RIKEN 2006–07 ANNUAL REPORT

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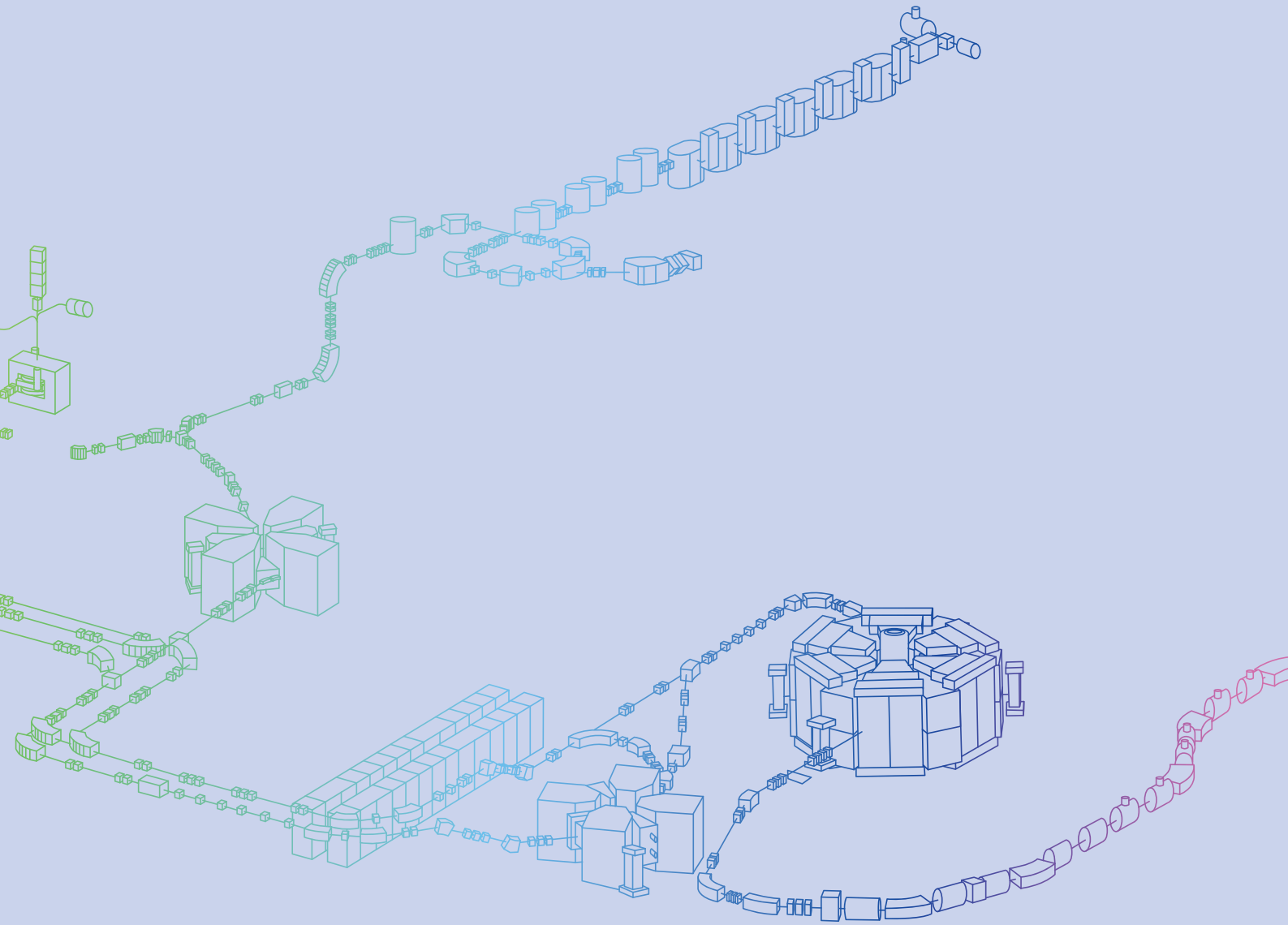


RIKEN

Towards a sustainable human society

Many things can be discovered from basic research in the natural sciences.

"The universe came into existence 13.7 billion years ago in the big bang,
and is still expanding. We only know of 4% of matter.
The rest is unknown dark matter and dark energy."

"The solar system came into existence 4.6 billion years ago,
and the earth rotates and orbits the sun. But even the land on the earth is not stationary;
it is continuously moving."

"Life on earth began 3.6 billion years ago.
All life evolved from the same origins. Early man emerged 1– 4 million years ago,
and Homo sapiens appeared 100,000 years ago in Africa.
Modern man has only existed for a tiny fraction of the history of the earth."

What is nature?

It is essential to understand ourselves and our environment objectively. This gives us a proper view of nature and our lives and teaches us humility. Mankind has put its knowledge of basic science to use in all sorts of ways to create a wide range of modern technology and build a comfortable society. We are only a tiny part of the history of the universe, the earth, and life. But through our remarkable creativity we have used science to pursue truth and build great civilizations.

On the other hand, mankind's excesses have led to serious environmental problems such as global warming and the depletion of natural resources. It is vital that we avoid passing this negative legacy on to future generations. The population of the world is now 6.5 billion, and we are faced with many serious problems, but I believe science and technology can play major roles in alleviating and solving these.

RIKEN's mission is firstly to make top-quality scientific achievements and then to return the benefits of its research to society in many different ways. But RIKEN is one of Japan's top research institutions, so this alone is not good enough. Another of our most crucial tasks is to convey the vital importance of natural science and scientific technology to ordinary people in Japan and around the world.

It is now only ten years until RIKEN's centenary. In this next decade I want RIKEN to increase and strengthen its activities. We are working to make RIKEN truly prominent, lead Japanese science to global pre-eminence, and respond to the wide-ranging demands of society.

I hope that this annual report will show you about our latest research achievements and that you will continue to give us your strong support in the future.

Ryoji Noyori (D. Eng.)
President
June 2007

Contents

Profile of RIKEN

With a 90-year history of cutting-edge research in the natural sciences, RIKEN is the only fully comprehensive research institute in Japan. RIKEN conducts basic and applied research covering a diverse range of fields including physics, chemistry, engineering, biology, and medical science. Not only does RIKEN participate in research collaborations with universities and corporations and undertake commissioned research projects, it also actively disseminates its scientific and technological findings and facilitates the transfer of technology to industry.

Mission

RIKEN's mission is to conduct research that extends the boundaries of science and technology. The aim is to produce internationally recognized results and maximize the social benefits of those results, making full use of RIKEN's unique research environment. This includes the pioneering of new research fields reflecting society's needs, and taking the initiative in undertaking research in particularly important areas.

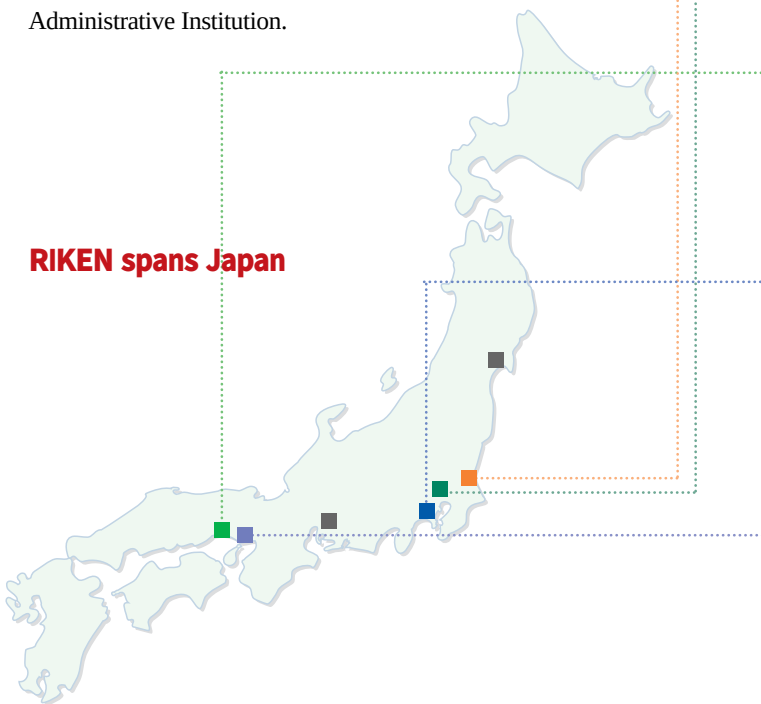
Expectations

RIKEN encourages active research by fostering a competitive environment and further developing its international character through the recruitment of researchers from around the globe. RIKEN is expected to maintain a process of constant self-improvement and to take the lead in renovating science and technology systems through collaboration with Japanese and foreign universities, research institutes, and corporations, as well as strengthening ties with local communities, taking active steps towards personnel mobility, actively recruiting young researchers, and introducing sophisticated systems of research evaluation.

History

RIKEN was established in 1917 as a private research foundation in Tokyo. After the Second World War, RIKEN was restructured as a private corporation named the Science Research Institute Ltd. (KAKEN), but in 1958 it became a semi-public corporation and was again called RIKEN. In 1967, RIKEN moved its main headquarters out of Tokyo to its current location in Wako, Saitama. With the continued expansion of RIKEN's research activities, the number of its research facilities is increasing and RIKEN now has research centers in the United Kingdom and the United States as well as throughout Japan. In October 2003, RIKEN underwent another administrative restructuring to become an Independent Administrative Institution.

RIKEN spans Japan



RIKEN's distinguished scientists

Hantaro Nagaoka
Physicist

Nagaoka proposed the Saturnian theory, postulating a planetary model of the atom as a nucleus with orbiting electrons. He was also the architect of Japan's platform for physical sciences and the director of the RIKEN foundation's Physics Division.

Kotaro Honda
Magnetic physicist

Honda pursued the study of metallurgy and magnetism, and raised the level of Japanese research in these fields to an international standard with the invention of KS steel, a type of magnetic resistant steel, and an enhanced NKS steel.

Umetaro Suzuki
Agricultural chemist

The founder of vitamin research in Japan, Suzuki successfully isolated vitamin B1 from rice bran, calling it oryzanin. Vitamin B1 proved effective in preventing and treating the vitamin deficiency disease beriberi, which flourished at the time. He was also instrumental in inventing and developing other products, including "RIKEN Vitamins," which financed much of the RIKEN foundation's activities.

Headquarters

- Research Priority Committee
- Policy Planning Division
- Public Relations Office
- General Affairs Division
- Personnel Division
- Finance Division
- Contract Management Division
- Facilities and Utilities Division
- Safety Division
- Auditing and Compliance Office
- Internal Communications and Systems Support Office
- Center for Intellectual Property Strategies
- Advanced Center for Computing and Communication
- Structural Genomics/Proteomics Initiative
- Next-Generation Supercomputer R&D Center
- SPring-8 Joint Project for XFEL

Wako Institute

- DRI/FRS Promotion Division
- Brain Science Promotion Division
- Research Program for Computational Science

- Discovery Research Institute
- Frontier Research System
- Brain Science Institute
- Nishina Center for Accelerator-Based Science

Tsukuba Institute

- Tsukuba Research Promotion Division
- Tsukuba Safety Center

- BioResource Center
- Research Collaborative Group

Harima Institute

- Harima Research Promotion Division
- Harima Safety Center

- RIKEN SPring-8 Center

Yokohama Institute

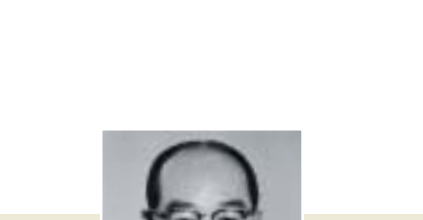
- Yokohama Research Promotion Division
- Yokohama Safety Center

- Genomic Sciences Center
- Plant Science Center
- SNP Research Center
- Research Center for Allergy and Immunology
- Center of Research Network for Infectious Diseases

Kobe Institute

- Kobe Research Promotion Division
- Kobe Safety Center

- Center for Developmental Biology



Terahertz-Wave Research Program (Sendai)
Bio-Mimetic Control Research Center (Nagoya)

Masatoshi Okochi
Scientist and executive

While promoting original, atypical basic research, Okochi sought ways to nurture emerging research achievements into full-fledged industries, founding the RIKEN Industrial Group (RIKEN Konzern) in the process. He is credited with creating RIKEN's unique environment as a "scientist's paradise" 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 kind of physics, and his laboratory in RIKEN inspired many scientists with its emphasis on researcher interaction and collaboration. He was president of the Scientific Research Institute Ltd. (KAKEN) after the war.

Shin-ichiro Tomonaga
Theoretical physicist

Tomonaga's RIKEN career started when he joined Nishina's laboratory in 1932. He shared the Nobel Prize in Physics with Richard Feynman and Julian Schwinger in 1965 for his contribution to quantum electrodynamics theory.

Hideki Yukawa
Theoretical physicist

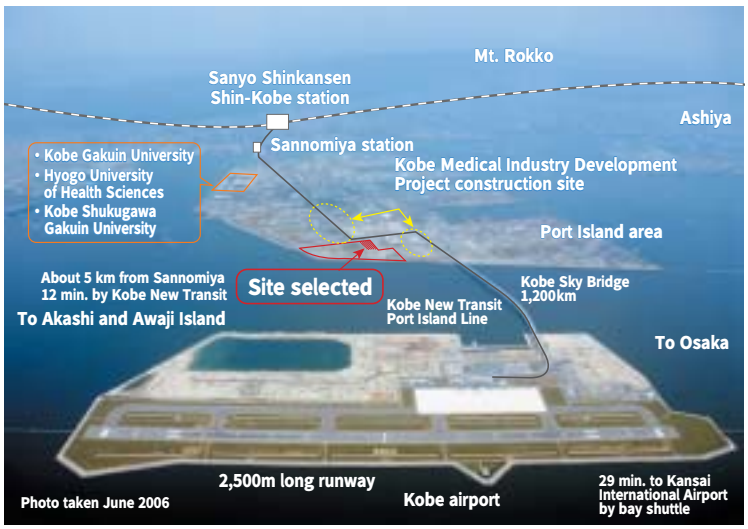
Another alumnus of Nishina's laboratory, Yukawa joined that laboratory in 1940 and later became a RIKEN Chief Scientist from 1961 to 1965, working on the properties of elementary particles. His prediction of meson particle existence earned him the Nobel Prize in 1949, making him the first Japanese national to be so decorated.

Events of 2006–2007

Kobe location selected for next-generation supercomputer

The next-generation supercomputer developed by RIKEN is expected to become the world's fastest supercomputer. It will be housed in a shared facility which will be maintained and operated by RIKEN in accordance with the law relating to the sharing of large-scale research facilities which came into effect in July 2006.

In order to select an appropriate location that could be used as a shared facility by researchers throughout Japan, and also as a base for R&D and human resource development, RIKEN organized a site-selection study group made up of external experts to ensure that the process was objective and rational. Based on this input, the decision was made in March 2007 to construct the facility on Kobe's Port Island at a site near the new airport.



The Emperor and Empress visit RIKEN's Wako Institute

On October 3, 2006, the Emperor and Empress paid a visit to the Wako Institute, where President Ryoji Noyori and DRI Director Koji Kaya presented an overview of research being conducted at the institute.

At the Nishina Center for Accelerator-Based Science, the newly discovered element 113 and breed-improvement techniques using heavy ions were explained. After viewing the world's largest superconducting ring cyclotron, the Emperor and Empress visited the Brain Science Institute to view the fMRI, which magnetically measures brain activity. They observed displays and heard explanations on research into Alzheimer's disease, structural analysis of the cerebral cortex, fluorescent proteins obtained from coral, and nerve cells that utilize proteins.

FRS Director Kohei Tamao receives the Japan Academy Prize

Kohei Tamao, Director of the Frontier Research System, was awarded the Japan Academy Prize in March 2007.

He was highly praised for his significant contribution in promoting industrial technologies as well as his academic studies on developing a number of useful chemical reactions and functional materials based on the concept of organic typical element compounds.

Awards and symposiums

RIKEN scientists received more than 100 awards and many symposiums were held in fiscal 2006.

Awards

Award		Recipient	Institute/Center	Position and lab or center
H. Kamerlingh Onnes Prize		Hidenori Takagi	DRI	Chief Scientist, Magnetic Materials Laboratory
Prizes for Science and Technology from MEXT (Research Category)		Katsumi Midorikawa	DRI	Chief Scientist, Laser Technology Laboratory
IEEE Fellow		Katsumi Midorikawa	DRI	Chief Scientist, Laser Technology Laboratory
20th IBM Japan Science Prize		Toshinori Suzuki	DRI	Chief Scientist, Chemical Dynamics Laboratory
JSPS (Japan Society for the Promotion of Science) Prize		Zhaomin Hou	DRI	Chief Scientist, Organometallic Chemistry Laboratory
4th RIKEN Frontier Research System Award	Grand Award	Yoshihiko Togawa	FRS	Quantum Phenomena Observation Technology Laboratory, Single Quantum Dynamics Research Group
	Promotion Award	Yu-xi Liu	FRS	Digital Materials Laboratory, Single Quantum Dynamics Research Group
	Promotion Award	Takashi Tsuboi	FRS	Fukuda Initiative Research Unit, Initiative Research Program
	Promotion Award	Seiichiro Ariyoshi	FRS	Terahertz Sensing and Imaging Laboratory, Terahertz-wave Research Program
	Technical Award	Asami Makino	FRS	Sphingolipid Functions Laboratory, Supra-Biomolecular System Research Group
Prizes for Science and Technology from MEXT (Research Category)		Takao K. Hensch	BSI	Group Director, Critical Period Mechanisms Research Group
Peter Gruber Neuroscience Prize		Masao Ito	BSI	Group Director, Advanced Technology Development
JSPS (Japan Society for the Promotion of Science) Prize		Atsushi Miyawaki	BSI	Team Leader, VCAD Applied FabricationTeam
6th JSDMT (Japanese Society of Die and Mould Technology) Best Presentation Award		Hitoshi Ohmori and four others	CIPS	Program Director, VCAD System Research Program
Doctor Honoris Causa University of Galati, Romania		Akitake Makinouchi	CIPS	Program Director, VCAD System Research Program
Gordon Bell Honorable Mention for Peak Performance		Makoto Taiji and nine others	GSC and others	Team Leader, High-Performance Molecular Simulation Team, Computational and Experimental Systems Biology Group
Prizes for Science and Technology from MEXT (Research Category)		Kazuo Shinozaki	PSC	Director, Plant Science Center
Honorary Foreign Member, Bulgarian Academy of Sciences		Yusuke Nakamura	SRC	Director, SNP Research Center
Medal with Purple Ribbon		Toshio Hirano	RCAI	Group Director, Laboratory for Cytokine Signaling
Japanese Society for Plant Cell and Molecular Biology, Thesis Award		Toshihiro Kobayashi	BRC	Research Scientist, Experimental Plant Division
Japanese Society for Plant Cell and Molecular Biology, Thesis Award		Masatomo Kobayashi	BRC	Head, Experimental Plant Division
Chairman's Award of the Saitama Prefecture High-pressure Gas Association		Gen Okada	BRC	Senior Research Scientist, Microbe Division, Department of Biological Systems
Hyogo Prefectural Science Award		Tetsuya Ishikawa	RSC	Director, RIKEN SPring-8 Center
13th SAS2006 Award for Outstanding Service (Sponsoring organization)		Tetsuro Fujisawa	RSC	Senior Research Scientist, Biometal Science Laboratory
Young Scientist Award, Biophysical Society of Japan		Ryo Kitahara	RSC	JSPS Young Scientist Research Fellow, RIKEN Visiting Researcher
Young Scientists' Prize from MEXT		Hiroki R. Ueda	CDB	Team Leader, Laboratory for Systems Biology

Symposiums

Event	Institute/Center	Dates
CDB Symposium 2006	CDB	2006/4/10–4/12
Third Symposium on Extreme Photonics	DRI	2006/4/13–4/14
Second Expert Meeting on Critical Issues on Next-Generation High-Intensity Fragment Separators	RNC	2006/5/10–5/13
Joint Retreat with DRI, BSI, CDB, and RCAI	DRI and others	2006/5/11–5/12
Frontier Research System Symposium 2006	FRS	2006/5/12
FIMRe (Federation of International Mouse Resources) Meeting	BRC	2006/5/22–5/23
BSI Tutorial Series	BSI	2006/6/26–2007/2/27 (once a week)
BSI Summer Program Internship Course	BSI	2006/6/28–8/28
The RCAI–JSI International Symposium on Immunology	RCAI	2006/6/16–6/18
BSI Summer Program Lecture Course	BSI	2006/7/25–8/5
Fifth Annual Meeting of Structural-Biological Whole Cell Project of *Thermus thermophilus* HD8	RSC	2006/8/11–8/13
Next-Generation Supercomputing Symposium 2006	NSC	2006/9/19–9/20
Second Workshop on Complex Electron System Science	DRI	2006/10/5–10/6
ICSB 2006 RTK Workshop	GSC	2006/10/12–10/13
VCAD System Research 2006	CIPS	2006/10/18–10/19
Frontier Research System 20th Anniversary Symposium	FRS	2006/10/25
Human Symbiotic Robotics in RIKEN	DRI	2006/10/26
Tenth RIKEN Workshop of the Quantum Materials Research Group	RSC	2006/10/27–10/28
RIBF International Collaboration Workshop	RNC	2006/11/6–11/9
First X-Ray Free Electron Laser Symposium	XFEL	2006/11/7
CDB Joint Graduate School Intensive Lecture Program	CDB	2006/9/6–9/7
Asian Research Forum on Emerging and Reemerging Infections 2007	CRNID	2007/1/15–1/16
First Symposium on Geometrical Teaching Materials and Solid Recognition for Visually Handicapped Persons	CIPS	2007/02/16
IBRO APRC/RIKEN BSI Advanced School	BSI	2007/2/27–3/9
Trends in Plant Hormones	PSC	2007/3/1–3/2
International Workshop: Joint JUSTIPEN-LACM Meeting	RNC	2007/3/5–3/8
CDB Symposium 2007	CDB	2007/3/26–3/28
Elucidation of Disease-Affecting Genes from SNPs	SRC	2007/3/29

Acronyms

BRC: BioResource Center, Tsukuba
BSI: Brain Science Institute, Wako
CDB: Center for Developmental Biology, Kobe
CIPS: Center for Intellectual Property Strategies, Wako
CRNID: Center of Research Network for Infectious Diseases, Yokohama
DRI: Discovery Research Institute, Wako
FRS: Frontier Research System, Wako
GSC: Genomic Sciences Center, Yokohama
NSC: Next-Generation Supercomputer R&D Center, Wako
PSC: Plant Science Center, Yokohama
RCAI: Research Center for Allergy and Immunology, Yokohama
RNC: Nishina Center for Accelerator-Based Science, Wako
RSC: RIKEN SPring-8 Center, Harima
SRC: SNP Research Center, Yokohama
XFEL: SPring-8 Joint Project for XFEL, Wako

Research

Twelve outstanding scientific achievements

Discovery Research Institute

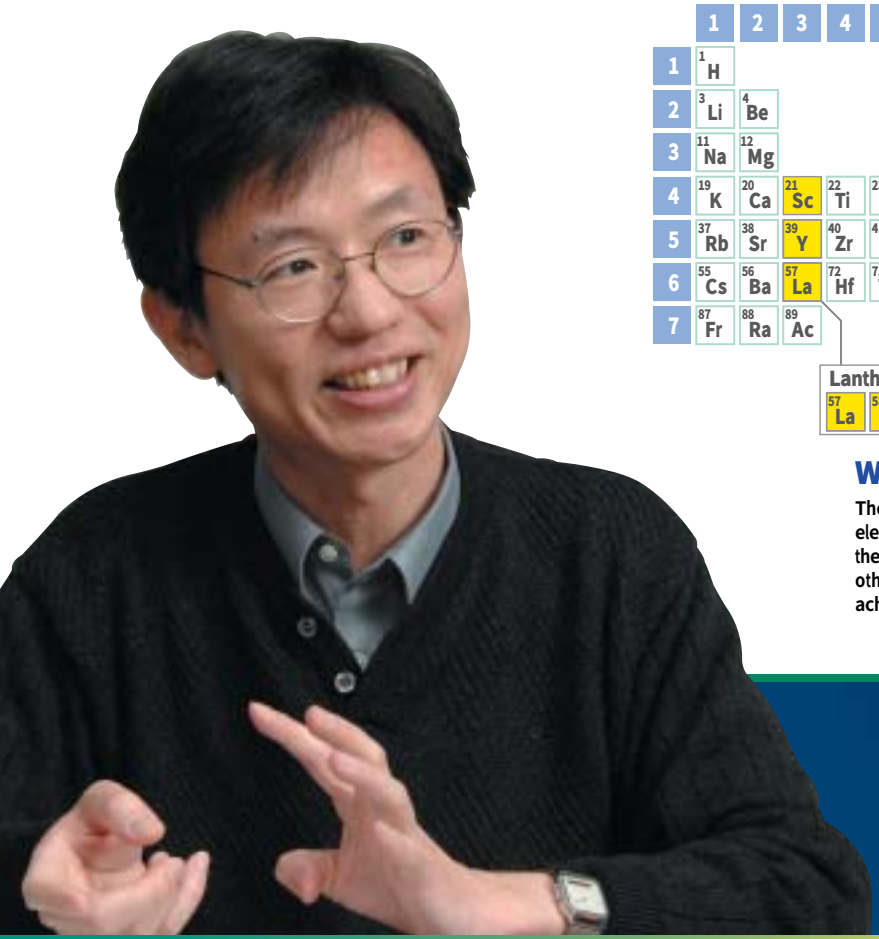
A new catalyst for creating synthetic rubber that is better than natural rubber

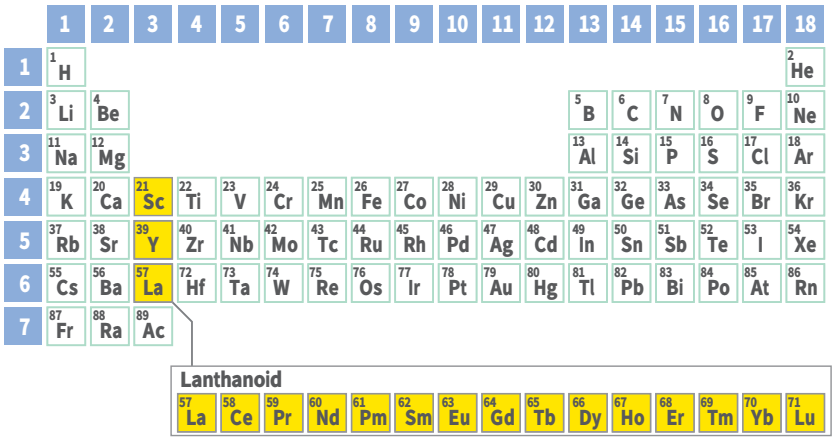
RIKEN has developed a new catalyst which precisely arranges the isoprene and butadiene units of synthetic rubber and synthesizes long chains of molecules (polymers). Synthetic rubbers are indispensable in our daily lives: they are used in tires, rubber belts and bands, footwear, adhesive compounds, medical products, and many other goods. To create a high-performance synthetic rubber, the positions, orientations, and lengths of the molecules all need to be controlled precisely. The new catalyst synthesizes polymers with all these controlled precisely, so it is now possible to develop synthetic rubbers with novel characteristics.

The two-percent gap

Rubber's physical properties, such as its elasticity, resistance to abrasion, and tensile strength, depend on how its component molecules are arranged. The main component of natural rubber, obtained from the latex of the rubber tree, is a polymer called polyisoprene, which is made from a large number of smaller identical building blocks of an organic molecule called isoprene linked in a chain. Although there are many different ways in which they can be joined together, in natural rubber all of the isoprene molecules are linked at each end with carbon-carbon double bonds having the same *cis*-1,4 arrangement, which gives good elasticity, resistance to abrasion, and tensile strength. Synthetic rubber has only 98% *cis*-1,4 microstructure. This 2% difference in *cis*-1,4 microstructure means that its physical properties are not as good as those of natural rubber.

However, natural rubber is not perfect. Plant proteins in natural rubber sometimes cause allergies, and its structure is not ideal because the lengths of the polyisoprenes in natural rubber are irregular. If the lengths of the polyisoprene could be made equal, and isoprene molecules could be artificially arranged so they are all in the *cis*-1,4 structure, it would be possible to make synthetic rubber that is harmless to humans and has better performance than natural rubber.





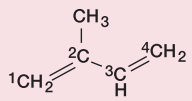
What is a rare-earth metal?

The rare-earth elements include scandium, yttrium, and the fifteen lanthanoid elements with atomic numbers from 57 to 71. The positive trivalent state is the most stable state for these elements, and they cannot easily change to other valencies during chemical reactions, so they are very suitable for achieving precisely controlled catalytic reactions.

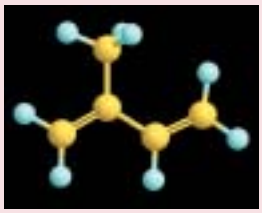
Zhaomin Hou
Chief Scientist
Organometallic Chemistry Laboratory
Discovery Research Institute

There are four types of polyisoprenes with different molecular positions and orientations.

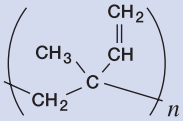
A molecule of isoprene

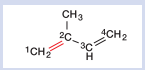


Polymerization

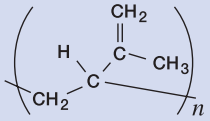


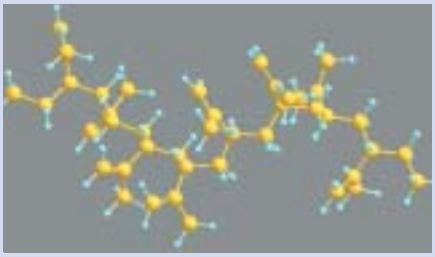
1,2-polyisoprene



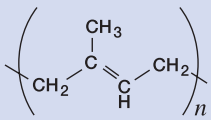
1,2-polyisoprene is a polymer that uses this type  of double bond. This polymer is theoretically possible, but the atoms are too closely packed, so it is impossible to synthesize.

3,4-polyisoprene

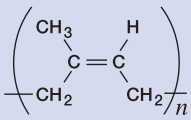


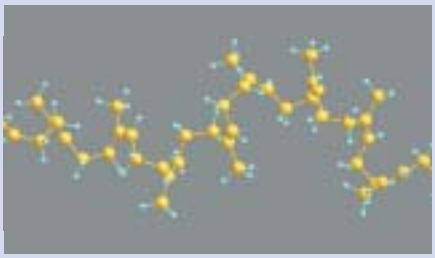


trans-1,4-polyisoprene



cis-1,4-polyisoprene



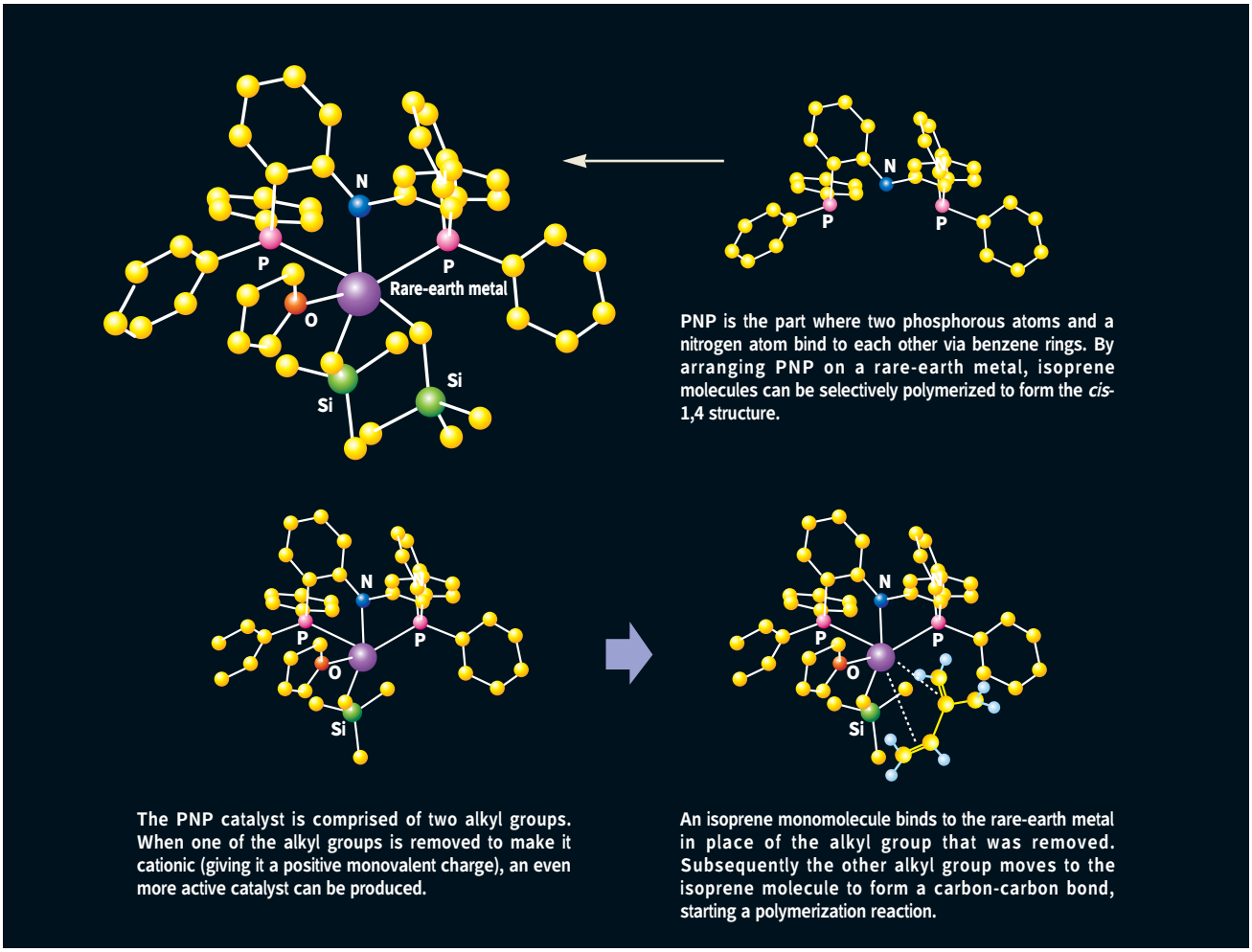


Positioning and orienting the molecules with PNP

Linking molecules of the same kind is called polymerization. Linking different kinds of molecules is called copolymerization. Polymerizing or copolymerizing molecules requires a catalyst. A catalyst is a substance that accelerates chemical reactions or causes reactions that would not normally occur. Chief Scientist Zhaomin Hou has been trying to develop new catalysts that uses rare-earth metals such as scandium, yttrium, and the lanthanides.

