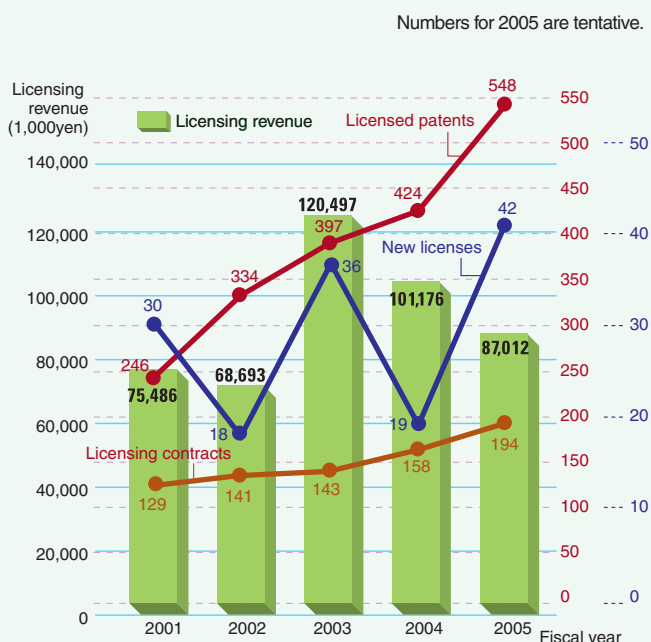


Fig. 2 ● Patent Income, Licenses and License Contracts



## 2 Transferring technology for practical application

Last fiscal year CIPS continued the Industrial Collaboration Program, the Integrated Collaborative Research with Industry, the use of coordinators, support

for RIKEN Ventures, and dissemination of research results through participation in scientific exhibitions and conferences and publicizing the effort over the internet. Some

of CIPS's other activities are as follows:  
1) Beginning in June 2005, RIKEN began to publish information about the patent rights it holds on the Internet in an open,

searchable database called R-BIGIN, or RIKEN Business Information for the Global IP Network (<http://r-bigin.riken.jp/>), allowing prospective corporate partners to access the data from outside RIKEN.

- 2) In November 2005, a Techno Conference was held to encourage technology transfer, to which a large number of prospective corporate partners were invited. This meeting was unusual in that, unlike the usual lecture meeting or exhibition, RIKEN researchers gave personal presentations of information often including previously undisclosed patents and their most recent, often unpublished research findings to corporate engineers and technicians charged with seeking out and incorporating new technologies in their operations.
- 3) CIPS, since its inception, has tied up with

trading companies in an effort to identify licensees of RIKEN-owned patents and to seek joint research partners.

These technology transfer efforts have brought about a 15.13% increase in patent licensing, greatly surpassing its target of 10% for the fiscal year. In addition, in an effort to draw itself even closer to industry, CIPS will begin, during FY 2006, publishing a newsletter regarding RIKEN's collaborative and technology transfer efforts with industry, supplying it by e-mail to corporate engineers and technicians charged with seeking out new technologies. (For more information about the newsletter, please contact the RIKEN Center for Intellectual Property Strategies at [r-bigin@riken.jp](mailto:r-bigin@riken.jp).)

### 3 Supplying bioresources

Bioresources are collected and maintained at the RIKEN BioResource Center (BRC) in

Tsukuba, and compiled into a database to actively promote supply to outside users.

Table2 ● Bioresources at BRC

	As of March 31, 2006
Laboratory animals (mice)	1,850 strains
Laboratory plants (seeds, DNA, cultured cells)	366,153 strains
Cell bank	4,857 cell lines
DNA samples	917,578 clones
Microorganisms	12,571 strains

### 4 Research collaboration

In 2005, a letter of intent was signed between RIKEN and Singapore's A\*STAR, the Agency for Science, Technology and Research, to pursue research collaboration in the life sciences and engineering fields, and a basic agreement concluded with Keio University

to engage in metabolic research. These are good examples of how RIKEN continues to promote collaborative relationships between governmental, private and academic interests to further the goals of science and technology.



A\*STAR



Keio University

### Joint Graduate School Programs

It has always been a RIKEN policy to promote collaborative relationships with universities by accepting university students into its laboratories as trainees. This policy culminated in 1989 with the creation of a first in Japan—the establishment of a joint graduate school program with Saitama University. As of FY2005, a total of 23 such programs have been established.

