RIKEN
ANNUAL REPORT
2008–2009

Science Serving Society

RIKEN

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Message from the President

The Spirit of RIKEN

The year 2008 was highly auspicious for the Japanese scientific community as it witnessed the awarding of Nobel Prizes to four Japanese-born researchers. These awards demonstrated to the world the resilient underlying strength of basic research in Japan.

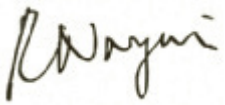
It should be noted that the prizes were awarded for the most basic of basic research. I hope that the promotion of basic scientific research, in a country that has tended to focus on economic matters, will only increase, and that this will lead more young people to discover the wonder of natural science and to devote themselves to its study.

Scientific research is a gradual process of building—piling up brick upon brick, some larger, some smaller—on the foundations built by our scientific predecessors. Provided these foundations are strong, and the science constructed thereupon is built in an elegant and well-ordered fashion, the results endure regardless of the passage of years. In its turn, scientific endeavor nurtures the growth of technology and all the benefits to society that this brings.

The role of science and technology is not fixed but changes with time. Furthermore, it is not introspective. Instead science points the way to solutions of problems critical to the continuation of the human line: from the environment, the food we eat and the water we drink; to energy, health, biodiversity and chronic poverty. In order for us to survive as a species on this crowded planet with its limited resources, we have a duty to promote the scientific understanding of the man-made and natural worlds, and provide scientific evidence to explain our current condition and make reliable forecasts of the likely shape of future society.

Over the last 90 years, the 'Spirit of RIKEN' has gradually evolved according to the values of its generations of scientists. A fundamental principle at the heart of the RIKEN philosophy is an emphasis on basic research at all times and in all places. The characteristic structure of RIKEN as a comprehensive research organization allows it to promote energetic and structured research activities while at the same time developing strategic technologies of national importance. This is combined with a dedication to delivering world-class research outcomes for the betterment of society.

I hope that this RIKEN Annual Report will provide an insight into our latest work and will encourage yet further interest in, and support for, the activities of RIKEN.



NOYORI Ryoji (DEng)
President

This report covers the research and global activities of RIKEN in the fiscal year 2008–2009, and is divided into three main sections. The first of these (pages 2–8) covers the history and organization of RIKEN, and its promotional activities in 2008–2009 both in Japan and the rest of the world. The second section (pages 9–37) introduces RIKEN's research achievements in six principle research fields in the 2008–2009 session. For each field, a short review summarizes the main trends during the past 12 months and outlines the research centers involved in that field, and is followed by a small number of research highlights exemplifying the cream of RIKEN research published in the primary literature. The report concludes (pages 38–50) with an introduction to several major new initiatives that will guide the work of RIKEN in the coming years as well as a comprehensive Facts and Figures section that tells the story of RIKEN's year in numbers.

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History

The RIKEN Foundation was originally established in 1917 as a private research foundation. Following the Second World War, the foundation was privately incorporated as the Scientific Research Institute Ltd, or *Kagaku Kenkyusho* (KAKEN), then in 1958 was renewed as a semi-public corporation under the original name of RIKEN. The RIKEN headquarters in Tokyo were relocated in 1967 to the current location in Wako, Saitama Prefecture, north of Tokyo. Since that time, RIKEN's research activities, which range from physics to medical science, have continued to grow through the establishment of new research centers and facilities. RIKEN currently maintains laboratories not only throughout Japan but also around the world, including South Korea, the UK and the US, with offices in Singapore and China. In October 2003 RIKEN became an independent administrative institution as part of the Japanese Government's initiative to make public research institutes more globally competitive.

Distinguished Scientists of RIKEN

Masatoshi OKOCHI (1878–1952) Scientist and Executive

Masatoshi Okochi was the third president of the RIKEN Foundation. In 1922 he abolished the traditional physics and chemistry divisions, and overhauled the structure of research with the aim of giving researchers more freedom and flexibility. He is credited with creating a 'researchers' paradise' during his tenure, in which chief scientists were allowed to run independent laboratories and manage research programs, budgets and personnel at their own discretion. Okochi also had a strong entrepreneurial spirit and established the 'RIKEN *konzern*', a group of companies that used RIKEN's research results to produce commercial products.

Kotaro HONDA (1870–1954) Physicist and Metallurgist

Kotaro Honda's research focused on metallurgy and magnetism. He earned great distinction early in his career in the first decade of the twentieth century for his invention of 'KS magnet steel', a steel capable of the strongest permanent magnetism at that time. Further development of this work brought impressive results, raising the quality of Japan's research on magnetism to an international level. In 1922 Honda opened the RIKEN–Honda Laboratory at Tohoku Imperial University (now Tohoku University), where he continued his research. He was also known as a skilled educator who mentored world-famous scientists such as Shoji Nishikawa, Hakaru Masumoto and Seiji Kaya.

Umetaro SUZUKI (1874–1943) Agricultural Chemist

Umetaro Suzuki is known as the father of vitamin research in Japan. His most important achievement was the isolation from rice bran of what he named Oryzanin, or vitamin B1, which proved to be an effective cure for the debilitating disease, beriberi. When the RIKEN Foundation was established in 1917, Suzuki became Director of the Chemistry Division and undertook research on nutrition and food. He invented and developed products such as 'RIKEN Vitamin' and 'RIKEN-Shu', a type of synthetic sake. Suzuki also contributed to the development of agricultural chemistry and biochemistry in Japan, while mentoring many leading scientists.

Yoshio NISHINA (1890–1951) Quantum and Nuclear Physicist

In 1928 Yoshio Nishina published what became known as the Klein–Nishina formula, which opened a new frontier of quantum physics. In 1931 Nishina became Chief Scientist at RIKEN, where he devoted himself to studying nuclear physics, cosmic rays and elementary particle physics. During the wartime period he also developed and operated Japan's first cyclotron. In 1948, when the RIKEN Foundation became an incorporated company (KAKEN), Nishina was appointed as its first president. As the founder of modern physics in Japan, he fostered many researchers including two Nobel Laureates in Physics: Hideki Yukawa and Shin-ichiro Tomonaga.

Shin-ichiro TOMONAGA (1906–1979) Theoretical Physicist

Shin-ichiro Tomonaga joined the Nishina Laboratory at RIKEN in 1932. In 1943 he published the 'super-many-time theory', which reconciled quantum mechanics with the theory of relativity. Tomonaga further developed these ideas in his 'renormalization theory' published in 1948. This new theory was key to the development of quantum electrodynamics and won him a share of the Nobel Prize in Physics in 1965 together with two US scientists. Tomonaga was an undergraduate classmate of Hideki Yukawa at Kyoto University. He once remarked that his determination to pursue a career in physics was inspired by Albert Einstein's visit to Japan in 1922.

Hideki YUKAWA (1907–1981) Theoretical Physicist

In 1935 Hideki Yukawa published his meson theory, proposing the existence of an elementary particle that produces the strong attractive force between protons and neutrons in the nucleus of an atom. As a result of this theory, in 1949 Yukawa became the first Japanese scientist to win the Nobel Prize, which acted like a fillip for many Japanese who were struggling to rebuild the country in the aftermath of the Second World War. In 1940 Yukawa joined Nishina's laboratory at RIKEN, where he continued his research on theoretical physics. He served as Chief Scientist at RIKEN from 1961 to 1967.

Introduction to RIKEN

Since its formation as a private research foundation in 1917, RIKEN has adopted a number of organizational forms in response to the needs of society; from a fully private corporation, to a semi-public body, and finally in its current incarnation as an independent administrative institution. However, throughout its more than 90-year history, the mission of RIKEN—to carry out high-quality experimental and theoretical research in all fields of science and technology, and to disseminate publically the fruits of its endeavors—has remain unchanged. The aim of RIKEN's activities is to produce internationally recognized results that not only extend the boundaries of science and technology, but also lead to tangible benefits to society. To achieve these goals, RIKEN has fostered a unique research environment that encourages constructive competition, prioritizes the championing of new emerging research fields, and promotes a proactive stance on research in areas that hold the promise of significant practical advances for society at large.

RIKEN people

The success of RIKEN is based on its people, and it is only by investing in the best people that RIKEN will continue to grow and develop in the future. As well as recruiting top scientists from Japan, RIKEN is actively pursuing greater internationalization and setting its sights on attracting the cream of scientific talent from around the world. These efforts take many forms, from forging closer links with Japanese and international universities, research institutions and corporations, to introducing dedicated programs aimed at assisting foreign researchers become established at RIKEN. The organization aims to help all its researchers realize their full scientific potential and establish long-term careers through enhanced, sophisticated systems of research and evaluation.

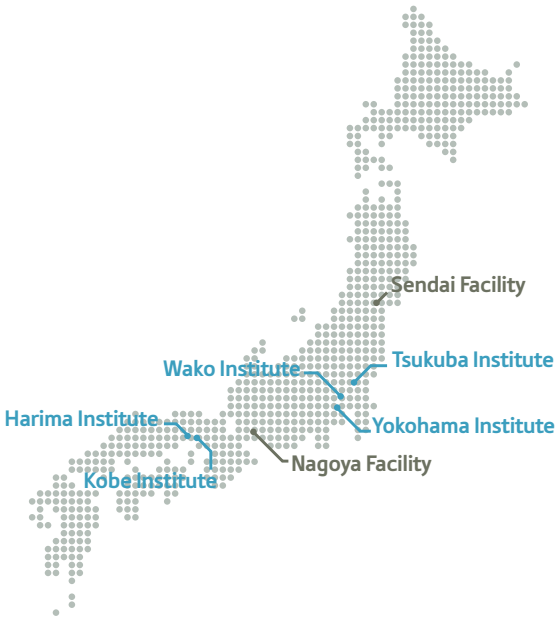
The second mid-term plan

The year 2008 marked the conclusion of the first five years of RIKEN's operation as an independent administrative institution. It also signaled the start of RIKEN's second mid-term plan, which maps out RIKEN's strategic direction for the next five years, to 2013. The guiding aims of this stage of the strategic renewal are to establish RIKEN as an institution that 1) delivers significant advances in science and technology, 2) makes a genuine contribution to society, and 3) is widely acknowledged as a recognized brand. To achieve these goals, RIKEN has set itself a series of ambitious targets that includes raising both the quality and quantity of research output, realizing improved budgetary efficiency, and promoting greater diversity in its personnel including significantly increasing the number of women and international researchers.

Structure and composition

In 2003 RIKEN was reconstituted as an independent administrative body, resulting in a significant overhaul of its operational framework. The management of RIKEN is based in its administrative headquarters in Wako, Saitama Prefecture, on the northwestern outskirts of Tokyo. This site is home to the office of the president of RIKEN and the executive directors, as well as all the administrative resources required for the smooth running of the organization.

The various research centers that form the core of RIKEN's operations are distributed among five institutes located throughout Japan, and six major offices and centers around the world.



RIKEN research institutions in Japan

The **Wako Institute** is located on the same site as the RIKEN headquarters and is home to the RIKEN Advanced Science Institute (formed in 2008 from the amalgamation of the RIKEN Discovery Research Institute and the RIKEN Frontier Research System), the RIKEN Nishina Center for Accelerator-Based Science, the RIKEN Brain Science Institute and the RIKEN Computational Science Research Program.

The **Harima Institute,** based in Harima Science Garden City west of Kobe, Hyogo Prefecture, was opened in 1997 and is home to the 'Super Photon ring-8 GeV' (SPring-8) synchrotron facility. It is also the site of the newly constructed X-ray Free Electron Laser (XFEL) facility scheduled for completion in 2010.

The **Kobe Institute,** located on an artificial island of reclaimed land in Kobe Bay, hosts the RIKEN Center for Developmental Biology and the RIKEN Center for Molecular Imaging Science. This site will also be home to the RIKEN Next-Generation Supercomputer, which is under construction and scheduled for completion by 2012.

The **Tsukuba Institute,** situated in Ibaraki Prefecture one hour northeast of Tokyo, is the site of the RIKEN BioResource Center. Since 2001, the center has established itself as one of the world's most important repositories and distribution centers for a wide range of living biological resources and human induced pluripotent stem (iPS) cell lines.

The **Yokohama Institute** south of Tokyo is home to the RIKEN Plant Science Center, the RIKEN Research Center for Allergy and Immunology, the RIKEN Center for Genomic Medicine, the RIKEN Center of the Research Network for Infectious Diseases, the RIKEN Omics Science Center, the RIKEN Systems and Structural Biology Center, and the RIKEN Bioinformatics And Systems Engineering division.

RIKEN also maintains laboratories as part of the Terahertz-Wave Research Program at the **Sendai Facility** in Miyagi Prefecture, and at the **Nagoya Facility** in Aichi Prefecture.

RIKEN facilities around the world

As well as research divisions in Japan, RIKEN maintains a strong presence overseas. In addition to its many joint research projects, it operates the following facilities and offices.

The **RIKEN BNL Research Center** was established in April 1997 at the Brookhaven National Laboratory (BNL) in New York, USA. The center is dedicated to the study of strong physical interactions, including spin physics, lattice quantum chromodynamics and Relativistic Heavy Ion Collider physics through the nurturing of a new generation of young physicists. **www.bnl.gov/riken**

Renamed in 2008, the **RIKEN-MIT Center for Neural Circuit Genetics** in Boston, Massachusetts, USA, was inaugurated in 1998 as the RIKEN-MIT Neuroscience Research Center. Formed by a collaborative agreement between RIKEN and the Massachusetts Institute of Technology, the center carries out cutting-edge research in such diverse fields as neural circuit genetics, neuroscience of learning and memory, and multiphoton imaging of synaptic plasticity. **web.mit.edu/picower/about/rikenmit.html**

The **RIKEN RAL Facility Office** at the Rutherford Appleton Laboratory (RAL) in Oxfordshire, UK, was established in 1995. Working with colleagues from RAL, scientists from the RIKEN Nishina Center for Accelerator-Based Science have constructed the RIKEN–RAL Muon Facility—the world's premier muon source and a hub for international muon research. **www.rikenresearch.riken.jp/profile/658**

The **RIKEN–Hanyang University Partnership** manages the Flucto-Order Functions Asian Collaboration Team (FOFACT) at the Fusion Technology Center, Hanyang University, Seoul, Korea. As part of an effort to establish a real-time research network in the Asian region, research at FOFACT centers on the development of novel technologies, recently dubbed 'fusion- and post- nanotechnologies', and on unconventional information-processing devices and technologies as well as new functional materials.