In September 2005, Hou was the first person in the world to successfully develop a catalyst that selectively polymerizes all the isoprene molecules in a *cis*-1,4 fashion while controlling their lengths. His catalyst also selectively copolymerizes the isoprene molecules and the butadiene molecules into the *cis*-1,4 structure. The new catalyst has a rare-earth metal in the center bound to two phosphorus (P) atoms and one nitrogen (N) atom, and the P and N bound to each other via benzene rings. Hou named this structure "PNP." When PNP is positioned above a rare-earth metal, it determines the spatial and the electronic properties around the metal. Only molecules in the *cis*-1,4 position and orientation can fit into this space and bind with each other. By binding to the catalyst, isoprenes that by themselves are unable to connect become able to connect. This is how all of the isoprene molecules can be arranged into the *cis*-1,4 structure.

The PNP catalyst that synthesizes *cis*-1,4-polyisoprene



Controlling the length with "livingness"

Another feature of the PNP catalyst is "livingness." Hou says, "In an ordinary catalyst, when a polymer reaches a certain length, it separates from the metal and a new polymerization reaction starts. With catalysts that have livingness, the polymer doesn't disconnect from the catalyst, so it can keep on extending until the monomers, run out." This means that the length of the polymer is determined by the number of molecules added to the catalyst.

Catalysts have parts called "active sites," which bind with molecules so as to generate chemical reactions. Most industrial catalysts have a variety of active sites with different properties. "For example, what can happen is that the reaction finishes when twenty molecules have been polymerized at some active sites, while others continue to 150,000 molecules, making it impossible to control the polymer's length. But all the active sites of the PNP catalyst have the same properties, so the polymerized molecules' lengths can be controlled precisely.

When butadiene molecules are added to the PNP catalyst after all the isoprene molecules have been completely polymerized, the butadiene molecules will link right next to the isoprene. If the catalyst does not have livingness, the polyisoprene molecules disconnect from the catalyst at the end of polymerization, and thus butadiene will not connect to the isoprene molecules, even when butadiene molecules are added. Only the PNP rare earth catalyst achieves copolymerization between isoprene and butadiene in a living *cis*-1,4 fashion . Each variety of rubber product requires different properties. By mixing multiple components, it is now possible to produce a rubber that has several useful properties. This is not possible with a single component.

The six glove boxes are put to full use to explore the possibilities of the new catalysts.

Producing new materials with the catalyst

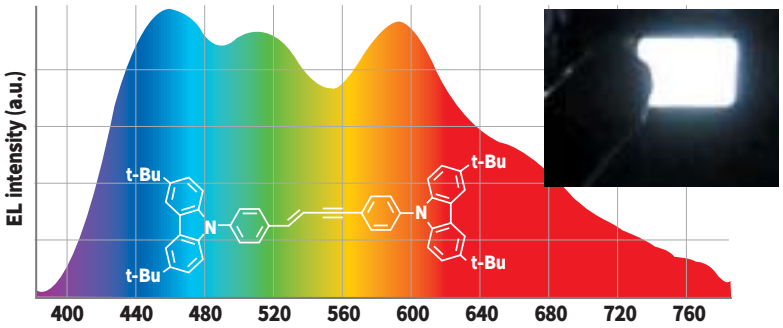
Most catalysts with livingness decompose more easily at high temperature, so during reactions the temperature is generally kept below 0°C. But the PNP catalyst remains stable even at 80°C without losing its livingness." Polymerization generates heat, so if the catalyst only works at a low temperature, cooling is necessary. "And that cooling requires a lot of energy. If the reaction temperature is about 80°C, we can use the waste heat from factories." In industrialization of the process, the PNP catalyst's stability at high temperature is a huge advantage.

These outstanding characteristics of the catalyst can only be achieved through the special combination of a rare-earth metal and a PNP structure. "We're always excited about whether we'll succeed. Sometimes we get a better result than we'd expected. The most attractive part of synthetic chemistry is that we can create high-value-added useful products from almost nothing—just raw materials. In a sense, we can *create* value." Not limiting himself to synthetic rubber, Hou is broadening his research to the development of innovative catalysts that can be used to create other new materials.

New materials produced by Hou's laboratory

A transparent polymer

Alternating norbornene-ethylene copolymer is becoming well known as a material for use in optical lenses and fibers, because of its high transparency and refractive index in addition to its high heat and chemical resistance.



π-conjugated aromatic compound with novel luminescent properties

Hou's laboratory has developed a luminescent molecule, for use in organic LEDs, that is capable of emitting an almost pure white light. This was the first time pure white light has been achieved with a single small organic molecule. Further developments are expected.

DIRECTOR'S MESSAGE

Fifty-six laboratories yield unique achievements in a cross-disciplinary research setting

Director, Discovery Research Institute **Koji Kaya**

Q. What were some of the noteworthy achievements of your institute in fiscal 2006?

A. Chief Scientist Katsumi Midorikawa and his colleagues in the Laser Technology Laboratory concentrated ultrashort intense laser pulses on gaseous atoms and molecules, successfully observing the motion of electrons in durations as short as 690 attoseconds. In addition, they created a new coherent control method that is essential for generating light pulses measured in attoseconds.

Q. What projects did your institute particularly focus on during fiscal 2006?

A. A new position of Associate Chief Scientist was introduced, with the objective of developing future leaders and providing highly motivated young scientists with the opportunity to preside over independent laboratories and develop new areas of research. The Discovery Research Institute recruited two Associate Chief Scientists in fiscal 2006. One has been evaluated highly for synthesizing functional ate complexes and developing new synthetic processes of high efficiency and high chemoselectivity, an achievement for which he received the Incentive Award in Synthetic Organic Chemistry. The other has achieved significant research results on the homologous recombination control mechanism in the DNA repair system and was appointed a professor at the University of Tokyo in April 2007.

In addition, the Scientists Assembly Secretariat, composed mainly of young scientists, has been entrusted with operating part of the in-house competitive funding system. This will contribute to the development of young researchers. Furthermore, opportunities for interdisciplinary interaction were provided through a number of internal and external exchange events.

Q. What new projects has your institute launched?

A. Aiming at the creation of new functional molecular materials, the Molecular Ensemble Research program was launched in fiscal 2006 to study molecular systems in which the molecules interact with each other in a coordinated manner. This study has been promoted within a framework of strong cooperation with other research centers and institutes and universities.

Q. What future plans do you have for the institute?

A. The Discovery Research Institute plays a central role in RIKEN. We will make an effort to lead research in a wide range of natural science and engineering fields and also serve as an international base for creating areas of study through interdisciplinary collaboration. We will also continue to encourage our Chief Scientists and their staff to pursue unique, cutting-edge research.

Frontier Research System

A membrane only 35 nm thick and 5×5 cm in size which does not break when sucked inside a pipette

"Thinner, larger, stronger" have been the three key criteria in the development of membranes, which are used in such everyday items as liquid crystal televisions, sensors, and water purifiers. RIKEN has developed a nanomembrane which meets these three criteria. It is 5 × 5 cm and only 35 nm thick, but it is strong enough not to break when sucked into and then blown out of a pipette. This new material is expected to have applications in seawater desalination and high performance fuel cells.

Nano but visible

RIKEN's new nanomembrane is made of zirconia and acrylic polymers and has a fine structure known as an IPN (Interpenetrating Polymer Network), where the molecular networks of two materials intertwine. The membrane is created by mixing and spin-coating acrylic monomers and zirconium alkoxide while irradiating them with ultraviolet light for several tens of seconds.

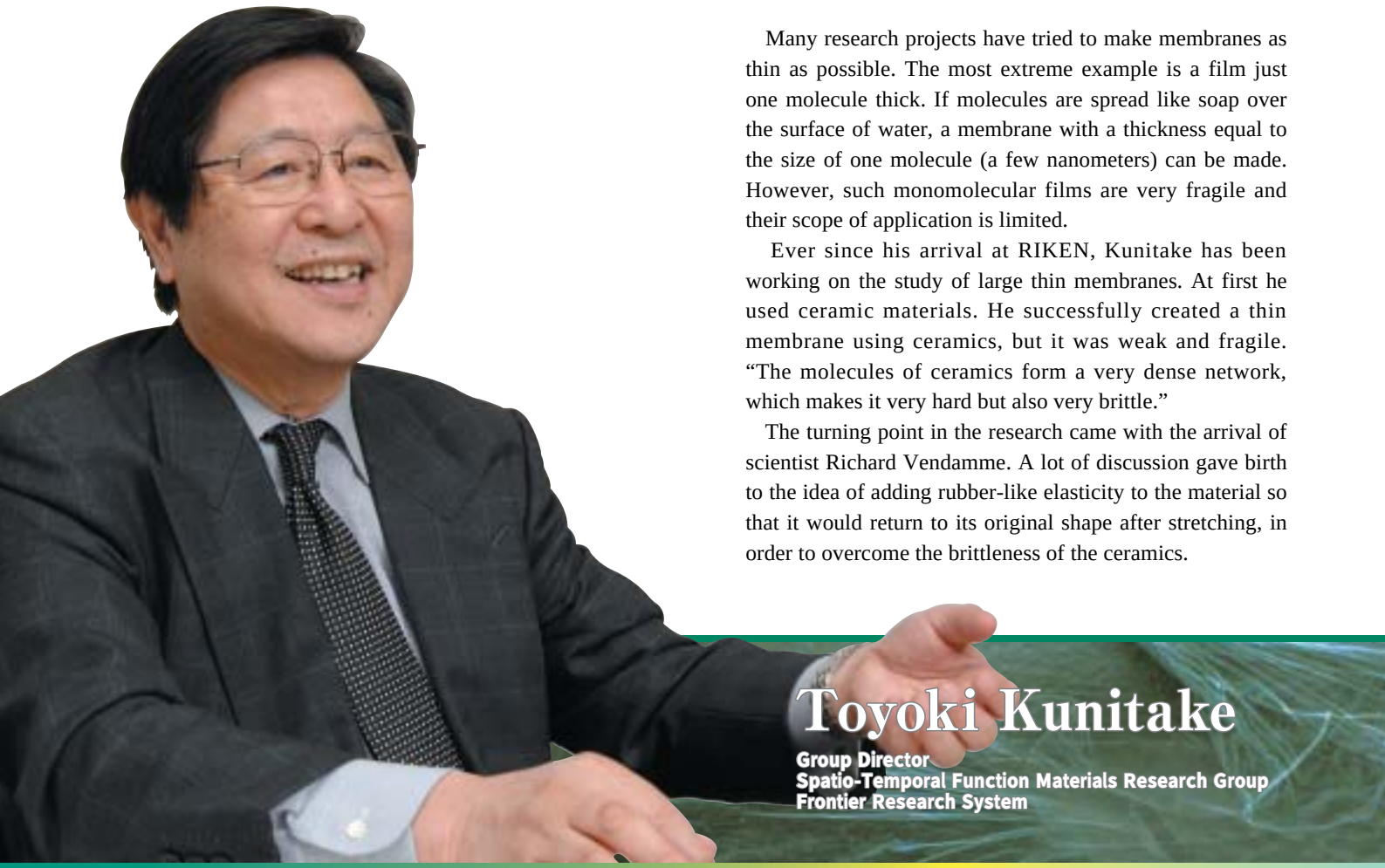
The research has gained attention because of the large 5×5 cm size of the nanomembrane. According to the group's director, Toyoki Kunitake, it could be made even larger. "Small thin membranes have been made up to now. They're interesting from a research perspective, but they can't be used unless they're big enough. A thin and fine material is suitable for embedding the dynamic functions of living organisms. In addition, the large size means that a wide range of artificial functions can be created."

Hard but flexible membranes

Many research projects have tried to make membranes as thin as possible. The most extreme example is a film just one molecule thick. If molecules are spread like soap over the surface of water, a membrane with a thickness equal to the size of one molecule (a few nanometers) can be made. However, such monomolecular films are very fragile and their scope of application is limited.

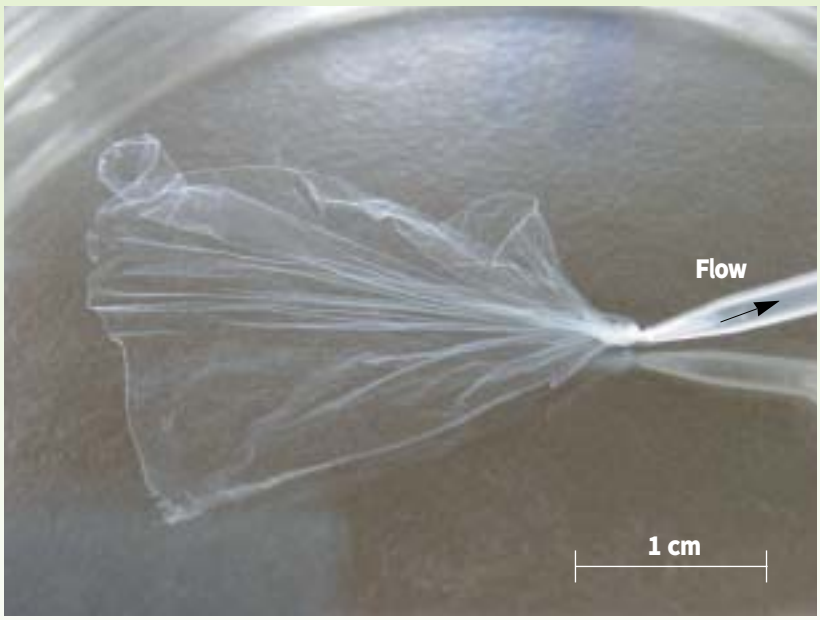
Ever since his arrival at RIKEN, Kunitake has been working on the study of large thin membranes. At first he used ceramic materials. He successfully created a thin membrane using ceramics, but it was weak and fragile. "The molecules of ceramics form a very dense network, which makes it very hard but also very brittle."

The turning point in the research came with the arrival of scientist Richard Vendamme. A lot of discussion gave birth to the idea of adding rubber-like elasticity to the material so that it would return to its original shape after stretching, in order to overcome the brittleness of the ceramics.

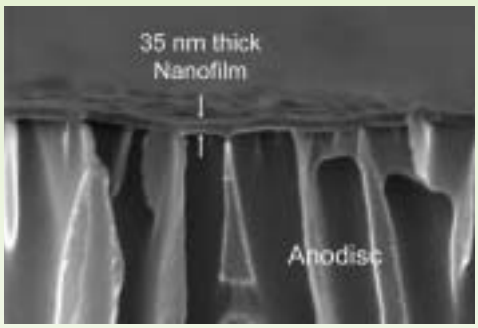


Toyoki Kunitake
Group Director
Spatio-Temporal Function Materials Research Group
Frontier Research System

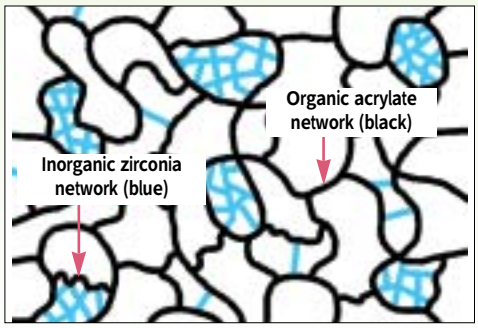
The hybrid giant nanomembrane



4 × 4 cm, 35 nm thick (1 nanometer (nm) = one billionth of a meter)
Even after the nanomembrane is sucked into a pipette and then blown out, it is strong enough to not lose its original size.



An SEM (scanning electron microscope) cross-section of a nanomembrane on an Anodisc



The structure of the giant nanomembrane

The elasticity of rubber is due to its special molecular structure, where long molecular chains partially link to each other. Kunitake and his colleagues considered that if flexible organic molecules and hard ceramics were combined to form a hybrid membrane, it could be strong and flexible, and large nanomembranes could then be created. In order to accomplish this, however, there was the technical problem of how to combine inorganic and organic molecules within a thin membrane in spite of their different properties. Kunitake and his colleagues successfully overcame this challenge by choosing a combination of inorganic and organic molecules that blended well with each other.

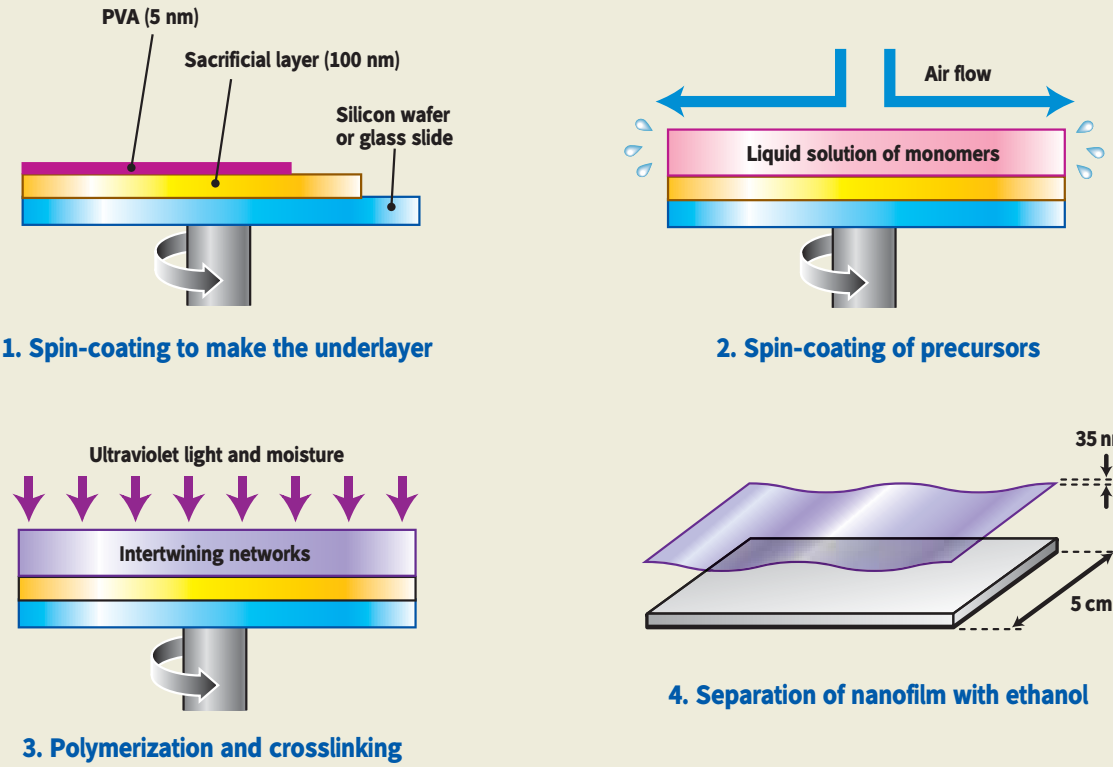
A huge nanomembrane was created from zirconia, a type of ceramic or inorganic material, and acrylic polymer, a type of organic material, forming a network structure and intertwining with each other. The thickness of the first huge nanomembrane was 35 nm, but they have now succeeded in making it as thin as approximately 20 nm.

Diversification of membrane materials

The materials for thin membranes do not have to be a combination of inorganic and organic materials. “The key to a thin strong membrane is a very dense network structure.” Kunitake and his colleagues have started creating a membrane using only organic materials, and they have already succeeded in producing a huge nanomembrane composed of epoxy oligomers and polyamine. Important organic materials include acrylic resin, epoxy resin, melamine resin, and urethane resin. As these thermosetting resins are comprised of molecules that form a network structure of very high density, they are extremely hard and strong.

“No one had thought of making a membrane using these thermosetting resin materials, because they are difficult to work with. However, when these materials are formed into nanomembranes, the same material behaves differently.” With nanoscopic formations, the network structure of the resins gives rise to a new property, that of flexibility.

How the giant nanomembrane is made



In the spin-coating process, the raw materials, macromolecules, are dissolved in solvent and then dripped on to the center of a spinning substrate. As the liquid spreads through centrifugal force, the solvent evaporates, leaving a thin membrane on the substrate. Thin membranes with a uniform thickness from several tens of nanometers to several micrometers can easily be created.

"Membranes made of organic materials are very interesting. If molecules with complex functionality, such as proteins, were embedded in them, those functionalities could be added to a thin membrane."

Widening the field of application to desalination and fuel cells

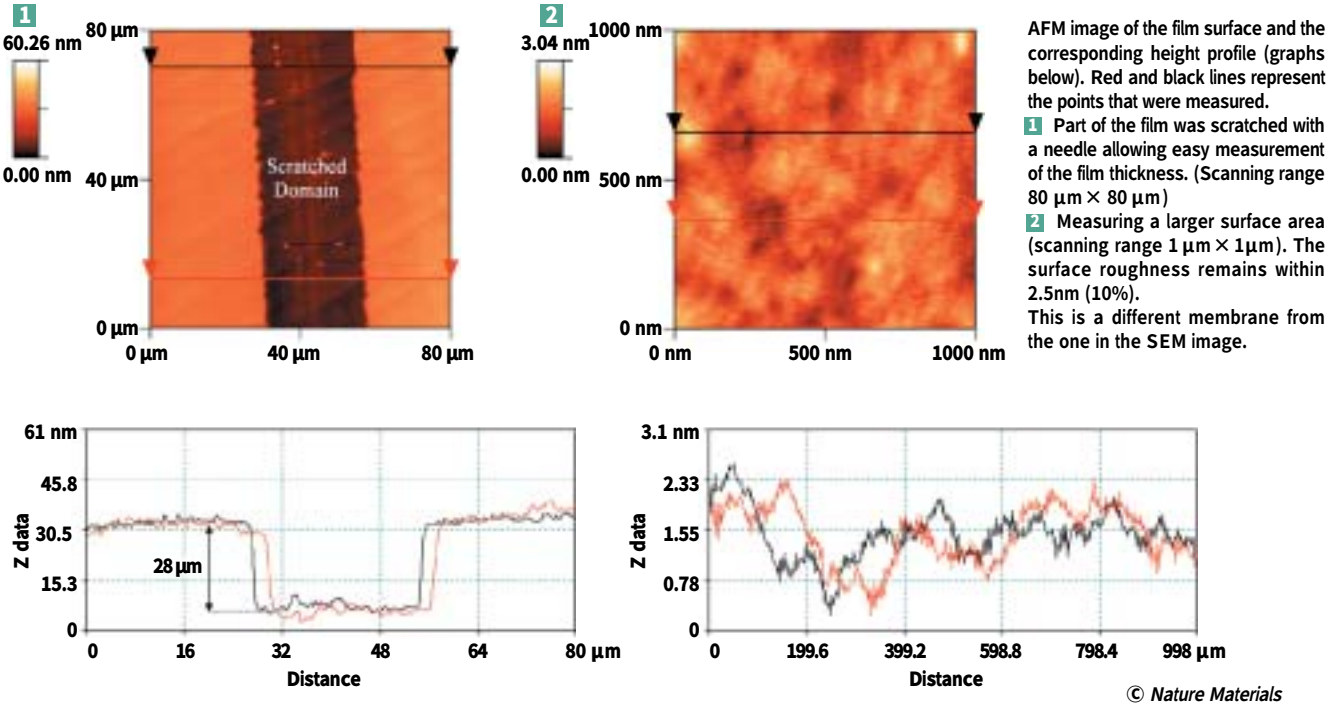
The first application of the thin membrane being considered is that of seawater desalination. The worst global shortage that mankind suffers could be that of fresh water. Countries such as Saudi Arabia have already started using desalination plants. Desalination plants apply high pressure to seawater to pass it through a reverse osmosis membrane, remove salt and impurities, and extract only the water. The thinner the reverse osmosis membrane, the less energy required to apply the necessary pressure. Today's commercially available reverse osmosis membranes have a thickness of micron to submicron order. Since the newly developed thin membrane has achieved an order-of-magnitude reduction in thickness, there are high expectations for its practical application.

Fuel cells use thin membranes as electrolytes in generating power from the chemical reactions of fuels such as hydrogen or methanol with oxygen. The efficiency of fuel cells is related to the function of the electrolyte membrane. The nanomembrane's high ionic permeability efficiency, high selective permeability, and fineness are expected to make it very useful.

The first step towards making spatio-temporal function materials

The body of a living organism, including cells, is constantly changing. However, an artificial material maintains its shape from its creation until the end of its lifetime. This means that while artificial materials have a spatial element and shape, they have no temporal element. So inquiries were made into whether or not an artificial material could be created that is equipped with a temporal element, similar to the material of an organism. "Unless it is based on a fine material, a new form with both time and space functions cannot be created," Kunitake believes. "For example, proteins are usually a few nanometers big. An artificial membrane can't work like a protein at the molecular level inside living bodies unless the membrane is

AFM observation of large-scale nanomembrane



AFM image of the film surface and the corresponding height profile (graphs below). Red and black lines represent the points that were measured.
1 Part of the film was scratched with a needle allowing easy measurement of the film thickness. (Scanning range 80 µm × 80 µm)
2 Measuring a larger surface area (scanning range 1 µm × 1µm). The surface roughness remains within 2.5nm (10%).
This is a different membrane from the one in the SEM image.

of a fineness of a few nanometers to a few tens of nanometers." Nanomembranes are suitable for addding the dynamic functions of organisms to, so large thin nanomembranes are the first step towards making a spatio-temporal functional material.

DIRECTOR'S MESSAGE

The Frontier Research System as RIKEN's "source of vitality": celebrating our 20th anniversary

Director, Frontier Research System **Kohei Tamao**

Q. What are some memorable events for the Frontier Research System (FRS) in fiscal 2006?

A. In May 2006 we held the first FRS Symposium, which had a total of 220 participants. During the symposium we held a ceremony to recognize the RIKEN Frontier Research System Award winners, who presented their research papers at this occasion.

In October we invited our former directors to give lectures to commemorate the 20th anniversary of the establishment of FRS. This event was attended by approximately 270 participants from various fields. Several constructive ideas were expressed regarding the roles FRS should play in the future.

Q. Have you launched any new projects?

A. The Functional RNA Research Program began in April 2006. It has now been one year since it was launched and research findings are accumulating. In addition, the Molecular Imaging Research Program (MIRP), which commenced in September 2005, has established its base adjacent to the Institute of Biomedical Research and Innovation in Kobe. Research has been in full swing at the Kobe location since the autumn of 2006. The MIRP has been designated as a center to support the development of new drugs. We are supporting R&D for new drugs on a nationwide basis with our molecular imaging technique, which enables greater efficiency in the drug production processes during the preclinical phase.

Q. What future plans do you have for FRS?

A. FRS occupies an intermediate, linking position between the Discovery Research Institute (DRI), RIKEN's core institute, which engages in a wide range of basic research projects, and RIKEN's other research centers and institutes, which pursue project-oriented research goals. We intend to play a pivotal role in germinating new research fields in line with RIKEN's future plans.

The first phase of our interim planning period ended with fiscal 2007 and the second phase begins with fiscal 2008. RIKEN is now in the process of undergoing a comprehensive review. At FRS we will take into account the proposals made during the external evaluation undertaken in 2006 to initiate further development in accordance with our long-term plans, and to expand our research into new fields.

Brain Science Institute

Creation of model mice, a major step toward understanding the mechanism of bipolar disorder

RIKEN has successfully created a strain of mice that display behavioral abnomalities and pharmacologic responses similar to those of bipolar disorder. Even though bipolar disorder is a long-known psychiatric disorder, how it works is still unknown. The mice created in this study may become the world's first model mice for exploring bipolar disorder, and they are expected to help us understand the mechanism of bipolar disorder and develop new therapeutic drugs.

Bipolar disorder's double threat to patients' lives

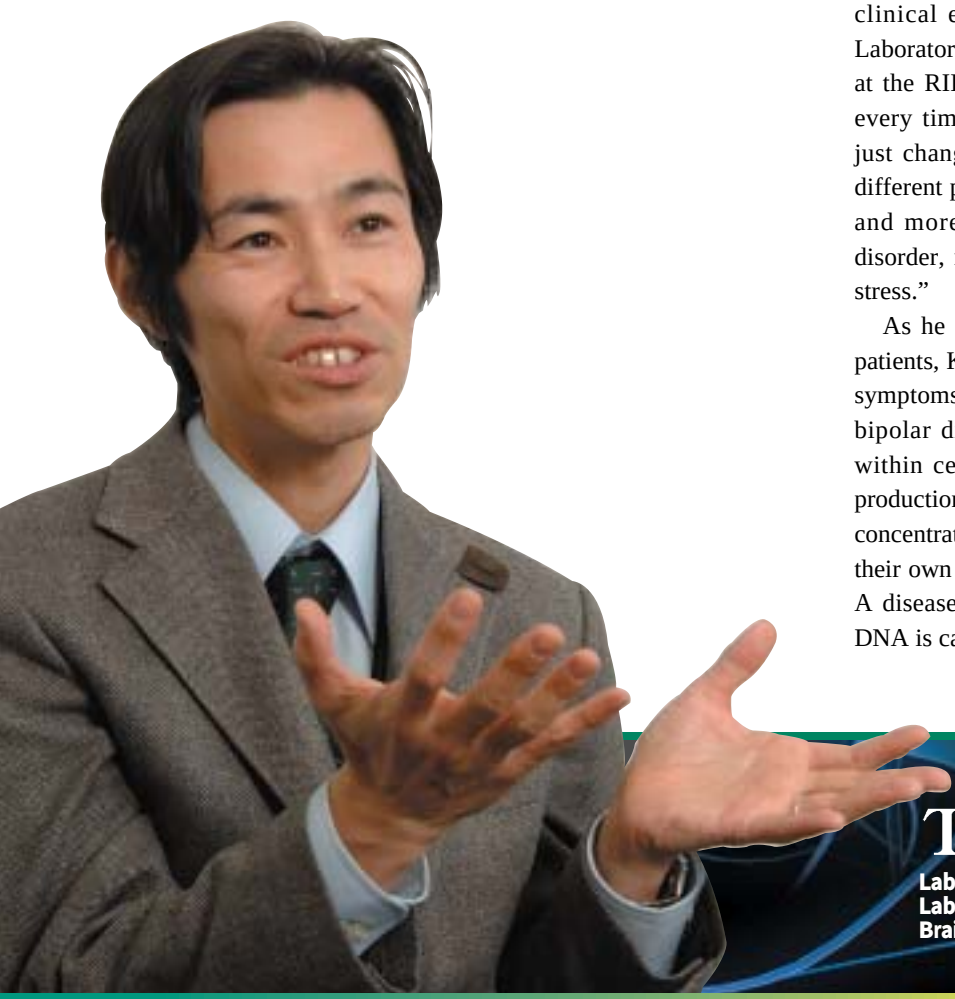
Bipolar disorder is a psychiatric illness in which sufferers alternate between a "manic" state, where they are overexcited and do not sleep, and a "depressed" state, where they lack energy and enthusiasm. When they are depressed, their unstable psychological state can lead to suicide, and in the manic state their outrageous behavior can destroy their relationships with other people. As the disease's recurrence rate is quite high, it can cause serious suffering for patients and their families over extended periods of time, and a severe deterioration in quality of life.

Although bipolar disorder is quite common, occurring in just under one in a hundred people in Japan, its pathogenic mechanism is still unclear. Possible causes are an abnormal metabolic process in the brain or the involvement of genes; however, there is currently very little consensus on the cause. One reason for this is that an animal model for bipolar disorder has not yet been created. An animal model is needed to understand the illness's pathology and develop a method of treatment.

A hypothesis derived from measuring metabolism in the brain

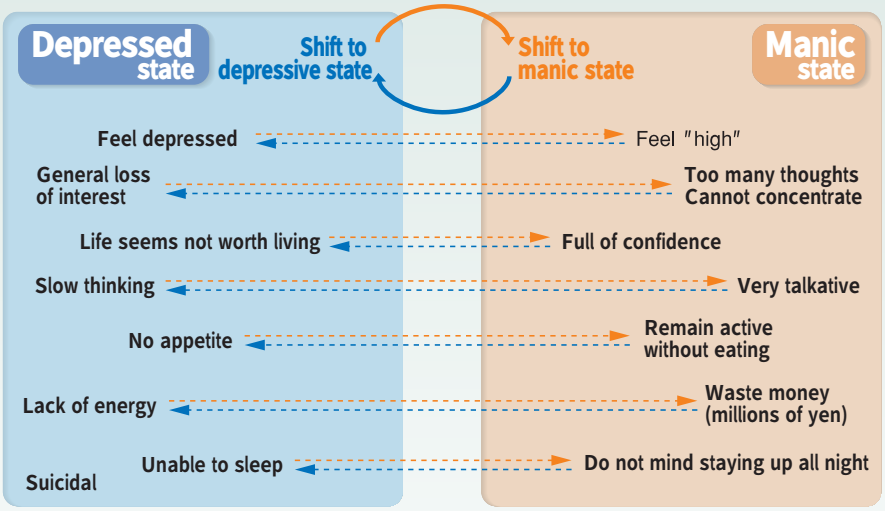
The creation of model mice in this study began from the clinical experience of Tadafumi Kato, the head of the Laboratory for Molecular Dynamics and Mental Disorders at the RIKEN Brain Science Institute. "In the late 1980s, every time I examined bipolar disorder patients who had just changed to the manic state, it was as if they were a different person from the previous day. I began to feel more and more that bipolar disorder was caused by a brain disorder, not by environmental or emotional problems like stress."

As he studied the brain metabolism of bipolar disorder patients, Kato discovered that mitochondrial diseases, whose symptoms are mostly physical, had some similarities with bipolar disorder. Mitochondria are minute organs found within cells. They have important functions such as the production of energy-carriers and the adjustment of calcium concentrations for intercellular signaling. Mitochondria have their own DNA, different from the DNA in the cell nucleus. A disease caused by an abnormality in this mitochondrial DNA is called a mitochondrial disease.



Tadafumi Kato
Laboratory Head
Laboratory for Molecular Dynamics of Mental Disorders
Brain Science Institute

A bipolar-disorder model mouse on a running wheel



Symptoms of bipolar disorder

"In the early 1990s, I was using magnetic resonance spectroscopy (MRS) to measure brain metabolism, and I discovered a drop in the levels of creatine phosphate in the brains of depressed patients." A survey of the literature indicated similar findings in mitochondrial diseases. Recently, it also has been reported that a type of mitochondrial disease called chronic progressive external ophthalmoplegia (CPEO), which interferes with muscle movement around the eyes, can be accompanied by depression. Kato therefore proposed a theory of mitochondrial dysfunction, where he hypothesized that an abnormality in mitochondrial DNA could interfere with the energy metabolism of the brain to cause an abnormality in calcium signaling, thus triggering bipolar disorder.