Joint Graduate School Programs Established with RIKEN (year of establishment)

- Saitama University (1989)
- University of Tsukuba (1992)
- Tokyo University of Science (1995)
- Toyo University (1997)
- Tokyo Institute of Technology (1997)
- Tohoku University (1997)
- Rikkyo University (1998)
- Chiba University (1998)
- University of Hyogo (1999)
- Tokyo Denki University (2000)
- University of Tokyo (2000)
- Yokohama City University (2001)
- Kyushu Institute of Technology (2001)
- Kobe University (2002)
- Kyoto University (2002)
- Nara Institute of Science and Technology (2003)
- Toho University (2003)
- Kwansai Gakuin University (2004)
- Niigata University (2004)
- Tokyo Medical and Dental University (2004)
- Nagaoka University of Technology (2004)
- Osaka University (2005)
- Hokkaido University (2005)

### Asian Joint Graduate School Program

In order to encourage the promotion of science in the wider Asian region, a network was established in 2001 among a number of Asian universities to promote the educational opportunities of doctoral students throughout Asia. The network consists of cooperative relationships established between RIKEN and the National Chiao Tung University (Taiwan), Hanoi University of Science (Vietnam), Pusan National University (S. Korea), Beijing University (China), University Sains Malaysia (Malaysia) and Kasetsart University (Thailand).

## Other activities in FY 2005

### RIKEN Honorary Fellow

The RIKEN Honorary Fellow is a new position for world famous scholars with distinguished careers and ideas from not only scientific research but also other fields. The RIKEN Honorary Fellow is invited to engage in positive interaction with RIKEN personnel through lectures and discussions, to broaden the horizons of RIKEN researchers,

and to enhance their awareness of their involvement in society and the international community. A ceremony to commemorate the first RIKEN Honorary Fellow was held on November 16, 2005, with the title being given to Leo Esaki, who received the Nobel Prize in Physics in 1973.

### RIKEN Culture Day

RIKEN Culture Day is held in the early spring when the cherry blossoms are in full bloom at RIKEN's campuses. The day is meant to remind RIKEN's scientists that they need to nurture their logical and emotional sensibilities as well as their scientific knowledge. On the first RIKEN Culture Day, Reiji Hiramatsu, one of Japan's foremost Japanese-style painters, was invited to present a special lecture on April 7, 2005.

The second RIKEN Culture Day was commemorated with a special lecture by Kunio Yonenaga, President of the Japan Shogi Association and holder of the permanent shogi title Eisei Kisei, on March 31, 2006.



### Awards

Many RIKEN researchers received awards and prizes in FY2005. Most notable was the Order of Cultural Merit conferred upon Koji Kaya, director of the RIKEN Discovery Research Institute, for his contributions to the development of a new field in nano-material science.

In addition to Dr. Kaya, 118 RIKEN researchers received awards acknowledging their contributions to science in FY2005.



### Visitors

RIKEN welcomed many visitors from Japan and around the world in FY2005.

We were especially honored by the visits of Peter Gruss, President, Max Planck Society(MPG), Germany; Tuula Haatainen, Finnish Minister of Education and Science; Susan. Hockfield, MIT President; and

Christian Brechet, Director General, French National Institutes of Health (INSERM).

Nariaki Nakayama and Kenji Kosaka, Japan's Ministers of Education, Culture, Sports, Science and Technology, and Iwao Matsuda, Minister of State for Science and Technology Policy also visited RIKEN in FY2005.