The **RIKEN Singapore Representative Office**, located at the Biopolis, a biomedical science research and development hub in Singapore, was officially opened on 24 April 2006 and is RIKEN's first overseas representative office. **www.riken.sg**

The **RIKEN China Office**, established in 2006, is situated in the Chao Yang district of Beijing, China. The China Office is the focal point for all of RIKEN's activities on the Chinese mainland. **www.riken.org.cn**

Annual roundup

A year of international outreach in the pursuit of excellence

RIKEN is a truly international organization and its mission is multi-faceted. The pursuit of scientific excellence is combined with the desire to create an organization with influence that does not stop at Japan's shores, but extends across the world to make real and long-lasting contributions to the international community and society. In 2008–2009 RIKEN continued in its quest to carry out world-class science and extend its global activities, as exemplified in the following small selection of highlights from the year.

Prime Minister Aso visits RIKEN facility in South Korea

In January 2009 Japanese Prime Minister Taro Aso visited the RIKEN Flucto-Order Functions Asian Collaborative Research Team at the Advanced Science Institute (ASI) in South Korea. Other VIPs at the event included Byong Man Ahn, South Korea's Minister of Education, Science and Technology, and RIKEN President Ryoji Noyori. The Collaborative Research Team is the third overseas base for RIKEN and its first in Korea, operating out of the new Fusion Technology Center at Hanyang University in Seoul.

The joint facility was established in summer 2008 as part of continuing efforts at RIKEN to build research networks with Asian nations. Researchers at the center are conducting investigations into new information-processing devices utilizing the phenomenon of self-organizing behavior with a view to developing electronic devices that exploit molecular fluctuation and instability, phenomena that until recently have been seen as obstacles to functionality. The center is also expected to produce new functional materials and information-processing technologies.

Following an introduction to the work of the Fusion Technology Center from Chong Yang Kim, President of Hanyang University, visitors were given a guided tour of the facilities by Prof. Haiwong Lee of Hanyang University, and Dr Masahiko Hara, Director of the Advanced Science Institute's Global Collaborative Research Group.

Prime Minister Aso's visit focused on cooperative activities in Asia, and RIKEN President Noyori explained that the collaborative research project is not just a one-sided exchange of researchers coming to Japan from South Korea, stressing the importance of cooperation in utilizing the complementary strengths of each country in science and technology diplomacy. ■

Japanese Prime Minister Taro Aso (third from left, in purple tie) meets with staff and students of the RIKEN–Hanyang University facility. RIKEN President Ryoji Noyori (third from right), the Korean Education and Science Minister Byong Man Ahn (second from left), and Prof. Chong Yang Kim (first from left) were among the VIPs attending the event.

Gender equality in research seminar

A delegation from RIKEN attended the US–Japan Roundtable Discussion on Equal Participation in Science and Engineering, which was held at Hokkaido University, 16–18 February 2009. The conference was jointly sponsored by the US National Science Foundation and the Support Office for Female Researchers, Hokkaido University.

Although RIKEN already has an active gender-equality program to support the various needs of all its researchers, including maternity support for female researchers and help with nursery and childcare for staff with small children, it is conscious that more needs to be done.

At the roundtable discussion, a group of 13 American and Japanese gender-equality experts discussed the issues and problem areas related to gender-equal participation, and gave ideas on how the two countries can cooperate to address these issues. The meeting also included presentations on equal participation promotion programs in Japan and the US, and workshops on career development, work-life balance and leadership training. ■

RIKEN president Noyori visits Malaysia

RIKEN President Ryoji Noyori visited Malaysia between 30 November and 3 December 2008 to sign an International Research Associate Program agreement between RIKEN and the University of Science, Malaysia (Universiti Sains Malaysia (USM)). He also delivered two lectures at the invitation of the Academy of Sciences, Malaysia (Academi Sains Malaysia) in a trip aimed at strengthening cooperation with the Southeast Asian nation.

The agreement concluded by President Noyori expands the current program, which has been in place since 2001, from the life sciences to include physics and chemistry. Under the expanded program, three or four graduate students per year, up to a total of 10, will receive research guidance for up to three years.

In addition, President Noyori discussed wider cooperation between RIKEN and USM in the future, and met with four doctoral students who will study at RIKEN from next year under the coordinated graduate school agreement.

RIKEN–Nishina Memorial Symposium

The RIKEN Wako campus welcomed around 150 delegates for the RIKEN–Nishina Memorial Symposium on 'Charging Molecules: Fundamental Chemical Physics and Analytical Applications' in December 2008. The symposium, which was organized by RIKEN and the Japan Academy of Sciences, and cosponsored by the Nishina Memorial Foundation, boasted a distinguished line-up of world-class scientists topped by Nobel Prize winners Yuan T. Lee and Koichi Tanaka, who gave plenary lectures. Several other distinguished researchers, including Haruo Shiromaru of the Tokyo Metropolitan University, RIKEN's Toshinori Suzuki and Maki Kawai, and Nagoya University chemist Hisanori Shinohara, spoke about the latest developments in their fields.

RIKEN hosts Chinese graduate students from earthquake-hit province

Five Chinese graduate students whose families and homes were affected by the devastating earthquake that hit China's Sichuan Province in May 2008 were invited to visit Japan as short-term researchers courtesy of RIKEN. The students, from the Chinese Academy of Sciences and Southwest Jiotong University, conducted experiments at RIKEN and visited other Japanese universities for three months beginning in January 2009.

The offer is part of ongoing relations between RIKEN and the Chinese research community that date back nearly three decades to the Memorandum of Understanding on Research Collaboration signed in 1982. More recently, in February 2008, RIKEN and Peking University entered into an agreement for strategic cooperation under RIKEN's Joint Graduate School Program.

RIKEN Brain Science Institute–Harvard summer internship program continues

The RIKEN Brain Science Institute (BSI) and Harvard University continued their collaboration on the RIKEN BSI–Harvard University Undergraduate Student Internship Program in 2008. Five Harvard students took part in the month-long internship, with one student joining each of the BSI's Hessler, Saido, Leeuwen, Hosoya and Okanoya groups.

Olivia Pure White blooms thanks to heavy ion beams

Researchers at the RIKEN Nishina Center for Accelerator-Based Science have succeeded in creating a new variant of dianthus flower by bombarding axillary buds of an existing strain of dianthus with heavy ions from the RIKEN Ring Cyclotron (RRC). The new flower, created over three years in cooperation with Hokko Chemical Industry Co., has been dubbed 'Olivia Pure White'. The flowers are a pure white and bloom throughout the year, and the plant has wide-spreading stems that reach a height of up to 10 cm.

BRC begins distribution of human iPS and ES cells

The RIKEN BioResource Center (BRC) in collaboration with Kyoto University began the distribution of human induced pluripotent stem (iPS) cells and human embryonic stem (ES) cells to nonprofit research organizations on 25 March 2009.

Pluripotent stem cells are a special type of cell that is capable of developing into any kind of cell in the body. As such, iPS cells have exciting potential in the development of medical therapies for a wide range of diseases that are currently untreatable. They can also be used to treat damage to the brain, spinal cord, skeletal muscles and heart.

Two lines of human iPS cells were deposited at the BRC by Prof. Shinya Yamanaka, head of the Center for iPS Cell Research and Application at the Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University. In addition to this service, the RIKEN BRC has also started providing KhES-1, an ES cell line, which was established by Norio Nakatsuji of Kyoto University.

To receive the iPS cells, the researcher wishing to use them and the institution's authorized representative must submit a Material Transfer Agreement to Kyoto University and the BRC. Copies of the forms may be obtained from:
www.saci.kyoto-u.ac.jp/ips/ips_index_e.html
www.brc.riken.jp/lab/cell/english/

The RIKEN BRC provides the iPS cells for free, but charges a small transport fee to cover preparation, handling and distribution costs.

Physics

A universe of discoveries

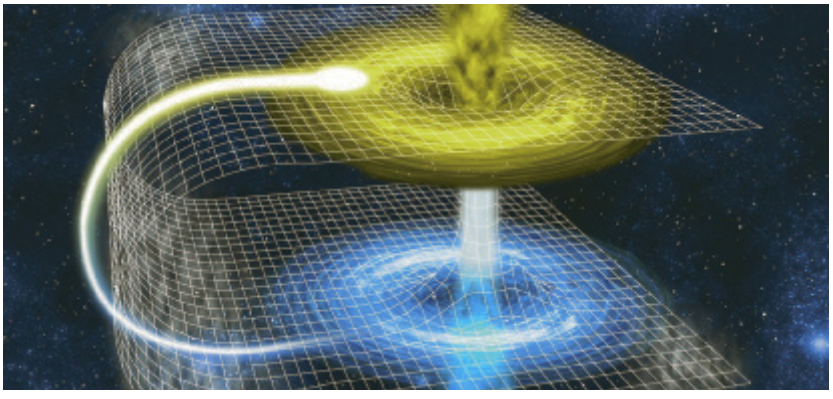
The breadth and strength of physics research at RIKEN has seen its researchers actively contribute in areas related to the topics that dominated physics headlines in 2008: the discovery of a new class of superconductors and answering questions on matters of matter using particle accelerators.

Stringing the universe together

One of the questions concerning particle physicists is the origin of sub-atomic particles, such as the electron, and forces, such as gravity. In this context, string theory is widely touted as a way to unify existing theories on these fundamental questions. Physicists at the RIKEN Nishina Center for Accelerator-Based Science in 2008 showed that string theory can indeed be used to describe gravity and extreme manifestations of its effects in objects such as black holes (Fig. 1)[1].

Meanwhile, physicists still struggle to explain why matter predominates in the universe and its counterpart, antimatter, does not. To address this basic discrepancy, one must investigate the properties of antimatter in detail. To this end, experiments at the RIKEN Advanced Science Institute (ASI) aimed at producing large numbers of cold antiprotons as well as entire antimatter atoms have been carried out[2].

Figure 1: An artist's impression of a pair of black holes.



Smaller, better, cheaper

In 2008 RIKEN researchers at SPring-8 in Harima were able to significantly reduce the scale of free-electron lasers (FELs) in the extreme ultraviolet wavelength range[3]. This unique design concept, called the 'SPring-8 Compact SASE Source' (SCSS), is crucial to the development and success of new compact high-performance X-ray free-electron lasers (XFELs), which are capable of generating coherent and brilliant X-rays with ultra-short pulse durations. XFELs promise to lead to innovations in research activities across many scientific fields. Unlike ring-based light sources that can simultaneously accommodate many users, however, XFELs are better suited to single users. By applying the SCSS concept to downsize XFELs, RIKEN has overcome this limitation.

Big physics at a small scale

Use of the quantum properties of energy states in 'artificial atoms' made from superconducting circuits is at the forefront of the quest to develop novel types of fast computers. At the ASI, researchers are continuing to manipulate quantum information toward the realization of quantum computers[4]. Another group at RIKEN

has concerned itself with trying to measure the 'superconducting gap'—an important energy associated with superconductivity—of high-temperature superconductors[5]. The team developed a new microscopy technique to investigate the properties of the superconducting gap in high-temperature superconductors. Although the critical temperature (the temperature below which a material becomes a superconductor) is strongly material dependent, little difference in the superconducting gap was observed among materials, indicating that superconductivity is more complex than previously thought.

To improve conventional electronics, the use of the electron's spin rather than its charge is a promising alternative. Novel device structures remained a focus of exploration at the ASI in 2008, and new materials such as silver were investigated for their improved 'spintronic' properties, such as the ability to maintain the orientation of electron spin over long distances[6].

RIKEN scientists at the ASI made another great advance in the investigation of electron spin properties with the discovery that a metal oxide, $Na_4Ir_3O_8$, exhibits 'quantum spin-liquid' behavior at temperatures close to absolute zero (–273.15 °C). They discovered that the electrons in the metal oxide lattice, dubbed a *kagome* structure due to its resemblance to a type of Japanese basket (Fig. 2), are in a constant state of flux as they try to minimize repulsions between adjacent electron spins. This is believed to represent the first confirmed example of a quantum spin-liquid in a material described as "a fascinating playground for quantum magnetism"[7].

Figure 2: The triangular lattice of $Na_4Ir_3O_8$ (top left) means that the spin of each electron will be aligned with that of one of its neighbors producing a repulsive force. To avoid this, electrons constantly flip their spin even at very low temperatures. The triangular pattern (bottom left) resembles that of the traditional *kagome* basket design (right).

Metal nanoparticles: cleaner hydrogen storage

RIKEN scientists also address important practical issues such as the development of cleaner energy. Metal nanoparticles, for example, show promise for use in improved hydrogen storage. The interaction of hydrogen with such nanoparticles was studied at the SPring-8 synchrotron facility as part of the development of greener energy based on hydrogen rather than oil[8].

Whether concerned with understanding our universe, or seeking to advance our way of life, RIKEN's physics research remains at the frontier of scientific knowledge. ■

1. *RIKEN RESEARCH*, July 2008, p.6 (also p.11 of this report)
2. *RIKEN RESEARCH*, December 2008, p.3 (also p.12 of this report)
3. *RIKEN RESEARCH*, December 2008, p.11 (also p.13 of this report)
4. *RIKEN RESEARCH*, August 2008, p.6
5. *RIKEN RESEARCH*, April 2008, p.4 (also p.14 of this report)
6. *RIKEN RESEARCH*, April 2008, p.7
7. *RIKEN RESEARCH*, April 2008, p.3
8. *RIKEN RESEARCH*, July 2008, p.1

RIKEN Nishina Center for Accelerator-Based Science

Nestled in the hills of Saitama, just outside Tokyo, the RIKEN Nishina Center for Accelerator-Based Science (RNC) is home to several large-scale projects investigating various aspects of fundamental nuclear physics. At the heart of the facility is the Radioactive Isotope Beam Factory (RIBF), consisting of five heavy ion particle accelerators with which RIKEN physicists study atoms under extreme conditions and produce novel atomic isotopes. In 2004 a new element, ununtrium, having the atomic number of 113, was discovered at RIBF. The facility is also important for the study of biological processes.

RIKEN SPring-8 Center

The RIKEN SPring-8 Center (RSC), which aims to become the world's leading center of excellence (COE) for synchrotron science, is located in Harima at the SPring-8 facility—the most advanced synchrotron X-ray source in the world. The RSC promotes cutting-edge, advanced research for innovative high-energy light sources, such as the X-ray Free Electron Laser (XFEL), and interdisciplinary photon science using the most advanced light sources. In one endeavor, the RSC is developing instrumentation to make these technologies available to general users. Moving forward, the RSC will continue to lead the development of XFEL instrumentation and the science associated with the mission of extending human knowledge.

Stringing it together

Superstring theory applied to the interior of a black hole is revealing the links between gravitational and quantum theory

Scientists have spent many years searching for a 'theory of everything' linking the standard model of particle physics—which explains electromagnetism and the weak and strong nuclear forces—with Einstein's theory of general relativity for gravity. One of the most promising candidates to provide the link is superstring theory, in which all particles and forces are represented as vibrations of strings.