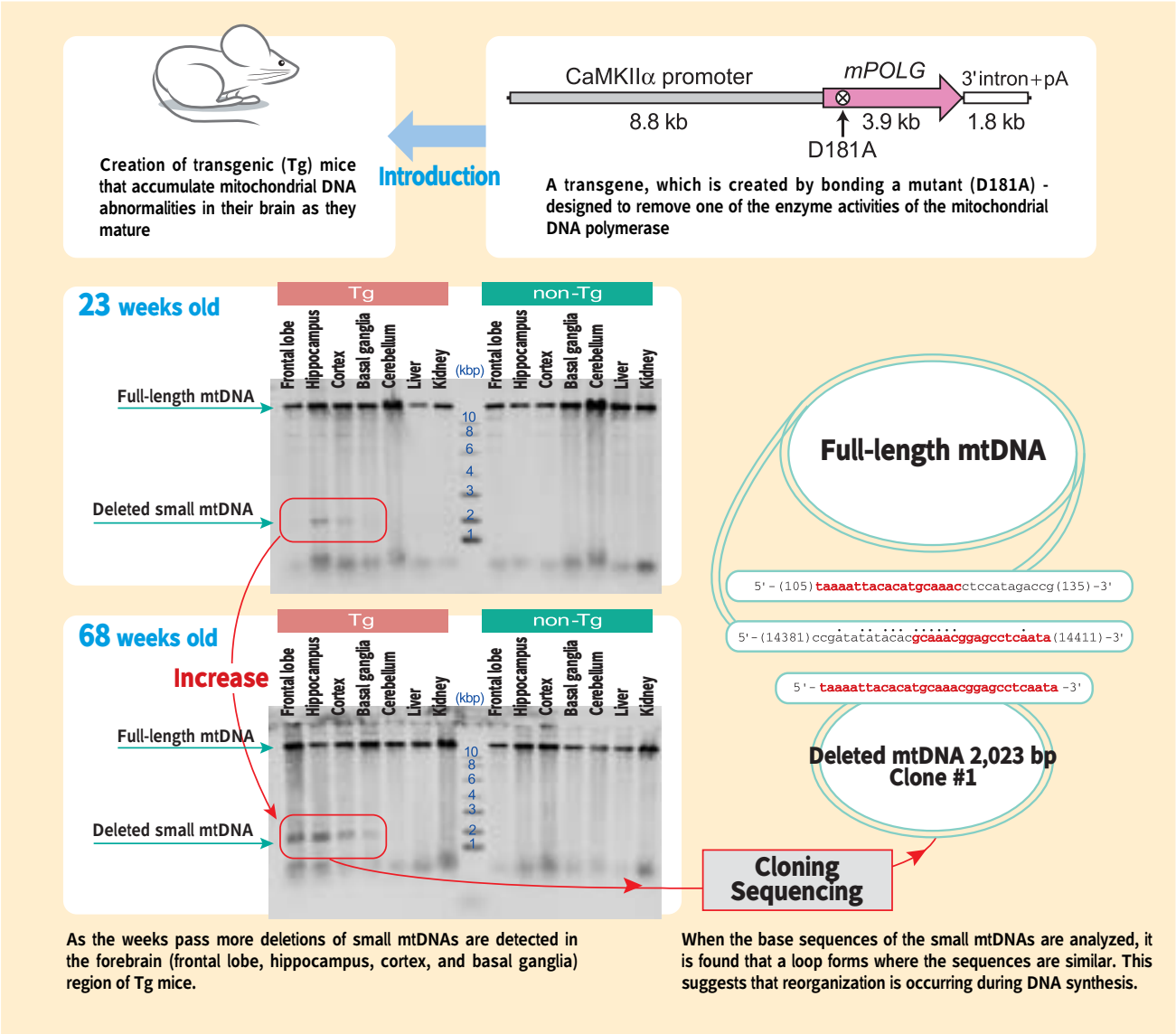
Following this, he had an opportunity to study the post-mortem brains of bipolar disorder patients in the United States, and he discovered an abnormality in their mitochondrial DNA. In CPEO patients, about 5,000 of the approximately 16,000 base pairs contained in mitochondrial DNA are missing. This type of abnormality was also observed in the brains of bipolar patients on a smaller scale. In addition, the same mitochondrial DNA variation as that in

History of the mitochondrial hypothesis of bipolar disorder

(Achievements by Kato et al. are in blue.)

1992	Report that an energy-carrier (creatine phosphate) decreases in the brain of depressed patients
1993	Report that the pH in the brain of a bipolar disorder patient tends to increase in acidity during remission
1994	The existence of "mitochondrial depression" is proposed
1995	Report that the mode of inheritance of bipolar disorder is similar to mitochondrial genetic inheritance (McMahon et al., Johns Hopkins University)
1996	Report that there is an increase in mitochondrial DNAs (mtDNA) deletion in the blood of bipolar disorder patients
1999	Report that treatments for bipolar disorder, lithium and valproic acid, can both increase the mitochondrial outer membrane protein Bcl-2 (Chen et al., US National Institutes of Health)
2000	Hypothesis of mitochondrial dysfunction in bipolar disorder
2001 April	Creation of the POLG mutant mice commences
July	Report that POLG is the causative gene for the chronic progressive external ophthalmoplegia family (accompanied by depression) (Van Goethem et al., University of Antwerp)
2003	Report of a family in which bipolar disorder and chronic progressive external ophthalmoplegia are linked (Siciliano et al., University of Pisa)
2004 March	A conspicuous variation is observed in genes related to mitochondria in the post-mortem brains of bipolar disorder patients, and it is claimed that the observation corresponds to the hypothesis of mitochondrial dysfunction (Konradi et al., Harvard University)
May	An accumulation of lactic acid is observed in the brains of bipolar disorder patients, and it is reported that this observation corresponds to Kato's hypothesis of mitochondrial dysfunction. (Dager et al., University of Washington)
June	*The Scientist* reports that mitochondria are found to be the cause of bipolar disorder
December	RepliGen Corporation, a US pharmaceutical company, tells the press that RG2417, a medication for mitochondrial disease, is effective for bipolar disorder
2005 January	The relationship between mtDNA 3644 mutation and bipolar disorder is reported
March	The observation regarding post-mortem brains by Konradi et al. is found to be an effect of sample pH
October	An accumulation of mtDNA 3243 mutation in the post-mortem brains of bipolar disorder patients is reported
	General remarks on the hypothesis of mitochondrial dysfunction (Stork and Renshaw, Harvard University)
2006 April	Report that mice with an abnormality in mtDNA show behavior similar to that of bipolar disorder
May	US Society of Biological Psychiatry holds a symposium titled "Mitochondrial-ER function in Bipolar Disorder" in Toronto
June	Collegium Internationale Neuro-Psychopharmacologicum holds a symposium titled "Mitochondrial Dysfunction in Psychiatric Disorders" in Chicago

Creation of model mice for bipolar disorder



patients with MELAS, a typical mitochondrial disease, was also observed, endorsing the theory of mitochondrial dysfunction.

Creation of mice with mitochondrial DNA abnormalities

Based on this hypothesis, Kato and his colleagues created mice that accumulated mitochondrial DNA abnormalities in their brain as they matured. When they studied these mice spontaneously running on wheels, they found that mice with mitochondrial DNA abnormalities turned the wheel less than healthy mice. They also had an abnormal circadian rhythm similar to that found with insomnia, and female mice showed a conspicuous variation in the amount of activity based on their estrous cycle.

What is more, these behavioral anomalies improved with the administration of lithium, a mood-stabilizer effective for bipolar disorder, and were exacerbated by administration of tricyclic antidepressants. Lithium is a known treatment for bipolar disorder, and tricyclic antidepressants are known to induce a manic state in bipolar disorder patients and increase the frequency of alternations.

This means that the reactions to the drugs can be considered similar to those of bipolar disorder patients. As mentioned above, the characteristics exhibited by the model mice are fairly similar to bipolar disorder symptoms; therefore, Kato and his colleagues hope that their mice will gain recognition as the world's first animal model for bipolar disorder.

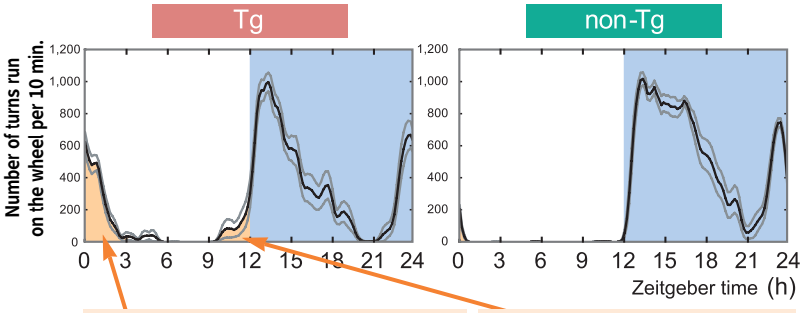
The possible involvement of cell death in the onset of disease

It has been suggested that not only bipolar disorder but also Parkinson's disease and diabetes are related to mitochondrial DNA abnormalities. There is a suggestion that mitochondrial dysfunction is involved in the cell death seen in Parkinson's disease and diabetes. In the late 1990s, scientists reported that lithium has the effect of protecting nerve cells.

"I think that bipolar disorder is triggered when the brain's mood-stabilizing system stops functioning properly. If nerve cells are damaged by mitochondrial dysfunction, it would

Abnormality in the circadian rhythm of wheel-running activity

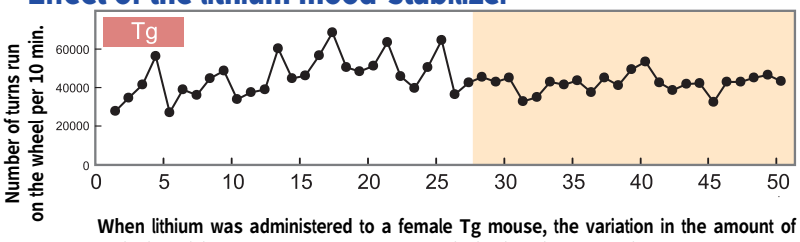
Healthy (non-Tg) mice are active when it is dark, but Tg mice continue running on the wheel even after daybreak and start running before nightfall.



Continue running on the wheel even after daybreak, although this is normally a rest period
→This may correspond to being unable to go to sleep for a human.

Start running on the wheel before it gets dark
→This may correspond to a tendency to wake up early for a human.

Effect of the lithium mood-stabilizer



When lithium was administered to a female Tg mouse, the variation in the amount of periodic activity decreased and the abnormality in circadian rhythm improved.

explain why lithium acts as a curative drug. The damaged nerve cells could be those that control mood in the brain. The model mice for bipolar disorder could also be of use in identifying those nerve cells."

Understanding psychiatric disorders through molecular biology

"People tend to think that they should be able to handle mental illnesses on their own, because they are matters of the mind. However, if the mechanisms of psychiatric disorders are explained through molecular biology, people will then start understanding that they are diseases that should be treated in hospitals."

The model mice for bipolar disorder developed in this study are going to be distributed through the RIKEN BioResource Center in Tsukuba. It is hoped that the model mice will be used by a large number of researchers and stimulate research on bipolar disorder that leads to the development of fundamental treatments and preventive methods for general psychiatric disorders.

DIRECTOR'S MESSAGE

The prospects for brain science study generated through integration and cooperation

Director, Brain Science Institute **Shun-ichi Amari**

Q. How would you characterize the Brain Science Institute?

A. Brain science has the noble target of understanding the human mind and our intellect. Moreover, it is an eclectic field of study, involving information science, human science, and mathematical science in addition to the life sciences. Therefore our research methodologies also need to be integrated. This is a major feature of research being conducted at the Brain Science Institute (BSI). This fiscal year significant advances were made in studies involving this integrated approach.

Q. What projects did you focus on during fiscal 2006?

A. We strengthened our ties with other research institutions. In Japan, we signed cooperative research and education agreements with the University of Tokyo and Waseda University. At present, a unit from the University of Tokyo is doing research at BSI. Internationally, we reached an agreement to establish a joint graduate school program with the Karolinska University in Sweden. In England, we have agreements with Newcastle University and the University of London and cooperative research has begun. We intend to further extend the cooperative framework both at home and overseas, while making steady progress in establishing cooperative arrangements with industry.

Q. What future plans do you have for BSI?

A. Brain science can be considered a core science for the 21st century. I would like to make BSI a hub for brain science research here in Japan and also have it play an important role in international collaborations. As part of this, the Japanese branch of the International Neuroinformatics Coordinating Facility (INCF) was established in BSI to facilitate the integration of brain science and information science.

In fiscal 2006, in order to improve the research level of young researchers, the IBRO APRC/RIKEN BSI Advanced School was hosted under the joint auspices of RIKEN and IBRO-APRC (International Brain Research Organization, Asia-Pacific Regional Committee). Education and public relations efforts to promote brain science are also being conducted in Japan through a symposium in cooperation with the Brain Century Promotion Conference. While conducting top-level brain science research is our main role, as you can see from the variety of our activities, BSI considers its educational role to be very important.

Nishina Center for Accelerator-Based Science

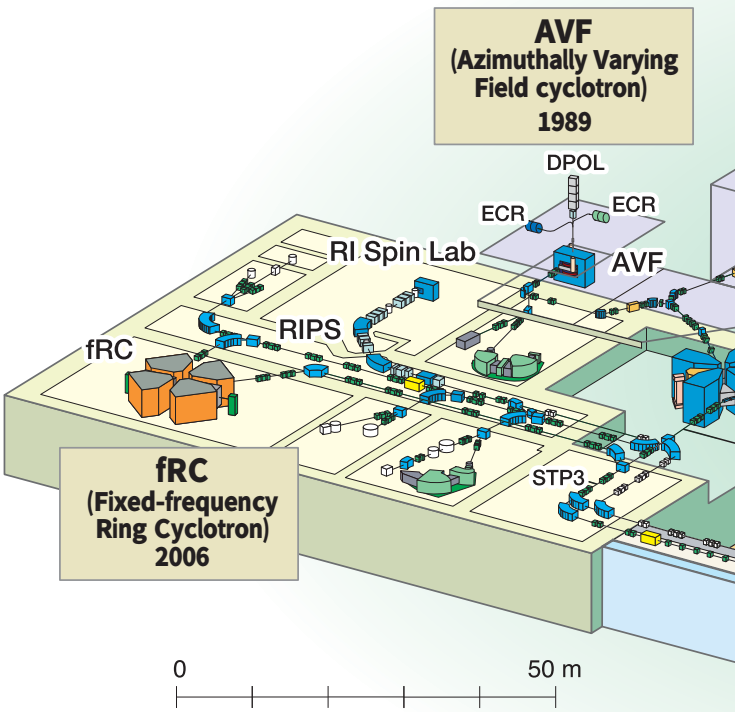
Successfully producing the first beam from the superconducting ring cyclotron

Ring cyclotrons are indispensable for study of the origin of the elements and the structure of atomic nuclei. In 2006, RIKEN completed the construction of the world's first superconducting ring cyclotron, and produced a beam of heavy ions (ions of elements heavier than lithium or carbon) that traveled at 70% of the speed of light for the first time ever. In the future, this cyclotron will be used in many fields, ranging from basic science such as nuclear physics to applied research in medicine and engineering.

The birth of the RI Beam Factory

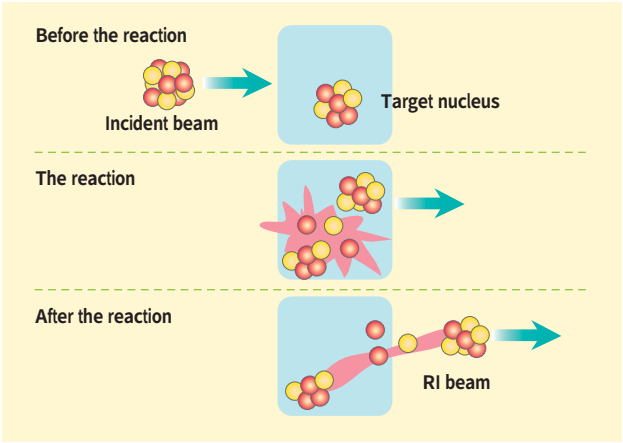
How did the various elements come into existence? The atoms which occur in nature are generally stable. In a stable state, the protons and neutrons in the atomic nucleus are thought to be mixed homogeneously and to each occupy the same volume. If this balance is broken, the atomic nucleus becomes unstable and it is called a radioisotope. All the naturally occurring nuclei from iron to uranium are thought to have been created from radioisotopes. Studying the properties of radioisotopes can provide important clues to the origin of the elements.

The RI Beam Factory is a facility that generates beams of radioisotopes. RIKEN already has three types of accelerator—the RIKEN linear accelerator, the AVF cyclotron, and the RIKEN ring cyclotron—and has achieved many results using them. In 2006, after ten years of development, RIKEN completed a radioisotope beam generator consisting of a group of three accelerators—a fixed-frequency ring cyclotron, an intermediate-stage ring cyclotron, and a superconducting ring cyclotron. This is called the RI Beam Factory, and it is capable of generating even more radioisotope beams.



Akira Goto
Group Director
Accelerator Development Group
Nishina Center for Accelerator-Based Science

A projectile fragmentation reaction



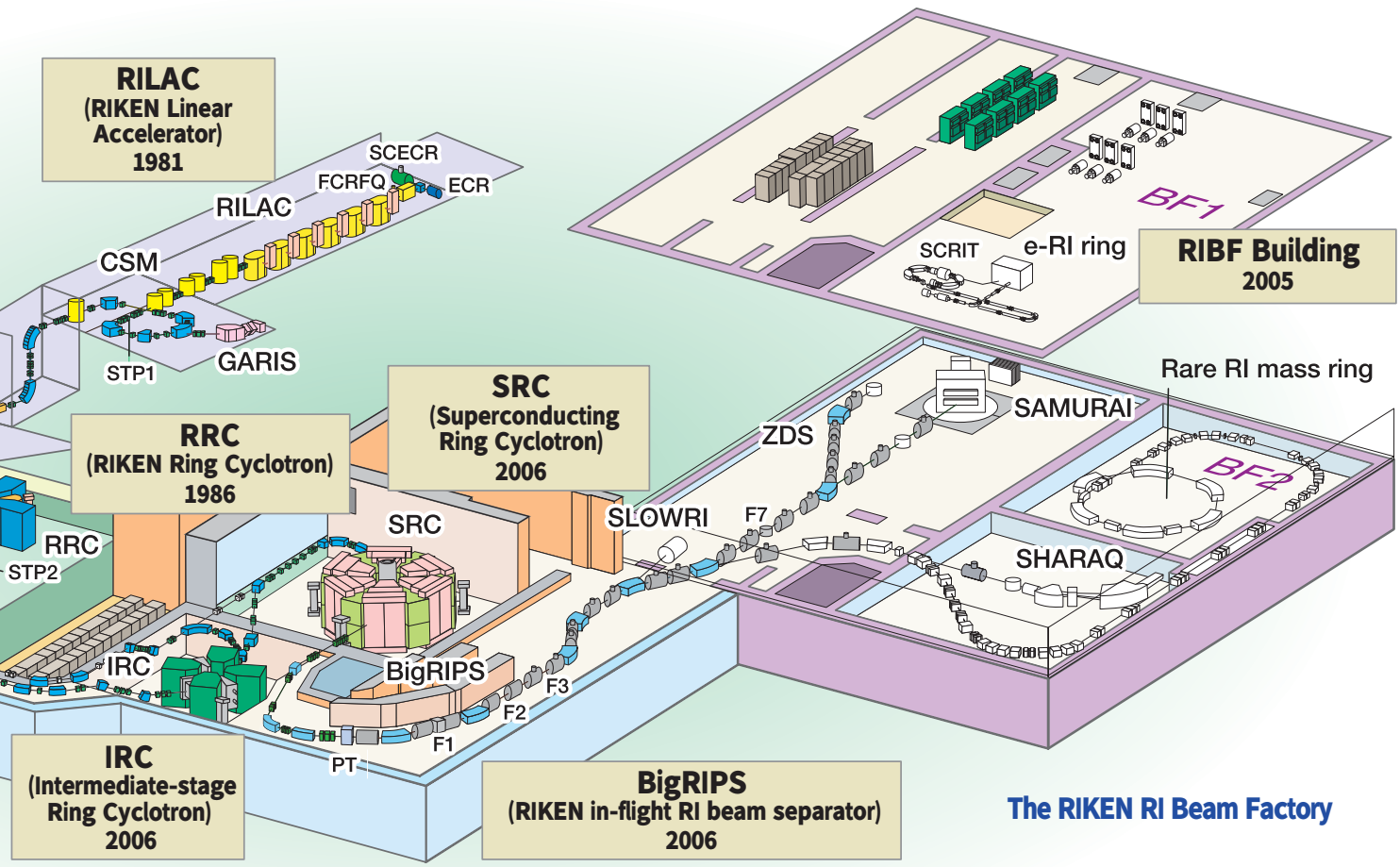
Accelerating uranium

The RI Beam Factory was designed to generate radioisotope beams of all the elements from hydrogen to uranium. In order to obtain radioisotope beams, a heavy ion is collided on a target nucleus to cause a projectile fragmentation reaction or a uranium fission reaction. Uranium above all gives a high probability of obtaining various kinds of radioisotope beams. However, the uranium ions need to be accelerated to about 70% of the speed of light. This was impossible with previous accelerators.

The RI Beam Factory's multi-stage acceleration system makes it possible by accelerating heavy ions in stages. The more positively charged a heavy ion is—in other words the fewer electrons it has—the more efficiently it can be accelerated. The RI Beam Factory was designed to make ions more positively charged as they are accelerated, by placing a carbon foil between the accelerators to remove electrons as the heavy ions pass through. The RI Beam Factory performs acceleration in five steps, a method unprecedented in the world, generating about four thousand different kinds of radioisotope beams, including approximately a thousand never seen before.

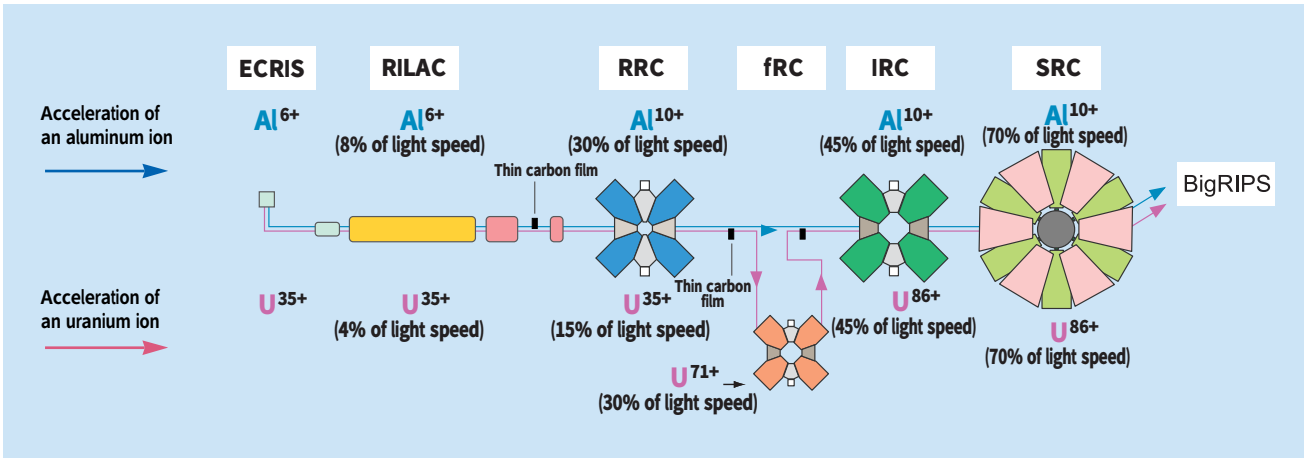
The world's first superconducting ring cyclotron

The ring cyclotron accelerates heavy ions as it rotates them in a spiral using magnetic and high-frequency electric fields.



The RIKEN RI Beam Factory

Heavy-ion acceleration



The highest accelerating power at the RI Beam Factory is generated by the superconducting ring cyclotron, the first in the world.

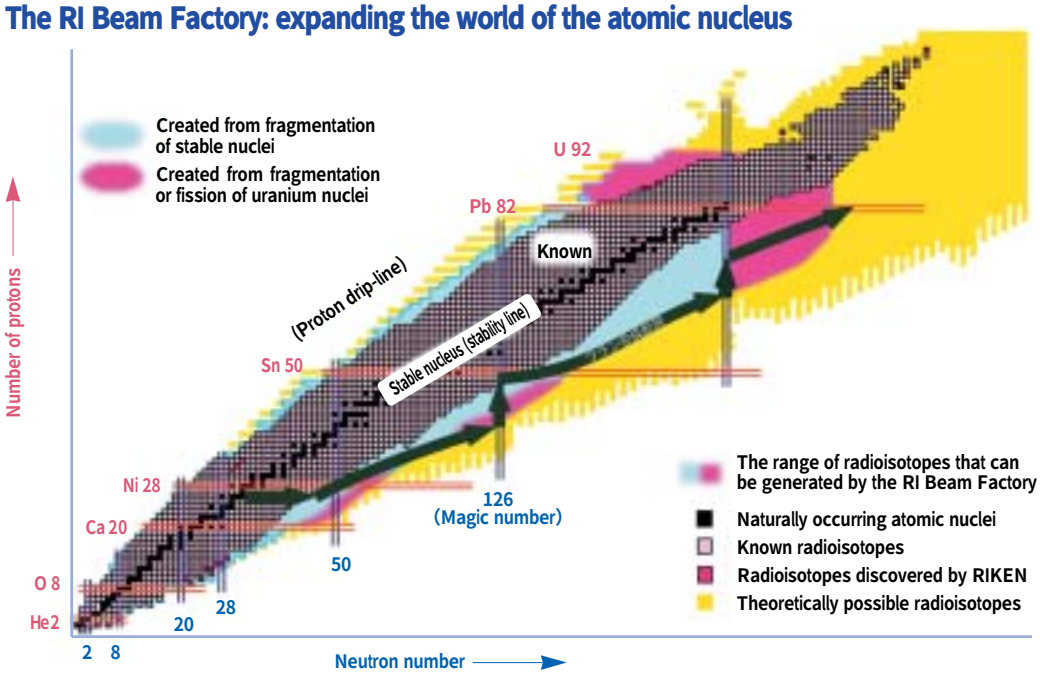
"There have been cyclotrons which used circular superconducting coils as magnets, but a cyclotron using wedge-shaped superconducting coils arranged in a ring had never been made, although some were planned," says Goto. "When superconducting coils generate a magnetic field, there is a strong force pushing the coils outward. A circular coil expands evenly, but since the coils of the ring cyclotron are wedge-shaped, the straight sections deform. So we faced the problem of how to reinforce the magnets."

The design team created the wedge-shaped superconducting magnets by employing an innovative structure where a long thin slit-like hole is made in the iron core of a room-temperature magnet, and a stainless-steel plate is then inserted into that hole to support the coil, which is cooled to a very low temperature. In addition, each of the gaps between the six superconducting magnets is covered with thick iron plates, which prevent the magnetic field from leaking outside the ring cyclotron. The magnetic field which bends the paths of the heavy ions has a power of eight Tesla meters, the highest in the world for a cyclotron. While Goto has experience in cyclotron development, this was the first time he had built such an enormous apparatus, with a total weight of 8300 tons. "I was used to making cyclotrons, but constructing three ring cyclotrons at the same time wasn't easy." Having overcome many challenges, the research group was at last ready to accelerate a uranium ion.

The first beam, and the successful production of a uranium heavy-ion beam

At 4 pm on December 28, 2006, the superconducting ring cyclotron accelerated an aluminum ion to 70% of the speed of light, and extracted it as a beam for the first time. "The first RIKEN ring cyclotron was built in December 1986.

The RI Beam Factory: expanding the world of the atomic nucleus



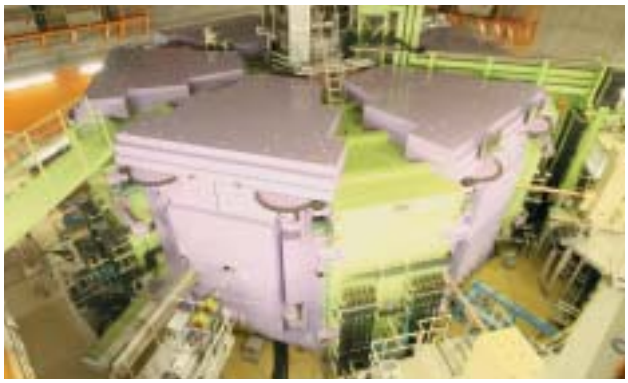
The vertical axis is the number of protons and the horizontal axis is the number of neutrons. Each small square represents an atomic nucleus. There are about 270 naturally-occurring stable atomic nuclei. Around these are many unstable nuclei (radioisotopes). The RI Beam Factory can use uranium or other heavy-ion beams to generate about 4000 kinds of radioisotopes, including about 1000 that were previously unknown. In this way it enables researchers to find new radioisotopes and study the origin of the elements.

We had been saying 'Let's extract the first beam from the superconducting ring cyclotron in December 2006, exactly 20 years after the first cyclotron was built.' We were very pleased to achieve that target." The multi-stage acceleration using three ring cyclotrons was an unprecedented achievement, and the first beam demonstrated the reliability and validity of the multi-stage acceleration system. On March 13, 2007, a krypton ion was accelerated in the same manner and collided into the target atomic nucleus, successfully generating a radioisotope beam.

At 9 pm on March 23, 2007, a targeted uranium ion was accelerated to 70% of the speed of light and the research group succeeded in producing a radioisotope beam. This was the first time that a uranium ion had been accelerated in Japan. For this acceleration, one more ring cyclotron was added, so, in total four were used. Although heavy-ion accelerators are being developed in Europe and North America, this series of successes indicates that the RI Beam Factory is one step ahead of anybody else.

December 28, 2006
Researchers celebrating the production of the first beam

From now to 2012, they are going to continue to develop devices to analyze the generated radioisotopes in detail from various perspectives. They are continually on the lookout for unknown radioisotopes, and they are also trying to construct the ultimate model of the atomic nucleus and understand the origin of the elements.



Superconducting Ring Cyclotron

DIRECTOR'S MESSAGE

Understanding the creation of matter with help from leading-edge particle beam technology

Director, Nishina Center for Accelerator-Based Science **Yasushige Yano**

The establishment of the Nishina Center for Accelerator-Based Science

Our center was established on April 1, 2006, to study accelerator-based science in a comprehensive manner, combining laboratories from the Discovery Research Institute and the Frontier Research System. Construction of the RI Beam Factory had been in progress since fiscal 1997. The core of the facility, the RI beam generation system, was completed and successfully produced its first beam in December 2006. Fiscal 2006 has proved to be a very memorable year.

Dr. Nishina and RIKEN's first cyclotron

Q. What specific issues did you emphasize in your first year of operation?

A. The RI Beam Factory will be ready for use in fiscal 2007 and in preparation for this we requested ideas for experiments using this facility from scientists all over the world. Subsequently we received submissions from both Japanese and foreign groups that included researchers from 13 countries other than Japan, a sure indication of our facility's high reputation abroad. We will continue to make the RI Beam Factory available to researchers from both Japan and abroad.

Another major undertaking aimed at developing the field of theoretical nuclear physics internationally is the establishment of the Todai–RIKEN Joint International Program for Nuclear Physics (TORIJIN) in collaboration with the University of Tokyo's Graduate School of Science.

Q. What are the future prospects for the center?

A. Our mission is to thoroughly investigate the atomic nucleus, and the true essence of the elemental particles that make up the atomic nucleus, so as to better understand the mysteries surrounding the creation of matter. While continuing to promote the RI Beam Factory, we will proceed with our cooperative research projects at the RIKEN BNL Research Center in the US and the RIKEN RAL Facility in England.

Center for Intellectual Property Strategies

The freely distributed VCAD system: supporting the Japanese style of production engineering

The VCAD system created by RIKEN supports the Japanese way of production engineering. Its strength is that it can import not only shapes, but also physical properties and actual measurements of objects, and use them in functional analysis simulations. The VCAD system can seamlessly handle the sequences of manufacturing processes. The system began with the release of nine basic VCAD software packages in July 2006. At present, ten packages are available for free distribution. There is a plan to expand into life science research in the future. The system is expected to have applications beyond manufacturing and be used as a basis for scientific and technological research.

Two aspects of "things"

The Japanese way of production engineering is classed as "on-site and actual object"—a way of working where highly experienced engineers at manufacturing sites solve any problems that could not be fully resolved at the design stage. This is done by repeatedly matching and rebuilding actual objects (prototypes). Although this process enables the development of highly finished and high precision products, the cost and manpower involved are huge.

"There are two types of things, things that exist and things that don't exist. CAD is a tool that can represent something that doesn't actually exist except inside the designer's head. In contrast, a measuring instrument is a tool for use with something that actually exists." The program's director, Akitake Makinouchi, considers that the "on-site and actual object" system needs to be able to handle these two types of things at the same time, and that it is necessary to seamlessly bridge the two processes of design and manufacture. At present, however, CAD tools are limited to merely drawing the shape of objects. They cannot incorporate information on the content of an object, its inner structure and physical properties, obtained by measuring it. Hence the Volume CAD (VCAD) system was developed.