Board members as of April 1, 2006 (from left to right)  
 Takeo KATOU (Auditor), Toichi SAKATA (Executive Director), Kenji OKUMA (Executive Director), Ryoji NOYORI (President),  
 Yoshiharu DOI (Executive Director), Kenji TAKEDA (Executive Director), Shin OHKOUCHI (Executive Director),  
 Takanobu HASHIMOTO (Auditor)

Headquarters and Wako Institute  
 Discovery Research Institute  
 Frontier Research System  
 Brain Science Institute  
 Nishina Center for Accelerator-Based Science  
 2-1 Hirosawa, Wako, Saitama 351-0198  
 Phone +81-48-462-1111  
 Fax +81-48-462-1554

Tsukuba Institute  
 BioResource Center  
 3-1-1 Koyadai, Tsukuba, Ibaraki 305-0074  
 Phone +81-29-836-9111  
 Fax +81-29-836-9109

Harima Institute  
 RIKEN SPring-8 Center  
 1-1-1 Koto, Sayo-cho, Sayo-gun, Hyogo 679-5148  
 Phone +81-791-58-0808  
 Fax +81-791-58-0800

Yokohama Institute  
 Genomic Sciences Center  
 Plant Science Center  
 SNP Research Center  
 Research Center for Allergy and Immunology  
 1-7-22 Suehiro-cho, Tsurumi-ku, Yokohama,  
 Kanagawa 230-0045  
 Phone +81-45-503-9111  
 Fax +81-45-503-9113

Kobe Institute  
 Center for Developmental Biology  
 2-2-3 Minatojima-minamimachi, Chuo-ku, Kobe,  
 Hyogo 650-0047  
 Phone +81-78-306-0111  
 Fax +81-78-306-0101

Terahertz-Wave Research Program  
 519-1399 Aoba, Aramaki, Aoba-ku, Sendai,  
 Miyagi 980-0845  
 Phone +81-22-228-2111  
 Fax +81-22-228-2122

Bio-Mimetic Control Research Center  
 Nagoya Science Park Research and  
 Development Center  
 2271-130, Anagahora, Shimoshidami,  
 Moriyama-ku Nagoya, Aichi 463-0003  
 Phone +81-52-736-5850  
 Fax +81-52-736-5854

Komagome Branch  
 2-28-8 Honkomagome, Bunkyo-ku, Tokyo  
 113-0021  
 Phone +81-3-5395-2800  
 Fax +81-3-3947-1752

Itabashi Branch  
 1-7-13 Kaga, Itabashi-ku, Tokyo 173-0003  
 Phone +81-3-3963-1611  
 Fax +81-3-3579-5940

Tokyo Liaison Office  
 7th fl. (Zone 739-740), Shin-Tokyo Bldg.,  
 3-3-1 Marunouchi, Chiyoda-ku, Tokyo 100-0005  
 Phone +81-3-3211-1121  
 Fax +81-3-3211-1120

Center of Research Network for Infectious  
 Diseases  
 North 7th fl., Yurakucho-Denki Bldg.,  
 1-7-1 Yurakucho, Chiyoda-ku, Tokyo 100-0006  
 Phone +81-3-5223-8731  
 Fax +81-3-5223-6060

Next-Generation Supercomputer R&D Center  
 6th fl., Meiji Seimei Kan  
 2-1-1 Marunouchi, Chiyoda-ku, Tokyo 100-0005  
 Phone +81-48-467-9265  
 Fax +81-3-3216-1883

RIKEN Facility Office at RAL  
 UG17, R3, Rutherford Appleton Laboratory,  
 Chilton, Didcot, Oxfordshire, OX11 0QX, U.K.  
 Phone +44-1235-44-6802  
 Fax +44-1235-44-6881

RIKEN BNL Research Center  
 Building 510A, Brookhaven National  
 Laboratory  
 Upton, NY 11973 U.S.A.  
 Phone +1-631-344-8095  
 Fax +1-631-344-8260

RIKEN-MIT Neuroscience Research Center  
 The Picower Institute for Learning and Memory,  
 Massachusetts Institute of Technology  
 77 Massachusetts Avenue, Building 46,  
 Room 1303  
 Cambridge, MA 02139, U.S.A.  
 Phone +1-617-324-0305  
 Fax +1-617-324-0976/+1-617-452-2588

RIKEN Singapore Representative Office  
 11 Biopolis Way, #07-01/02 Helios, Singapore  
 138667  
 Phone +65-6478-9940  
 Fax +65-6478-9943

**RIKEN Public Relations Office**

2-1 Hirosawa, Wako, Saitama 351-0198, Japan

Tel. +81-48-467-4098 Fax +81-48-462-4715

<http://www.riken.jp/>

[koho@riken.jp](mailto:koho@riken.jp)