Now, Masanori Hanada at the RIKEN Nishina Center in Wako and co-workers have studied the interior of a black hole (Fig. 1), where string theory simplifies to the Super-Yang-Mills theory—a quantum mechanical gauge theory for interacting fields. Their work shows that string theory can reproduce the known gravitational properties of a black hole[1].

Superstring theory involves a concept of particle physics called supersymmetry, which links different types of particles in pairs. "Some black holes are well-approximated by both the Super-Yang-Mills theory and supergravity, which is a supersymmetric generalization of Einstein gravity—so the theories are equivalent," says Hanada. This so-called gauge/gravity duality is especially likely at low temperatures. Hanada's group set out to find further evidence of gauge/gravity duality by directly analyzing the Super-Yang-Mills theory.

"Analyzing Super-Yang-Mills theory is very difficult … and we need to rely on numerical simulation," says Hanada. In such simulations, space is usually divided into a discrete lattice—and the larger the number of lattice points, the more accurately the calculations represent real continuous space. The researchers invented a more powerful 'non-lattice' method and used supercomputers to perform a Monte-Carlo simulation (repeated computation with random sampling) on near-continuous space. They found strong agreement with supergravity.

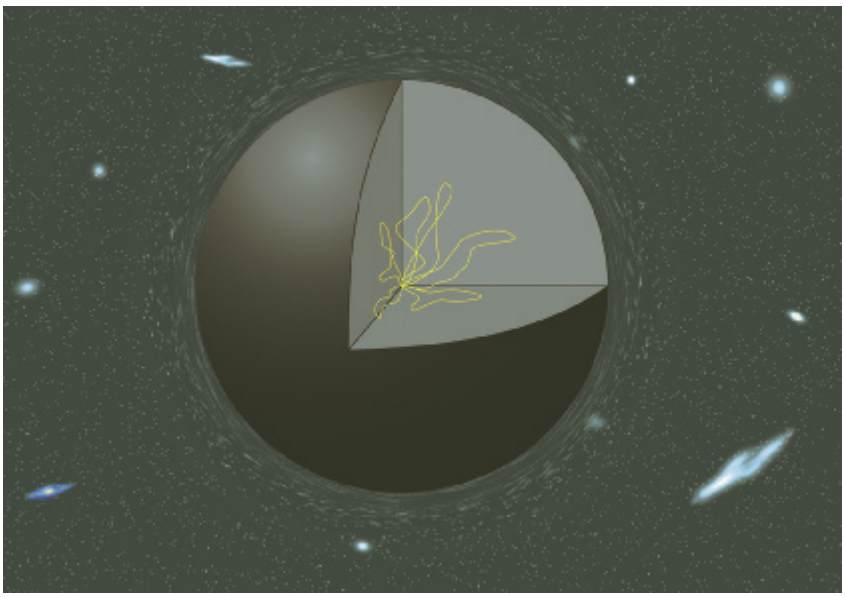


Figure 1: Superstring theory can be used to understand the region of space inside a black hole.

"Our result provides a very non-trivial check for gauge/gravity duality," says Hanada. "Also, because Super-Yang-Mills theory provides a stringy description of a black hole, our results can be regarded as evidence that a black hole is a stringy object."

The black hole they studied is defined in ten dimensions, but has many things in common with black holes in our four-dimensional world (three spatial dimensions plus time). The work suggests that realistic black holes can also be described by string theory.

The next step in the group's research will be to study lower temperatures under even more accurate simulations. "Then we can check the gauge/gravity duality more rigidly, and better understand the nature of black holes," says Hanada. ■

1. Anagnostopoulos, K.N., Hanada, M., Nishimura, J. & Takeuchi, S. Monte Carlo studies of supersymmetric matrix quantum mechanics with sixteen supercharges at finite temperature. *Physical Review Letters* **100**, 021601 (2008).

Antimatter trap to test nature's symmetry

Origins of our Universe could be probed by detailed study of antihydrogen atoms

RIKEN scientists have developed a method for trapping and manipulating antimatter that could be key to solving one of the universe's biggest mysteries.

The technique will allow scientists to "test the most fundamental symmetry of nature," says Yasunori Yamazaki of RIKEN's Advanced Science Institute, Wako.

"It is believed that our Universe started as the Big Bang some 13 billion years ago," he explains. From that burst of energy coalesced the fundamental particles of matter.

But according to a key part of quantum theory—known as charge, parity and time symmetry (CPT)—the Big Bang should have produced equal amounts of matter and antimatter, which annihilate whenever they meet. So why is our Universe mostly made of matter?

"One possibility... is that CPT symmetry is broken in some way," says Yamazaki. "So we are going to test this CPT symmetry by comparing hydrogen and antihydrogen with high accuracy."

Hydrogen is made from a positive proton and a negative electron, while antihydrogen is made from their antimatter equivalents: a negative antiproton and a positive anti-electron, known as a positron.

One of the most important techniques to advance the CPT symmetry test with antihydrogen is to manipulate an antiproton cloud to efficiently synthesize cold antihydrogen atoms. Yamazaki is leading an international group called MUSASHI, a part of the ASACUSA (Atomic Spectroscopy And Collisions Using Slow Antiprotons) collaboration, which has now developed a way to compress a cloud of antiprotons,

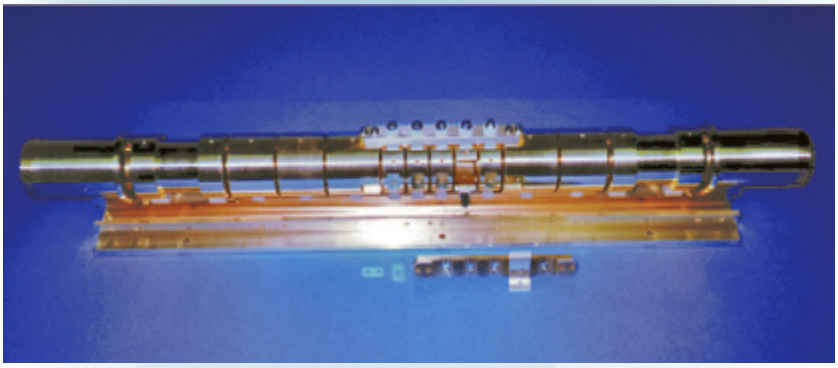


Figure 1: The multi-ring trap, which is used to trap and manipulate a large number of antiprotons.

an essential precursor to making antihydrogen that can be trapped by a magnetic field[1].

First, the team captured and decompressed a cloud of electrons in a trap that uses multi-cylindrical ring electrodes to confine the particles (Fig. 1). The strong magnetic field forces the electrons to emit so-called synchrotron radiation, which cools the electrons. Then about 50,000 energetic antiprotons were injected and mixed with the electrons, which resulted in a sympathetic cooling of the antiprotons by the electrons.

After the cooling process, the electrons were ejected from the trap, and a rotating electric field was applied to compress the antiproton cloud. This reduced the radius of the antiproton cloud to 0.25 mm, an order of magnitude smaller than the original cloud.

It's surprising that antiproton compression can be done with a rotating electric field, says Yamazaki, even after the coolant electrons have been removed. He adds that the team now hopes to synthesize and trap a large enough number of antihydrogen atoms for detailed study, which should help to answer key questions about CPT. ■

1. Kuroda, N., Torii, H.A., Shibata, M., Nagata, Y., Barna, D., Hori, M., Horváth, D., Mohri, A., Eades, J., Komaki, K. & Yamazaki, Y. Radial compression of an antiproton cloud for production of intense antiproton beams. *Physical Review Letters* **100,** 203402 (2008).

Smaller, better, cheaper

A new design for compact free-electron lasers leads the way towards exploiting extremely short wavelengths

Physicists are greatly interested in free-electron lasers (FEL) because they are capable of generating high-intensity laser radiation across a very broad wavelength spectrum, even down to the extreme ultraviolet rays and x-rays. Worldwide, several multi-billion-dollar efforts are underway to build next-generation free-electron lasers at x-ray wavelengths. As part of these efforts, a compact and efficient design has been realized by researchers from the RIKEN XFEL Project Head Office, collaborating with the Japan Synchrotron Radiation Research Institute (JASRI). They report on the superior properties of extreme ultraviolet FEL laser radiation from a first-test system in *Nature Photonics*[1].

Figure 1: A view at the beam hall of the FEL test facility. The electron gun is contained in the grey box on the left.

Free-electron lasers consist of two fundamental components: an accelerator that produces high-energy electrons, and so-called 'undulators' that send these electrons on a periodically curved path. The wiggling of the electrons along the path causes the emission of high-energy laser radiation through electro-magnetic interaction between the electrons and the radiation field.

Currently, x-ray FELs require large-scale electron accelerators of a few kilometers in length. It is important to reduce this length to enable the fabrication of cheaper FEL systems. The project team's compact FEL design of 55 m has produced a high-quality laser beam at the RIKEN Harima Institute.

To achieve this significant reduction in accelerator length, the team used special undulators with a shorter electron oscillation period, which allows the generation of x-rays with lower energy electrons. However, for this novel scheme to work effectively, "a stable and high-quality electron beam is needed, where all electrons propagate nearly parallel and with high density," comments Hitoshi Tanaka from the team. To attain such good beam properties, the team used a 'thermionic electron gun' (Fig. 1), which has a CeB6 single crystal cathode. This type of cathode is commonly used as an electron emitter in the electron microscope.

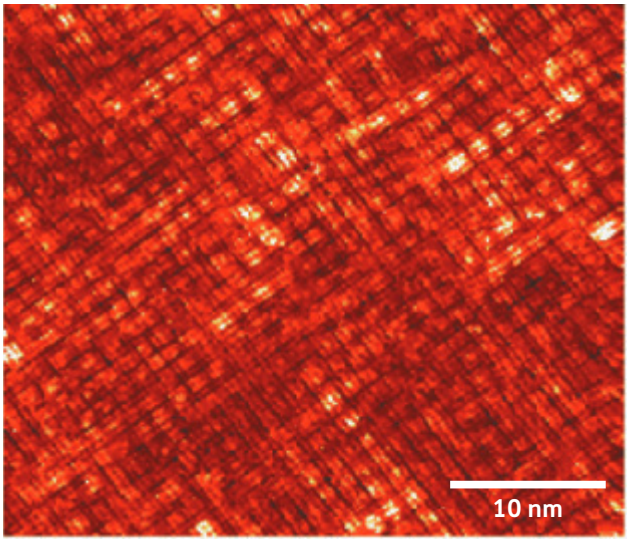
The full system presently being constructed next to the SPring-8 storage ring will reach a total length of about 700 m, which is less than a third of the length of competing designs. This shorter length reduces the construction cost, which is estimated at 370 billion yen, compared to 750 and 1,500 billion yen, respectively, for international competitors.

A future aim of the researchers is to also realize FELs at much shorter wavelengths, down to the x-ray region at around 0.1 nm, which will enable new research applications. Indeed, Makina Yabashi from the research team is convinced that this can be achieved and that "the compactness of our design will considerably expand the opportunities for engineering and medical research." ■

1. Shintake, T., Tanaka, H., Hara, T., Tanaka, T., Togawa, K., Yabashi, M., Otake, Y., Asano, Y., Bizen, T., Fukui, T. *et al.* A compact free-electron laser for generating coherent radiation in the extreme ultraviolet region. *Nature Photonics* **2,** 555–559 (2008).

'Virtual' reality check for superconductors

New clues important to our understanding of superconductivity are provided by precise measurements of electronic states



Nature Physics

Figure 1: Periodic variations of the electronic states at the surface of a superconductor. The actual quasiparticle signatures are embedded in signals originating from unrelated surface effects and need to be filtered out using mathematical techniques.

Researchers at RIKEN's Discovery Research Institute in Wako, in collaboration with researchers from Cornell University in the US, and Kyoto University, have refined a method that measures small electronic excitations in superconductors. Comparisons of these properties for different materials have provided valuable clues towards our understanding of superconductivity.

The classical theory of superconductivity describes the superconducting state arising through the pairing of electrons into pairs. The properties of these electron pairs, however, are difficult to model mathematically. Physicists therefore prefer to describe them as a virtual single 'quasiparticle'. "Although these quasiparticles are fictitious, they really govern the electronic states of superconductors, particularly at low energies," explains Tetsuo Hanaguri from the research team.

Many details of the electronic states of quasiparticles and the precise amount of energy it takes to break up the electron pairs are difficult to measure, and remain poorly understood. This 'break-up energy', referred to as the 'superconducting gap', is traditionally considered as being directly related to the critical temperature where superconductivity persists. The larger the gap, the greater the difficultly to break up the electron pairs, thus the higher the critical temperature is for superconductivity. However, this relation has never been confirmed for the so-called 'high-temperature' superconductors, whose mechanism of superconductivity remains a mystery.

Reporting in the journal *Nature Physics*[1], the RIKEN researchers have now measured the properties of the quasiparticles using a scanning tunneling microscope that scans the surface of a superconducting material with an atomic resolution and records tiny variations in the electronic structure (Fig. 1). However, the observed periodic variations in the electronic properties are difficult to analyze as a number of effects contribute to these regular patterns. Therefore, Hanaguri and colleagues developed a novel mathematical technique to successfully pick out the quasiparticle signatures.

This mathematical technique allows the researchers to characterize several materials and compare their superconducting properties. Surprisingly, the relative variation in the superconducting gap was found to be the same for two different high-temperature superconductors, although their critical temperature differs by a factor of three. This shows that, contrary to conventional assumptions, the superconducting state is influenced by more than just the size of the superconducting gap.

To better understand the relation between superconducting gap and superconductivity, Hanaguri says that further measurements are needed to determine the effect of temperature and magnetic field on the quasiparticles. Ultimately, these measurements may provide vital clues on the fundamental mechanisms governing high-temperature superconductors. ■

1. Hanaguri, T., Kohsaka, Y., Davis, J. C., Lupien, C., Yamada, I., Azuma, M., Takano, M., Ohishi, K., Ono, M. & Takagi, H. Quasiparticle interference and superconducting gap in $Ca_{2-x}Na_xCuO_2Cl_2$. *Nature Physics* **3**, 865–871 (2007).

Chemistry, materials science and nanoscience

Embracing diversity

Chemistry, by providing us with ways to manipulate molecules for specific purposes, is at the core of a wide range of fields. Research at RIKEN is at the forefront of advances across a broad spectrum, with environmental and pharmaceutical issues topping the agenda.