A new format for data

One of the strengths of VCAD is its data format. Conventional CAD represents the shapes of objects with lines and planes, but VCAD represents them as aggregates of small boxes called cells. Each cell holds information. For example, the outline of an object is represented as a plane through the cells. The same cells can store physical properties such as the elasticity and density of each part, and they can also store the structure of the object obtained as a result of actual measurements. This means that each cell contains all the

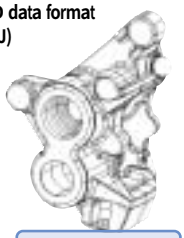
Akitake Makinouchi
Program Director
VCAD System Research Program
Center for Intellectual Property Strategies

Overview of the VCAD system and downloadable software

Importing a motorcycle part into the VCAD system

From design data to the VCAD system

Data conversion from commercially available 3D CAD format to the VCAD data format (VOBJ)



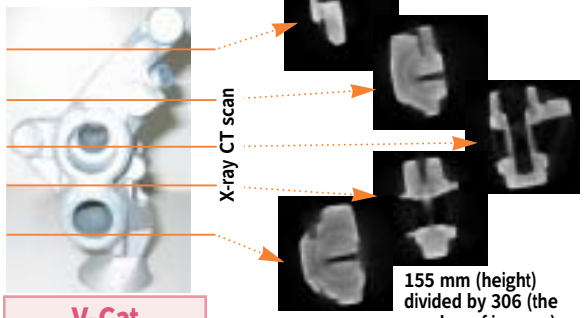
CAD data

V-Objcreator

Input

From measurement data to the VCAD system

Generation of a VCAD data format (VOBJ) 3D model from an actual 3D image



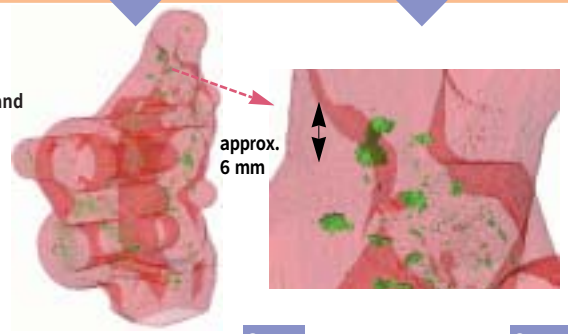
155 mm (height) divided by 306 (the number of images) = approx. 0.5 mm pitch

V-Cat

Input

VCAD Framework

The system's core, which can generate and edit VCAD models



Close-up

Analysis model showing casting defects

(Number of elements: 1,968,666
Number of nodes: 875,288)

Output

Structural analysis

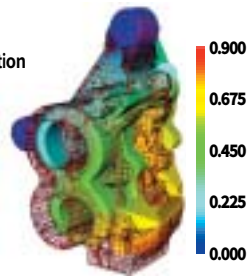
Using VCAD models to simulate the strength and deformation of products

V-DualGrid

Structural analysis settings

V-Struct

Structural analysis computation



V-X3D

Deformation (mm; magnified 30 times)

Output

Thermo-fluid analysis

Using VCAD models to simulate fluids inside products

V-Sphere

V-Sphere-SvCubes2D

V-Isio

Output

Forming and casting analysis

Using VCAD models to simulate forming and casting processes with metal molds

V-Cast

V-Forge

V-Stamp

Output

Fabrication system

Generating data for product-machining tools with VCAD models

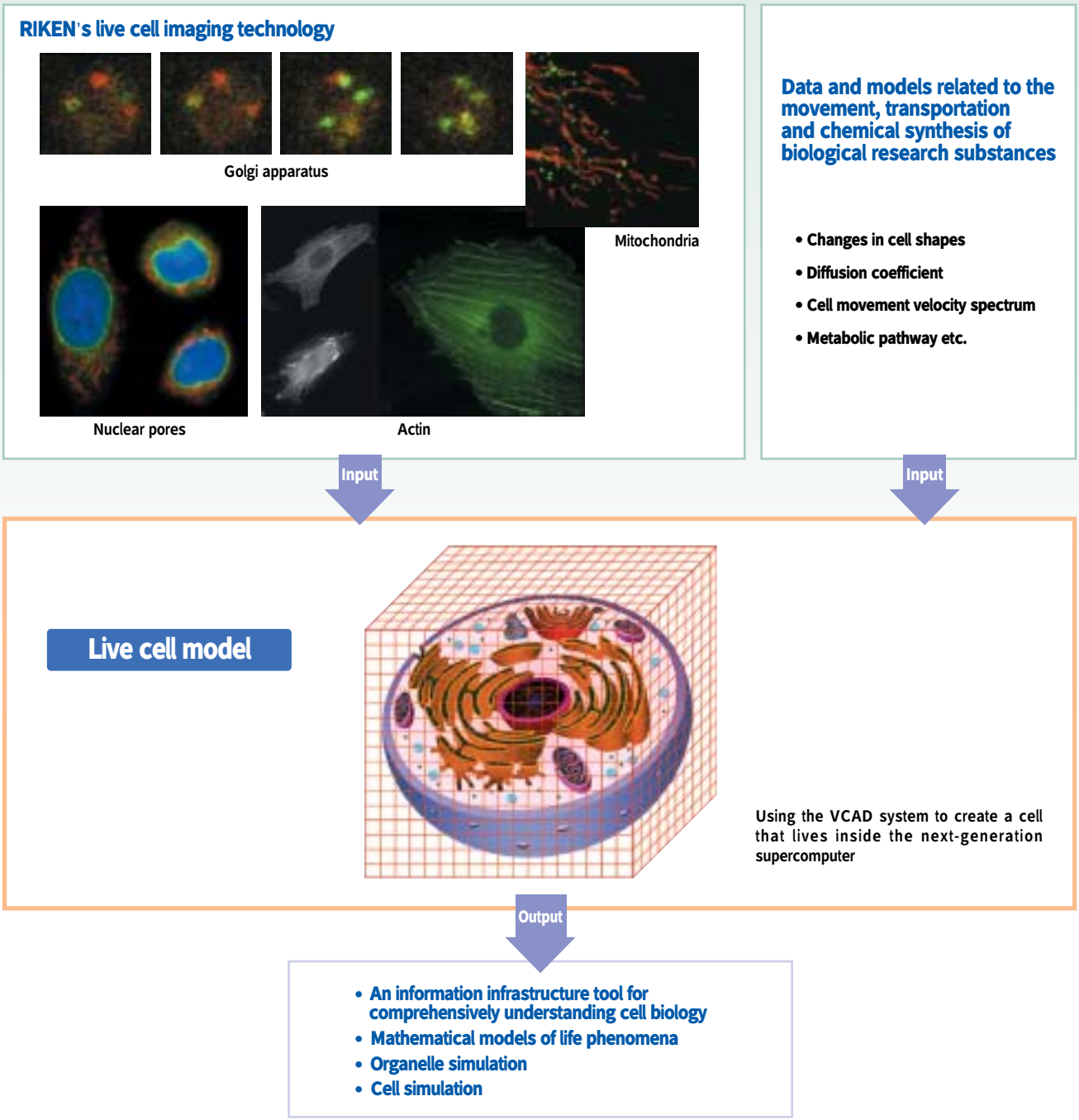
N-Cam

V-CAM

Downloadable software. Ten software packages are currently available (June 2007).

Software under development. To be released in the future.

Live cell modeling



information on that location, and hence the system is able to represent the entire object while also holding information about all its parts.

The most impressive aspect of VCAD is its ability to do computer analysis of objects that actually exist. “For example, if you take an image of an engine using an X-ray CT scanner or some other apparatus and import the data into a computer, you can then obtain a 3D model of the actual, existing engine. This is called X-ray CT measurement. And then by using that model, you can check for shape and other defects such as casting pores—pores inside the metal created in the casting process. Moreover, you can carry out structural and fluid analysis on the computer.” The VCAD system makes it possible to know the special characteristics of a product more precisely, using a computer for measurement. This should play an important role in improving product reliability.

In addition, the software’s functions can easily be enhanced. Since conventional CAD software is designed for drawing, it needs to be combined with other software to be able to perform functional analysis. The problem with this is data compatibility. A huge amount of coordination is required just to transfer data from one piece of software to another. The VCAD system’s data format, on the other hand, is completely unified. VCAD does away with the cumbersome tasks required to overcome compatibility problems, because the shape models are created and the simulation handled using the same data format. This is expected to dramatically reduce both cost and time.

Free distribution of software

In order to start using the VCAD system, users need software to import information into the VCAD framework. Makinouchi and his colleagues have developed software that converts shape data from commercially available 3D CAD systems to the VCAD format, and software that integrates the sectional views obtained with X-ray CT measurement or MRI scanner measurement and converts them to VCAD-format data as a 3D model.

Software for structural and fluid analysis has also been developed, in order that the VCAD system can be used in functional analysis. Nine software packages that are essential for starting to use the VCAD system are currently available for free distribution (at http://vcad-hpsv.riken.jp/). And in order to make the VCAD system easier to use and more versatile, new software and new functions are planned, and the distribution service will be expanded and improved.

Applications to life science research

Applications of the VCAD system are not limited to manmade objects. A project has been launched to simulate living cells on a computer. Local intracellular phenomena are gradually becoming understood through painstaking research. However, there has been almost no research that deals with a single cell as an entire system, for example, studying how substances move within the whole cell, how subcellular organelles are arranged in three dimensions, and how they divide.

"With the VCAD system, we're trying to import a cell into the computer as it is. It's the world's first 'live cell modeling.'" One laboratory at RIKEN is leading the world in live cell imaging technology. It plans to create a model of a cell by importing the data obtained on subcellular organelles by other labs into the VCAD system. "As the next step, we hope to perform simulations using this cellular model on a computer. If this is possible, we might even be able to control and improve cells and engineer them. "

Live cell modeling has already been selected as one of the fields RIKEN's next-generation supercomputer will be used for, so this research is expected to accelerate. There are great hopes that the Japanese-style VCAD system will play a major role in building bridges between science and technology.

DIRECTOR'S MESSAGE

The "baton zone" for technology transfer

Director, Center for Intellectual Property Strategies **Eiichi Maruyama**

Q. What projects did you launch in fiscal 2006?

A. The VCAD System Research Program was launched in April 2006 in response to strong demand from industry. The program is to be continued for five years. By limiting the term of the project, we hope to achieve a seamless transfer of our research results to industry.

We also have the RIKEN Ventures program which has become quite active. Our researchers are starting their own companies to accelerate practical applications and propagate their research findings. As of March 2007, there are 21 RIKEN venture companies.

Q. What was the most outstanding achievement in fiscal 2006?

A. The Integrated Collaboration Research Program with Industry. From its start in 2004, the technology transfer success rate has always been over 40% and is now nearly 50%. At nano tech 2007 held in February, the Innovative Nanopatterning Research Laboratory program was highly evaluated for its successful technology transfers to businesses and won the grand-prize award. The Integrated Materials Research Laboratory completed its team mission by successfully transferring technology to Toray Industries, and one of the RIKEN ventures, OM Chem Tech, succeeded in transferring its technology to Bridgestone. In addition, as an investment support framework for RIKEN venture businesses, the RIKEN Business Investment and Consultation Limited Partnership, established through the RIKEN Venture Capital Corporation, has invested in two RIKEN venture companies. We continue to strive to form new relationships with industry in order to continue the "RIKEN spirit," the Okochi spirit, and to promote new ideas.

Q. What future plans does the center have?

A. We will actively listen to the ideas and proposals we receive from our industrial partners. In order to make a seamless "baton zone" for technology transfer, we will provide unwavering support for technological development, both in organizational and financial terms. We will continue to promote a RIKEN that is useful to the world through our various activities, and that serves society in order to accelerate the procurement of external funds for energizing further research and development.

BioResource Center

Mass-producing red blood cells from cord blood to relieve blood shortages

RIKEN has developed a new method of producing red blood cells from the blood found in the umbilical cord connecting a baby and its mother. Conventional methods use cells from mice to culture red blood cells, but RIKEN's new method uses nothing but human cells. These new red blood cells can be transfused to people without risk of rejection or infection. The method is suitable for mass production, and so we hope it will relieve the chronic shortage of blood for transfusions.

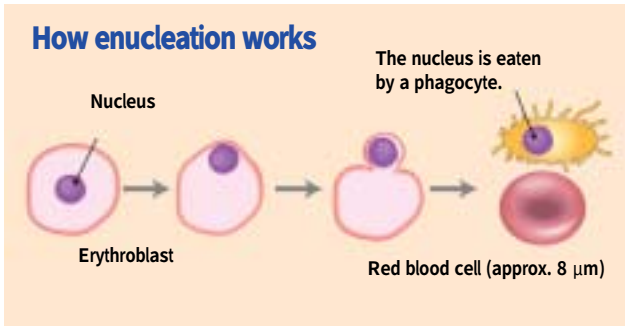
Blood stem cells in cord blood

Blood is produced in our bodies every day. Red blood cells, for example, have a lifetime of about three months, and every day about fifty milliliters of new red blood cells are produced to replace old ones. Blood stem cells produce the red and white blood cells and blood platelets that constitute blood. It used to be thought that blood stem cells were only found in bone marrow. However, today we know that they are also found in abundance in umbilical cord blood. Blood stem cells from cord blood multiply faster than those found in bone marrow, and cause fewer rejections.

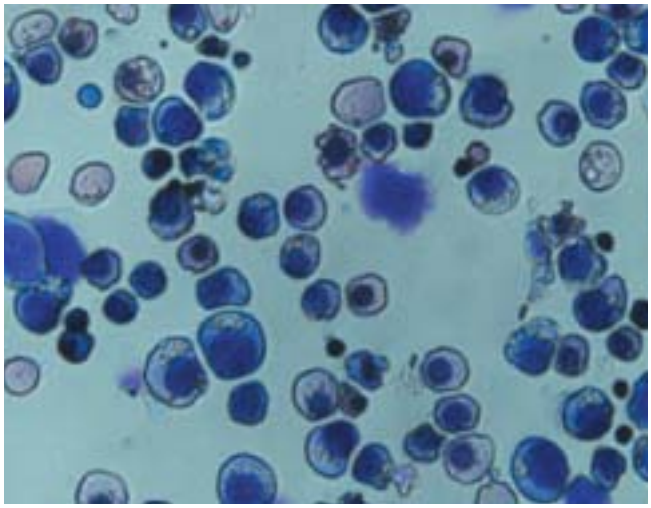
At present, eleven umbilical cord blood banks in Japan hold donated cord blood frozen for use in transfusions for leukemia patients. However, these transfusions only use cord blood containing at least six hundred million cells with a nucleus. In the past, cord blood not meeting this standard was discarded. But now, with the cooperation of five blood banks, the discarded blood has been made available for research. "Blood which can't be used for transfusions is just going to be thrown away anyway, so if the donor gives consent, there aren't many ethical problems. We're cultivating stem cells from this discarded cord blood to try to make red blood cells," says Yukio Nakamura, the director of the Cell Engineering Division.

The enucleation problem

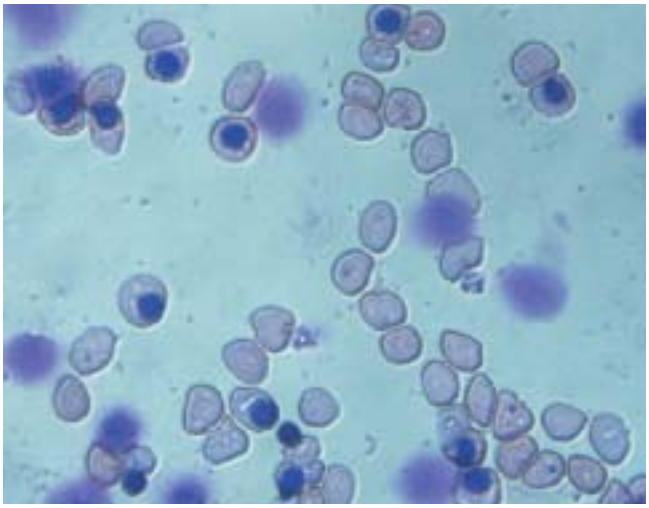
Red blood cells are grown from blood stem cells using a nutrient-containing agent called a culture medium. Up to now, red blood cells have been mass-produced from mouse cells. However, using mouse cells means there are risks of contamination from microbes within the cells and rejection caused by constituents of the mouse cell. A safer artificial culture medium to produce red



Yukio Nakamura
Director
Cell Engineering Division
BioResource Center



Cells before enucleation



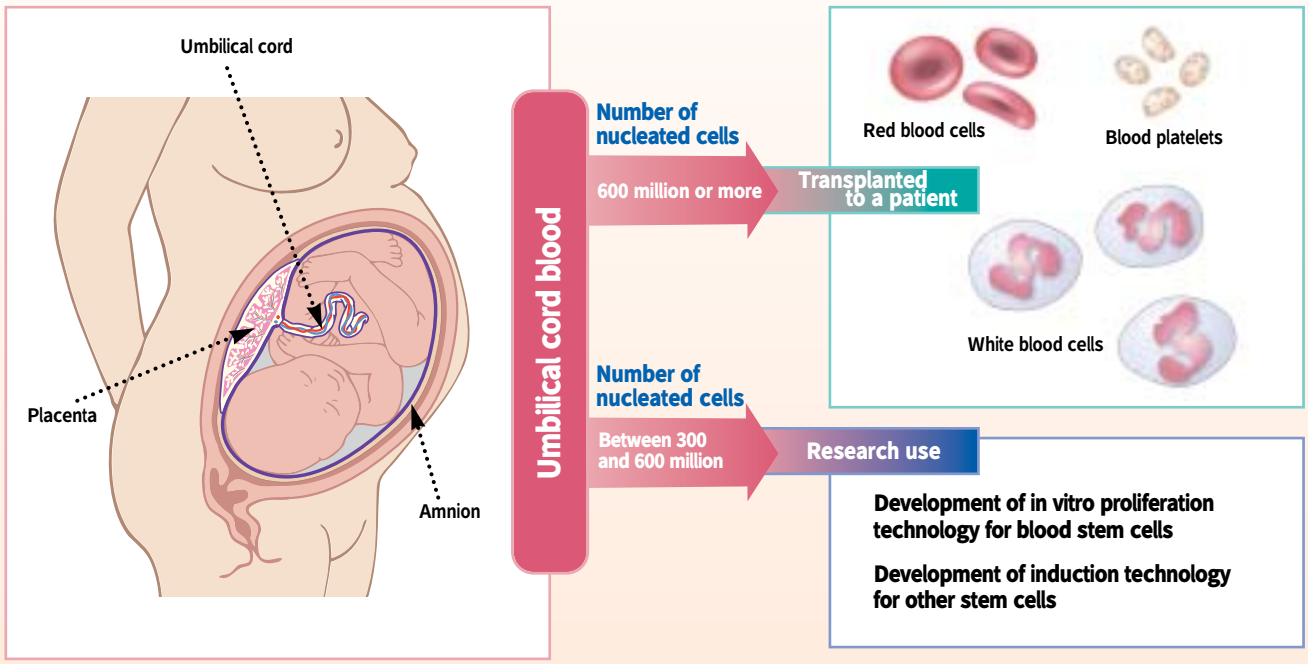
Cells after enucleation

blood cells was tried, but it could not successfully mass-produce cells. The obstacle to mass production using an artificial medium was the enucleation of the red blood cells.

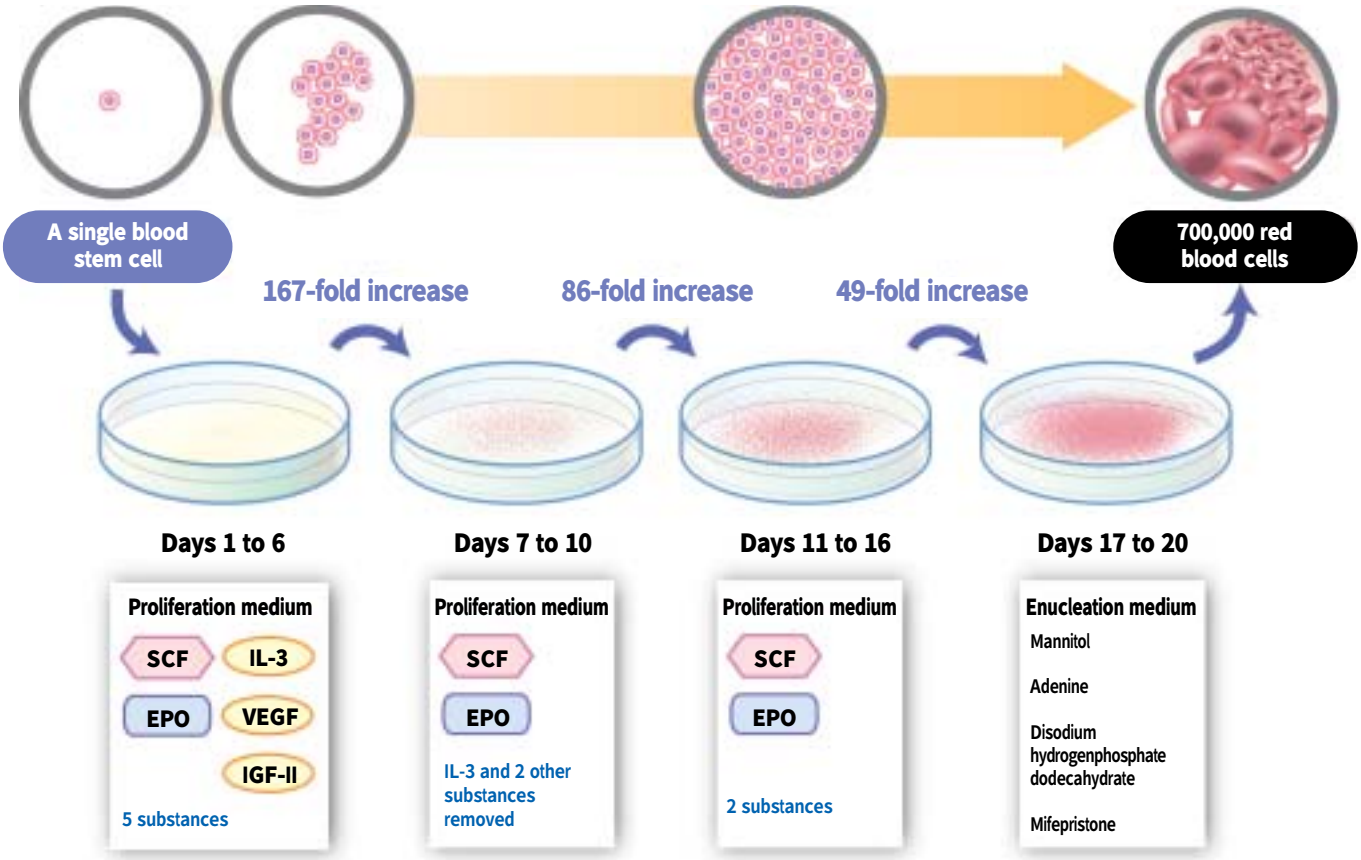
Enucleation is the following process. Because red blood cells do not have a cell nucleus, they are flexible and can change their shape to flow through fine capillary blood vessels and deliver oxygen to every part of the body. When a blood stem cell differentiates into a red blood cell, it first becomes a cell called an erythroblast. As the erythroblast matures, its nucleus emerges from one of its sides in a process similar to cell division. The cell empty of its nucleus is now a red blood cell.

When mouse cells are used for the culture medium, 100% of the erythroblasts can be enucleated. Although the artificial medium could mass-produce erythroblasts, only 20% to 30% of the erythroblasts produced could be enucleated. It was not clear how enucleation worked, or how it could be stimulated.

Uses of umbilical cord blood



Culturing of red blood cells from erythroblasts on an artificial medium



Better enucleation on an artificial medium

"Actually we weren't thinking about enucleation." The initial purpose of the research was to increase the number of red blood cells that could be produced from a single blood stem cell. "Before we did this research, we were using agents called VEGF and IGF-II to stimulate the proliferation of blood cells from monkey-embryo stem cells. Because these substances worked rather well, we thought that VEGF and IGF-II would be effective for poorly differentiated blood system cells. So we thought that these substances might be effective in proliferating red blood cells from human blood stem cells."

However, adding VEGF and IGF-II to the artificial medium did not increase the number of cells as much as expected. "They only increased by ten or twenty percent, which wasn't very much. But then we had a surprise. When VEGF and IGF-II were used in the early stages of culturing, the enucleation was very good." Enucleation rates in the artificial medium, which had been only 20% to 30%, rose to as much as 80%.

Most important in achieving a higher enucleation rate was the administration of VEGF and IGF-II, but there was another key substance. At the start of the culturing, the artificial medium contained five different substances including VEGF and IGF-II. It was discovered that enucleation could be stimulated by removing a substance called IL-3 from the medium from the seventh day onwards.

A universal system for blood transfusions

With the new method, 700,000 red blood cells can be produced from just one blood stem cell. Enough blood for one transfusion can be produced from the cord blood of a single baby.

Moreover, because quality control is easier, artificial mediums are more suitable for industrialization. "Because it doesn't use any cells or proteins from non-human species, it can be applied clinically as soon as culturing of large quantities can be achieved. Although a million babies are born every year in Japan, we only store less than ten thousand of their umbilical cords at the moment. It's important to establish a nationwide system for collecting cord blood."

Nakamura's next goal is to produce a cell strain of erythroblasts. A cell strain means a cell that can be semi-permanently cultured on a medium while maintaining its original characteristics. Establishment of a human cell strain is difficult, and so far the only strains of human cells which have been successfully established are cancer and embryo-stem cells. Embryo-stem cells can differentiate into any kind

This tank, refrigerated with liquid nitrogen, stores the umbilical cord blood of 7000 people. At a temperature of −196°C the cells can be stored almost indefinitely.

of cell, and so they should play an important role in regenerative medicine where tissue is artificially produced and transplanted. Some people worry that transplanted tissue may proliferate abnormally and cause cancer. "Red blood cells don't have a nucleus, so they can't proliferate, and there's no risk of them causing cancer. If we can establish cell strains corresponding to the eight ABO and Rh± blood types, we'll be able to supply any type of blood on demand."

Henceforth, RIKEN is planning to do research on the establishment of an erythroblast strain. Due to a falling birth rate and an aging population, the number of people needing blood transfusions is expected to increase just as the blood-donating younger population decreases. Nakamura and his team hope that their results will support the blood transfusion systems of the future.

DIRECTOR'S MESSAGE

Aiming to be the world's most advanced bioresource facility

Director, BioResource Center **Yuichi Obata**

Q. What are some of your noteworthy achievements in fiscal 2006?

A. A large quantity of bioresources was transferred to our center in 2006. They included approximately 3000 micro-organism cultures from the Institute of Molecular and Cellular Biosciences at the University of Tokyo, cell samples from 5000 individuals of the Mongoloid race from Professor Sonoda of Kagoshima University and Director Tajima of the Aichi Cancer Center Research Institute, cell samples from 50 progeria patients from Professor Goto of Toin University in Yokohama, and cell strains from the Cell Resource Center for Biomedical Research of the Institute of Development, Aging and Cancer, Tohoku University. These transfers demonstrate the high degree of trust the research community places in our center and our ability to make an important contribution by preserving these valuable resources. In addition, our Bioresource Engineering Division successfully developed a freezing method for preserving mice. This is an achievement that goes beyond the bounds of what has become accepted as common sense in our field. We expect it will be useful for the efficient preservation and transportation of laboratory animals.

Q. Have you launched any new projects?

A. Our center has been conducting training programs in the utilization and handling of bioresources since 2004. Since then a total of 72 people have participated, from both academia and industry. In 2006, we opened our doors to foreign participation and accommodated three engineers from Taiwan and a key Chinese researcher for a month of training. Our center will continue to play a leadership role in developing resources comparable to those in Western countries while making the most of Asian qualities.

Q. What are the future prospects for the center?

A. With trust, sustainability, and leadership as our primary principles, we will endeavor to promote RIKEN BRC as a "brand." We will strive to improve both our quantity and quality in order to establish an efficient supply framework. In addition, to demonstrate that we are trustworthy leaders in the field, we intend to undertake a variety of new research projects. Science is the "Foundation for Discoveries and Access to the Future." As research scientists we must work for the benefit of all mankind.

RIKEN SPring-8 Center, SPring-8 Joint Project for XFEL

Successful lasing with an X-ray free electron laser prototype accelerator

RIKEN has set up the SPring-8 Joint Project for XFEL (the SPring-8 Joint Project) to build an X-ray free electron laser (the XFEL), in collaboration with the Japan Synchrotron Radiation Research Institute (JASRI). In June 2006, an XFEL prototype accelerator successfully created a free-electron laser in the vacuum ultraviolet range. When XFEL, the so-called dream light source, becomes available, it will enable major progress in the structural analysis of proteins and the development of new materials, which is expected to lead to the creation of new fields of science. The successful lasing of the prototype accelerator is a major step toward this.

XFEL: the "dream light"

X-rays are well known from their uses in medicine, but they are also widely used in advanced science. When observing objects, nothing smaller than the wavelength of the light can be seen. To observe smaller objects, a shorter wavelength needs to be used. Using X-rays even the individual atoms of an object can be seen. SPring-8, in Hyogo prefecture, can produce the brightest light in the world over a wide range of wavelengths including X-rays, and is being used in life science and materials science research.

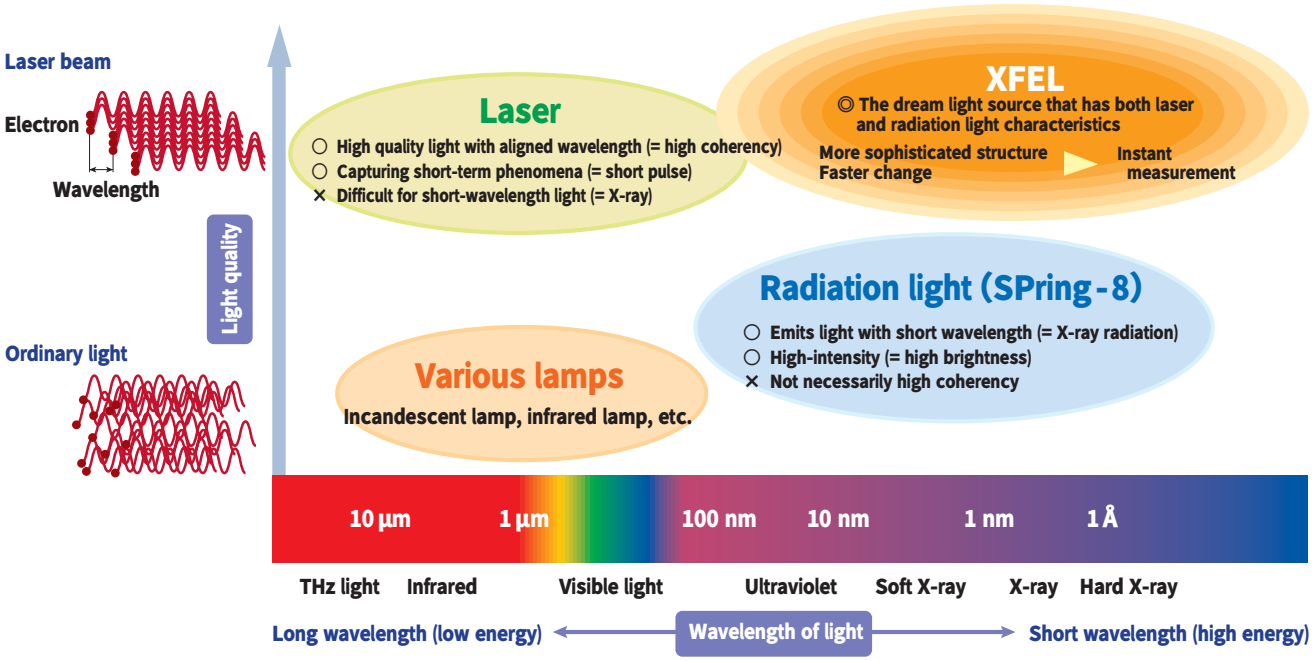
The X-rays produced at SPring-8 are ten billion times brighter than the sun. However, the peaks and troughs of the light waves are not aligned. Laser light is light with its waves aligned. The light produced by the XFEL will be a billion times brighter than SPring-8. A brighter light will be a major step forward and enable us to observe faster movement in a smaller region.

The site where the XFEL facility will be built

The XFEL facility (red border) will be next to SPring-8 (the circular building). The yellow border shows the prototype accelerator.

In Japan, the SPring-8 Joint Project between RIKEN and JASRI has been developing the XFEL with the aim of completing it in fiscal 2010. The prototype accelerator which succeeded in creating a laser beam this time has basically the same structure as the XFEL itself will, and was designed for use in demonstration experiments that can check the component technologies needed for the actual XFEL.

What is an X-ray free electron laser?



Three new technologies for the XFEL

XFELs are also under development in the United States and Europe, but the XFEL facility planned in Japan is the most compact, with a total length of 700 meters. In order to achieve a working XFEL of this size, the team developed three original technologies: a monocrystal cerium boride thermal electron gun, a C-band accelerator, and an in-vacuum undulator.

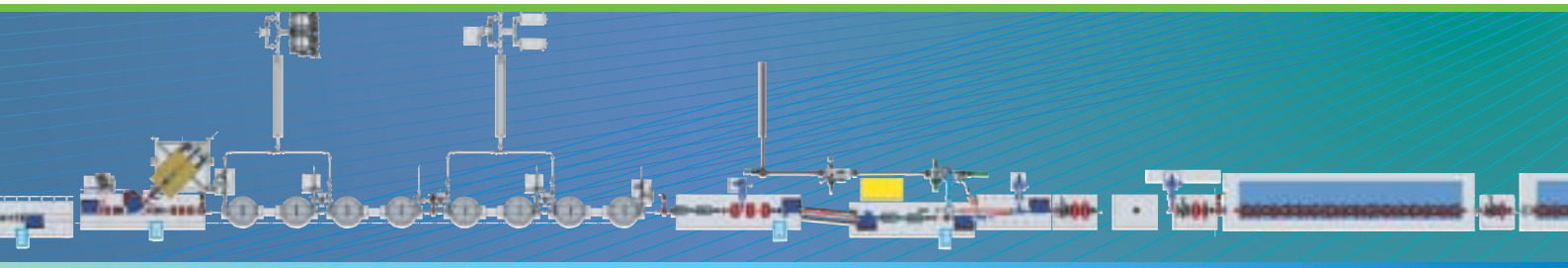
Lasing requires the production of a dense and narrow electron beam. The monocrystal cerium boride thermal electron gun can generate the narrowest electron beam in the world. The beam is then accelerated with a high-frequency electric field. Since the C-band accelerator uses a frequency of 5712 MHz, twice as high as conventional, only half the usual distance is required for the acceleration.

Next, the accelerated electron beam passes through the undulator. In traditional free-electron lasing, the light generated with a zigzagging electron beam is reflected back and forth using the mirrors in the undulator, and the phase of the light is aligned as it repeatedly interacts with the electron beam. However, this method would not work with X-rays, because they pass through mirrors.

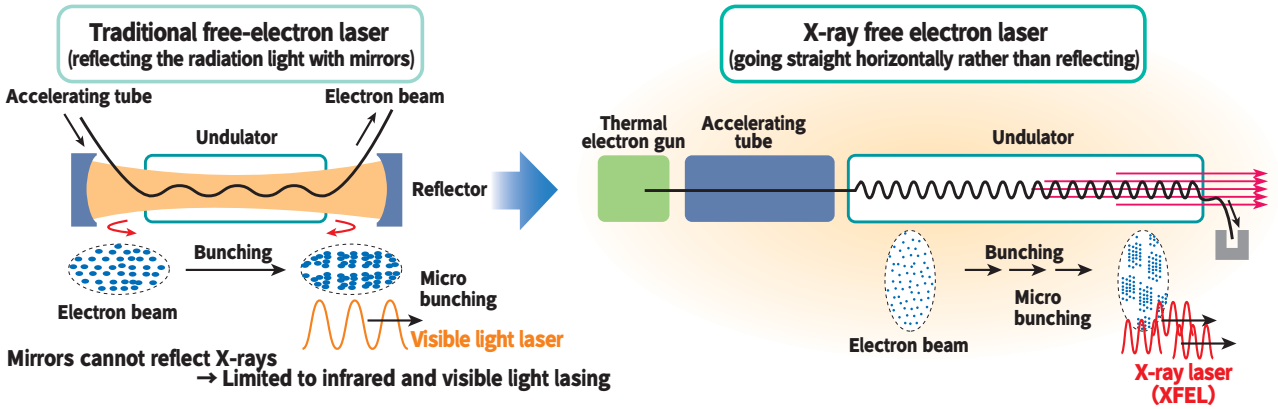
Therefore, several undulators are aligned separated by a length equivalent to the distance of return, so that the phase of the light becomes aligned by a similar kind of interaction as the electron beam and light go through them. Whereas magnets are usually located outside the vacuum chamber, the in-vacuum undulator has magnets sealed within it, so that the width of the magnets can be 15 mm, half the conventional size. This contributes to the reduction of size of the whole facility. Insiders call these three original pieces of technology, which are the key to building the XFEL, the "three sacred treasures," after the three imperial regalia of the Japanese emperor.

Insisting on stability

After all the components were ready in May 2006, the project team started to adjust the system so it would produce a fine dense electron beam. "Every single beam was observed and fine adjustments were made over and over again. Since we have a very good understanding of each process of the thermal electron gun, we can refer to the results of prior simulations and refine the adjustments step by step. In addition, the electron gun itself is highly stable, and the operating status of the prototype accelerator can be accurately monitored based on previously obtained results. Therefore, beam performance could be smoothly improved up to the target level," says Team Leader Hitoshi Tanaka.



Principles of the X-ray free electron laser



Thermal electron gun

C-band accelerator

In-vacuum undulator

The prototype accelerator successfully produced a vacuum ultraviolet laser beam. It is comprised of a thermal electron gun, two S-band accelerators, four C-band accelerators, and two undulators, and has a total length of about 60 m. On the other hand, the XFEL facility (planned for completion in fiscal 2010) will have an electron gun, two L-band accelerators, eight S-band accelerators, 128 C-band accelerators, and 20 undulators, and a total length of 700 m.

Full picture of the prototype accelerator

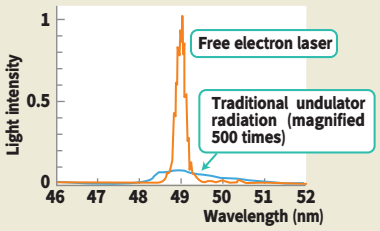
On June 20, 2006, an electron beam generated by the thermal electron gun was delivered to the undulator, and a vacuum ultraviolet laser was fired at a wavelength of 49 nm with maximum output of 110 kW. This was an extraordinarily quick accomplishment—the lasing was achieved just a month after beam adjustment commenced. In fact, while the monocrystal cerium boride thermal electron gun is suitable for generating fine beams, its electron density is comparatively low. Therefore, the electron density needs to be increased during the process of beam acceleration. In some cases this can be a very time-consuming task. However, adopting a thermal electron gun with familiar characteristics allowed for shortcuts in achieving a stable laser.

"If a stable laser is used, better experiments can be performed. Previously, people considered that any kind of electron beam would be good enough. However, they now demand quality, so we use every scrap of knowledge we can to try to improve it. And as a result, we've succeeded in producing a highly stable laser that can easily be reproduced. This experiment showed that it should be possible to produce a laser in the X-ray range," Deputy Director Noritaka Kumagai confidently stated.

Creating a new world of science

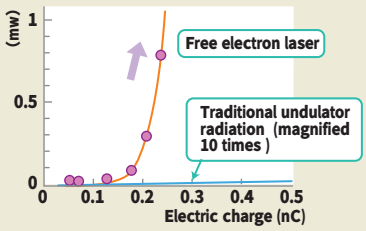
When the XFEL becomes available, proteins that can currently be observed only in crystallized form will be able to be viewed even as single molecules. In addition, the planned XFEL will enable observation of objects every 100 femtoseconds (in other words, every 10 trillionths of a second). If used as a strobe light, the XFEL will make it possible to observe how chemical reactions proceed in cells or substances frame by frame. Furthermore, the high energy of XFEL could be used for synthesizing new materials.

Spectrum comparison



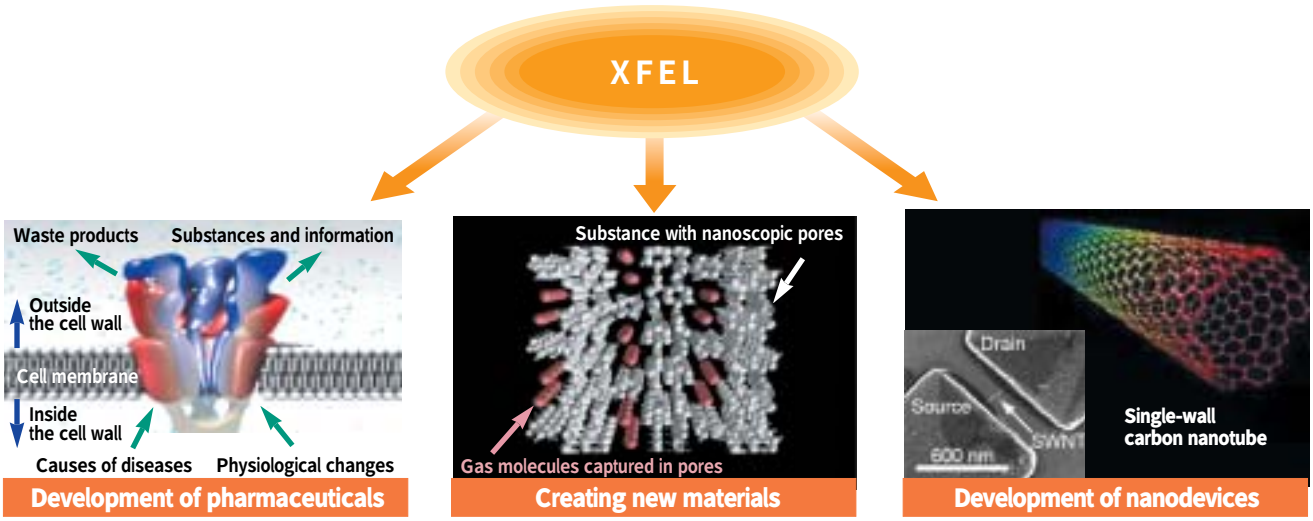
Laser beam spectrum. At a wavelength of 49 nm, the light emitted is 6000 times stronger than with the traditional undulator.

Peak power comparison



Peak power of laser beam. When the electric charge increases, the laser beam power increases exponentially. This is laser oscillation.

What will the XFEL make possible?



The XFEL will make a significant contribution to the structural analysis of membrane proteins, which will be useful for pharmaceutical development.

Movement of atoms and molecules can be directly observed. This will contribute to the design and development of new materials.

Evaluation and analysis become possible at the atomic and molecular level. This will make contributions to the development of nanodevices.

"The initial goal is to instantaneously capture the atomic world. However, as I felt when I worked on the SPring-8 project, I am sure that XFEL will also contribute to unknown fields beyond our expectations," says research scientist Makina Yabashi.

The vacuum ultraviolet laser produced by the prototype accelerator is also important in itself. It is scheduled to be used in a variety of research experiments from autumn 2007. Looking forward, Tanaka and his team members will continue to do demonstration experiments using the prototype accelerator. They continue to put their full efforts into the development of the world-leading XFEL.

DIRECTOR'S MESSAGE

Sciences of the photon, by the photon, for the photon

Director, RIKEN SPring-8 Center **Tetsuya Ishikawa**

Q. What are some of your noteworthy achievements in fiscal 2006?

A. We succeeded in developing a spectrometer that can instantly capture the color of the X-ray Free-Electron Laser (XFEL) beam. This device will play a valuable support role in XFEL experimentation. We also reached an understanding of a system that controls the recording speed of a DVD-RAM. This finding, for which the high-intensity radiation of SPring-8 was used, will contribute to the development of materials used in high-speed mass-storage optical media. In biology, we succeeded in structurally analyzing various proteins including sphingomyelinase, which produces ceramide, a substance necessary for maintaining healthy skin, "Cut A1," a protein having the highest thermal stability, and a "proton pump" which could lead to the realization of bio-nanomachines.

Q. What are some projects that you have recently launched or completed?

A. The Advanced Protein Crystallography Research Group has just finished its research and made a large contribution to establishing a foundation for X-ray crystallography of proteins. The Quantum Materials Research Group has also concluded its research. This group used the high-intensity radiation light of SPring-8 to study substances in terms of their magnetic, electronic, and nanotechnological properties. A new group is the Structural Physiology Research Group, recently launched to perform structural studies through a combination of X-ray analysis and microscopy with the aim of elucidating the physiological functions of the bimolecular complex that is responsible for cell signaling. The SR System Biology Research Group also commenced work, taking a systems biology approach in aiming to understand the life phenomena of an entire cell, using an extremely thermophilic bacterium as a model organism.

Q. What are your plans for the future?

A. In 2007, SPring-8 celebrates its 10th anniversary, as does the RIKEN Harima Institute. Attention will continue to focus on the mission of promoting synchrotron radiation research centered on SPring-8, advancing research and development in the field of high-intensity radiation, and R&D on the next-generation synchrotron radiation source, while striving to construct the world's first operating XFEL facility in close cooperation with JASRI.

Center for Developmental Biology

Creating varieties of cells: studying the mechanism of asymmetric division

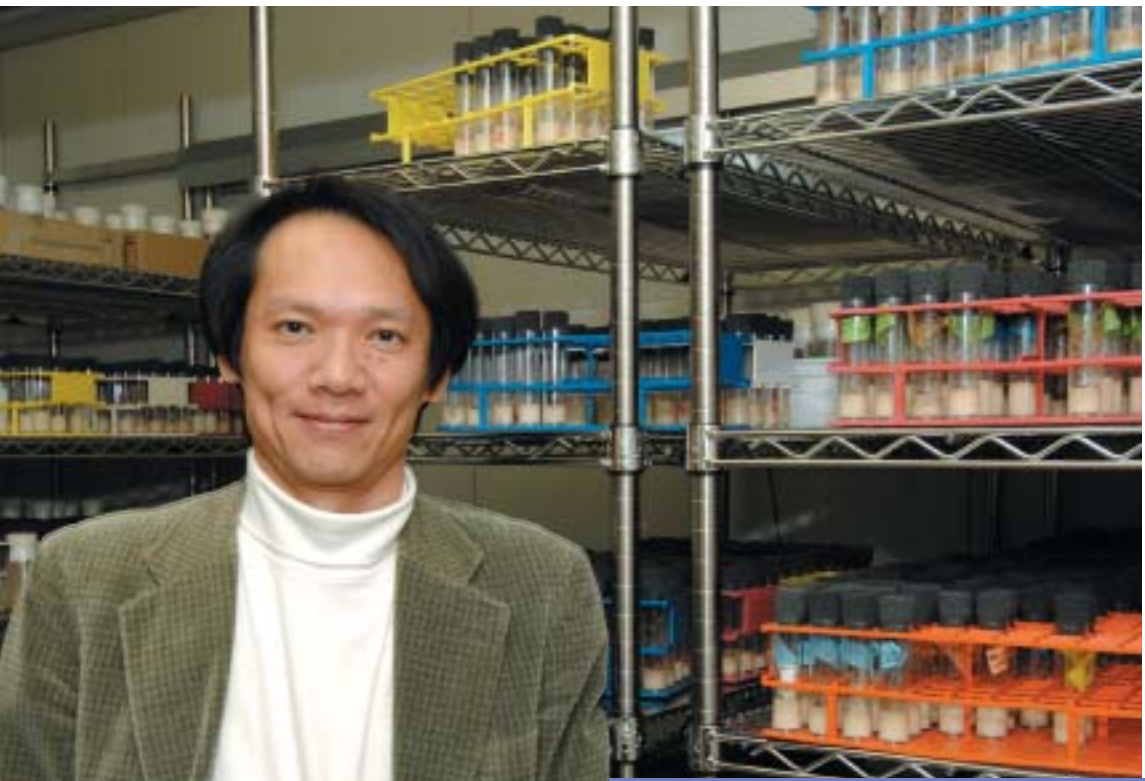
The human body consists of a variety of organs, which are comprised of cells having many different functions. Asymmetric division is one of the ways that cells of different types are generated. RIKEN has found a clue to understanding the mechanism of asymmetric division in the process of Drosophila neural development. This will shed light on the mystery of the emergence of multicellular organisms, and is expected to lead to an understanding of asymmetric division in vertebrates, including humans.

Asymmetric division's two roles in proliferation and differentiation

Multicellular organisms consisting of many cells grow from a single cell, namely a fertilized egg. In order for a fertilized egg to grow into an organism with all its necessary organs, it must first increase its number of cells and then produce different varieties of them.

For example, the brain of Drosophila (the fruit fly) is comprised of neural stem cells, neural mother cells, and various kinds of neurons and glial cells. First, the fertilized egg undergoes cell division and becomes an embryo, and then the epidermal cells, the equivalent of the epidermis of the embryo, move toward the center of the embryo and become neural stem cells. From these neural stem cells, other more differentiated cells develop.

Asymmetric division is essential for this process. Asymmetric division is when a mother cell splits into two daughter cells with different properties. "One of the daughter cells has the same properties as the mother cell, while the other has different properties. This mechanism is very effective in creating a variety of different cells and increasing their number," says Group Director Fumio Matsuzaki.

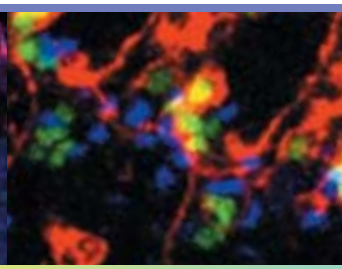


Matsuzaki's group constantly has around 1000 kinds of Drosophila mutants on hand.

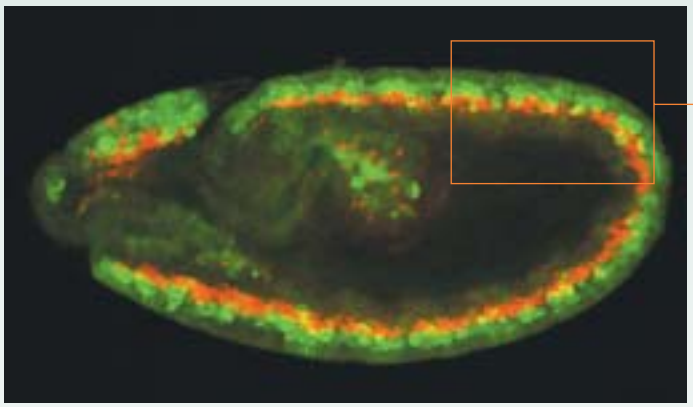
The orientations of polarity and division

How do the two daughter cells come to have different properties? In 1992, Matsuzaki discovered a type of protein called Prospero, which is produced by Drosophila neural stem cells and active in neural mother cells. In 1995, he discovered that only one of the daughter cells inherits the Prospero protein during the division of neural stem cells, and as a result the properties of the two daughter cells differ. The

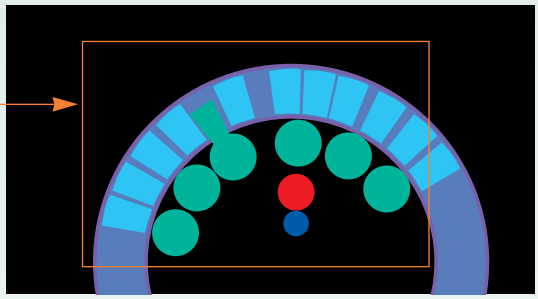
Fumio Matsuzaki
Group Director
Laboratory for Cell Asymmetry
Center for Developmental Biology



The neurogenesis of Drosophila



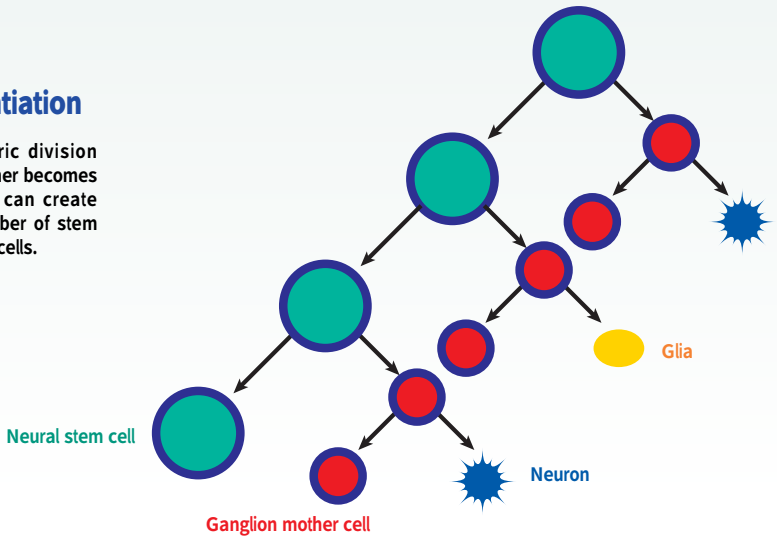
The embryo's outermost epidermal cells move inside and create neural stem cells (green). The image above shows the neural stem cells actively creating neural mother cells (red).



The epidermal cells identify the outside of the embryo as the front, and the inside of the embryo as the back. This is inherited by the neural stem cells and neural mother cells.

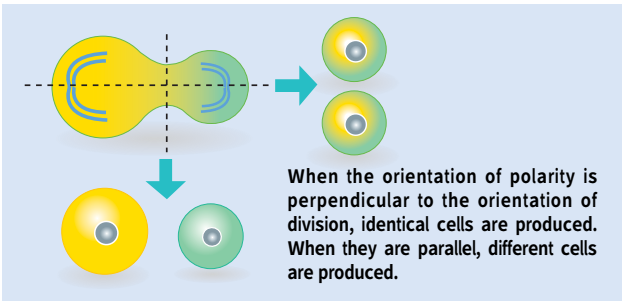
Both proliferation and differentiation

One of the cells produced from asymmetric division becomes identical to the parent cell, and the other becomes a more differentiated cell. This mechanism can create differentiated cells while maintaining the number of stem cells, which are the sources of different kinds of cells.

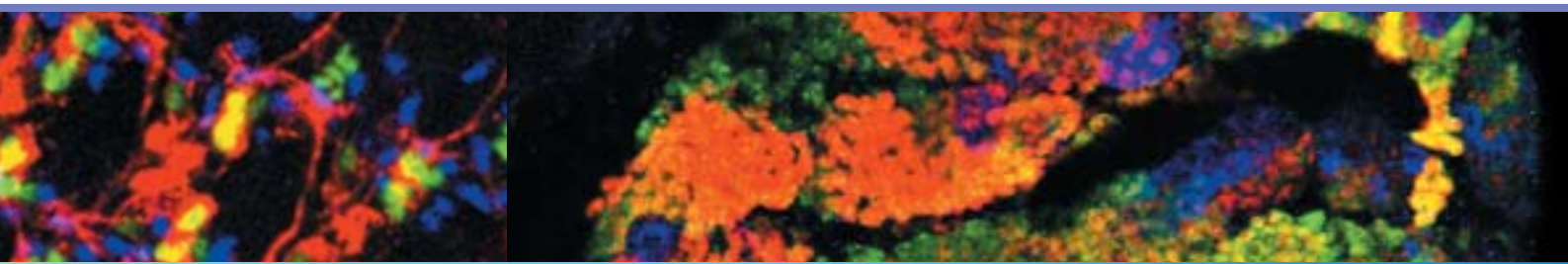


daughter cell that inherits the Prospero protein becomes a neural mother cell, while the daughter cell that does not inherit the Prospero protein becomes another neural stem cell, the same as the parent cell. A substance that determines the properties of daughter cells in this way is called a cell fate determinant. When cells are asymmetric, this is called cell polarity. "The parent cell being polar is important for asymmetric division."

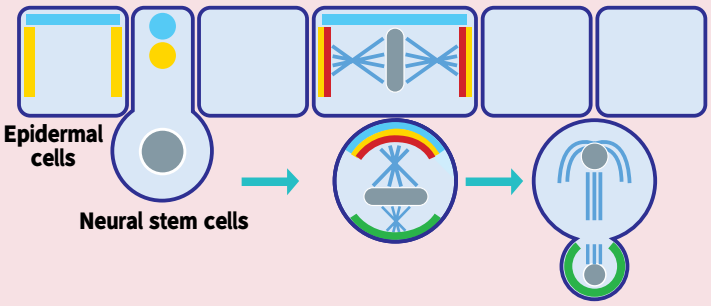
However, even when a cell is polar, the two daughter cells sometimes have the same properties. This depends on the orientation of the cell division. In fact, epidermal cells, the source of neural stem cells, divide into two identical epidermal cells even when they are polar. So the orientation of cell division is also an important factor in asymmetric division, along with whether the cell is polar or not. When the orientations of polarity and division match each other, two daughter cells with different properties can be created. "From past research, we understood quite a lot about how cells become polar. However, we didn't really understand how the orientation of division comes to match the orientation of polarity."



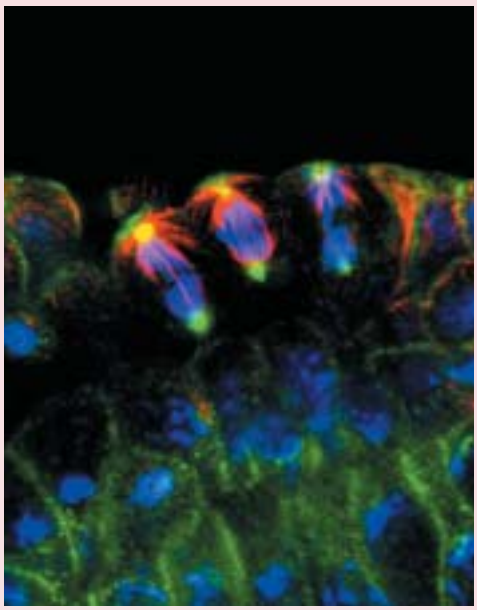
When the orientation of polarity is perpendicular to the orientation of division, identical cells are produced. When they are parallel, different cells are produced.



The Mud protein determines the orientation of division



There are two types of protein complexes (light blue and yellow) that create polarity in cells. One of them is the Pins-G protein complex (yellow). The Mud protein (red) is bound to the Pins-G complex and influences the mitotic apparatus in determining the orientation of division. In epidermal cells and neural stem cells, the alignments of the Pins-G protein complexes are different by 90 degrees, and so the orientations of the divisions are also 90 degrees different to each other. As a result, the epidermal cells undergo symmetric division and the neural stem cells undergo asymmetric division.



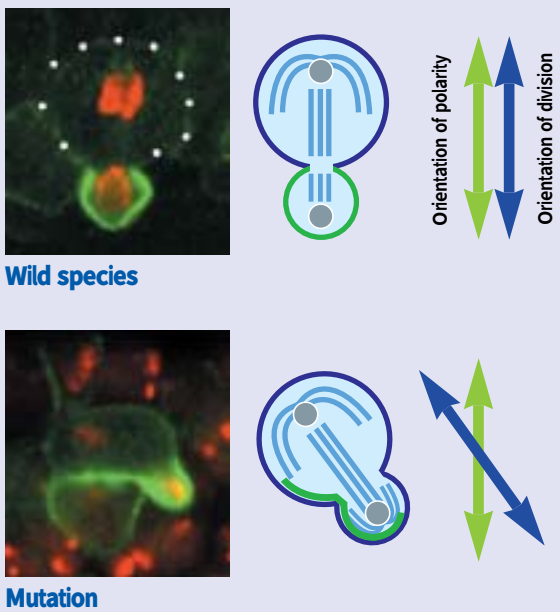
Asymmetric division of a Drosophila neural stem cell. The Mud protein, mitotic apparatus, and chromosome are green, red, and blue respectively.

Looking at the 90 degree difference

Matsuzaki's group artificially induced a mutation in a Drosophila gene, and then investigated the relationship between the orientation of the polarity and the orientation of cell division in the mutant Drosophila that were born. In this investigation, they discovered cells that were polar, as they should be, but where the orientation of division did not line up with the orientation of the polarity. If the gene that caused this abnormality could be found, it should allow the discovery of the essential factor that is needed for lining up the orientations of polarity and division. "Even though Drosophila has only a small number of genes, this factor is still not easy to find. We knew that it must exist somewhere. But we couldn't find it straight away."

During the search, Yasushi Izumi, one of the members of Matsuzaki's group, attempted to resolve this problem from a different angle. As described above, both epidermal cells and neural stem cells have polarity, but there is a 90 degree difference between the orientations of division. There are several types of proteins involved in the creation of cell polarity, one of which is a complex of the Pins protein and the G protein. This complex exists on the side of epidermal cells and at the top of neural stem cells, in positions that are at 90 degrees to each other. "This led us to suspect that cells may be determining the orientation of division with reference to the position of this complex. Thus, we looked for substances that bind with this complex, and succeeded in finding a protein called Mud."

Disorder in the orientation of division



Correct division creates the correct structure

This discovery confirmed that the Mud protein combines with the Pins-G protein complex and guides the division into the correct orientation. The orientation of division is determined by the orientation of the mitotic apparatus, which takes chromosomes from the parent cell to the daughter cells. The Mud protein bound to the Pins-G protein complex controls the relationship between the orientations of polarity and division by pulling the mitotic apparatus in its own direction. The position of the Mud protein in the cell determines whether the cell continues to divide symmetrically, creating identical cells, or whether it undergoes asymmetric division to become more differentiated cells.

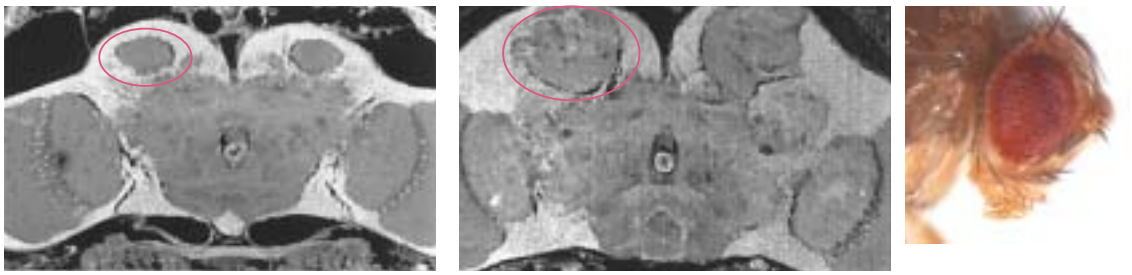
When the Mud protein cannot be produced correctly, the

orientation of division remains undetermined, and the cell may divide into an orientation different from how it was supposed to be. In fact, it was already known that when an insect gene that creates the Mud protein causes a mutation, the insect's brain deforms. The biggest abnormalities are found in the shape of the olfactory center. "This means that if one cell doesn't divide itself into the proper orientation, the brain will not be constructed properly."

Mammals have a protein very similar to Mud. One of these is NuMA, a protein often expressed in cancerous cells in humans. It is suspected that NuMA is related to the abnormal proliferation of cancer cells. "These results suggest that species share a common mechanism that controls the orientation of cell division." Matsuzaki is now extending his research to mice, and by comparing various species, working toward a full understanding of how different kinds of cells are created and how the structures of organisms are properly created.

Tomogram of Drosophila brain

Wild species **Mud mutation**



A Drosophila with a mutation in its gene that produces the Mud protein has an abnormally shaped olfactory center. The cause of this was discovered to be an abnormality in the orientation of nerve-cell division.

DIRECTOR'S MESSAGE

Contributing to both science and medicine through research in developmental biology

Director, Center for Developmental Biology **Masatoshi Takeichi**

Q. What are some noteworthy achievements of your center in fiscal 2006?

A. Our achievements directly reflect the great variety of research we conduct at our center. They include the control of gene expression with DNA methylase and the discovery of a new system for diversification and recognition of nerve cells. In addition, significant technical developments were made which could contribute to scientific research worldwide, including a method of efficiently performing PCR from a single cell, and a method of visually labeling individual cells. There were also many other research achievements which will contribute to the field of medicine including the discovery of a gene involved in the malignant processes of pediatric tumors of the nervous system, and the development of a technology for safely culturing stem cells.

Q. Have you launched any new projects at your center?

A. Masayo Takahashi, team leader of the Retinal Regeneration Medical Research Team, is undertaking basic research on regenerative medical techniques for the treatment of retinitis pigmentosa, one of the causes of blindness. Since the team has already successfully differentiated retinal photoreceptor cells from embryonic stem cells, this research is expected to make even further progress. We have only just started our translational research (TR), which allows our achievements in basic research to be used in clinical applications. Dr. Takahashi is the ideal TR researcher in this area of medicine since she is an experienced ophthalmologist.

Q. What future plans do you have for your center?

A. Our center has already produced excellent achievements in embryonic stem cell research. Additionally, in order to support embryonic stem cell research activities, particularly in humans, we have established the Division of Human Stem Cell Technology in fiscal 2007. Through this division we will be able to share the knowledge we have accumulated with other researchers. We will promote international exchange in the field of developmental biology, including providing support for the International Congress of Developmental Biology, the Asia-Pacific Developmental Biology Network, and the Asia Reproductive Biotechnology Society. Through these activities we will play a central role worldwide in developmental biology research, as well as making an important contribution to the growth of developmental biology throughout Asia.

YOKOHAMA 横浜

Genomic Sciences Center

MDGRAPE-3, the world's fastest special-purpose computer

Computer simulations are becoming widely used in scientific research. In June 2006 RIKEN announced the completion of MDGRAPE-3, a special-purpose computer for protein simulation. With a speed of one petaflops (10^{15} floating-point operations per second), MDGRAPE-3 is the fastest special-purpose computer in the world. It will lead to new knowledge and understanding of how proteins work and major advances in pharmaceutical development.

The ease of use of a general computer with the speed of a special-purpose computer

Between the atoms in a protein molecule there are several different forces at work: chemical bond forces, electrostatic forces, and intermolecular forces. MDGRAPE-3 is specially designed to perform molecular dynamics simulations of these complicated interactions. It calculates the forces between the atoms, and uses Newton's equation of motion to calculate how each one moves. The movements of the atoms can then be shown on a screen.

A handmade m-TIS circuit diagram from his student days

MDGRAPE-3 was developed by RIKEN's High-Performance Molecular Simulation Team, led by Makoto Taiji. In 1986, Taiji hand-built the m-TIS, a special-purpose computer for simulating how the properties of magnets change. Taiji came up with the idea of connecting a normal desktop computer with a special-purpose computer that would do certain calculations. "The desktop computer or workstation sends data to the special-purpose computer, which then does the calculations and returns the results back to the desktop computer. This configuration allows us to use the software on the desktop computer, so it is easier to set up and easier to use. It's also cheaper."

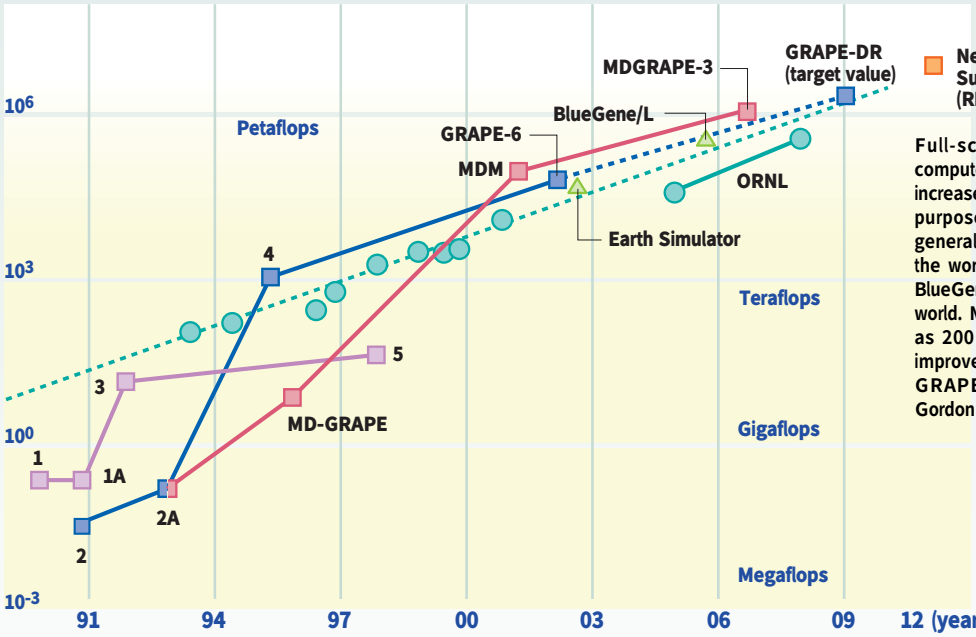
Later, Taiji was part of the team that built the fourth-generation machine for the GRAPE project, which started at the University of Tokyo in 1989. The GRAPE computers were special-purpose machines for astronomical simulation. The same configuration was used in GRAPE and its successor MDGRAPE-3.

Achieving one petaflops using broadcast parallelization

GRAPE was originally built to calculate the forces of attraction between stars. But it was possible to use it to simulate molecular dynamics by replacing stars by atoms and replacing gravity by the chemical bond force. "There are basically two ways of modeling nature. One is with 'fields.' For example, electric and magnetic fields have physical quantities at each point in space, and exert an effect via the surrounding field. The other is with 'particles.' Individual particles directly affect all the other particles at the same time. With stars and

Makoto Taiji
Team Leader
Genomic Sciences Center
Computational and Experimental Systems Biology Group
High-Performance Molecular Simulation Team

Increasingly fast special-purpose computers

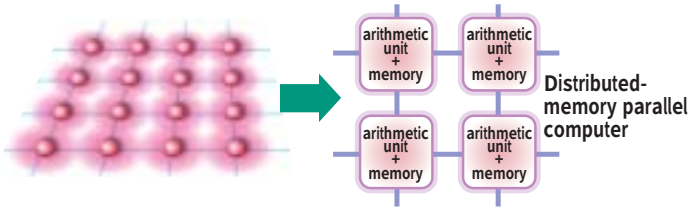


Full-scale development of special-purpose computers started in the late 1980s. Speeds have increased dramatically over the last decade. Special-purpose computers are somewhat different from general-purpose ones, but MDGRAPE-3 overtook the world's fastest computer, the general-purpose BlueGene/L, and is now the fastest computer in the world. MDGRAPE-3's power consumption is as low as 200 kW, but its electrical efficiency has been improved by a factor of 100. From 1995 to 2006, GRAPE received the IEEE Computer Society's Gordon Bell Prize no less than eight times.

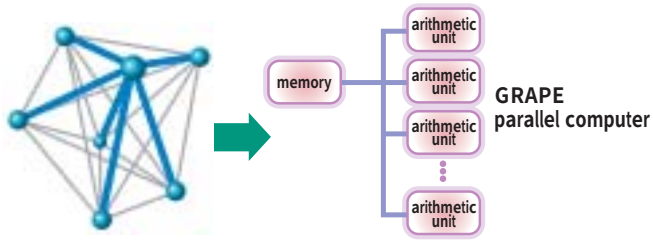
- General-purpose commercial supercomputers
- MD-GRAPE, a special-purpose computer for simulating molecular dynamics
- GRAPE (highly accurate model), a special-purpose computer for astrophysics
- GRAPE (lower accuracy model), a special-purpose computer for astrophysics

Choosing the best set-up for the subject

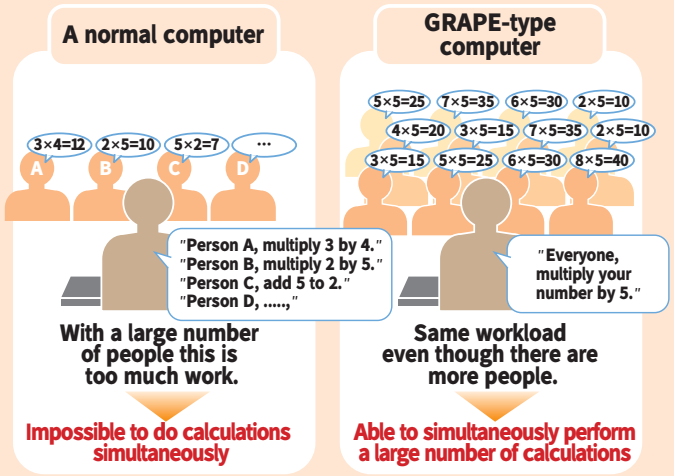
A field Each particle affects its surroundings via the field.



A particle One particle affects the others at the same time.