Super cuprates

Using carbon dioxide gas as a source of carbon for the synthesis of various chemicals would be an attractive alternative to its release into the atmosphere (Fig. 1). In reality this is difficult, as current reagents based on manganese, lithium or rhodium complexes are either too dangerous for large-scale use or too fragile. A team at RIKEN has now circumvented these issues by using copper rather than rhodium to catalyze efficiently a reaction between carbon dioxide and boron compounds[1]. In a similar manner, benzene—a ring-like organic compound found in fossil fuels—is a potential feedstock for the preparation of many chemicals. A drawback is that all its carbon–hydrogen bonds exhibit very similar behavior making selective reactions difficult. Another copper-based compound developed at RIKEN[2] can now steer additional groups toward a particular position, thus enabling good control of the molecules prepared (Fig. 2).

Figure 1: Carbon dioxide is a greenhouse gas that accelerates global warming—but it could also become a versatile synthetic chemical.

Materials world

Human activities are largely based on a variety of materials with properties such as strength, conductivity or biodegradability tailored for specific purposes. For example, rubber—a chain of isopropene molecules produced by some plants—is commonly used to make objects ranging from surgical gloves to tires. Rather than depleting natural resources, chemists can prepare this elastic polymer synthetically, but because isopropene units can be linked in different ways, a range of other products are also obtained. A group at RIKEN has now found that the pairing of two catalysts can influence polymer synthesis, allowing the selective formation of either rubber or another polymer that could be further modified to suit other applications[3].

Pharmaceuticals: from diagnosis to drug development

Most bioactive molecules are chiral—meaning that they have distinct three-dimensional structures that cannot be superimposed onto their mirror

image counterparts—and this 'handedness' is inherent to their activity. Asymmetric reactions, which favor the creation of one chiral form over the other, are crucial in order to synthesize only the active form of a molecule. RIKEN chemists have prepared a palladium complex that, when added to the aldol reaction, can help form only the desired 'handed' product[4]. In addition to the synthesis of drugs, chemistry also works hand-in-hand with biology when it comes to diagnostic and therapeutic applications. Another RIKEN team has designed an assembly of a DNA sequence, an organic linker and a metal ion, which could enable the detection of methylcytosine—a modified nucleotide present in excess in cancerous tissues—much faster than currently possible[5].

Chemical reactions: one step at a time

Viewed from the outside it is not possible to see the change in individual molecules during a chemical reaction. The reaction of single molecules, however, can be probed using a scanning tunneling microscope. Yet, until recent work by RIKEN researchers, the reactions studied were nonselective and irreversible, such that the products of a completed reaction could not be converted back to their starting state. In 2008 researchers at the Advanced Science Institute (ASI) observed the addition of individual hydrogen atoms to a molecule of methylisocyanide absorbed to a platinum surface, which produced a product called methylaminocarbyne. They also observed its removal, which regenerated the starting methylisocyanide. This is the first time that scientists have been able to break and then reform a single chemical bond at a time, representing a major step forward in surface chemistry and, potentially, molecular electronics[6].

Across these diverse fields, research carried out at RIKEN provides significant advances that could lead to a better use of our resources and the development of novel compounds for applications in materials or pharmaceutical fields. ■

1. *RIKEN RESEARCH*, November 2008, p.9
2. *RIKEN RESEARCH*, July 2008, p.11
3. *RIKEN RESEARCH*, September 2008, p.7 (also p.17 of this report)
4. *RIKEN RESEARCH*, October 2008, p.13 (also p.18 of this report)
5. *RIKEN RESEARCH*, March 2008, p.10
6. *RIKEN RESEARCH*, February 2008, p.1

Figure 2: Crude oil can be turned into medicines and useful materials with the help of cunning chemistry that replaces hydrogen atoms.

RIKEN Advanced Science Institute
Formed in 2008 and located at the main RIKEN site at Wako in Saitama Prefecture, the RIKEN Advanced Science Institute (ASI) is a relatively new addition to the RIKEN family, although its origins are much older. The institute came into being as the result of consolidation of the RIKEN Discovery Research Institute and the RIKEN Frontier Research System. Researchers at ASI carry out explorative research in new areas of all natural science with a strong emphasis on interdisciplinary research. The institute retains a flexible structure that is capable of quickly adapting to new concepts and trends in science. This is assisted by the absence of a rigidly fixed mission or a focus on particular research areas. The aim of researchers at ASI is simply to advance the frontiers of science.

RIKEN Center for Molecular Imaging Science
Molecular imaging, in which molecular probes are used to target specific cells in living organisms and produce an image of their biological processes, offers exciting possibilities in terms of diagnosis and therapeutic applications. Reflecting the multidisciplinary character of this field, the RIKEN Center for Molecular Imaging Science (CMIS) gathers researchers from very diverse backgrounds and areas of expertise. In October 2008 the CMIS was reorganized into three laboratories and three units. Each of these are advancing the drug discovery process in Japan through activities ranging from the design and synthesis of novel molecular probes, focusing on radio-labeled species in particular, to the development of new imaging technologies.

Rubbery reactions

It only takes the addition of a simple aluminum compound to a new polymerization system to switch between rubber polymers

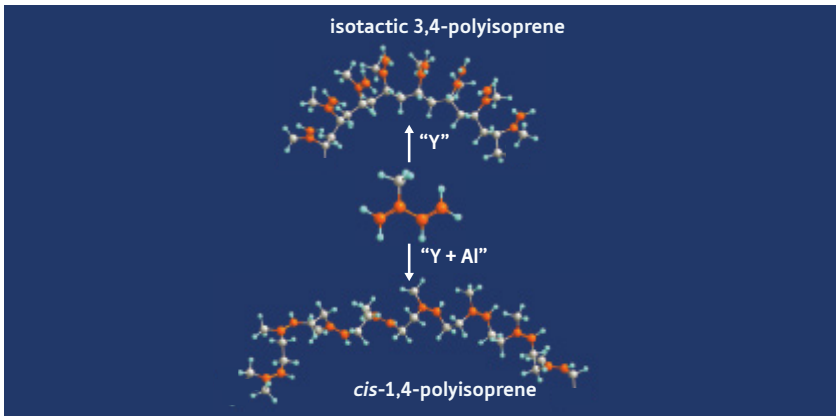


Figure 1: Isoprene (center) can form the new polymer, isotactic 3,4-polyisoprene (top) using an yttrium-based catalyst, but when trimethyl aluminum is added in sufficient quantity, 1,4-*cis* polyisoprene (bottom), the main component of natural rubber, is produced.

Researchers from RIKEN Advanced Science Institute in Wako, using a rare earth-based catalyst, have produced a novel polymer or chain of isoprene molecules with unique properties. In addition, much to their surprise, they found their polymerization system can be dramatically switched, simply by adding an aluminum-based compound, to produce a different isoprene polymer which is the main component of natural rubber.

The two polymers vary in which of the carbon atoms of the four-carbon isoprene molecules connect together to form the chain. The rubber chain (1,4-cis polyisoprene) is formed by joining the two end carbons of the isoprene molecules, whereas in the new polymer the molecules are joined at two adjacent carbons in a particular three-dimensional arrangement (isotactic 3,4-polyisoprene) (Fig. 1). It leaves the other two carbon atoms double-bonded on a side chain all along the same side of the main or polymer chain, a construction which allows a range of groups with different chemical functions to be added easily. The researchers are collaborating with a chemical company on employing this facility to transform 3,4-polyisoprene into further useful polymers.

The research group has been exploring how catalysts based on rare-earth metals—a group of elements which includes scandium, yttrium and the lanthanides—can be used to produce high-performance synthetic rubber[1]. "We need a chemical way to produce rubber," says project leader Zhaomin Hou. "Not only is the natural supply limited, but a big advantage of chemical synthesis is that it allows us to modify the properties of rubber in the laboratory."

In their latest paper published in *Angewandte Chemie International Edition*[2], the researchers discuss their work with a catalyst made up of an yttrium ion with bulky nitrogen-based groups called amidinates attached. The shape of the catalyst restricts the polymerization reaction to the two adjacent carbons at positions 3 and 4 in the isoprene molecule. The result is the new polymer 3,4-polyisoprene. But when they added trimethyl aluminum ($AlMe_3$), widely recognized as a co-catalyst which can potentially increase the activity of the catalyst system, they found the reaction began to change.

At levels below two $AlMe_3$ molecules to one catalyst molecule they were still producing 3,4-polyisoprene, but by five $AlMe_3$ molecules to one catalyst molecule, 98% of their product was rubber (1,4 *cis*-polyisoprene). "The finding that an aluminum alkyl compound can switch the selectivity of isoprene polymerization suggests that we should reconsider the role of aluminum compounds in such catalyst systems," Hou says. ■

1. Zhang, L., Suzuki, T., Luo, Y., Nishiura, M. & Hou, Z. Cationic alkyl rare-earth metal complexes bearing an ancillary bis(phosphinophenyl)amido ligand: A catalytic system for living *cis*-1,4-polymerization and copolymerization of isoprene and butadiene. *Angewandte Chemie International Edition* **46,** 1909–1913 (2007).
2. Zhang, L., Nishiura, M., Yuki, M., Luo, Y. & Hou, Z. Isoprene polymerization with yttrium amidinate catalysts: Switching the regio- and stereoselectivity by addition of $AlMe_3$. *Angewandte Chemie International Edition* **47,** 2642–2645 (2008).

Twisting around the palladium

A metal catalyst teaches an old chemical reaction new tricks

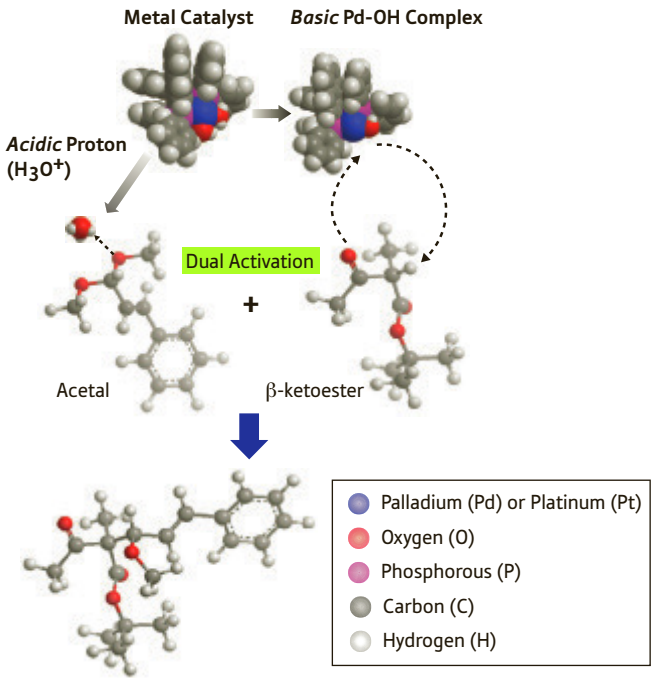


Figure 1: An asymmetric aldol-type reaction catalyzed by a palladium acid-base catalyst.

A new twist on a common chemical reaction has enabled RIKEN scientists to create molecules that are useful building blocks for making new pharmaceuticals.

The aldol reaction is a very reliable way to stitch together two carbon-based organic molecules that each contain a carbonyl group—a carbon atom doubly bonded to an oxygen atom.

Organic chemists have devoted enormous effort to developing asymmetric forms of this reaction. The products of these reactions cannot be superimposed on their 'mirror image' molecule—just as your left hand cannot be superimposed on your right.

Nature often selects molecules of a particular handedness; so many pharmaceuticals must be the correct mirror image form. But it is often difficult to synthesize a chemical of one handedness without also producing an equal amount of its twin.

Pilot molecules are often added to these reactions to steer their progress, ensuring that the correct form of the desired chemical is produced. Ideally, these molecules should speed up the reaction even though they are present in only trace amounts, and should not be consumed by the reaction. Chemists call them asymmetric catalysts.

Mikiko Sodeoka and colleagues at RIKEN's Advanced Science Institute in Wako have now developed an asymmetric catalyst that connects two different types of molecular building blocks—β-ketoesters and acetals—in an aldol reaction to form new compounds of a single handedness (Fig.1)[1]. "This type of aldol reaction has long been recognized to be notoriously difficult, and the key to success is the double activation by the Pd complex as an acid-base catalyst," says Sodeoka.

The catalyst is made from the metal palladium, attached to a bulky molecule called binap which has a twist in its structure. This twist ensures that the β-ketoester molecule sticks to the central palladium metal atom in a specific way—which, in turn, determines the orientation of the acetal connecting to it.

Sodeoka and her team tried a range of different β-ketoester and acetal combinations, and found that in most cases the catalyst helped to form the product in almost entirely the correct handedness. The compounds can in principle be converted into important building blocks for many drugs, which would otherwise be difficult to make catalytically using conventional methods.

The team also developed an alternative catalyst, which used platinum in place of palladium, and found that it was more resistant to decomposition in those reactions which took a long time to complete. They now hope to refine the catalysts' design, and use them to create more complex, bioactive molecules. ■

1. Umebayashi, N., Hamashima, Y., Hashizume, D. & Sodeoka, M. Catalytic enantioselective aldol-type reaction of β-ketoesters with acetals. *Angewandte Chemie International Edition* **47,** 4196-4199 (2008).

Engineering and computer science

Visualizing connections

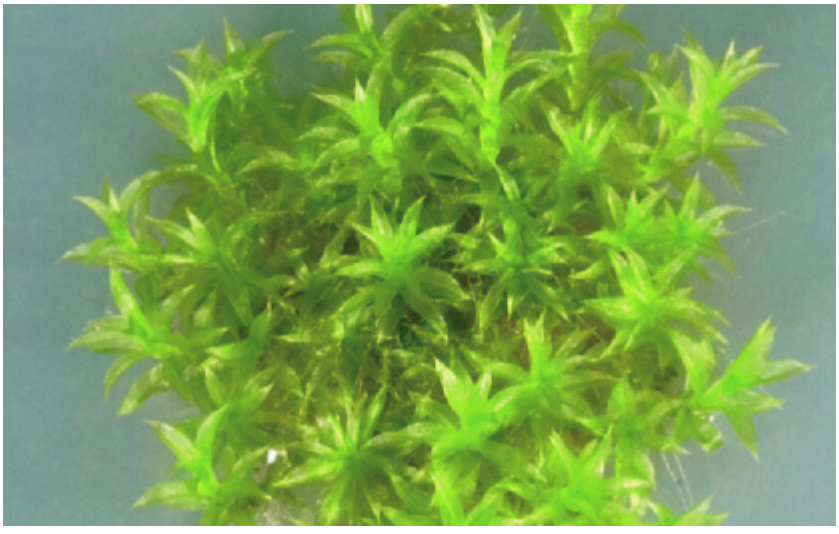
Seeing the seemingly invisible is a still a major goal of many areas of scientific research. In 2008 RIKEN's engineers and computer scientists applied their 'visualization' skills to provide faster, sharper and more accurate answers to a wide range of hot science topics.