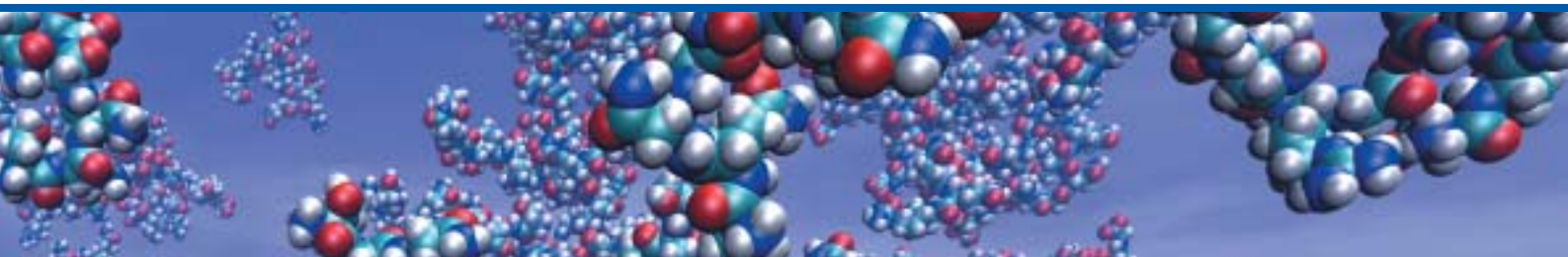


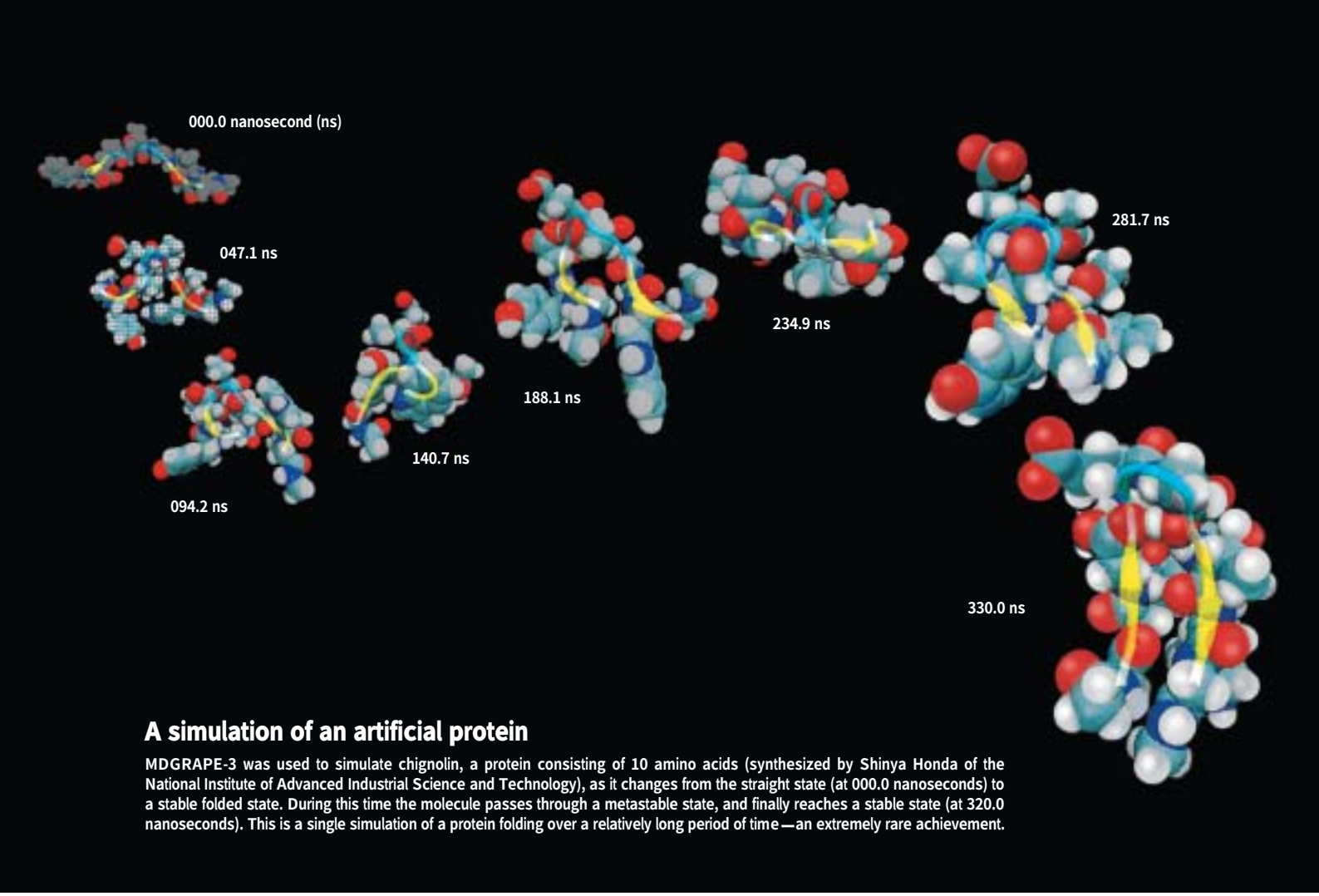
How MDGRAPE-3's structure enables high-speed computation



proteins, it's more effective to represent them as particles."

To achieve high-performance simulations, it is important to specially design the computer for the phenomenon that is going to be modeled. MDGRAPE-3 uses broadcast parallelization, in which each piece of memory is connected to several arithmetic units. This enables high-speed calculation of the forces between the atoms. Each arithmetic unit deals with a different atom, so the information about an atom can be sent from the memory to the arithmetic units, and the arithmetic units can then calculate the forces between their atoms and this one all at the same time. A normal desktop computer's CPU can only do about four





A simulation of an artificial protein

MDGRAPE-3 was used to simulate chignolin, a protein consisting of 10 amino acids (synthesized by Shinya Honda of the National Institute of Advanced Industrial Science and Technology), as it changes from the straight state (at 000.0 nanoseconds) to a stable folded state. During this time the molecule passes through a metastable state, and finally reaches a stable state (at 320.0 nanoseconds). This is a single simulation of a protein folding over a relatively long period of time—an extremely rare achievement.

calculations at the same time, but the MDGRAPE-3LSI can do 720. This is how MDGRAPE-3 as a whole is able to achieve a speed of one petaflops.

Revealing how proteins work

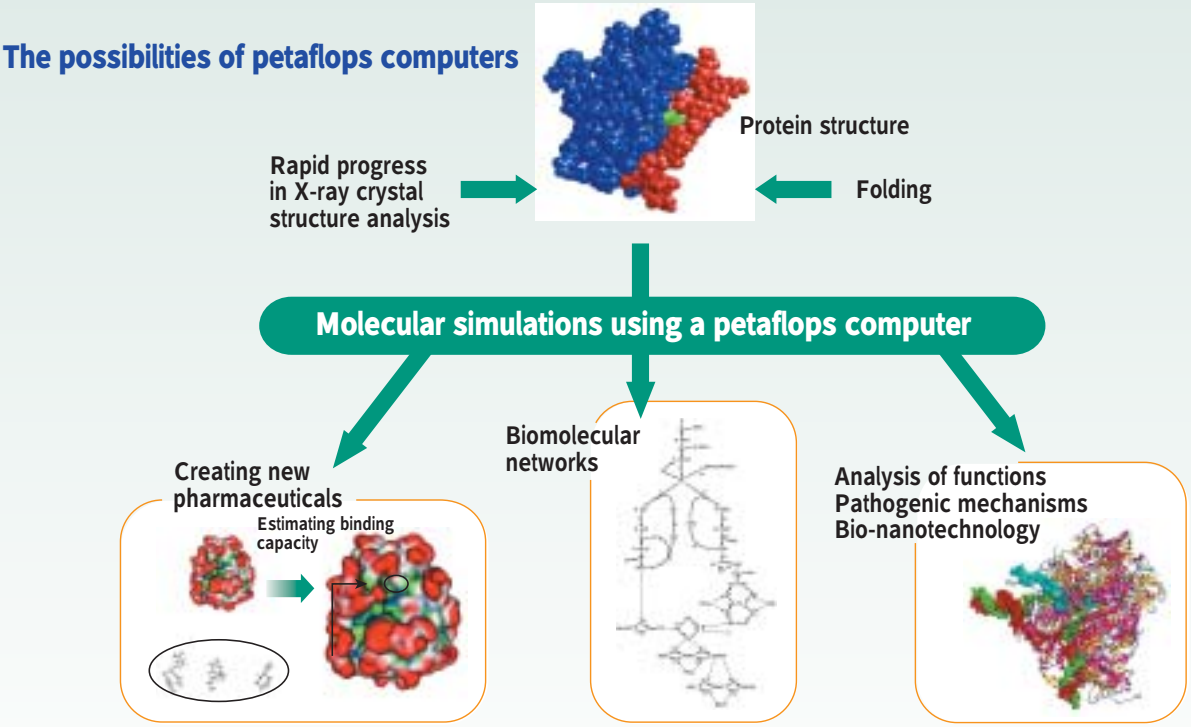
What can MDGRAPE-3 be used for? Japan is now carrying out a National Project on Protein Structural and Functional Analyses, to work out the structures of 3000 especially important proteins. Proteins have many functions that are essential for life. But when they perform their functions their shapes change. So to understand how proteins work it is essential to understand their structures. Simulating how proteins link with pharmaceutical chemicals is also useful for evaluating the effectiveness of pharmaceuticals and developing new ones. MDGRAPE-3 has already proved itself in testing the effectiveness of potential pharmaceuticals, and starting this year it is going to be used for searching for new pharmaceuticals in earnest. One other use for MDGRAPE-3 relates to molecular motors. These are found in living organisms and work like machines. If the mechanism of molecular motors could be understood, it would be useful for biology, and could also provide ideas that would be useful in designing micromachines.

MDGRAPE-3's system

MDGRAPE-3 only needs 100 m^2 of floor space

Twin parts of life science research

When Taiji was a graduate student, he undertook a study where he irradiated a protein called rhodopsin, which is capable of sensing light, with a laser beam, and then explored how it changed spectrographically. From that time on Taiji has dreamed of the possibility of "simulation based on structure." Now his dream has come true. Measuring instruments have improved greatly, and we can now collect data that is vastly more accurate than before. "However, having this accurate data doesn't mean that there's no need for any more simulations. The more precise the data, the more precise the models that we will need to deal with. We actually expect that simulations will be used more." With the protein structures obtained by the national protein-structure



analysis project, and MDGRAPE-3's high-performance simulations, life science research will take another step forward. Moreover RIKEN is developing a next-generation supercomputer that will run at 10 petaflops. This supercomputer is due to be completed in 2011. The experience gained in large-scale simulation with the MDGRAPE-3 will help in the development of the next-generation supercomputer.

DIRECTOR'S MESSAGE

Understanding biological processes: from elements to systems

Director, Genomic Sciences Center **Yoshiyuki Sakaki**

Q. What are your important achievements for fiscal 2006?

A. The successful construction of MDGRAPE, the dedicated calculator for protein simulation. Makoto Taiji, who leads the High-Performance Molecular Simulation Team, was awarded the 2006 Gordon Bell Prize in the peak performance category for this achievement. The development of a rapid isothermal method for SNP detection has enabled the SMAP process, which can detect genetic mutations from a single drop of blood in only 30 minutes. In addition, we released OmicBrowse, free open-source software which can search for and provide visual images of a number of gene-related databases simultaneously. With this in place, research into disease-causing genes is expected to accelerate.

Q. What are some of the projects that were completed or just launched in fiscal 2006?

A. The National Project on Protein Structural and Functional Analyses just finished. This was a systematic study of the functions and 3D structures of proteins, and we have succeeded in working out the basic structures of 2500 proteins. The next step will be to concentrate on the structural and functional analysis of highly complicated proteins, as they could be key factors in medical and pharmaceutical science, nutrition, the environment, and basic life phenomena, and will contribute to our understanding of the protein network. The National BioResource Project has also been completed. This project developed over 300 types of mouse mutants, and 236 strains are now publicly posted on the project's website. We are also providing resources to external researchers.

Q. What are the center's future prospects?

A. Since the center's establishment, all of its research groups have made significant progress in their individual projects, and their achievements are highly evaluated internationally. We have achieved our initial targets, and at the end of fiscal 2007 we will bring to an end our integrated operation. From here on, each group will make the most of its abilities to develop new research fields in cooperation with other groups.

YOKOHAMA 横浜

Plant Science Center

Closing in on clarifying the morphogenesis of organisms: identifying the gene involved in a cell cycle

Through functional gene analysis using the model plant Arabidopsis thaliana, RIKEN has discovered a gene that controls the cell cycle known as endoreduplication (ERD). Since this gene seems to be involved in the cell cycles of not only plants but also animals, there are hopes that it will help in understanding morphogenesis (the development of tissues and organs) in organisms. This research has led to the development of the world's first method for genomic functional analysis, the FOX Hunting system.

Understanding the gene functions of plants

Crops resistant to cold and disease yield more and need less fertilizer and other agricultural chemicals. Controlling the properties and morphology of plants could solve both food supply and environmental problems. What is very important is to clarify the gene functions of plants. The RIKEN Plant Science Center is tackling this problem by taking advantage of state-of-the-art genome research technology. Minami Matsui, the director of the Plant Functional Genomics Research Group, has successfully identified a gene involved in endoreduplication, a process which increases the size of plant cells.

Endoreduplication: another cell cycle

Organisms create their bodies through cell proliferation. One well known method of proliferation is somatic division. After the cell's DNA has been duplicated, its cytoplasm divides, producing daughter cells identical to the original one. Animals grow mainly by somatic division, but plants also have another cell cycle called endoreduplication (ERD). In ERD the cell does not divide even though the DNA is duplicated. Since the amount of DNA within each cell is multiplied, the cell's metabolic rate and size increase.

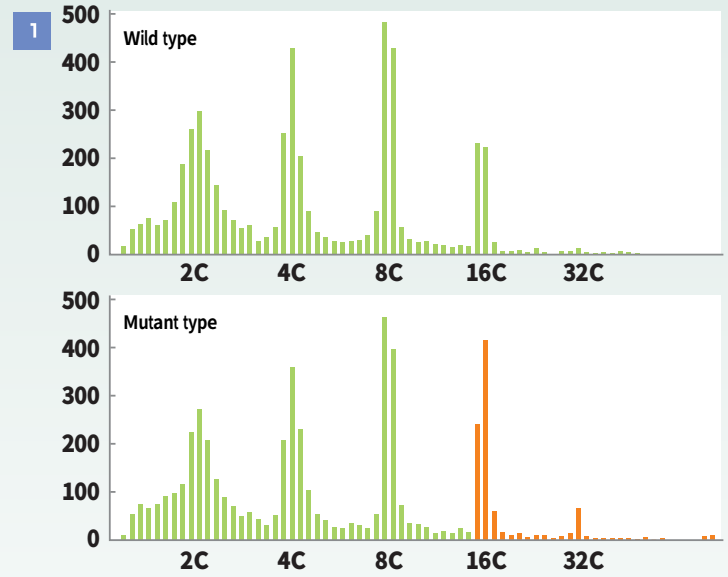
For example, hypocotyls (embryonic stems of seedlings

Increase in Arabidopsis hypocotyl size

Germination of Arabidopsis in the light (left) and the dark (right). The hypocotyl cells grow longer in the dark.

Minami Matsui
Group Director
Plant Functional Genomics Research Group
Plant Science Center

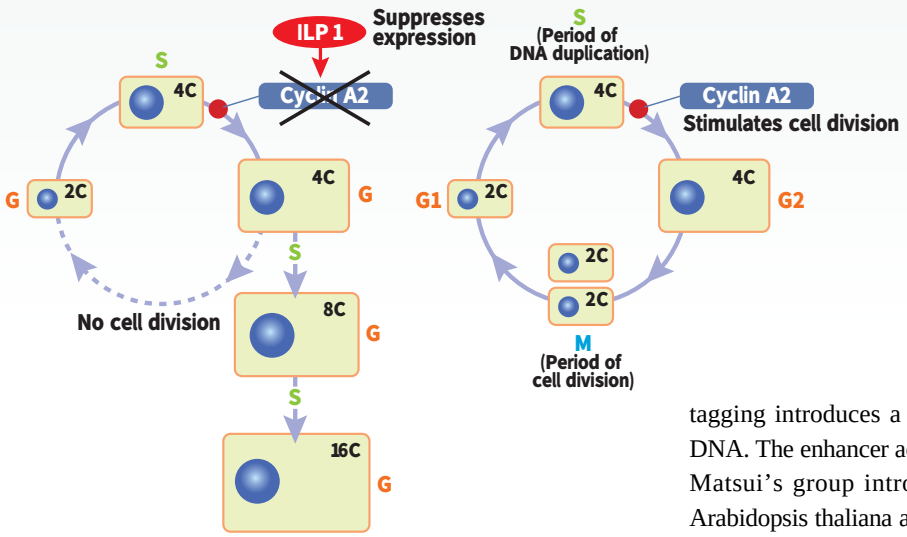
Phenotypes in mutant strains



1 Histograms indicating the amount of DNA in a wild type (top) and a mutant (bottom). The vertical axis is the number of cells measured, and the horizontal axis is the amount of DNA. The mutant shows an increase at the peak indicating 16C compared to the wild type. C represents one set of chromosomes.

2 Germination of wild type (upper) and mutant (lower). The mutant has a cotyledon area 30% larger than that of the wild type.

Endoreduplication (left) and somatic division (right)



Since somatic division has one S phase (DNA duplication) and one M phase (cell division) for each cell cycle, the cell never has more than 4C of nuclear DNA. In contrast, because endoreduplication has no M phase, nuclear DNA continues to multiply, becoming 4C and 8C and then 16C.

without roots and cotyledons) germinated in the dark will grow longer than those germinated in light. This is because the difference in the amount of light stimulates ERD. In this way, ERD is intimately involved in the morphogenesis of plants. However, how this happens remains unclear.

The gene that increases cell size

Matsui and his group used a technique called activation tagging to search for the genes involved in ERD. Activation tagging introduces a base sequence called an enhancer into DNA. The enhancer activates the expression of adjacent genes. Matsui's group introduced an enhancer into the DNA of Arabidopsis thaliana and produced over 70,000 mutant strains. Of these, the mutant that showed an even great increase in the amount of DNA than in the wild type were analyzed, and it was discovered that a gene coding the ILP1 protein was overexpressing. Then it was found that, of the cyclins, the ILP1 protein only suppresses the gene expression of Cyclin A2. This confirmed that the ILP1 protein suppresses the expression of the Cyclin A2 gene, thus stimulating ERD.

Furthermore, when the group studied cultured mouse cells, they found that here too, a protein similar to ILP1 suppresses the expression of the Cyclin A2 gene. These discoveries are expected to lead to a better understanding of morphogenesis in animals and other organisms.

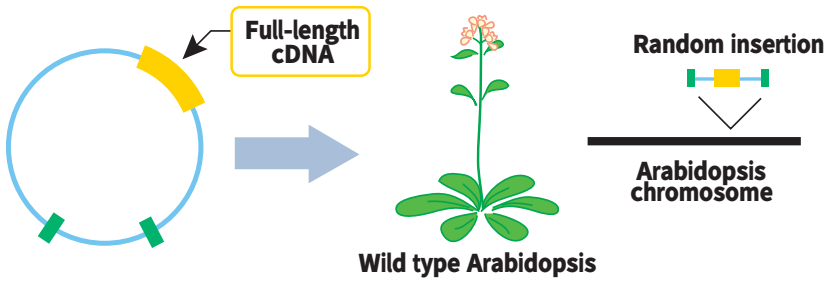
Development of a unique analysis technique

The broad effect of the enhancer used for activation tagging makes it time-consuming to identify genes. This means that the gene expressions of a huge number of mutants need to be examined and base sequences analyzed.

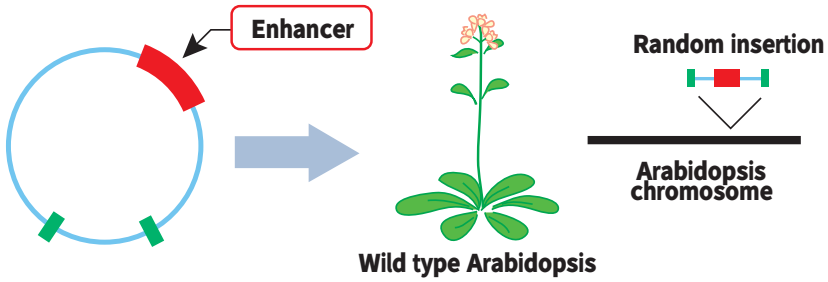
To find a more efficient way to identify genes, Matsui's group developed the FOX Hunting system, which uses RIKEN's own cDNA collection technique. cDNA is DNA that is created using an mRNA (messenger RNA) template, which is assembled only from the protein-coding sequences by discarding unnecessary sequences. Full-length cDNA contains all the design information for protein synthesis. RIKEN has developed a world-leading technique that efficiently synthesizes full-length cDNA.

In the FOX Hunting system, full-length cDNA is introduced into the genome of Arabidopsis thaliana in order to create a mutant strain. The full-length cDNA contains all the information carried by a single gene. And, since the targeted gene shows overexpression, the gene functions can be identified with certainty.

FOX Hunting system



Activation tagging



Gene manipulation of the wild type

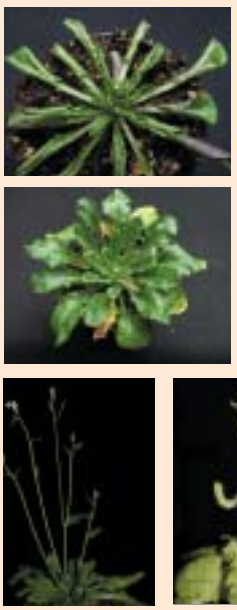
Insertion of the base sequence into the plasmid of a soil bacterium

Gene manipulation of the wild type

Wild type and mutant of Arabidopsis

Wild

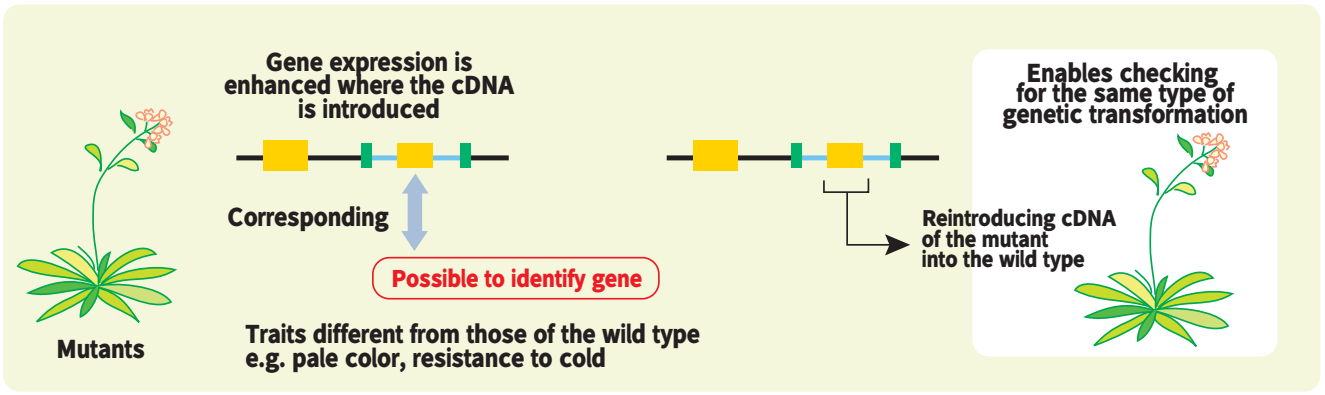
Mutants

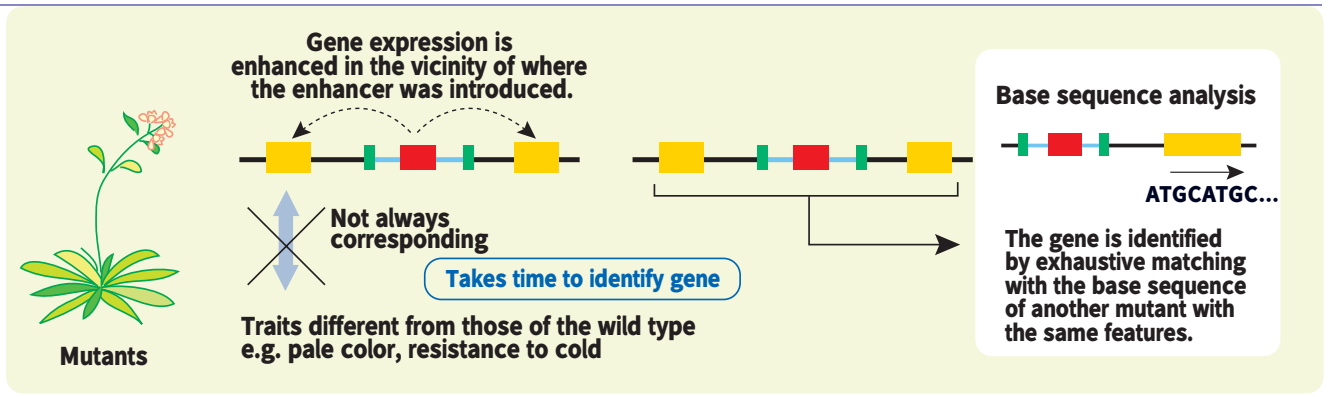


Application to other plants

"The major advantage of using full-length cDNA is that the gene expressions can be studied by introducing cDNA of a different species into Arabidopsis thaliana." In cooperation with the National Institute of Agrobiological Sciences and the Research Institute for Biological Sciences Okayama, Matsui has launched a project to investigate the useful genes of rice by introducing rice cDNA into Arabidopsis thaliana. "Rice takes half a year to reach maturity, but Arabidopsis thaliana only takes about three months, so our research is that much more efficient. The benefits of using Arabidopsis thaliana for trees, which take decades to grow, would be even greater."

The Arabidopsis thaliana mutants produced by activation tagging have already been published as a database. Based on this research using FOX Hunting, a database containing the useful traits of rice will be created in the future. In collaboration with other research organizations, the RIKEN Plant Science Center will continue its work on new plants with useful characteristics.





Growing the mutant from a processed wild type seed

Mutant analysis

DIRECTOR'S MESSAGE

Promoting plant science for a sustainable society

Director, Plant Science Center **Kazuo Shinozaki**

Q. What were some of the achievements at your center in fiscal 2006?

A. As we entered our second term, one major milestone was the metabolome analysis facility becoming fully functional, enabling us to begin several collaborative research projects. In collaboration with the Research Institute of Agricultural Resources, we are studying desirable genes in the rice plant using metabolome analysis and the FOX Hunting system. With the Kihara Institute for Biological Research at the Yokohama City University we are conducting research on genome analysis and metabolome analysis of wheat. In addition, in a collaborative research project with the University of Tokyo, we discovered that genes related to the metabolism of plant hormones are useful for breeding plants.

We hosted an international symposium on plant hormones, where we were able to release to the world our discoveries in plant hormone research, a traditionally strong area for RIKEN.

Q. What projects did you particularly focus your attention during fiscal 2006?

A. In cooperation with research teams involved in metabolome analysis, transcriptome analysis, and phenome and comparative genomics analysis, bioinformatics research was conducted to explore crop and tree genes. We have also discovered a new metabolic network. Database integration is underway in cooperation with the University of Tokyo, the Nara Institute of Science and Technology, the Kazusa DNA Research Institute, and the Max Planck Society.

Q. What future plans do you have for your center?

A. We aim to use genomic information to analyze the various physiological systems found in plants. Of these systems, the metabolic system will be the core of our study. We also plan to use comparative genomics analysis to learn about biological functions in model plants for crop and forestry applications. For this purpose the collection and analysis of full-length cDNAs is currently underway.

The Plant Science Center's mission is to contribute to the solving of various problems, including those of food, energy, and environmental conservation, through the application of research findings obtained from basic plant science. We are currently promoting our Green-Techno Plan nationwide in a drive to improve plant productivity.

YOKOHAMA 横浜

SNP Research Center

Finding an explanation for osteoarthritis: the discovery of a new gene

Osteoarthritis is a disease where the cartilage in the joints becomes worn and deformed with aging. It is a common disease, with around 10 million sufferers in Japan. However, its pathogenic mechanism is yet to be clarified. RIKEN has recently discovered that a gene called GDF5 causes osteoarthritis. This may guide us in diagnosing osteoarthritis and in customizing medical care to provide treatment suitable for each patient's constitution.

Osteoarthritis, a multifactorial disease

"If aging alone were the cause of this disease, everybody would suffer from it in the same way, but even among people with similar lifestyles and stress levels, some are prone to getting it and others aren't. That's why we thought that it had to be gene-related," says the head of the laboratory, Shiro Ikegawa. He has been trying to find the genes involved in this disease for twelve years. Two years ago, Ikegawa discovered Asporin and Calmodulin 1, two genes which cause osteoarthritis, the first in the world to be discovered.

What is osteoarthritis?

The bone and joint disease with the highest incidence rate. Only palliative treatments such as sedatives, weight control, or building up of muscles are currently available, and if the symptoms become severe, the diseased joint has to be replaced with an artificial joint through surgery.

- Around ten million patients in Japan
- Develops with advancing age
- Symptoms such as aches and deformations
- Interferes with daily activities

When a disease occurs with a probability of nearly 100% because of a mutation in a single gene, it is called a monogenic disorder. Osteoarthritis, on the other hand, is called a multifactorial disease, because more than several genes are involved.

"With multifactorial diseases, even if one of the genes for the disease has the mutation, the disease doesn't necessarily occur. It just increases the probability of getting the disease. If you have two mutations rather than one, or three rather than two, the risk increases, of course, but the risk can't be determined just from the number of genes. Some genes significantly affect whether a person gets the disease, but others don't. Basically, the likelihood of developing the disease increases with the number of genes and the degree to which they have an effect." When people say things like "I tend to have high blood

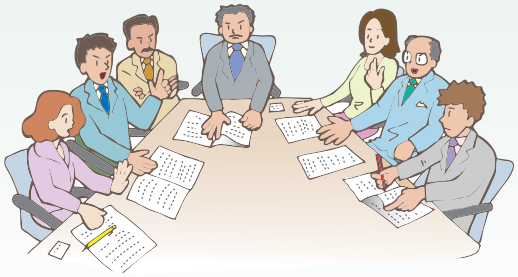
Shiro Ikegawa
Laboratory Head
Laboratory of Bone and Joint Diseases
SNP Research Center

Monogenic disorders and multifactorial diseases: how genes affect whether people get diseases

Dictatorship

The mutation of a single gene determines whether or not the disease will appear. This type of disease is called a monogenic disorder, and the gene which causes it is called a disease gene.

Committee



The combined influence of more than several genes determines whether or not a disease develops. This type of disease is called a multifactorial disease and its causative genes are called susceptibility genes. Whether or not a disease actually develops is determined by the combined influence of the susceptibility genes and environmental factors.

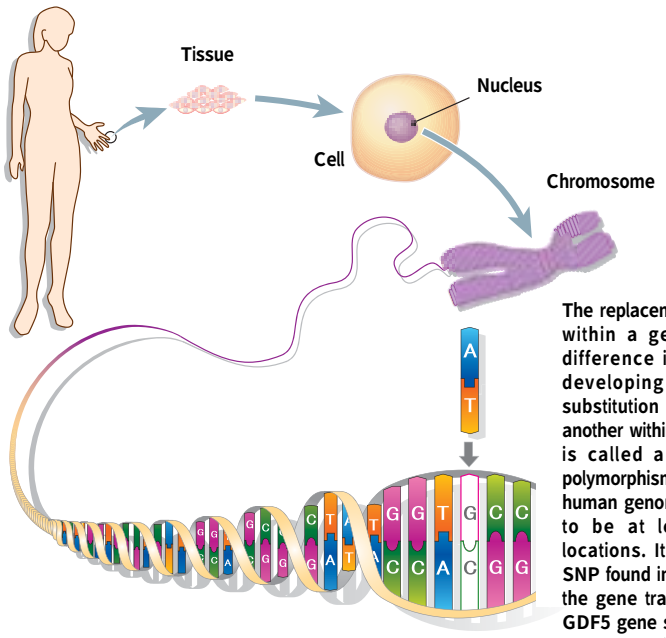
pressure," or "I have a family history of cancer," what they are actually talking about is multifactorial disease.

Search for a common factor

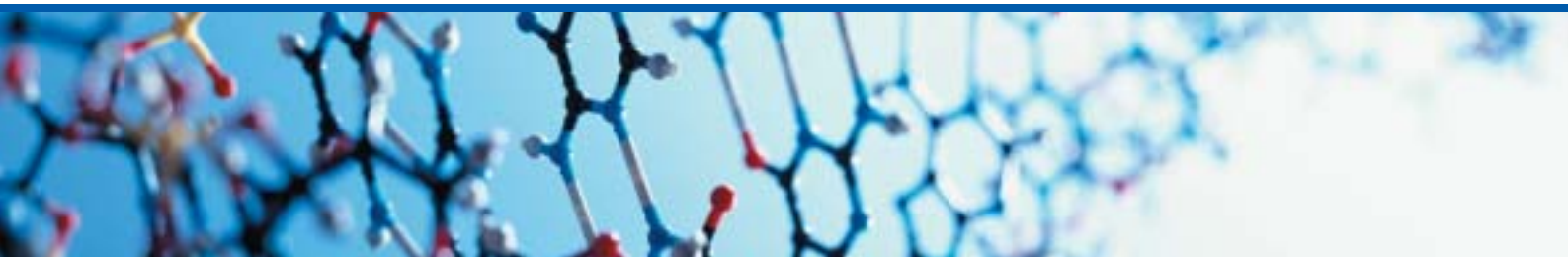
A method called "association study" was used to search for the disease-susceptiblity gene. By comparing the gene sequences of diseased and healthy people, the sequence specific to the diseased people can be found. Although humans have 99.9% of gene sequences in common, there are tiny differences between individuals. These are called polymorphisms, and they act as markers when searching for disease genes. If polymorphisms are frequently observed in people with a disease, but not in those who are healthy, the gene is highly likely to be involved in the disease.

In this study, Ikegawa focused on comparing polymorphisms in a gene called GDF5 (Growth and Differentiation Factor 5). GDF5 is known to be related to the formation of joints and the differentiation of cartilage cells, and so Ikegawa suspected that GDF5 could be involved in the development of osteoarthritis. Although osteoarthritis is a disease in which various joints are affected, a gene that causes a disease in a certain joint does not necessarily cause one in other joints as well. Therefore, Ikegawa's team first compared the gene

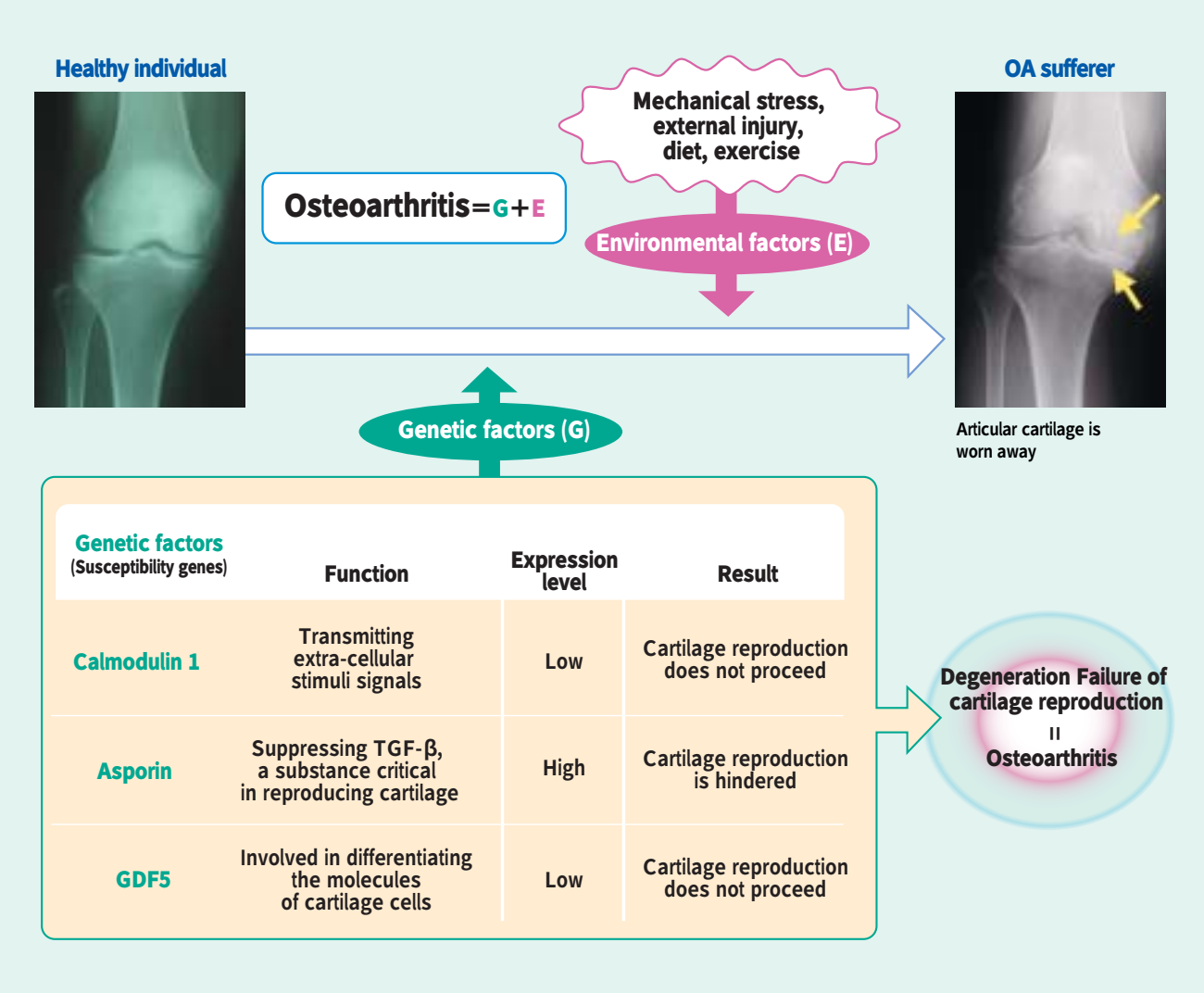
A single base determines the likelihood of developing a disease



The replacement of a single base within a gene can make the difference in the likelihood of developing the disease. A substitution of a single base for another within the DNA sequence is called a single nucleotide polymorphism(SNP). In the entire human genome there are thought to be at least three million locations. It is now known that SNP found in a site which adjusts the gene transcription within the GDF5 gene sequence is common to osteoarthritis patients.



Known causative genes of osteoarthritis



Genetic factors (Susceptibility genes)	Function	Expression level	Result
Calmodulin 1	Transmitting extra-cellular stimuli signals	Low	Cartilage reproduction does not proceed
Asporin	Suppressing TGF-β, a substance critical in reproducing cartilage	High	Cartilage reproduction is hindered
GDF5	Involved in differentiating the molecules of cartilage cells	Low	Cartilage reproduction does not proceed

sequences of patients suffering from osteoarthritis in the hip joints to those of patients without the disease. From all the polymorphisms contained in the GDF5 gene, they discovered one polymorphism commonly seen in many of the patients. Moreover, it was found that people with this polymorphism are 1.8 times more likely to get hip osteoarthritis.

Polymorphism in GDF5 makes cartilage difficult to maintain

Ikegawa next performed research on osteoarthritis patients with affected knee joints, and the polymorphism in question also showed a correlation with the disease, even though it was not as strong as with hip joints. In addition, joint research with Nanjing University in China and others confirmed that this correlation could be found not just in the Japanese but also in the Chinese population. These results showed that the polymorphism in GDF5 is involved in the disease regardless of the joint affected or the patient's race.

Within the gene sequence, this polymorphism exists in a particular site that adjusts the expression level of GDF5. From the research, it was discovered that when this polymorphism is present, the expression level of the GDF5 gene decreases. "Thus, we suspect that the increase and maintenance of joint cartilage, which is GDF5's job, becomes inadequate, causing the osteoarthritis. Since hip joints in particular take a heavy load, we think that greater damage occurs, which increases the likelihood of developing the disease."

By testing for the presence of mutations in the two genes discovered, the likelihood of developing osteoarthritis can be predicted in advance. In addition, if the relationship of GDF5 to cartilage formation becomes clear, this could lead to the development of a drug that enhances the performance of GDF5 and suppresses the onset of the disease.

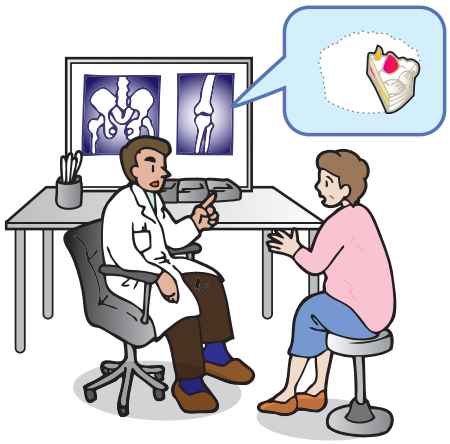
Understanding the risks and preventing the disease

Until the human gene sequence was mapped by the Human Genome Project, progress was slow in understanding the

causes of bone and joint-related diseases. This was due to the difficulty of work such as extracting proteins from hard bone. "The genome research changed everything. This discovery confirmed that our association study method is effective for determining the causes of bone and joint diseases. What we need to do now is to find as many susceptibility genes as possible, and then clarify what they do," says Ikegawa, who is eager to find another gene.

"Many people think that genes or genetic factors determine their fate, but that's a misunderstanding. Genetic factors don't determine whether you get a disease or not, they just determine how you react to stimuli." With multifactorial diseases, some people get the disease but others do not, even though they have similar disease-prone genes, because of their environments and lifestyles.

"The gene only determines susceptibility, so we can change the risk of getting the disease by changing the environmental factors. If every one of us knows our own individual risk and understands how to handle it, we can prevent the disease. What we are aiming at is to evaluate the risk for each individual person and to manage them accordingly." Ikegawa's next challenge is to customize medical care to the individual.



Customizing medical care

Knowing how many susceptibility genes each person has tells us their chances of developing a disease, making possible preventive lifestyle guidance as well as treatment specific to each individual person.

DIRECTOR'S MESSAGE

Understanding our bodies from our genes, aiming for effective patient-friendly medical care

Director, SNP Research Center **Yusuke Nakamura**

Q. What did you focus on at your center in fiscal 2006?

A. We widened our research collaboration networks both at home and overseas. We developed relationships with overseas research institutions through international cooperation on SNP research. We also established a cooperative framework in the BioBank Japan Project on the implementation of personalized medicine, in which we accepted applications from universities and research institutions that implement research on diseases using SNP analysis information.

Q. What were your center's most memorable activities in fiscal 2006?

A. To start collaborative research programs I visited Thailand, Malaysia, and Bulgaria, where I saw many young, serious researchers with a clear sense of mission. This is something I cannot help but feel is being lost in today's young Japanese, who seem to be interested only in their research. I believe it would be very stimulating for our center to welcome researchers from abroad who have a sense of mission toward both their countries and their patients.

Q. What are some of your center's newly launched projects?

A. We launched an international cooperative SNP research project to support overseas researchers, mainly in Asia. In fiscal 2006, we accepted researchers from Thailand, Malaysia, and Bulgaria after signing agreements with their respective research institutions. Using DNA samples imported from these three countries, we will carry out a genome-wide association study on how genes affect proteins. Through this cooperative study we plan to make international contributions in the fields of medical care and health.

Q. What future plans do you have for your center?

A. Our center is playing an important role in developing the field of personalized medicine in Japan and communicating our findings to the rest of the world. By the end of fiscal 2007, we will have completed a gene data bank based on 300,000 people through the BioBank Japan Project. We will attempt to obtain findings relating to each of the 47 targeted diseases, as our way of responding to the trust put in us by the patients who participated in this project. We look forward to making a contribution on a global scale by developing our international cooperation scheme for SNP research.

YOKOHAMA 横浜

Research Center for Allergy and Immunology

Understanding how interferon antiviral agents are produced

When pathogens enter our body, the body produces antiviral agents that cause inflammation and suppress the growth of the pathogen. Interferons are one type of antiviral agent. RIKEN has discovered a molecule that is needed for the production of interferons and discovered how this molecule is made. Interferons are also involved in autoimmune diseases, and it is hoped that the discovery of this molecule will contribute to the development of antiviral drugs and treatments for autoimmune diseases.

Toll-like receptors, the molecules that detect pathogens

When a pathogen enters a mammal, it triggers an immunoreaction. There are two stages of immunoreaction: innate, where a cell called a phagocyte ingests and destroys the pathogen, and adaptive, where the body identifies the pathogen using information from phagocytes and then produces antibodies.

In recent years, however, it has been discovered that pathogens are also identified in the innate immunity stage. The main role in this process is played by a type of phagocyte called a dendritic cell. Dendritic cells are equipped with sensors called toll-like receptors (TLR) which identify pathogens. Identification of a pathogen by a TLR triggers production of interferon or inflammatory cytokine. There are twelve types of TLR. Each type combines with a specific substance and identifies intruders.

Of the twelve types of TLR, TLR3, TLR7, and TLR9 are known to combine with nucleic acids such as viral RNA and bacterial DNA to produce type-I interferon or inflammatory cytokine. Until now, however, it was not known how the TLR recognizing a virus led to the production of interferon.

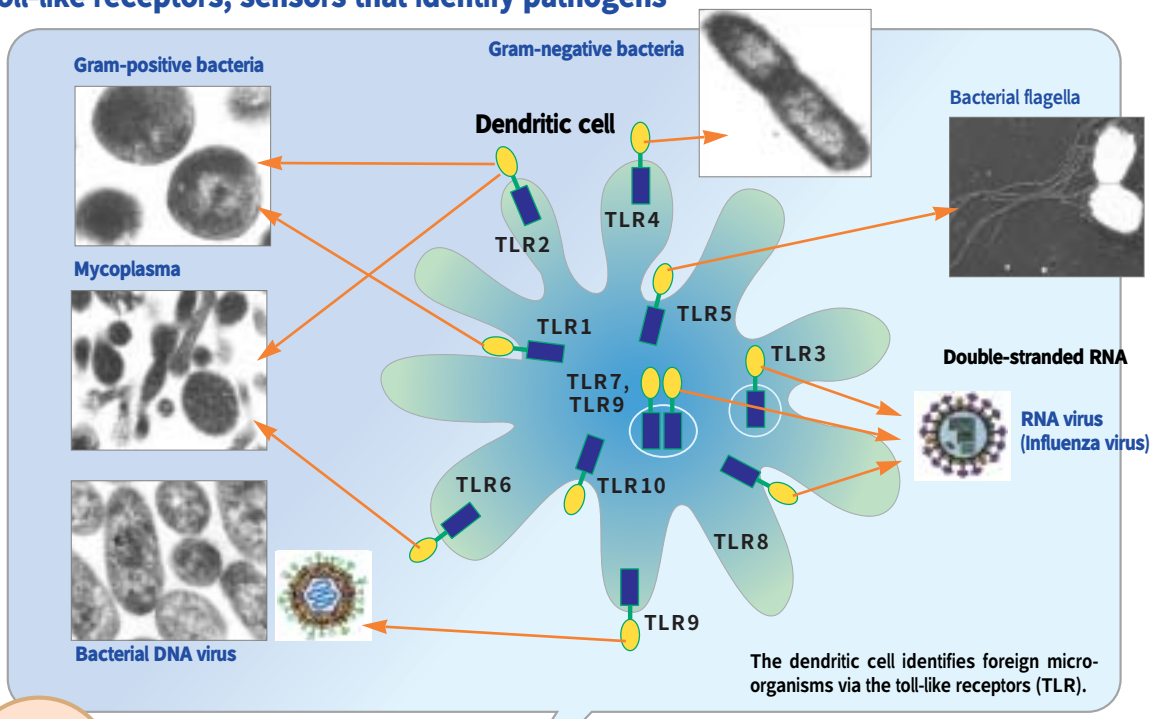
Plasmacytoid dendritic cells and IKKα

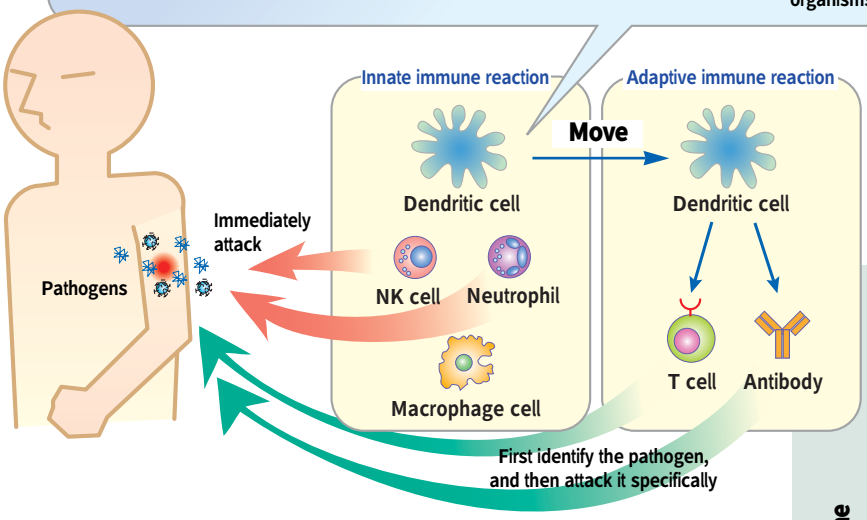
Team Leader Tsuneyasu Kaisho has been studying dendritic cells for a long time. “Dendritic cells don’t just enable innate immune reactions. They also play an important role in transmitting the signals generated in the innate stage to the adaptive immune system. So studying dendritic cells is a good way to get an overall understanding of immune reactions.” A very small number of dendritic cells are of a type called “plasmacytoid dendritic cells.” Kaisho became interested in these cells, which only contain TLR7 and TLR9 and produce large amounts of type-I interferon alpha (IFNα) when they encounter a virus.

A family of molecules known as I kappa B kinase (IKK) plays an important role in the production of interferon and inflammatory cytokine by dendritic cells. There are four types of molecules in the IKK family. Three of them have already been shown to play a part in innate immunity. The other one is IKKα. “IKKα was known to play a part in adaptive immunity. People used to think that this was all IKKα did, so they didn’t study it in

Tsuneyasu Kaisho
Team Leader
Laboratory for Host Defense
Research Center for Allergy and Immunology

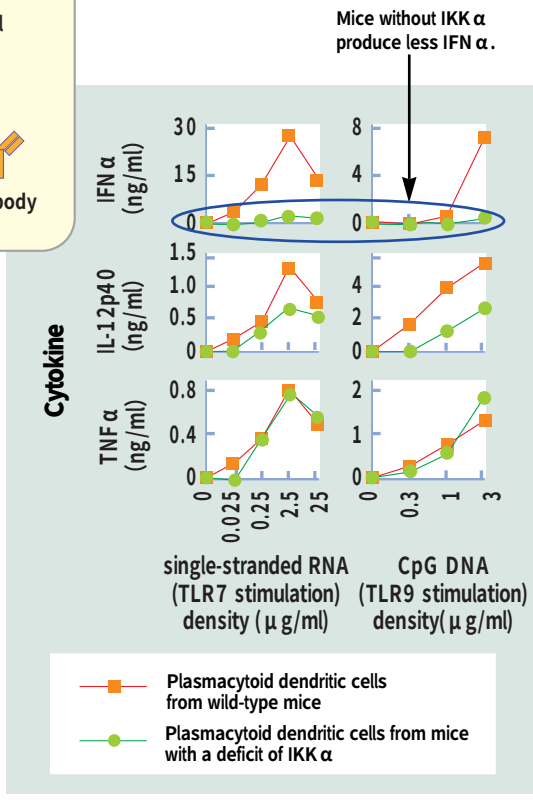
Toll-like receptors, sensors that identify pathogens





The mechanism of an immunoreaction

innate immune reactions. However, we thought that IKKα did also play a part in innate immune reactions, like the other IKK molecules. We performed experiments by removing a small number of plasmacytoid dendritic cells from mice from which the gene that produces IKKα had been knocked out."



When TLR7 and TLR9 in the plasmacytoid dendritic cell are stimulated…

Another role of IKKα

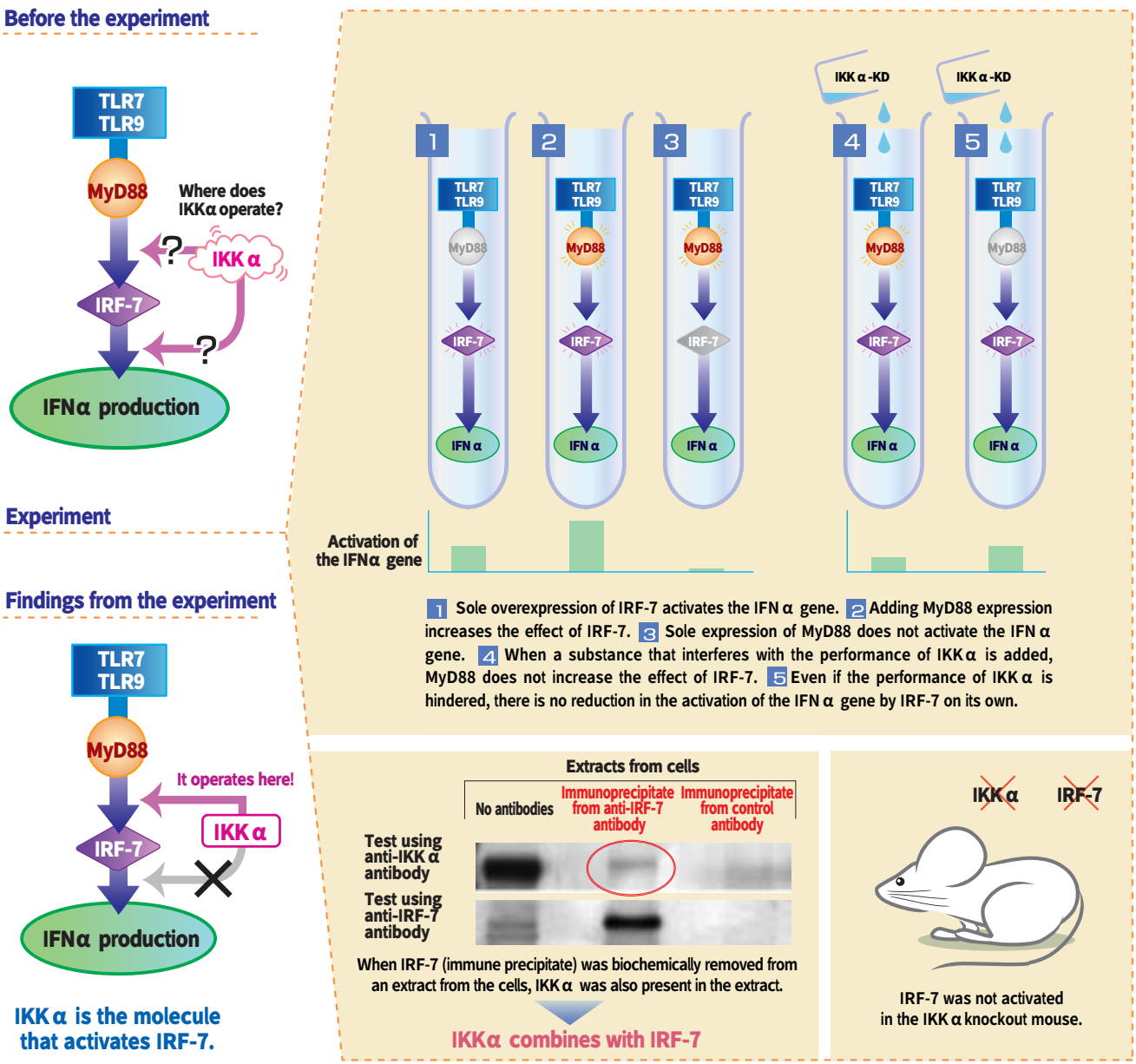
Kaisho removed plasmacytoid dendritic cells from the IKKα knockout mouse, and administered nucleic acid that combines with TLR7 and TLR9 into these cells. There was no significant change in the amount of inflammatory cytokine produced, but much less IFNα was produced. "Removing IKKα meant that less IFNα was produced, which showed that IKKα must be especially important in the production of IFNα. The next question was, how is it important?"

When TLR7 or TLR9 combine with a nucleic acid, they activate a molecule called MyD88. The MyD88 then activates another molecule, and signals announcing the infection are successively transmitted. It was already known that finally the transcription factor Interferon Regulatory Factor-7 (IRF-7) is activated, and that IRF-7 then causes a gene to produce IFNα. However, what actually activates the IRF-7 was unknown. Kaisho's experiments showed that IKKα combines with IRF-7 to control the production of IFNα. "We discovered that IKKα is the molecule that activates IRF-7, and that the reason less IFNα was produced in the knockout mice was that the IRF-7 hadn't been activated."

Towards treatment of autoimmune diseases

The understanding of this mechanism is expected to contribute to the development of antiviral drugs. A substance that can boost the production of IFNα by increasing the performance of IKKα, or conversely, a substance that can suppress an excess immunoreaction by hindering it, are both possible drug candidates. Even if the IKKα is stopped from working, inflammatory cytokines other than IFNα are still produced. Therefore it is still possible to control the immune reaction by maintaining the minimum necessary inflammation.

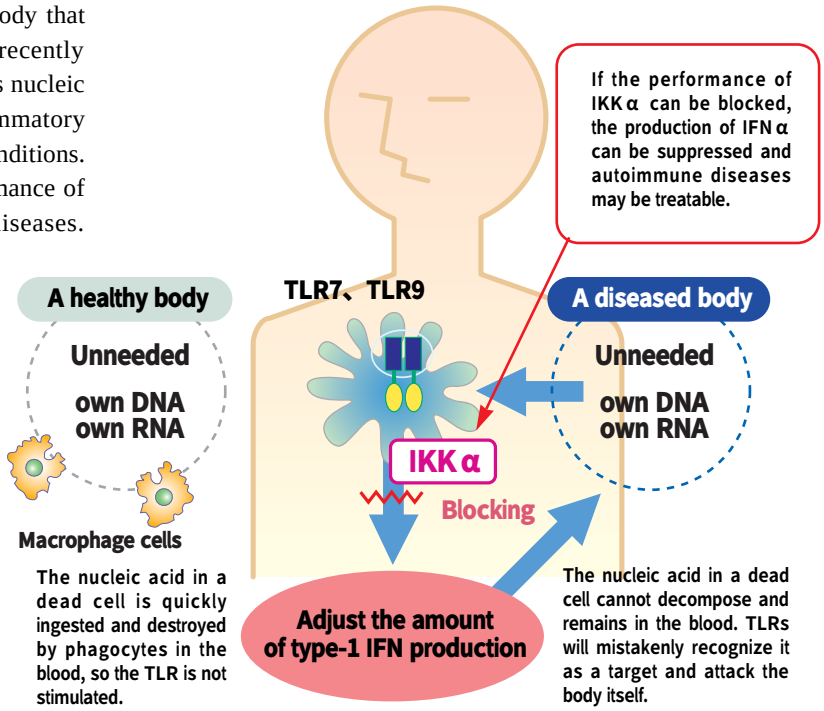
TLR7 and TLR9 also recognize some nucleic acids that exist in human cells. In healthy people, when cells die the



nucleic acid enters the blood and is quickly destroyed. In patients with autoimmune diseases, however, the nucleic acid does not break down easily, because an antibody that acts against the nucleic acid is produced. It has recently been suggested that TLR mistakenly recognizes this nucleic acid as a pathogen, and that this causes an inflammatory immunoreaction and may be related to clinical conditions. According to this hypothesis, inhibiting the performance of IKK**α** might be useful in treating autoimmune diseases. IKK**α** itself has been studied for a long time, and many inhibitors have already been discovered.

"Although it's not likely to be reflected in clinical applications in the near future, we'll keep on researching whether IFN**α** production can be controlled in human dendritic cells." Kaisho believes that another important molecule besides IKK**α** must also be involved in the production of IFN**α**. This achievement is a first step; future research will aim at understanding the entire mechanism.

Towards treatment of autoimmune diseases



DIRECTOR'S MESSAGE

A transitional "baton zone" from basic science to utilization: launching a project for the practical application of immunological research

Director, Research Center for Allergy and Immunology **Masaru Taniguchi**

Q. What are some of your center's noteworthy achievements in fiscal 2006?

A. Working out the relationship between the maturity of immuno-dendritic cells and intracellular zinc concentration was an epoch-making event. Zinc, previously regarded only as a nutrient, was discovered to play a role in immunological signaling. In addition, the world's first artificial lymph node was transplanted into a mouse with a critical immunological disorder, after which its immune system recovered. In allergology, we discovered the mechanism whereby allergies are suppressed by the BCG vaccine, empirically proving the hygiene hypothesis. Our efforts have resulted in many achievements, such as our discovery that memory T cells are required in allergic reactions.

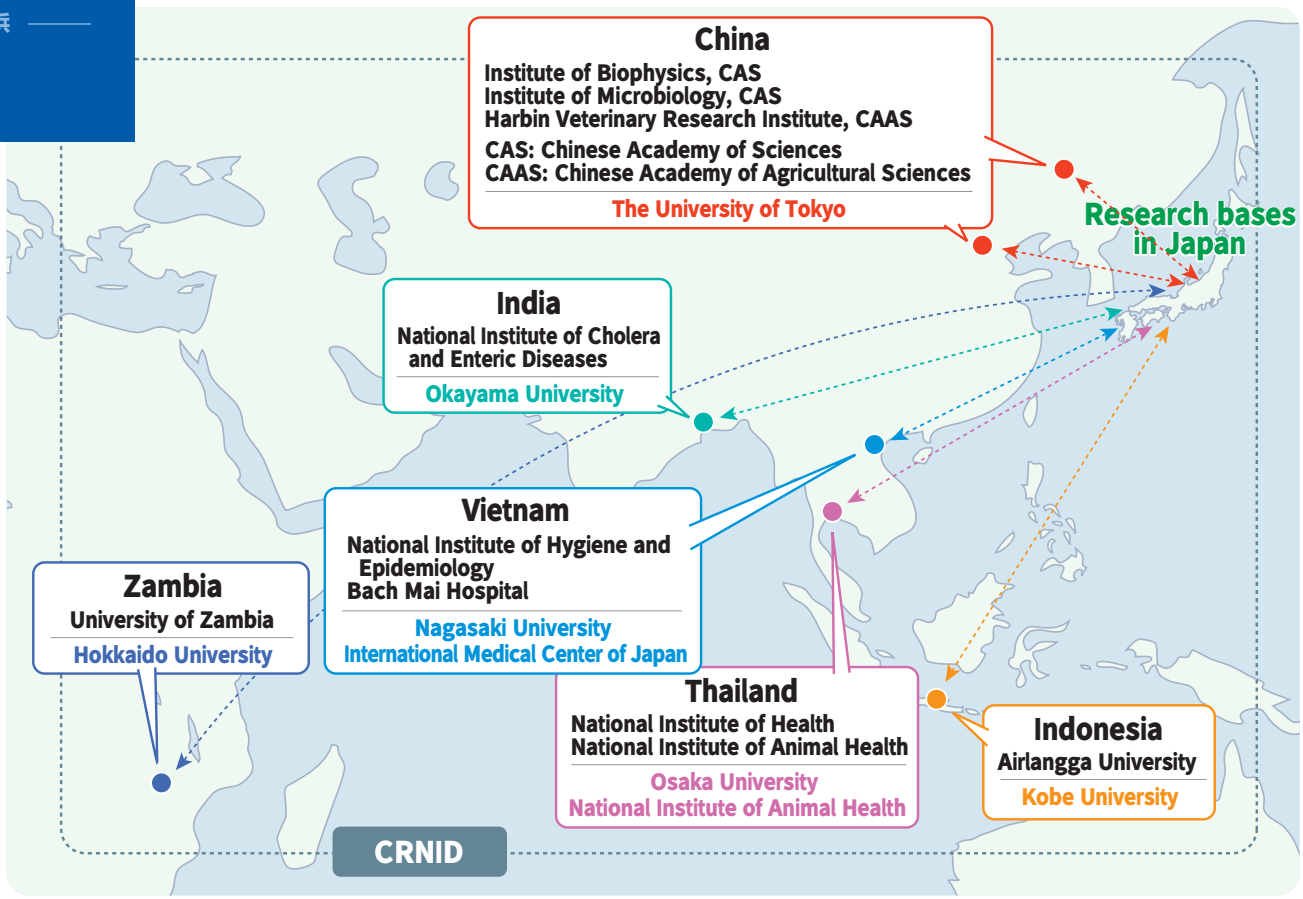
Q. Has your center launched any new projects?

A. The Humanized Mouse Project. We can now transplant human hematopoietic stem cells into mice to establish complete human immune systems with hematopoietic capability. Comprehensive analysis of human immune reactions is then possible . This can lead to individually-tailored medical treatments. The Primary Immunodeficiency Network Project was launched in cooperation with the Clinical Study Group for Primary Immunodeficiency at the Ministry of Health, Labour and Welfare. This project analyzes test samples taken from patients, and performs gene diagnosis to seek out possible medical treatment, as well as to understand the cause and status of the disease. Our aim is to apply this research to other diseases in the future so that it can serve as a bridge between basic research and applications.

Q. What future plans do you have for your center?

A. We are aiming to establish a new integrated field. Last fiscal year it became possible to observe in real-time the molecular movement of cells by using a single-molecule imaging microscope developed at our center. Based on information obtained with this system, we would like to establish a new field of system biology for immune cells by performing quantification and simulations. In addition, studying the pathology of allergies and developing methods of treatment and prevention have also been important missions for the center since its establishment. Additionally, we are putting a lot of effort into developing vaccines to control allergies.

Center of Research Network for Infectious Diseases



DIRECTOR'S MESSAGE

No borders for infectious diseases: toward greater security and safety for Japan and the world

Director, Center of Research Network for Infectious Diseases **Yoshiyuki Nagai**

Q. What events of particular interest do you remember from fiscal 2006?

A. The launching by MEXT of the Program of Founding Research Centers for Emerging and Reemerging Infectious Diseases was particularly memorable. Three major research bases were established in our first fiscal year of 2005, in Thailand (with Osaka University), Vietnam (Nagasaki University), and China (The University of Tokyo). Smaller projects, such as the ones at the National Institute of Animal Health in Thailand, Bach Mai Hospital, and Harbin Veterinary Research Institute, have also commenced activities. While the research bases are not yet in full-scale operation, we are pleased that they have started functioning on their own. Some of our major difficulties were settling issues of intellectual property rights, duties, and income tax rules and regulations. In January 2007, the second Asian Research Forum on Emerging and Reemerging Infections was held in Nagasaki. Research results were presented and relationships were expanded.

Q. What specific issues did you focus on in fiscal 2006?

A. We established new overseas research bases, in addition to those that already exist, so as to expand our network. Beginning with preliminary inquiries, Hokkaido University, Okayama University, and Kobe University all decided to establish their own new research bases, in Zambia, India, and Indonesia respectively. These three projects will be officially inaugurated during fiscal 2007 and will utilize research facilities provided through aid from the Japan International Cooperation Agency. To further expand the network, we also invited public, nation wide participation in new research projects that will use existing research bases. To date, there are six such projects in progress.

Q. What are the center's future prospects?

A. The Center for Tropical Medicine at Oxford University in England has established over its thirty-year history a network of roughly 15 research bases throughout the world. The Institut Pasteur in France has established a worldwide network of about 30 research bases during its 100-year history. Overseas bases require long periods of time to mature. Since the term of this program is relatively short, at five years, one of the greatest challenges in the future will be how to expand the network and make the program permanent.

Facts & Figures

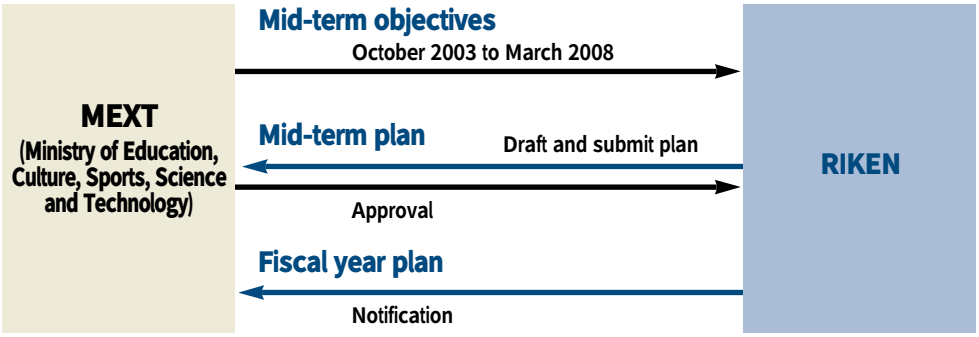
RIKEN's administration and management: fulfilling our responsibilities to society

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
1. Improvement of operations	
1) Publication and utilization of research results	
Publish original results	1,820 or more papers annually
Publish in journals that are highly regarded in the relevant fields	50% or more
Register intellectual property	610 applications in fiscal 2007
License patents	12%
Issue press releases	40 a year
Publish *RIKEN News*	12 times a year
2) Training and development of researchers and technical staff	
Special Postdoctoral Researchers	Maintain constant level of 200 researchers
Initiative Research Scientists	10 researchers by fiscal 2007
Junior Research Associates (JRA)	Maintain constant level of 140 JRAs
2. Improvement of operational and managerial efficiency	
Increase operational efficiency	Reduce expenditure by 1% annually
Increase procurement efficiency	Reduce expenditure by 2% annually
Increase managerial efficiency	Reduce administrative costs by 15% (before taxes)

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.

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

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.

RIKEN Science Council

The objective of the RIKEN Science Council is to respond to inquiries from the President, and report its findings to the President. The council consists of approximately thirty members, including Directors, Chief Scientists, and Group Directors. It has lively debates on topics such as the broad and long-term issues of what fields RIKEN should research and formulating a vision for researchers at RIKEN. In 2006, it produced reports such as "The Future of the Life Sciences: from Discovery of Scientific Principle to Application in Society" and "The Future of Nanoscience and the role of RIKEN."