Glowing success

Even the best microscopes are limited by optical rules governing the smallest object that can be viewed clearly. To overcome this, scientists from the RIKEN Advanced Science Institute (ASI) have developed a new method of fluorescence spectroscopy, which uses higher harmonic overtones of light to bypass classical limits. The technique, which requires no special training to use and can be modified to generate three-dimensional images, will likely have a huge impact on microscopy of biomolecular systems requiring nanometer resolution[1].

A team at the RIKEN Brain Science Institute (BSI) at Wako has applied the fluorescent emission of genetically modified versions of two proteins, Cdt1 and Geminin, to visualize cellular processes directly in real time. The process allows the monitoring of cell division, migration and development, which could give detailed insights into processes controlling the growth of cancer cells[2].

Figure 1: The moss *Physcomitrella patens* could hold the secret to drought-resistant crops.



Genetic genius

The effect of minute variations in gene sequences is a topic of major importance in genetics. A team of RIKEN scientists at the Center of Genomic Medicine (CGM) has developed a computational tool for CNV haplotype inferences, a technique that examines sequence differences between DNA samples. Using this algorithm, the team analyzed precise haplotypic variations of the number of sequence copies in the DNA of human populations in Nigeria and the US. This technique can be applied to association studies in medicine for finding genes that are susceptible to diseases[3].

Another RIKEN team was amongst 70 researchers worldwide who adumbrated the genome of *Physcomitrella patens*, a moss found on the margins of lakes and rivers that forms a link between algae and flowering plants (Fig. 1). The work will shed light on the evolution of land-dwelling plants and may provide clues to enhancing drought resistance in crops[4].

It is just this kind of work—distinct but related—that could be snared by a new search engine being developed by researchers from the RIKEN Bioinformatics and Systems Engineering (BASE) division (Fig. 2). Their new software, called the General and Rapid Association Study Engine (GRASE), assists with solving gene search problems by ranking genes based on intelligent inferences over bio-medical publications and collection of omics data[5].

The heart (and lungs) of the matter

The ability to peer inside a working, living body was, until recently, the stuff of science fiction. Now, a RIKEN-led team at the ASI has made a major advance in ultra-high resolution computed tomography (CT). Using synchrotron radiation from the SPring-8 Center at Harima, the scientists have produced images of a beating heart, coronary arteries and small airways of live rodents with high contrast and minimized blurring. The work allows the calculation of important physical parameters in the heart and lungs, and represents a significant step toward a computer model of the human body[6].

Figure 2: Numerous databases containing scientific papers and omics data can now be analyzed statistically using GRASE.

These and other reports show how the overlap of engineering and computing with other disciplines leads to both fascinating science and practical applications with potentially far-reaching benefits for society. ■

1. *RIKEN RESEARCH*, June 2008, p.1
2. *RIKEN RESEARCH*, September 2008, p.1
3. *RIKEN RESEARCH*, December 2008, p.17 (also p.21 of this report)
4. *RIKEN RESEARCH*, July 2008, p.14
5. *RIKEN RESEARCH*, October 2008, p.3
6. *RIKEN RESEARCH*, December 2008, p.12 (also p.22 of this report)

RIKEN Center for Intellectual Property Strategies

The RIKEN Center for Intellectual Property Strategies (CIPS) was set up in 2005 to manage interactions between RIKEN, a public body, and private industry with the idea of creating a RIKEN that is "useful to the world". Sited at the RIKEN headquarters in Wako, 25 minutes from central Tokyo, the division undertakes such diverse activities as nanofunctional materials research, manufacturing process simulation and computational cell biomechanics. CIPS also oversees the technology transfer activities of RIKEN and manages the portfolio of RIKEN venture capital companies (currently numbering 24), as well as the VCAD structural analysis software system developed in-house.

Computational Science Research Program

Located at the Wako Institute, researchers at the RIKEN Computational Science Research Program (CSRP) develop software for the simulation of natural phenomena. The teams in this program will make use of the RIKEN Next-Generation Supercomputer to conduct petaflop-scale experiments in order to develop algorithms for the elucidation of the molecular basis of biological processes such as blood-flow, drug metabolism, the dynamics of brain and neural systems, genomic data assimilation and systems biology. The ultimate aim of the division is to create new and better prediction-based methodologies for real-world applications in science.

Mapping multiplicity mathematically

A new algorithm crunches genomic data to predict maps of variable chromosomal regions that may yield valuable indicators of disease susceptibility or drug response

Every copy of the human genome generally consists of the same set of genes, but considerable variability exists between individuals at the sequence level. Variations can include single nucleotide polymorphisms (SNPs), in which one DNA base is substituted for another; or copy-number variations (CNVs), in which entire blocks of gene sequence are deleted or duplicated. Individual variations can alter the function or activity of affected genes, and thus have important health implications.

Also important, however, is an individual's 'haplotype'—the set of variations that co-occur on a given chromosome. Human chromosomes typically come in pairs, and the combined data from two haplotypes is referred to as a 'diplotype'; in some cases, the impact of a specific diplotype can be just as important for predicting drug response or disease susceptibility as the variations it contains.

Tools for high-throughput SNP haplotype analysis are already part of the clinical diagnostic arsenal, but equivalent methods are not as well developed for CNVs. "CNVs are getting more widely recognized as useful indicators," says Tatsuhiko Tsunoda of the RIKEN Center for Genomic Medicine in Yokohama (formerly the SNP Research Center), "but they are still challenging to handle."

Since CNV patterns can be highly complex (Fig. 1), effective high-throughput CNV haplotype analysis will require sophisticated mathematical strategies. To this end, Tsunoda's group developed a computational tool called CNV phaser, which applies an algorithm to CNV datasets to infer the most probable individual haplotypes[1]. Their system can perform calculations based on information about each individual's combined copy number for both chromosomes or, for CNVs that also contain SNP variants, based on the frequency of occurrence of individual nucleotides within this set of copies.

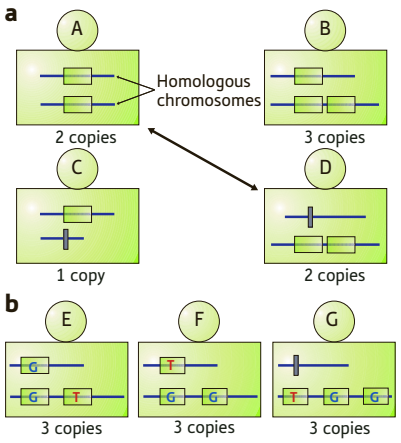


Figure 1: Copy-number variation (CNV) can occur in ambiguous patterns. (a) Individuals in a population may have different copy numbers on homologous chromosomes at CNV loci. For example, here individual A and D have two copies, although the patterns are different: A has one copy on each chromosome, whereas D has two on one chromosome and zero on the other. (b) Individuals may also have CNVs that contain SNPs. For example, individuals E, F, and G each have three copies, but the patterns can be distinguished by the numbers of copies on each chromosome and variations defined by SNPs.

CNVphaser accurately estimated haplotype frequencies in initial tests using simulated genomic datasets, and the team noted that the algorithm was especially effective for analyzing variant regions in which a small number of specific haplotypes occur with much greater frequency than other potential haplotypes.

The algorithm also performed well in a real-world test, in analyses of gene variants from two distinct human populations—Nigerian Yoruba and individuals of European ancestry in Utah. "CNV patterns showed quite different frequencies—up to dozens of percentage points—between the two populations," says Tsunoda. "This shows the algorithm's big power for identifying differences in copy patterns between two groups." Based on this initial success, Tsunoda is optimistic that his method will also prove valuable in the clinic, and is now exploring its effectiveness for performing genetic association studies with patient samples. ■

1. Kato, M., Nakamura, Y. & Tsunoda, T. An algorithm for inferring complex haplotypes in a region of copy-number variation. *The American Journal of Human Genetics* **83,** 157–169 (2008).

Catching the heart and lungs in action

A newly developed micro-CT system produces images sharp enough to detect the motion of arteries and small airways in rats and mice

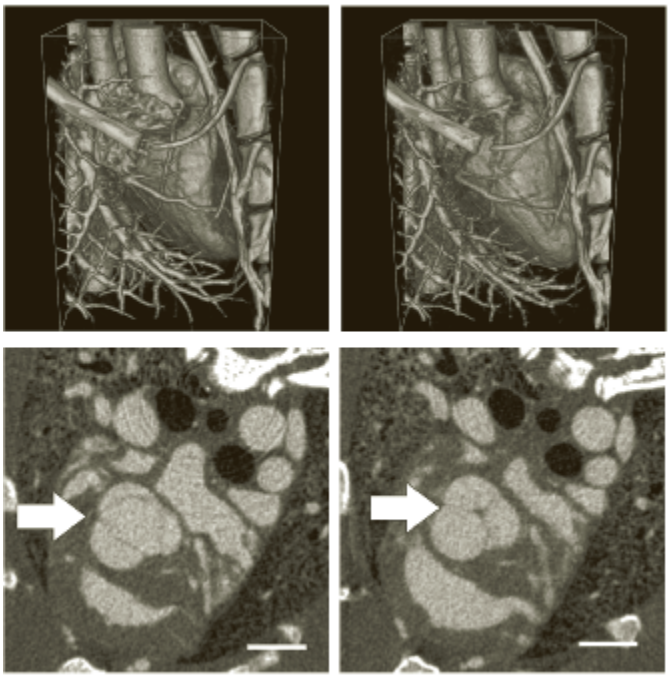


Figure 1: Examples of high-resolution images of a beating rat's heart produced using the new micro-CT system (top: whole heart; bottom, cross-section at aortic valve).

A RIKEN-led team has designed and constructed a high-resolution, computed tomography (CT) system that can visualize the motion and deformation of the heart, coronary arteries and small airways of live rats and mice, the animals most often used as models for human disease.

These internal movements are integral to understanding respiratory and cardiovascular diseases, and therefore to the development of effective treatments. They are also influenced by drugs, and hence can be used in testing and development of new therapeutic compounds.

The condition of the heart is manifested in its rhythmical beating, and the location of fatty deposits, which can lead to heart disease, is influenced by motion of the arteries. Deformation of the airways affects gas exchange and deposition of particles, and initial results from the new system already show that changes in diameter are larger in smaller airways.

In the past five years, several systems have been proposed and developed for imaging the heart and lungs of small living animals, but none have been sharp enough to detect the motion of arteries and small airways. The highest potential resolution can be obtained using x-ray based, micro-CT, but the sample animal needs to be as still as possible. When imaging the heart, the movement of the lung needs to be minimized, and vice versa. So, data to construct the images needs to be collected under certain prescribed conditions.

In a recent paper in *Physics in Medicine and Biology*[1], researchers from the RIKEN Advanced Science Institute in Wako and other Japanese institutions explain how they dealt with these problems.

They used synchrotron radiation at the SPring-8 Center in Harima, which is much more powerful and predictable than standard laboratory sources, and so achieves high contrast resolution and minimizes blur (Fig. 1). The shutters for x-ray source and detection were synchronized. The sample rodents were anaesthetized, put onto a ventilator, and connected to an electrocardiogram (ECG) machine. The researchers were then able to acquire data at controlled airway pressures and time observations for the periods between heart contractions. For heart and arteries, image acquisition could be timed for the end of breath expiration.

The sharp images during dramatic motion thus obtained allow calculation of gas exchange in small airways, and of shear stress in blood vessels, an important factor in deposition of plaques. "This development is a significant step in our program to create a computer model of the human body," says Ryutaro Himeno, who heads the research team. ■

1. Sera, T., Yokota, H., Fujisaki, K., Fukasaku, K., Tachibana, H., Uesugi, K., Yagi, N. & Himeno, R. Development of high-resolution 4D *in vivo*-CT for visualization of cardiac and respiratory deformations of small animals. *Physics in Medicine and Biology* **53**, 4285–4301 (2008).

Neuroscience and developmental biology

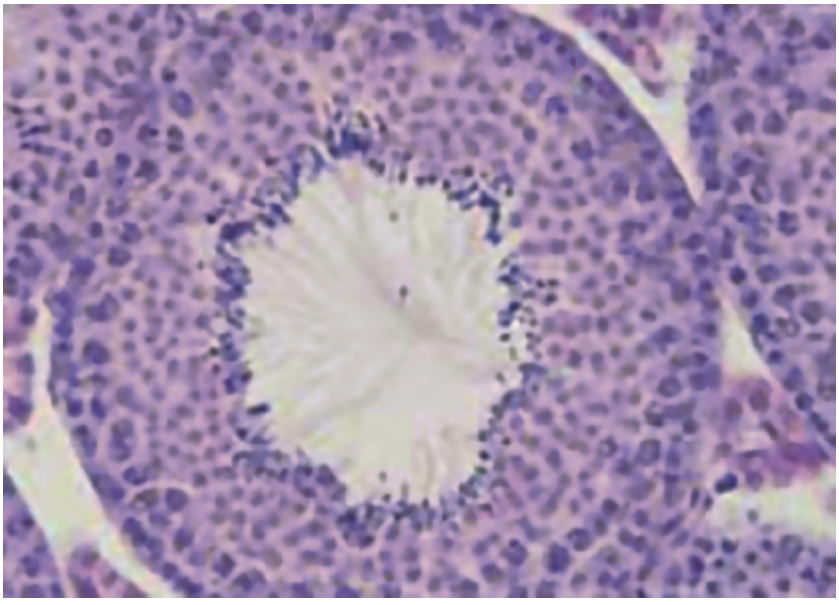
Advances for the body and brain

Knowledge in the broad fields of neuroscience and developmental biology continued to expand rapidly throughout 2008. RIKEN added to this with research illustrating the remarkable phenomena that occur during maturation of the body and brain.

Forming the embryo

In the past year two research groups at the RIKEN Center for Developmental Biology (CDB) helped resolve the question of how cells in the developing embryo are specified into layers—the ectoderm, endoderm and mesoderm. One group identified an ectodermal protein called XFDL that blocks mesoderm formation[1]. The other group discovered that basement membrane breakdown is required to initiate migration of cells that will become the mesoderm, in a process called gastrulation[2].

Figure 1: Cross-section of mice testes showing sperm in the center.



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Meanwhile, other researchers at the CDB found that a gene called Prdm14 is required for the production of the primordial germ cells in the embryo that go on to become the eggs or sperm of the individual (Fig. 1)[3].

Making the brain

During brain development, neural progenitor cells divide to create young neurons, which then migrate from where they are formed until they reach their final position. Altering the plane of cell division of the progenitor cells results in their depletion, according to research completed at the CDB[4].

In another development, a discovery by a group at the RIKEN Brain Science Institute (BSI) overturned a prevailing hypothesis that an organelle called the centrosome is responsible for pulling the neuronal nucleus along while young neurons are migrating. The new work suggests that the nucleus is instead pulled along by rope-like bundles of filaments called microtubules[5].

After birth, significant plasticity in the brain leads to more efficient processing of external information. Researchers at BSI last year found that a protein called Otx2 travels from the eye to the brain during early visual experience (Fig. 2), and controls this plasticity in the visual cortex[6].

Shaping behavior

Scientists have long puzzled over how different parts of the brain work together to control movement. An international team of researchers, including two scientists from BSI, found that a part of the brain called the cerebellum creates similar frequencies of oscillations to those found in the cerebral cortex. This suggests that these two brain areas interact with each other to modulate body movement[7].

Environmental factors can also affect behavior. Light exposure at inappropriate times, for example, can lead to jet lag or sleep disturbances. Until now, scientists thought that a flash of light affects our internal daily clock by altering the rhythms of entire groups of cells. However, a group at CDB discovered that light instead desynchronized the rhythm of individual cells[8].

Motor systems and higher cognitive processes are both required for animals to determine how using tools can help them achieve their goals. In 2008 researchers at BSI determined that small mouse-like rodents called degus can be trained to use tools. Degus could serve as a model system to understand how tool use modifies brain circuits[9].

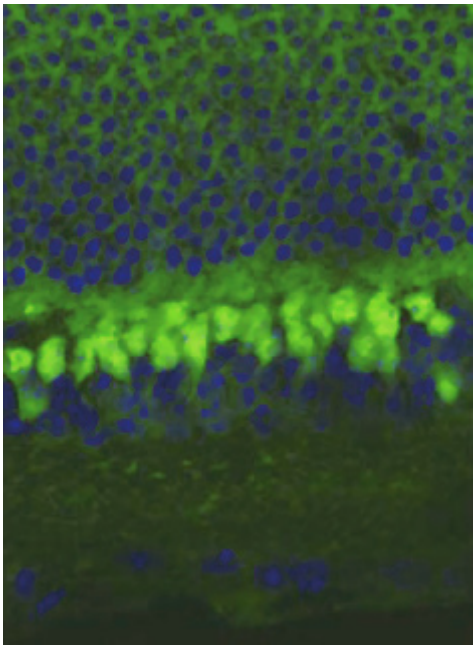

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Figure 2: Otx2 protein (green) is found in the retina.

Collectively these findings provide important insights into how growth and development shapes differentiation, migration and communication between cells, which can then modify animal behavior. ■

1. *RIKEN RESEARCH*, November 2008, p.19 (also p.25 of this report)
2. *RIKEN RESEARCH*, November 2008, p.20
3. *RIKEN RESEARCH*, December 2008, p.22
4. *RIKEN RESEARCH*, June 2008, p.5
5. *RIKEN RESEARCH*, March 2008, p.1
6. *RIKEN RESEARCH*, December 2008, p.1
7. *RIKEN RESEARCH*, November 2008, p.1
8. *RIKEN RESEARCH*, April 2008, p.11
9. *RIKEN RESEARCH*, September 2008, p.19 (also p.26 of this report)

RIKEN Center for Developmental Biology

Since April 2000, researchers at the RIKEN Center for Developmental Biology (CDB) in Kobe have provided the world with insights into the processes that see a single-celled fertilized egg develop into a complex system of functioning tissues and organs.

As developmental biologists must understand how cells divide, mature, migrate and work together as a unit of tissue, research at CDB spans the fields of embryology, developmental cell biology, neural developmental biology, stem cell and tissue regeneration research, evolutionary biology and genome research.

Discoveries made at the CDB could pave the way to regenerative therapies for a variety of developmental and degenerative disorders.

RIKEN Brain Science Institute

At the RIKEN Brain Science Institute (BSI), situated in Wako on the outskirts of Tokyo, researchers are busily working to determine how genes, proteins, cells and neural circuits work individually—and in concert—to regulate emotions, intelligence and behaviors.

The interdisciplinary and collaborative research at BSI falls within four core research areas: Mind and Intelligence Research, Neural Circuit Function Research, Disease Mechanism Research and Advanced Technology Development.

The work is yielding important information on the processes that regulate how the brain is formed by genes and shaped by our environment during development, injury and aging and will lead to mechanism-based interventions.

Guiding the decision-making process

Identification of a novel protein involved in embryonic development leads to new insights into the first stage of neural development

In developing animal embryos, stem cells soon differentiate into three distinct layers of tissue, the primary germ layers. These are the endoderm, mesoderm and ectoderm, and each subsequently develops into a specific subset of tissues and organs. These differentiating cells follow a highly complex 'decision-making' process, and a lot of ambiguity still remains as to why, for example, an ectodermal cell became an ectodermal cell.

Yoshiki Sasai of the RIKEN Center for Developmental Biology in Kobe views the exploration of this process as a long-term mission. "Fifteen years ago, I isolated the neural inducer chordin, which induces neural progenitors from uncommitted ectoderm," he says. "However, how the uncommitted ectoderm develops from pluripotent cells has remained unknown—so it has been my 15-year-old homework to elucidate it!"

In the frog species *Xenopus laevis*—a popular animal model for developmental studies—germ-layer differentiation is triggered via two sets of signals: some derived from maternally produced factors, and others generated by the zygote itself. Previous research has identified several candidate maternal factors, but the mechanisms involved in the latter pathway have proven more elusive, and Sasai's team has focused much of their recent effort on finding zygotic factors potentially responsible for ectoderm formation.

In their most recent study, Sasai's team identified a previously uncharacterized protein, XFDL, which exhibits a marked ability to block mesoderm formation[1] (Fig. 1). Elevated XFDL levels lead to inhibition of mesoderm-specific genes, while reduced levels of the protein lead to broader expression of these genes in embryonic regions that normally form ectoderm.

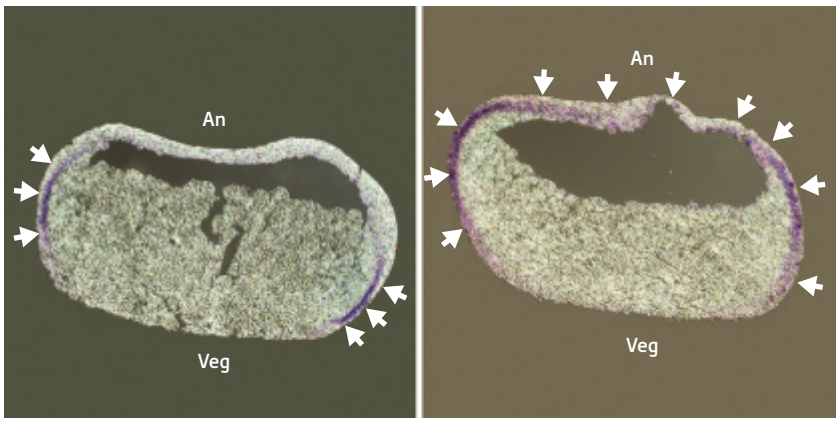


Figure 1: *Xenopus* embryos stained to indicate expression of a mesodermal marker. In the left panel, an unmodified embryo exhibits the marker in the region between the ectodermal 'animal pole' region (An) and the 'vegetal pole' (Veg), where the endoderm is formed. The embryo in the right panel has greatly reduced XFDL production, resulting in the formation of mesoderm in a typically ectodermal region of the embryo.

Subsequent experiments revealed that XFDL acts by interacting with p53, a transcription-regulating protein with a known role in mesoderm formation, and directly interfering with its ability to bind to DNA and activate its target genes. When XFDL was prevented from interacting with p53, it lost its ability to regulate ectoderm differentiation—an unexpected finding, according to Sasai. "Although p53 is implicated in the regulation of mesodermal development, we did not think it had such a profound function in the binary decision of ectodermal versus mesodermal determination," he says.

The researchers have identified two XFDL-related proteins in mice, both of which also inhibit mesoderm formation in *Xenopus*, indicating that mammalian germ layer formation may also be regulated via a similar pathway—a possibility that Sasai's team is currently exploring more closely. "Our preliminary studies suggest that this is the case at least with *in vitro* differentiation of mammalian embryonic stem cells," he says. ■

1. Sasai, N., Yakura, R., Kamiya, D., Nakazawa, Y. & Sasai, Y. Ectodermal factor restricts mesoderm differentiation by inhibiting p53. *Cell* **133,** 878–890 (2008).

Rodents rake for rewards

A RIKEN study shows that rodents can be trained to use tools just as well as primates

In the past, the use of tools enabled humans to adapt to different ecological niches. The resulting new experiences presented more learning opportunities, extending our brain capacity.

Now researchers at the RIKEN Brain Science Institute in Wako have trained degus, a medium-sized rodent native to Chile, to use tools. The study shows that degus could be a useful animal model for directly observing how tool use modifies brain and behavior[1].

"Rodents are smaller and less costly to maintain than primates," explains project-scientist Kazuo Okanoya. "Also, techniques for genetic manipulations are more advanced for rodents and we could modify these existing procedures for degus."

The researchers originally chose to study degus because they noticed that the animals are playful, highly inquisitive, and have good manual skills (Fig. 1). Adult degus were placed in a chamber with openings that the degus could put their hands through. Food was placed just beyond the animals' reach, while a rake-like tool was placed within their reach.

To begin with, the food was placed behind the rake's blade, so that all the degus had to do was pull the rake handle. Once they had mastered this, the task was made more difficult by placing the food in front or to one side of the tool. The degus soon began to try out new movements such as pushing the tool or wiggling sideways. With more practice the movements merged into one smooth trajectory and the degus were seen to stare at the food rather than at the tool, suggesting that the tool was becoming an intuitive extension of their own arms.

Figure 1: The RIKEN researchers chose degus for tool-use training after noticing their high level of curiosity and manual dexterity.

Furthermore, the degus adapted to tools of different sizes, shapes and colors, and quickly learned to ignore tools that didn't work. This shows that the animals gained a mental appreciation of the tool's function.

The results for degus compare favorably with previous studies on primates. The researchers expect that tool use produces new connections between different areas of the brain, leading to improved hand–eye co-ordination. "We are confident that other rodents could also be trained to use tools, although it might take longer than for degus," says Okanoya.

In the future, Okanoya would like to study the links between tool use and voice. "We think the site where these two activities overlap could be a precursor for the brain areas related to language production," he says. "Thus, the current tool use study can lead to the study of the origin of language." ■

1. Okanoya, K., Tokimoto, N., Kumazawa, N., Hihara, S. & Iriki, A. Tool-use training in a species of rodent: the emergence of an optimal motor strategy and functional understanding. *PLoS ONE* **3**, e1860 (2008).

Genetic science, plant science and environmental science

Looking deeper

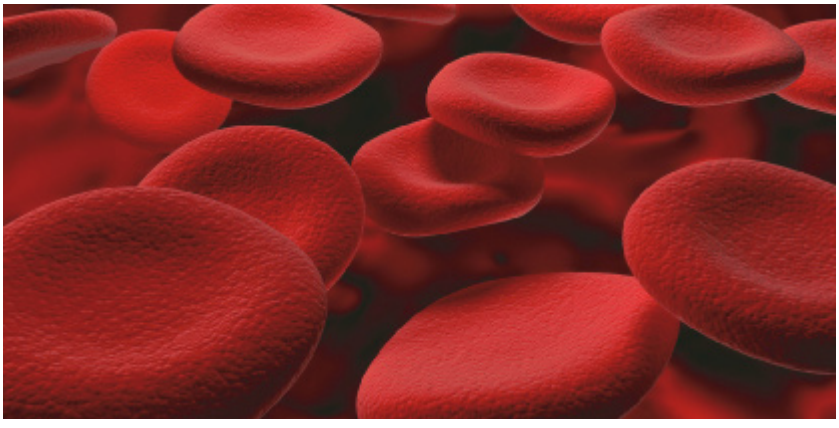
Diverse achievements emanating from life sciences research at RIKEN throughout 2008 are leading scientists across the globe to a better understanding of how the internal machinery of cells governs their responses to drugs, environmental changes and other challenges.

Disease strategies

With the theoretical capacity for being reprogrammed to mature into virtually any cell type, embryonic stem cells (ESCs) represent an especially promising resource in strategies for treating human disease. A team at the RIKEN BioResource Center (BRC) recently demonstrated this potential by coaxing mouse ESCs into forming transfusion-ready red blood cells—a breakthrough that could alleviate hospitals' dependence on donors (Fig. 1)[1].

Other teams focused on strategies for drug development, such as a new approach for the stabilization of synthetic RNA therapeutics in the bloodstream of patients. This could help move RNA interference, a powerful method for modulating gene activity, from the laboratory bench to the clinic[2].

Figure 1: A new approach for deriving red blood cells from embryonic stem cells could offer new hope for transfusion patients.



Nature also offers a rich source of potential new drugs. The fungal compound methylgerfelin, for example, may limit the bone-destroying effects of osteoporosis and bone cancer, according to findings by a collaborative effort between Japanese university scientists and the RIKEN Advanced Science Institute (ASI)[3].

Inner workings

Even after a drug candidate has been identified, it is important to determine its mode of action. For example, RIKEN scientists investigating the basis for resistance to the plant-derived anticancer drug camptothecin have identified specific mutations in its target enzyme that enable both plant and cancer cells to survive the toxin[4]. Careful analysis of another protein, Rbf1, enabled a team at the RIKEN Systems and Structural Biology Center (SSBC) to understand how it helps cells protect themselves from another hostile condition—extreme cold[5].

In 2008 RIKEN research teams continued to make considerable progress in exploring the processes by which many proteins undergo additional chemical modifications that alter their functional behavior, such as determining how conditions within the cell affect the addition of sugar molecules to protein targets[6]. Another breakthrough came from the RIKEN Plant Science Center (PSC), where researchers

completed a detailed analysis of protein phosphorylation, an essential modification that plays a role in most major cellular processes. Their findings represent the first large-scale mapping of the plant cell 'phospho-proteome'[7].

Part of the community

The internal and external environments of cells are inextricably interconnected, and many cells rely on their 'neighbors' for survival. Pioneering genome-sequencing work from the ASI has yielded valuable new insights into how the interdependent community of single-celled microbe species in the termite gut collaborate with their host and each other—findings that could guide the engineering of biological systems to convert plant matter to energy[8].