Strengthening scientific governance

The report of the 6th RIKEN Advisory Council: "RIKEN: Leading Japanese Science to Global Pre-eminence"

The RIKEN Advisory Council (RAC) serves as an external advisory body and evaluates RIKEN's scientific and administrative activities for the President. RAC is made up of highly influential and successful people from outside RIKEN. The 6th RAC meeting was held in June 2006. In the report of that meeting, "RIKEN: Leading Japanese Science to Global Pre-eminence" (available on the RIKEN website at http://www.riken.jp/engn/r-world/info/report/rac/pdf/6report.pdf), RIKEN was praised highly for having taken its place among the most prestigious international scientific research organizations. The organizations cited in the report include the National Institutes of Health (USA), the Weizmann Institute (Israel), the Max-Planck Society (Germany), the British Medical Research Council, and the French national research organizations CNRS and INSERM. Furthermore, the report analyzes RIKEN's management style and praises current management initiatives and reforms, saying: "The President has established a strong system of advisory committees and a transparent, broadly-based governance regime that balances 'top-down' and 'bottom-up' management."

For further development of the organization, and in order to play a leading role in the international scientific community, RAC recommended that RIKEN strengthen its recruiting efforts by seeking talented personnel from around the world, create a strong international RIKEN brand, increase its international visibility, and cultivate scientific relationships with other countries in Asia. Additionally, with regard to RIKEN's role in providing scientific infrastructure, it recommended that RIKEN become "a source of innovative science," and that its relationships with universities and other research institutions be enhanced.

RIKEN is following these excellent recommendations. We have budgeted for these areas in fiscal 2007, and will be including them when our second mid-term plans are discussed, starting in 2008.

Evaluation at RIKEN

Evaluation of R&D activities

Overall evaluation of RIKEN by RIKEN Advisory Council (RAC)

All AC chairs are also RAC members

Evaluation Report

Evaluation of each RIKEN research institute/center by its Advisory Council (AC)

Evaluation report

Individual research evaluations of each laboratory by research review committees

Independent Administrative Institution evaluation

Evaluation by a committee from MEXT (the Ministry of Education, Culture, Sports, Science and Technology)

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 the 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 research institutes and centers

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 the laboratory level

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

Governmental evaluation

A MEXT committee will evaluate the extent to which RIKEN met its mid-term objectives.

The members of the 6th RIKEN Advisory Council (RAC)

Affiliations and titles are as of June 2006

Chair

Zach W. Hall

President, California Institute for Regenerative Medicine, USA

Vice-Chair

Yuan T. Lee

President, Academia Sinica, Taiwan;
Nobel Prize (in Chemistry, 1986)

Henry G. Friesen

Distinguished Professor Emeritus, University of Manitoba; Former RAC Chair

Geraldine A. Kenney-Wallace (absent)

Director, Learning & Information Technology, Group e-Strategy, City & Guilds of London Institute, UK

Guy Ourisson (absent)

Professor, Louis Pasteur University; former President, French Academy of Sciences, France

Hans L. R. Wigzell (absent)

Professor and former Director, Karolinska Institute, Sweden

Paul R. Williams

Former Chairman, Council for the Central Laboratory of the Research Councils, UK

Hiroo Imura

Chairman, Foundation for Biomedical Research and Innovation; Counselor to the President, Japan Science and Technology Agency; former member, Council for Science and Technology Policy

Shigehiko Hasumi

Professor Emeritus and former President, the University of Tokyo

Toshiaki Ikoma

Director-General, Center for Research and Development Strategy, Japan Science and Technology Agency; former FRAC Chair

Mitiko Go

President, Ochanomizu University

Hidetoshi Fukuyama

Professor, Faculty of Science, Department of Applied Physics, Tokyo University of Science; former Director, Institute for Solid State Physics, the University of Tokyo; Chair, Institute Laboratories Advisory Council (ILAC)

Yoshihito Osada

Executive and Vice President, Hokkaido University; Chair, Frontier Research System Advisory Council (FRAC)

Yoshitaka Nagai

Professor Emeritus, the University of Tokyo; former President, Mitsubishi Kagaku Institute of Life Sciences; Chair, BioResource Center Advisory Council (BRAC)

Tim Hubbard

Head, Human Genome Analysis Group, Wellcome Trust Sanger Institute; Chair, Genomic Science Center Advisory Council (GSAC), UK

Wilhelm Gruissem

Professor, Swiss Federal Institute of Technology Zurich; Chair, Plant Science Center Advisory Council (PSAC)

Mark Lathrop

Director General, Centre National de Génotypage, France; Chair, SNP Research Center Advisory Council (SRAC)

Max D. Cooper

Investigator, Howard Hughes Medical Institute, University of Alabama at Birmingham, USA; Chair, Research Center for Allergy and Immunology Advisory Council (AIAC)

Yo-ichi Nabeshima (in place of Yoshiki Hotta)

Professor, Graduate School of Medicine / Faculty of Medicine, Kyoto University; Acting Chair, Center for Developmental Biology Advisory Council (DBAC)

Yoshiki Hotta (absent)

President, Research Organization of Information and Systems, Japan; Chair, Center for Developmental Biology Advisory Council (DBAC)

Tairo Oshima

Professor Emeritus, Tokyo Institute of Technology; Director, Institute of Environmental Microbiology, Kyowa Kako Co., Ltd.; Chair, RIKEN SPring-8 Center Advisory Council (RSAC)

Sydney Gales

Director, Grand Accelerateur National D'Ions Lourds (GANIL), France; Chair, RIKEN Nishina Center for Accelerator-Based Science Advisory Council (RNAC)

Sten Grillner

Professor, Department of Neuroscience, Karolinska Institute, Sweden; Member, Brain Science Institute Advisory Council (BSAC)

Endeavoring to diversify funding

The government remains RIKEN's primary financial supporter

Like other Independent Administrative Institutions, RIKEN is responsible for deciding how to distribute the funds it receives from the government. While the government does not impose requirements on how its funds are used at RIKEN, it does monitor and evaluate spending closely.

The subsidies for facilities that RIKEN receives from the government can only be used for acquiring tangible assets, such as for the purchase of land or for constructing buildings. Costs for the maintenance and operation of SPring-8 and the Next-Generation Supercomputer R&D Center are shared with the government under a law related to the use of such advanced facilities for the benefit of the public.

RIKEN also works hard to get funding from other sources to reduce its dependency on government subsidies. These other types of funding 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

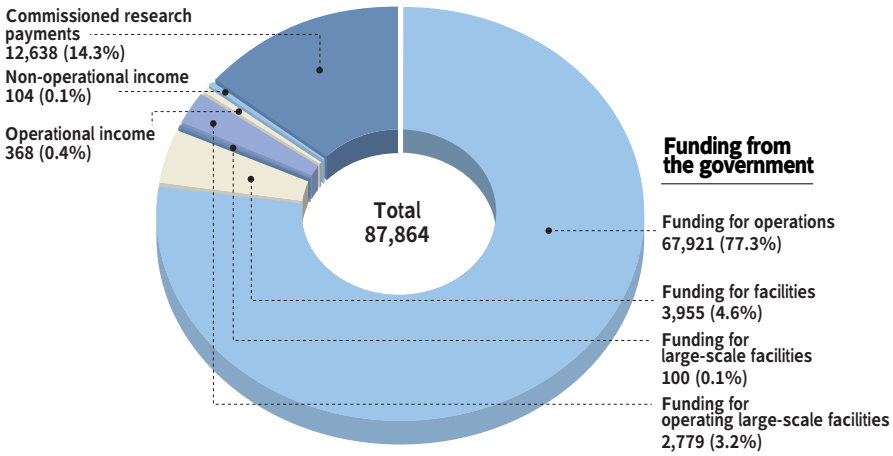
3. Payment for research that RIKEN is commissioned to do

Projected 2006 budget

Income

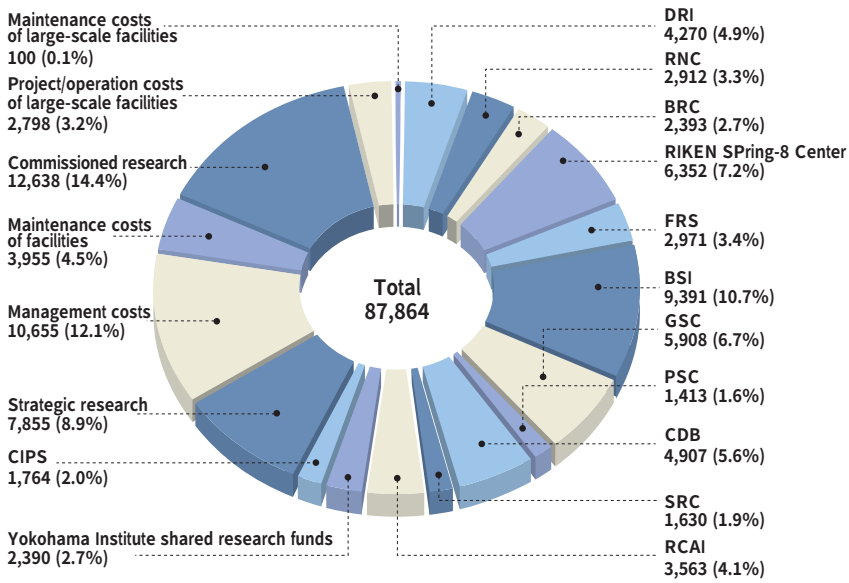
(unit: million yen)

Self income

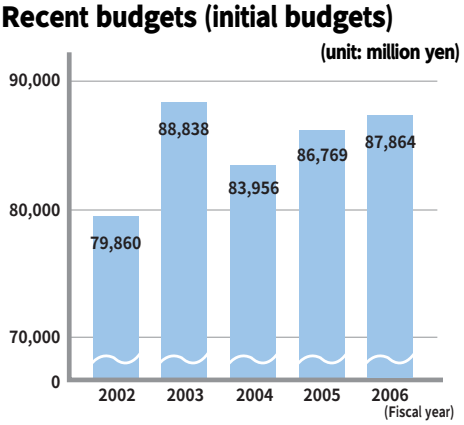


Expenditure

(unit: million yen)



Recent budgets (initial 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 2006.

Acquisition of external funds

Category	Description		FY2004		FY2005		FY2006	
			million yen	cases	million yen	cases	million yen	cases
1. Competitive funds	Grants-in-aid for Scientific Research		2,458	426	2,538	484	2,634	574
	Grants-in-aid for Scientific Research (Ministry of Health, Labour and Welfare and Ministry of Environment)		61	2	133	4	38	2
	Special Coordination Funds for the Promotion of Science and Technology		534	10	417	8	328	6
	Projects funded by organizations that fund science and technology		1,457	70	1,318	64	1,228	65
	Basic Research Programs (Japan Science and Technology Agency)		0	0	556	2	544	4
	Other publicly supported projects		208	8	277	14	354	18
Sub-total			4,718	516	5,239	576	5,126	669
2. Non-competitive funds	Commission	Government-commissioned research	8,279	25	9,488	27	10,136	39
		Government-related commissioned research	148	25	263	28	261	30
	Grants	Government grants	98	31	76	13	90	15
		Private grants	61	46	51	36	115	57
	Collaborative research	Contributions	114	14	127	20	267	19
Sub-total			8,700	141	10,006	124	10,870	160
Total			13,418	657	15,245	700	15,996	829

The above has been rearranged since the previous year in line with changes made in selection criteria that went into effect in fiscal year 2005.

Acquisition of external funds, grouped by center

(unit: million yen)

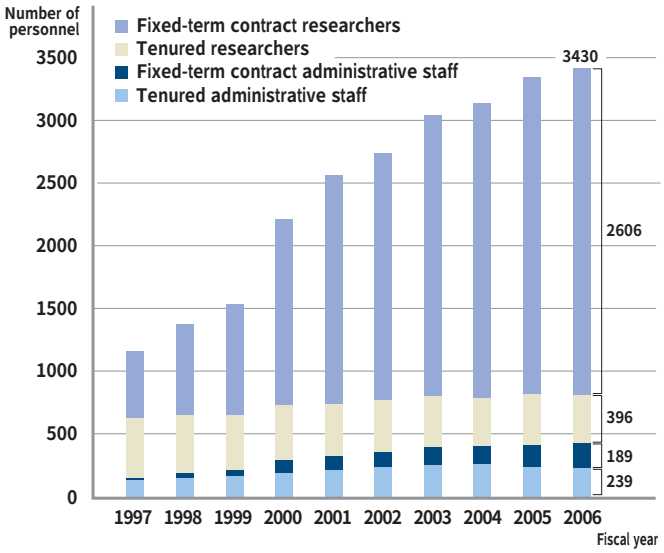
Institute		FY2004		FY2005		FY2006	
		cases	amount	cases	amount	cases	amount
Wako Institute	Discovery Research Institute	238	2,241	245	2,302	261	2,391
	Frontier Research System	52	198	48	703	62	955
	Brain Science Institute	108	817	122	579	153	792
	Center for Intellectual Property Strategies	0	0	7	25	6	50
	Nishina Center for Accelerator-Based Science	0	0	0	0	19	97
	Others	13	188	23	243	3	287
	Sub-total	411	3,444	445	3,852	504	4,573
Tsukuba Institute	BioResource Center	26	126	28	131	27	147
Harima Institute	RIKEN SPring-8 Center	22	1,273	25	2,043	37	1,896
Yokohama Institute	Genomic Sciences Center	36	5,627	35	5,792	51	5,476
	Plant Science Center	20	98	27	200	47	486
	SNP Research Center	8	1,240	12	1,730	13	1,616
	Research Center for Allergy and Immunology	68	496	65	488	74	453
	Center of Research Network for Infectious Diseases	0	0	1	170	1	293
	Sub-total	132	7,460	140	8,380	186	8,323
Kobe Institute	Center for Developmental Biology	66	1,116	62	839	75	1,058
Total		657	13,418	700	15,245	829	15,996

Enabling the best people to achieve the best results

At RIKEN, tenured employees with mandatory retirement age are mostly employed in the Discovery Research Institute, in laboratories headed by Chief Scientists, and in administrative departments. Scientists working on fixed-term projects are usually fixed-term contract employees, with one-year renewable contracts.

To stimulate innovative research, a bonus system has been introduced for fixed-term contract researchers, and annual salaries are decided based on original evaluation methods established in each research center. By constructing a transparent, fair, and satisfying employment system, RIKEN is working to forge employment policies that will encourage scientists in their endeavors.

RIKEN personnel



Fixed-term contract researchers

(fiscal year)

	2001	2002	2003	2004	2005	2006
Discovery Research Institute	248	239	223	206	212	200
Frontier Research System	126	124	134	175	168	217
Nishina Center for Accelerator-Based Science	-	-	-	-	-	62
Brain Science Institute	426	488	457	499	531	540
BioResource Center	7	16	37	45	53	52
SPring-8 Center	56	80	97	117	93	86
Genomic Sciences Center	346	243	396	390	408	393
Plant Science Center	99	110	92	99	94	134
SNP Research Center	66	94	131	131	115	115
Research Center for Allergy and Immunology	79	138	163	177	238	229
Center for Developmental Biology	119	210	269	293	308	318
Center for Intellectual Property Strategies	-	-	-	-	51	68
Other	232	220	231	218	236	192

International diversity

International cooperation is a cornerstone of scientific research, and RIKEN employs many researchers from overseas. Various services are provided to help them and their families adjust to living and working in Japan.

Foreign employees receive a handbook called *Life in RIKEN* and a monthly English-language newsletter called *ICO News*, and English-speaking staff are available in ICO Room and other offices.

Foreign researchers at RIKEN by area of origin
(includes visiting researchers)

Asia (excluding Korea and China)	90
Africa	4
Oceania	16
Europe	293
Korea	58
China	137
Middle East	14
Central and South America	9
North America	64
Total	685

Foreign researchers by center/institute
(includes visiting researchers)

Discovery Research Institute	144
Frontier Research System	82
Nishina Center for Accelerator-Based Science	57
Brain Science Institute	184
BioResource Center	14
SPring-8 Center	33
Genomic Sciences Center	56
Plant Science Center	20
SNP Research Center	12
Research Center for Allergy and Immunology	16
Center for Developmental Biology	40
Center for Intellectual Property Strategies	13
Units and Initiative Research Units	12
Next-Generation Supercomputer R&D Center	2
Total	685

New salary system

For Japanese science and technology to advance, RIKEN believes that an appropriate degree of mobility is necessary so that scientists can acquire experience in a wide range of work settings. RIKEN also believes that appropriate remuneration for outstanding achievements is one way to motivate and encourage young scientists.

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

As this system is more widely applied at RIKEN and other organizations, we hope that it will stimulate greater mobility among young Japanese scientists, making them more internationally competitive and raising the standards of science and technology in Japan.

Fostering the development of young researchers

Junior Research Associate Program

The Junior Research Associate (JRA) program employs young doctoral candidates to work at RIKEN laboratories as part-time staff. The intent of the program is to foster the next generation of researchers. The JRA is expected to complete his or her doctoral degree within the contract term.

Contract term: one year
(renewable subject to evaluation up to a maximum of three years)
Total number of JRAs in FY2006: 144

Special Postdoctoral Researcher Program

RIKEN's program for Special Postdoctoral Researchers (SPR) was instituted in fiscal 1989 to provide young and creative scientists with the opportunity to be involved in autonomous and independent research. Candidates must be under the age of 35 and must have a doctoral degree in the natural sciences or equivalent research capability, and must independently and responsibly pursue a research topic of their own choosing at RIKEN.

Contract term: one year
(renewable subject to evaluation up to a maximum of three years)
Total number of SPRs in FY2006: 195

Initiative Research Unit System

The purpose of this new system is to recruit young, creative scientists and give them the opportunity to pursue independent research to open up hitherto unexplored fields. Initiative Research Scientists are selected based on the originality of their research and the validity and feasibility of their proposals. They serve as the leaders of Initiative Research Units, which conduct independent research. Beginning in fiscal 2007, RIKEN is recruiting Initiative Research Scientists internationally, especially in fields we consider strategically important.

In fiscal 2006, eleven units were brought together to form the Initiative Research Program, part of the Frontier Research System. As of March 2007, there are nine active units in this Program. The one-year contract term is renewable subject to evaluation up to a maximum of five years.

- **Imakubo Initiative Research Unit**
  Creating 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 behavior in the central nervous system
- **Manabe Initiative Research Unit**
  Developing a new catalytic system for novel organic synthesis
- **Okamoto Initiative Research Unit**
  Designing functional biopolymers on an atomic scale using organic synthesis
- **Miyagishima Initiative Research Unit**
  Identifying and characterizing novel organelle division proteins (in chloroplasts and mitochondria) that are contributed by the eukaryotic host

Sponsored Laboratories

To build stronger bonds between RIKEN and industry, RIKEN has created the Sponsored Laboratory Program, whereby an invited scientist can establish a laboratory at RIKEN using only corporate and other private funds. As of March 2007, the Abe Laboratory is studying physiologically active substances produced by hornets.

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 holds 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 public on open days, and hosts a variety of scientific lectures and other activities to encourage greater understanding of its science and technology.

RIKEN Gallery, Wako

Research presentations in FY2006

Center / Institute	Original papers published		Articles in journals		Oral presentations		Total
	English	Japanese	English	Japanese	Overseas	In Japan	
Discovery Research Institute	464	31	42	136	627	1160	2460
Frontier Research System	329	87	18	61	384	444	1323
Nishina Center for Accelerator-Based Science	91	5	11	10	76	163	356
Brain Science Institute	278	27	28	131	455	426	1345
BioResource Center	88	5	5	41	68	150	357
SPring-8 Center	175	4	11	68	263	296	817
Genomic Sciences Center	152	4	14	79	227	248	724
Plant Science Center	74	3	19	18	120	176	410
SNP Research Center	29	0	3	21	25	54	132
Research Center for Allergy and Immunology	87	2	23	43	87	178	420
Center for Developmental Biology	133	1	12	41	80	97	364
Center for Intellectual Property Strategies	13	5	1	15	29	86	149
Others	0	0	0	0	0	1	1
Total	**1,913**	**174**	**187**	**664**	**2,441**	**3,479**	**8,858**

Comparison of total number of citations, number of citations per paper, and number of citations per paper within Japan of published RIKEN papers (1996–2006)

Fields	Total number of citations	Number of citations per paper	Number of citations per paper within Japan
Biology and biochemistry	39,047	17.67	12.56
Physics	38,871	8.91	7.11
Molecular biology and genetics	38,130	27.08	20.14
Chemistry	19,927	9.56	8.54
Neuroscience and behavior	19,417	21.62	12.21
Plant and animal science	16,493	20.98	5.83
Clinical medicine	9,762	15.47	8.74
Immunology	6,803	35.07	18.97
Microbiology	5,003	4.46	3.01
Engineering	4,968	11.16	10.28
Materials science	2,095	5.56	4.83
Multidisciplinary	1,025	48.81	11.31
All fields	209,600	13.67	8.11

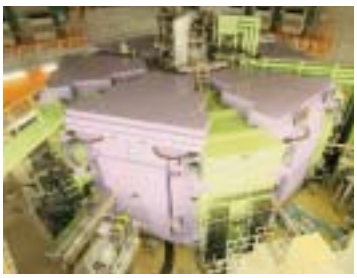
(Source: Thomson ISI Essential Science Indicators)

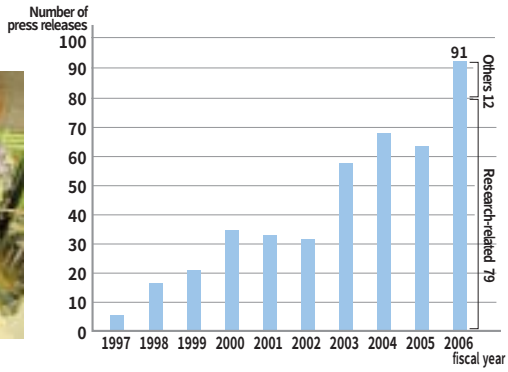
RIKEN Seminars and Symposiums

	2002	2003	2004	2005	2006
RIKEN Seminars	142	179	205	205	242
RIKEN Symposiums	37	39	40	40	34

Press releases

In fiscal 2006, RIKEN made 79 research-related press releases (including ones for RIKEN-initiated joint research with other organizations) and 12 press releases regarding other matters. Additionally, there were 10 press releases related to joint research initiated by other organizations, and reference materials were distributed on 18 occasions.





Enhancing RIKEN's public image

Open day visitors (fiscal year)

		2005	2006	
Wako Institute		7,103	Apr. 22	6,664
Tsukuba Institute	General Open Day	551	Apr. 19	622
	Special Open Day	381	Apr. 22	481
Harima Institute		2,506	Apr. 23	2,898
Yokohama Institute		1,663	June 24	1,644
Kobe Institute		1,401	May 20	1,010
Terahertz-Wave Research Program (Sendai)		Not held	Oct. 27	61
Bio-Mimetic Control Research Center (Nagoya)		645	Nov. 11	583
Total		14,250		13,963

RIKEN Science Lectures 2006

A vision of the future led by computer science—people, goods and environment

Date: 26 October **Venue:** Marunouchi Building Hall,Tokyo **Audience:** 391

Lectures: **Is a computer with a mind feasible?**
(Kenichiro Mogi, Senior Researcher, Sony Computer Science Laboratories)

World's fastest specific computer MDGRAPE-3 and protein simulation
(Makoto Taiji, Team Leader, Genomic Sciences Center, Computational and Experimental Systems Biology Group, High-performance Molecular Simulation Team)

Simulation using a supercomputer and next-generation development project
(Ryutaro Himeno, Chief, Advanced Center for Computing and Communication; Group Director, Next-Generation Supercomputer R&D Center)

Science research in the era of forecasting
(Koji Kaya, Director, Wako Institute)

Research Ethics Committees

With recent advances in the life sciences, RIKEN is very aware that ethical issues must be given the attention they deserve. For example, ethical issues arise in experiments involving the use of human subjects, and experiments involving blood and other materials collected from humans and the handling of medical records. Life scientists cannot conduct their research without the consent of the people who cooperate as subjects.

Since the first research ethics committee was established in the Brain Science Institute in 1998, several RIKEN institutes have established research ethics committees. Currently four RIKEN institutes have their own research ethics committees, and a system whereby the committees oversee all clinical research, including joint research with outside organizations, was set up in 2006. We have invited eminent persons from outside organizations to become members of the committees to ensure objectivity. Transparency is maintained through public disclosure of committee review summaries on our websites.

	No. of committee meetings held	Total no. of cases reviewed
Wako Institute	18	96
Tsukuba Institute	7	21
Yokohama Institute	11	59
Kobe Institute	5	12

The Center for Intellectual Property Strategies

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 President Noyori's call for making RIKEN useful to the world. CIPS is responsible for the licensing of intellectual property produced through research activities, collaboration with industry through joint research, and the acquisition of external and competitive funding. Through these functions, CIPS acts as a gateway between RIKEN and the outside world for intellectual property matters. In addition to this, there are three research projects directly under the auspices of CIPS to assist industry with technology transfer.

1. Acquiring patents

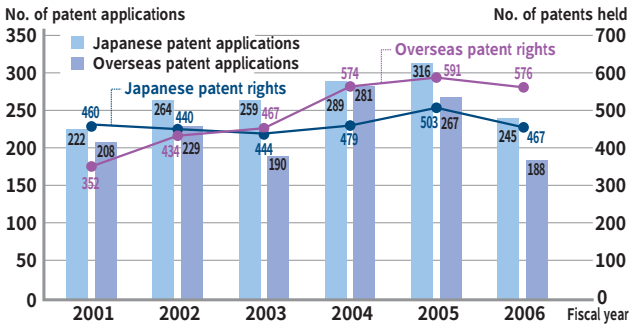
RIKEN works with its researchers to identify patentable intellectual property and provides advice on patenting inventions. It also holds patent seminars and provides instruction on inventions and intellectual property tailored to specific fields of science and technology and projects being conducted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

Overseas patent applications: The possibilities of applying in other nations for inventions for which Japanese applications have already been completed are also thoroughly investigated.

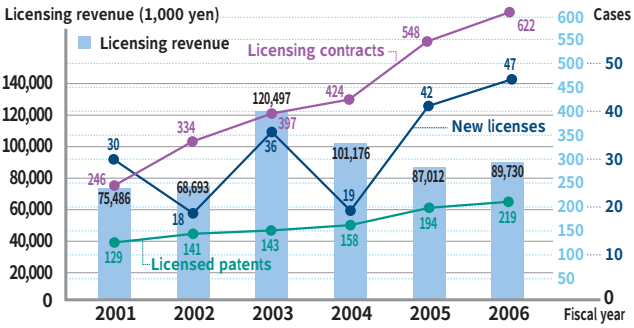
Patent rights: The licensability of patent rights possessed by RIKEN or its scientists or collaborators are also regularly checked and verified to efficiently manage them as necessary.

Applications filed in FY2006: 433 patents, 2 trademarks
(in FY2005: 583 patents, 1 utility model registration, 2 trademarks)

Patent applications and registrations



Patent income, licenses and license contracts



2. Technology transfer for practical applications

Email newsletter on collaboration with industry

In July 2006, RIKEN launched an email newsletter on collaboration with industry. The newsletter contains information on new inventions and events related to technology transfer. The main subscribers to this newsletter are companies interested in incorporating technological advances in their products and operations. The newsletter has 500 subscribers, from 285 companies.

Technology transfer seminars

Since fiscal 2006, technology transfer seminars have been held on five occasions. These seminars are announced in the email newsletter described above and provide opportunities for specialists to provide technology transfer information to interested parties.

Center for the Promotion of Collaboration with the Industrial Sector

This new program for collaborating with the industrial sector was started in February 2007. Unlike as in our earlier joint research projects, in this new scheme RIKEN and industry collaborate in areas such as research support and technology deployment. Typically, RIKEN and a company enter into a contract based on proposals made by the company and a center is established within RIKEN for collaborative research on a broad range of themes and objectives. The objective is to foster new fields and encourage talented personnel. The company's name may appear in the name of the center.

The RIKEN Incubation Plaza

Using our research expertise as a basis, RIKEN has cooperated with Saitama Prefecture, Wako City, and the Organization for Small and Medium Enterprises and Regional Innovation, Japan (SMRJ) to launch this project. A building is being constructed at RIKEN's Wako campus to serve as an incubation facility for ventures, and to provide a support framework for the venture companies which will have offices there. Preparation for the facility began in February 2007, and its opening is scheduled for January 2008.

3. Supplying bioresources

Bioresources are collected and maintained at the RIKEN BioResource Center (BRC) in Tsukuba, and recorded in a database to actively promote supply to outside users.

	FY2006 (as of March 31, 2007)
Laboratory animals (mice)	2,285 strains
Laboratory plants (seeds, DNA, cultured cells)	390,185 strains (including clones)
Cell bank	5,888 cell lines
DNA samples	1,027,471 clones
Micro-organisms	16,459 strains

4. Research collaboration

RIKEN collaborates with Japanese and overseas research institutions, as well as with various industrial, academic, and governmental institutions. RIKEN signed the following collaborative research agreements during fiscal 2006: research cooperation with the University of Helsinki, cooperation and collaboration with the Japan Agency for Marine-Earth Science and Technology (JAMSTEC), and an agreement on the development of cutting-edge supercomputers with the University of Tsukuba and the National Institute of Informatics.

Joint Graduate School Programs

It has always been RIKEN's policy to promote collaborative relationships with universities by accepting university students into its laboratories as trainees. This policy was expanded in 1989 with the launching of a joint RIKEN–Saitama University graduate program, the first time such a program was introduced in Japan. As of fiscal 2006, RIKEN has joint programs with the 24 universities listed below.

Saitama University
University of Tsukuba
Tokyo University of Science
Toyo University
Tokyo Institute of Technology
Tohoku University
Rikkyo University
Chiba University
University of Hyogo
Tokyo Denki University
The University of Tokyo
Yokohama City University
Kyushu Institute of Technology
Kobe University
Kyoto University
Nara Institute of Science and Technology
Toho University
Kansai Gakuin University
Niigata University
Tokyo Medical and Dental University
Nagaoka University of Technology
Osaka University
Hokkaido University
Ritsumeikan University

Asian Joint Graduate School Program

In order to encourage the promotion of science in the wider Asian region, a network was established in 2001 with 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).

International Associate Program

In 2006 the International Associate Program was established for RIKEN to accept foreign doctoral candidates in cooperation with domestic and overseas graduate schools. The purpose of the program is to train talented young researchers and help build an international research collaboration network.

For this program, RIKEN has made agreements with the Graduate School of Frontier Science of the University of Tokyo, Tokyo Medical and Dental University, and Tokyo Institute of Technology. RIKEN intends to enhance this program by collaborating with other educational institutions, both in Japan and abroad.

Organizational structure of RIKEN (as of March 31, 2007)

President
Ryoji Noyori

Executive Directors
Kenji Okuma
Shin Ohkouchi
Toichi Sakata
Kenji Takeda
Yoshiharu Doi

Auditors
Takeo Katou
Takanobu Hashimoto

Senior Advisors
Akito Arima
Kunio Iwatsuki
Shunichi Kobayashi
Fumitaka Sato
Fumimaro Takaku
Ken Taneichi
Norihito Tanbo

RIKEN Headquarters
- Research Priority Committee
- Policy Planning Division
- Public Relations Office
- General Affairs Division
- Personnel Division
- Finance Division
- Contract Management Division
- Facilities and Utilities Division
- Safety Division
- Auditing and Compliance Office
- Internal Communications and Systems Support Office
- Center for Intellectual Property Strategies
- Advanced Center for Computing and Communication
- Structural Genomics/Proteomics Initiative
- Next-Generation Supercomputer R&D Center
- SPring-8 Joint Project for XFEL

Wako Institute
- Discovery Research Institute
- Frontier Research System
- Nishina Center for Accelerator-Based Science
  - DRI/FRS Promotion Division
- Brain Science Institute
  - Brain Science Promotion Division
- Research Program for Computational Science

Tsukuba Institute
- BioResource Center
- Research Collaborative Group
  - Tsukuba Research Promotion Division
  - Tsukuba Safety Center

Harima Institute
- RIKEN SPring-8 Center
  - Harima Research Promotion Division
  - Harima Safety Center

Yokohama Institute
- Genomic Sciences Center
- Plant Science Center
- SNP Research Center
- Research Center for Allergy and Immunology
- Center of Research Network for Infectious Diseases
  - Yokohama Research Promotion Division
  - Yokohama Safety Center

Kobe Institute
- Center for Developmental Biology
  - Kobe Research Promotion Division
  - Kobe Safety Center

RIKEN facilities

Japan

RIKEN 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, Japan
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Fax +81-48-462-1554

Tsukuba Institute
BioResource Center
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Fax +81-29-836-9109

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

Yokohama Institute
Genomic Sciences Center
Plant Science Center
SNP Research Center
Research Center for Allergy and Immunology
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Fax +81-45-503-9113

Kobe Institute
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Molecular Imaging Research Program
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Fax +81-78-304-7112

Terahertz-Wave Research Program
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Fax +81-22-228-2122

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(in the Nagoya Science Park Research and Development Center)
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RIKEN BNL Research Center
Bldg. 510A, Upton, NY 11973, USA
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Fax +1-631-344-8260

RIKEN-MIT Neuroscience Research Center
MIT 46-2303N, 77 Massachusetts Avenue, Cambridge MA 02139, USA
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Fax +1-617-324-0976 or +1-617-452-2588

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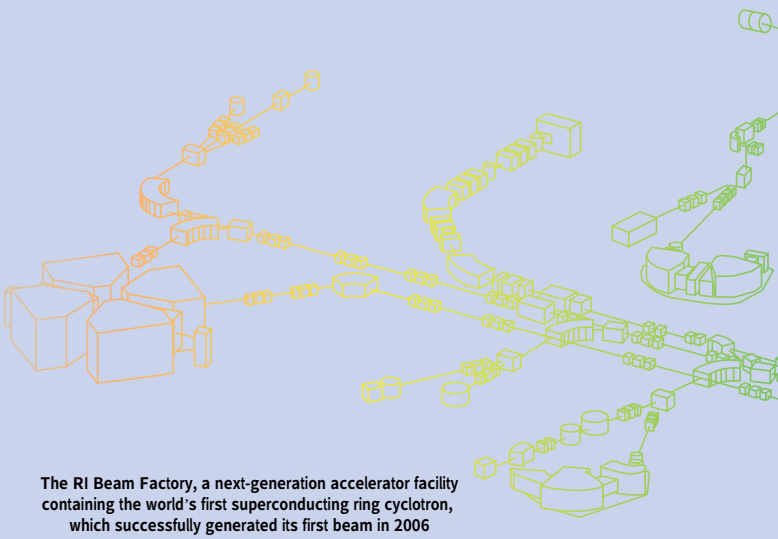
Fax +65-6478-9943

RIKEN China Office
c/o JST Beijing Representative Office, #1121 Beijing Fortune Bldg., No.5
Dong San Huan Bei Lu, Chao Yang District, Beijing 100004, China
Tel. +86-10-6590-8077
Fax +86-10-6590-8270

www.riken.jp
koho@riken.jp



The RI Beam Factory, a next-generation accelerator facility containing the world's first superconducting ring cyclotron, which successfully generated its first beam in 2006

RIKEN Public Relations Office

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