Developing optimized plant strains for research is a major biotechnology objective. An international team, also at the PSC, has identified an essential protein involved in pollen coat formation (Fig. 2), which may represent a means for engineering plants with non-functional pollen, giving researchers tighter control over plant breeding and propagation[9].

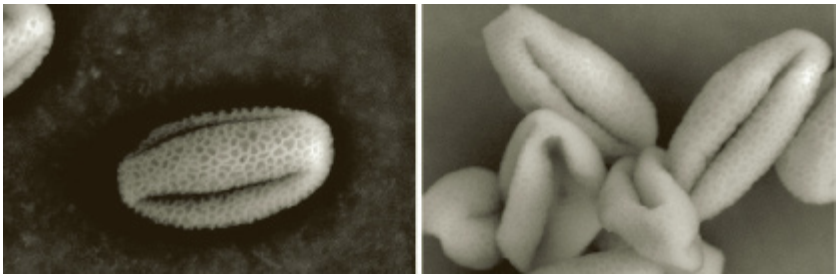


Figure 2: Wild-type thale cress plants produce pollen grains (left) with a rigid protective protein coat. By comparison, grains from plants with a mutation in the MS1 gene fail to develop this coat (right), resulting in plants that are effectively male-sterile.

These and other findings illustrate how parallel efforts in basic and applied research facilitate the translation of biochemistry and molecular biology advances into medical and technological breakthroughs—an approach RIKEN will continue to pursue in the future. ■

1. *RIKEN RESEARCH,* August 2008, p.1
2. *RIKEN RESEARCH,* May 2008, p.3
3. *RIKEN RESEARCH,* December 2008, p.19 (also p.29 of this report)
4. *RIKEN RESEARCH,* October 2008, p.20 (also p.30 of this report)
5. *RIKEN RESEARCH,* June 2008, p.10 (also p.31 of this report)
6. *RIKEN RESEARCH,* Aug 2008, p.11
7. *RIKEN RESEARCH,* October 2008, p.1
8. *RIKEN RESEARCH,* September 2008, p.12 (also p.32 of this report)
9. *RIKEN RESEARCH,* May 2008, p.12

RIKEN Systems and Structural Biology Center

In recent years a rapidly growing base of biological knowledge has enabled scientists to begin to approach cells not as mere pouches of organic molecules, but rather as highly integrated miniature machines. The RIKEN Systems and Structural Biology Center (SSBC) in Yokohama is at the forefront of efforts to understand how these machines work. Its scientists are pursuing parallel lines of research to identify and explore the underlying mechanisms for, and interconnections between, essential cellular processes, and to develop tools and strategies to modulate and re-engineer these pathways to unearth treatments for human disease and produce useful new biomaterials and chemical products.

RIKEN Omics Science Center

Just as the maturation of genomic research helped lay a foundation for the now-flourishing fields of transcriptomics and proteomics, the RIKEN Omics Science Center (OSC) in Yokohama has evolved from the knowledge and expertise of the former the RIKEN Genomic Sciences Center (GSC). Since its launch in April 2008, scientists at the OSC have worked toward mapping the complex networks of interactions between nucleic acids and proteins that guide an organism's development and survival. To this end, the OSC is spearheading the ambitious 'life science accelerator' (LSA) project, an innovative experimental and analytical framework that promises to greatly expedite the identification and integration of these networks.

RIKEN Plant Science Center

Plants may harbor effective solutions for a broad variety of global needs, and the researchers at the RIKEN Plant Science Center (PSC) in Yokohama are working to achieve new breakthroughs in diverse areas, including food and energy production, environmental remediation and drug discovery. Fundamental priorities at the PSC include unraveling the biological mechanisms underlying plant growth and productivity, and learning how better to protect crops from environmental challenges including climate shift, insects and infections. These findings will be applied to the development of plant strains that have been optimized for agricultural use or the generation of useful compounds and materials.

Stop the loss

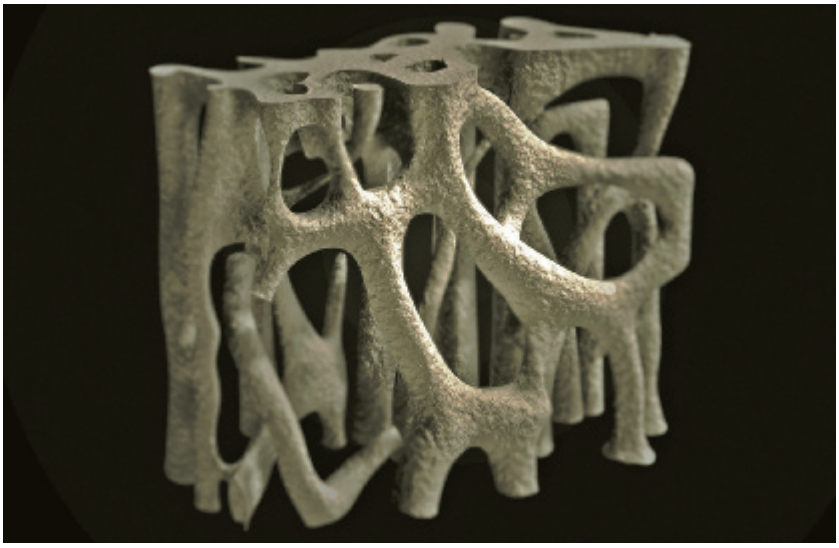
The discovery of an inhibitor of the production of bone-resorptive cells opens new possibilities for regulating bone loss

A RIKEN-led research group has discovered that the methyl form of a small molecule—first found in fungi—inhibits production of the bone resorptive cells known as osteoclasts. And by immobilizing the compound on gel beads, the researchers have begun to unravel the biochemical mechanism involved.

The work is important because an excess of osteoclasts has been implicated in several significant human diseases including osteoporosis (Fig. 1), rheumatoid arthritis and bone cancer. An inhibitor to the production of osteoclasts might be useful for developing drugs to treat such conditions. The compound the researchers found, methyl-gerfelin (M-GFN), also can be employed to probe how osteoclasts differentiate and function.

Osteoclasts develop from bone marrow-derived macrophages in the presence of factors released by bone-forming osteoblasts. The two cell types work in tandem to build, model and renew bones. But an oversupply of osteoclasts can break down bone inappropriately, leading to bone disease.

In a recent paper in *Proceedings of the National Academy of Sciences*[1], the research group from the RIKEN Advanced Science Institute in Wako together with colleagues from three Japanese universities detail how they used an assay involving the differentiation process to screen small molecules from the chemical library of the RIKEN Natural Products Depository for inhibitors. They found that while GFN had a weak inhibitory effect, M-GFN suppressed osteoclast differentiation in a dose-dependent manner. The difference between the compounds appears to be in their ability to be absorbed by cells.



Medical RF/amanaimages

Figure 1: Bone affected by osteoporosis is thinner and less dense than normal and more prone to fracture.

The researchers then attached M-GFN to agar gel beads by means of a linker activated by light—a process which they had developed earlier—and exposed the beads to macrophage breakdown products. Two of the proteins bound directly to M-GFN.

They then suppressed the activity of the genes coding for those two proteins using RNA interference techniques, and found that one of them, the antioxidant enzyme glyoxalase I (GLO1), was required for production of osteoclasts. By analyzing the crystal structure of the complex that forms between M-GFN and GLO1, the researchers were able to show that M-GFN inhibits its function by binding to its active site.

"M-GFN might be useful as an anti-resorptive agent if it has pharmacological activity. We plan to examine the activity of M-GFN in live mice, particularly in mouse models of osteoporosis," says the paper's lead author, Makoto Kawatani. "We are also looking at creating compounds with stronger inhibitory activity based on the structure we see in the GLO1/M-GFN complex." ■

1. Kawatani, M., Okumura, H., Honda, K., Kanoh, N., Muroi, M., Dohmae, N., Takami, M., Kitagawa, M., Futamura, Y., Imoto, M. & Osada, H. The identification of an osteoclastogenesis inhibitor through the inhibition of glyoxalase I. *Proceedings of the National Academy of Sciences USA* **105,** 11691–11696 (2008).

Why plants can resist their own deadly toxins

Resistance to self-produced anticancer toxins could help the study of drug resistance in cancer patients

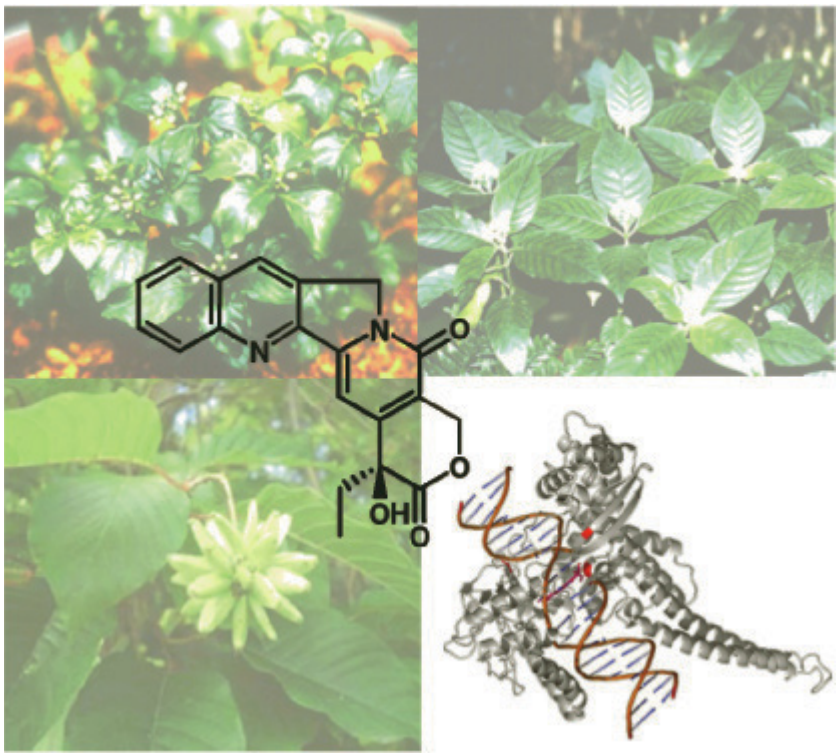


Image courtesy of Supaart Sirikantaramas and Hiroshi Sudo

Figure 1: Three plant species producing camptothecin and its interaction with DNA and topoisomerase I.

Japanese researchers have explained the mechanism of self-resistance in plants to their own lethal toxins. This new information will help medical researchers to tackle resistance in humans to anticancer drugs that are often based on these plant toxins.

Camptothecin (CPT) is a plant-derived anticancer drug that kills cancerous cells by disrupting the action of an enzyme called topoisomerase 1 (Top1) (Fig. 1), which is essential to DNA maintenance in almost all living organisms. Although CPT is deadly to most life forms, resistance to the toxin is found in its source plants and in some CPT-treated human cancer cells.

Now Kazuki Saito of the RIKEN Plant Science Center in Yokohama and his team from Chiba University and the Japan Science and Technology Agency in Chiba, have shown for the first time how plant self-resistance works at a molecular level. Understanding these processes is becoming increasingly important because of the expanding use of plant-derived compounds as medicines and the evolving drug resistance in the human cells they are used to target.

By comparing Top1 genes from CPT-producing and non-producing plants, the team found three mutations in the toxin producers that cause amino acid changes in the resulting enzyme and make it immune to the drug's poisonous attack. Remarkably, one of the amino acid substitutions found by Saito and his colleagues in plants is identical to one that has been found previously in CPT-resistant human cancer cells.

The team's genetic comparisons, reported recently in the *Proceedings of the National Academy of Sciences*[1], suggest that CPT resistance in the source plant has developed gradually in parallel with the ability to produce the drug. Consequently, the team proposes that low-level CPT production may have triggered the resistance-giving mutation to occur in Top1. The importance of this suggestion is exemplified by the observation that continuous exposure of human cancer cells to CPT results in a Top1 mutation conferring CPT resistance.

The team's findings will help to uncover similar self-resistance mechanisms in other plants and for different toxins. Furthermore, understanding the molecular interaction between cancer drugs and their target molecules will facilitate the design of drug therapies that prevent resistance in their human targets. Saito's team intends to explore CPT biosynthesis with a view to the feasible production of anticancer compounds. They also "look forward to establishing the evolutionary genomic basis of chemical diversity in plants through the study of plant toxins," says Saito. ■

1. Sirikantaramas, S., Yamazaki, M. & Saito, K. Mutations in topoisomerase I as a self-resistance mechanism coevolved with the production of the anticancer alkaloid camptothecin in plants. *Proceedings of the National Academy of Sciences USA* **105**, 6782–6786 (2008).

A cure for the cold

A recent structural biology study reveals how one protein helps keep bacteria running through a cold spell

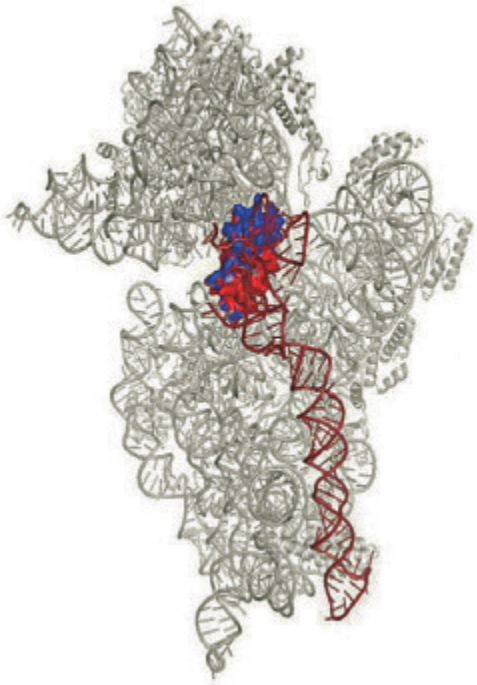


Figure 1: The structure of the RbfA-30S complex, revealing the interaction of the RbfA (red and blue) with helices (brown) on 30S involved in ribosomal assembly and RNA translation.

The translation of RNA into protein is managed by cellular machines known as ribosomes. A ribosome consists of two subunits, each composed of an RNA-based scaffolding with a number of specialized proteins attached.

The formation and assembly of ribosomes within a living cell seems to be a complicated process, which can be strongly affected by environmental conditions. For example, extreme cold has a very negative impact on bacterial protein production. "Cold shock results in an increase in the level of non-translating ribosomes, and produces a temporary cessation of bacterial growth," explains Shigeyuki Yokoyama of the RIKEN Systems and Structural Biology Center in Yokohama. "Growth is then restored through the action of a set of cold-shock response proteins."

Previous studies have implicated the bacterial protein RbfA as an important component of this cold-shock response, and Yokoyama's team recently joined up with German and American scientists to explore the RbfA-ribosome interaction in order to better understand the mechanism of this process[1]. RbfA binds to the smaller 30S subunit of the bacterial ribosome, and so the researchers began by acquiring detailed structural data for the subunit alone and bound to RbfA.

These data showed that RbfA binds in the immediate vicinity of helix h1, a specific domain of 30S that is known to fold improperly under cold-shock conditions. They also revealed a dramatic conformational change in 30S after RbfA binding, affecting a separate ribosomal domain directly involved in the RNA decoding process as well as assembly of the large and small ribosomal subunits (Fig. 1). Subsequent comparison of the RbfA binding site on the ribosome against the binding sites used by other proteins associated with 30S subunit maturation indicated that these various proteins interact with many of the same ribosomal domains, suggesting mechanistic overlap.

Collectively, these results indicate that the binding of RbfA to 30S serves a dual purpose: enabling proper formation of the ribosomal subunit, as well as ensuring that mRNA transcripts do not associate with premature, incompletely folded subunits. The findings from this work should be broadly applicable with regard to understanding ribosomal maturation, for although RbfA production is markedly increased at temperatures where ribosome formation becomes inefficient, the protein is generally present at low levels under other cellular conditions. "Our results not only provide insight into the role of RbfA during maturation of the 30S subunit," says Yokoyama, "but they also suggest how RbfA confers a translational advantage to cells under conditions of cold shock." ■

1. Datta, P.P., Wilson, D.N., Kawazoe, M., Swami, N.K., Kaminishi, T., Sharma, M.R., Booth, T.M., Takemoto, C., Fucini, P., Yokoyama, S. & Agrawal, R.K. Structural aspects of RbfA action during small ribosomal subunit assembly. *Molecular Cell* **28,** 434–445 (2007).

Bugs helping bugs

Scientists get their first glimpse into the workings of the complex bacterial community residing within the termite gut

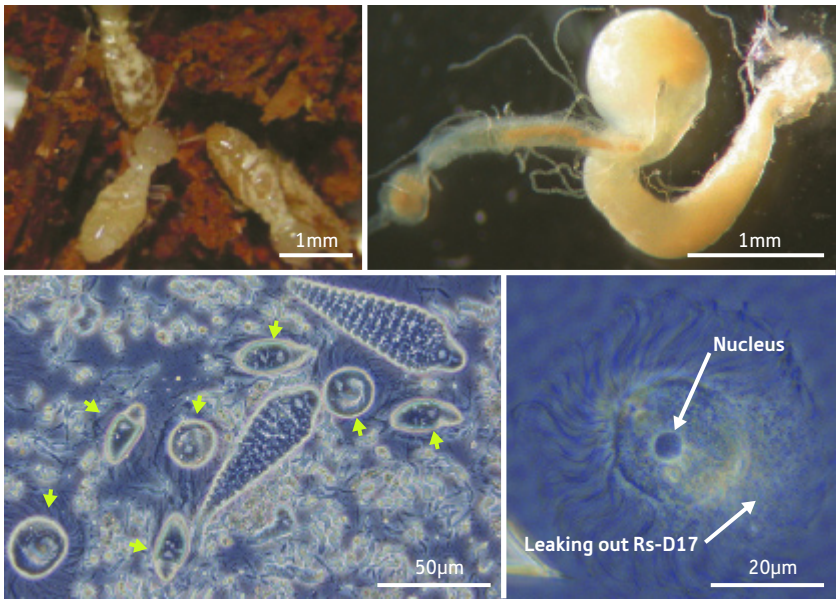


Figure 1: Rs-D17, a gut microbe isolated from the termite species *Reticulitermes speratus* (top left). Within the gut (top right) of the termite is a thriving ecosystem of microbial species (lower left). The Rs-D17 bacterium can be seen leaking out of a gut protist cell in which it resides (lower right).

Left unchecked, a band of termites can eat their way through a house, but they can't do it alone. Within every termite is a thriving ecosystem of bacteria that maintain an essential symbiotic relationship with their hosts, taking shelter within the insect's gut and contributing to its survival by various means, including facilitating the digestion of plant matter.

Little is known about these symbiont species, as these bacteria have proven virtually impossible to cultivate in the laboratory and thus difficult to characterize in detail. "One termite gut harbors several hundred species of microbes," explains Yuichi Hongoh, a postdoctoral fellow in Moriya Ohkuma's research group at RIKEN's Advanced Science Institute in Wako, "and it is not realistic to collect a large enough amount of a specific species to analyze with general methodologies."

Fortunately, recent years have seen the development of new tools for obtaining detailed genomic sequence information from limited sample quantities and Hongoh, in partnership with the RIKEN Bioinformatics And Systems Engineering division (formerly the RIKEN Genomic Sciences Center), in Yokohama, was able to take advantage of these new amplification and sequencing methods to finally assemble the first comprehensive genomic sequence from a termite gut symbiont species[1].

The team analyzed Rs-D17 (Fig. 1), a representative species that is thought to account for approximately 4% of all termite gut bacteria. The analysis revealed that the Rs-D17 genome consists of a single chromosome containing 761 putative protein-coding genes, as well as several smaller non-chromosomal DNA molecules.

The researchers were surprised to find that a large percentage (>15%) of the genes identified were actually pseudogenes, non-functional evolutionary descendants of known genes. Although these pseudogenes no longer generate protein, comparative analysis of the genes lost or maintained by Rs-D17 yielded some valuable hints about how the bacterium evolved to adapt to its host environment over time.

In general, Rs-D17 appears to have sacrificed its regulatory and cellular defense mechanisms in favor of maintaining robust pathways for synthesizing organic molecules required by the termite. "This indicates that this bacterium has been 'domesticated' by the host like an organelle, which synthesizes the nitrogen compounds critically deficient in wood food material," says Hongoh.

He indicates that the team is now looking to extend their strategy to assemble genomic maps for additional symbiont species, in the hope of clarifying the complex relationships between the various members of this gut ecosystem. "By combining these data," concludes Hongoh, "our understanding of termite gut symbiosis will be greatly enhanced."

1. Hongoh, Y., Sharma, V.K., Prakash, T., Noda, S., Taylor, T.D., Kudo, T., Sakaki, Y., Toyoda, A., Hattori, M. & Ohkuma, M. Complete genome of the uncultured Termite Group 1 bacteria in a single host protist cell. *Proceedings of the National Academy of Sciences, USA* **105,** 5555–5560 (2008).

Medical science

Combating cancer and juggling genes

The human body works in mysterious ways, but scientists around the world continue to unlock its secrets. This includes building up the complex map of 'which gene does what' in the body, testing new drugs and improving tools such as imaging and computer modeling. RIKEN's medical sciences research program, although still relatively new, has made enormous contributions to this process over the past year.

Digging into diseases

Fascinating work has emerged from the RIKEN Center for Allergy and Immunology (RCAI) in Yokohama, where researchers bred mice that support the mutated stem cells from humans that generate acute myeloid leukemia. The cells maintain their human gene expression patterns in mice, providing an accurate model for testing cancer drugs[1].

Another exciting discovery at RCAI is a possible vaccine against cancer. A group identified a compound from a rather exotic source—a sea sponge—that protects mice against four common types of tumor[2].

Researchers at RCAI are also finding potential treatments within our own bodies. One group showed how common components of the immune system called dendritic cells can suppress chronic inflammation associated with conditions such as asthma (Fig. 1)[3]. Meanwhile, another group discovered how cells in the gut arrange themselves into complex structures that act to prevent infection, while managing the growth of benign bacteria[4].

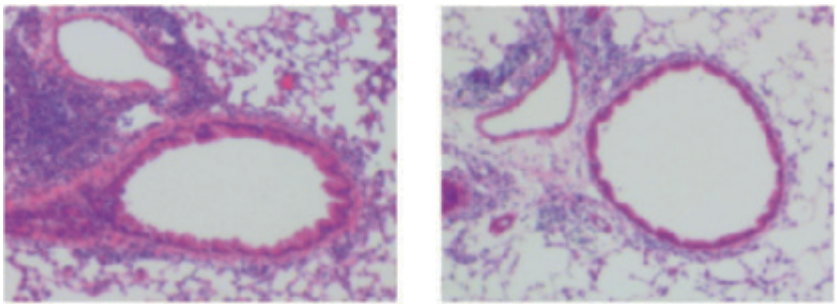


Figure 1: Dendritic cells make a clear difference. The airways of a section of an inflamed mouse lung (left) are constricted by immune cells (purple stain). Following treatment with dendritic cells, the inflammation is much reduced thus opening the airways (right).

Spotting the targets

Researchers at the RIKEN Center for Molecular Imaging Science (CMIS) in Kobe are improving medical imaging techniques to detect and monitor diseases without the risks of surgery. For example, a research team labeled biomolecules with gallium so that they can be detected in the body by positron emission tomography (PET). The technique allows PET imaging of much larger molecules than before[5].

The numbers game

Another very important medical research tool is something that all scientists have to do, but many dread: statistics. Researchers at the

Figure 2: Diabetes, particularly the Type 2 variant, is a growing problem in many countries and requires some patients to monitor their own blood sugar levels.

RIKEN Center for Genomic Medicine (CGM) in Yokohama have been pooling large amounts of data in international collaborations in order to spot important trends.

In 2008 a research team combined data representing over 11,000 people from studies in Europe and Asia. The team's statistical analysis revealed a genetic variation that increases susceptibility to osteoarthritis[6].

Similarly, a second group of researchers at the CGM compared the genomes of people in Japan, Denmark and Singapore. They identified a new single nucleotide polymorphism (SNP)—a variation in which only one of the base pairs in DNA is changed—on the KCNQ1 gene that was strongly associated with Type 2 diabetes in all the populations studied (Fig. 2)[7].

It is only recently that such tiny changes in the genome became detectable, but progressive work in the field once again put RIKEN researchers at the forefront of developments in medical science. The remarkable achievements at these RIKEN institutes in 2008 will improve the health of present and future generations all over the world. ■

1. *RIKEN RESEARCH*, May 2008, p.1
2. *RIKEN RESEARCH*, April 2008, p.8
3. *RIKEN RESEARCH*, July 2008, p.15
4. *RIKEN RESEARCH*, November 2008, p.16 (also p.35 of this report)
5. *RIKEN RESEARCH*, July 2008, p.13 (also p.36 of this report)
6. *RIKEN RESEARCH*, October 2008, p.18 (also p.37 of this report)
7. *RIKEN RESEARCH*, December 2008, p.18

RIKEN Center for Genomic Medicine

Researchers at the RIKEN Center for Genomic Medicine (CGM) in Yokohama are on a mission "to understand individual gene variation and to apply this knowledge to healthcare in order to promote full and healthy lives". They scour the genomes of thousands of patients in search of tiny variations that could link genes to diseases.

The researchers know that different people respond to drugs in different ways, and so are moving towards personalized medicine that targets specific complaints while avoiding negative side-effects. The same work could identify which individuals are susceptible to diseases, and help them to adjust their lifestyle accordingly.

RIKEN Research Center for Allergy and Immunology

Our immune systems provide an impressive array of defense mechanisms to protect us against disease. It is vitally important to understand how the immune system works and, more importantly, why it sometimes breaks down or attacks the body itself.

The RIKEN Research Center for Allergy and Immunology (RCAI) in Yokohama was established in 2001 to provide answers to some of these questions. The researchers are involved in international collaborations to identify mechanisms that develop, maintain and regulate the immune system. Using this knowledge they are working towards therapies for common allergies, autoimmune diseases and cancer, and learning why the body often rejects tissue implants.

How the gut manages bacteria

A previously unknown mechanism enables the immune system in the gut to respond rapidly to changes in bacteria

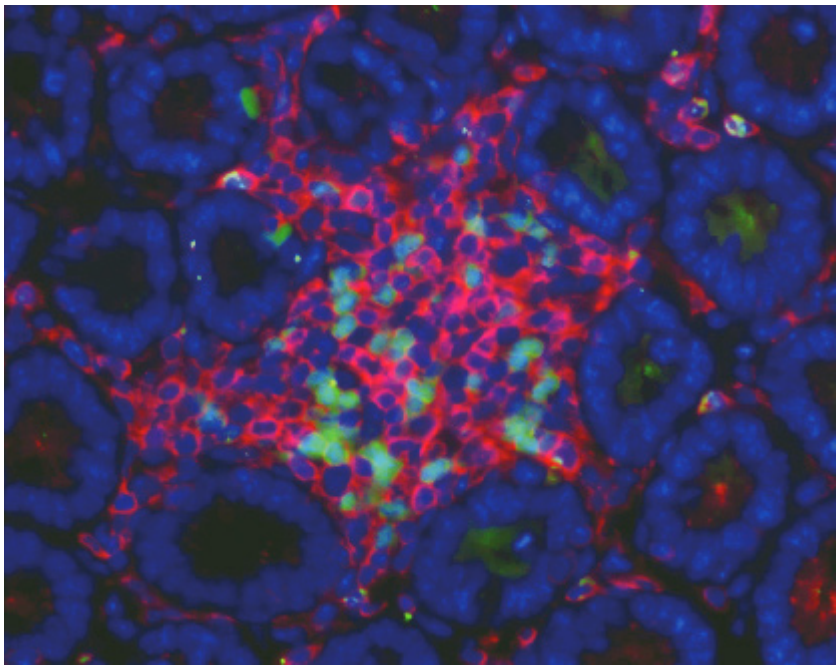


Figure 1: Adult LTi cells (green) interact with underlying stromal cells in the gut to recruit lymphocytes (red) in the small intestine. The nuclei of cells are stained in blue to reveal the gut structure.

A RIKEN-led international research group has puzzled out details of the intricate mechanism by which the immune system in the gut can respond rapidly to changes in its bacterial environment. Eventually, the work could lead to better treatment and control of gut infections and inflammatory bowel diseases.

The gut is in direct contact with the external environment and houses at least 400 different species of bacteria in vast numbers. It maintains a finely tuned immune system built around immunoglobulin A (IgA) antibodies produced by B cells to protect the body against pathogens and manage the growth of benign organisms. Previous research by other researchers unraveled a mechanism whereby T cells control the formation of these IgA-producing B cells in organized multi-cellular structures called Peyer's patches, which develop in the embryo. But such a system could take weeks to respond to invasive bacteria.

The latest work reveals a second mechanism that operates without intervention of T cells, and develops only after colonization of the intestine with bacteria, hence after birth. It involves another set of cellular structures called isolated lymphoid follicles (ILFs).

In a recent paper in the journal *Immunity*[1], the researchers, led by Sidonia Fagarasan of the RIKEN Center for Allergy and Immunology in Yokohama, detail how these ILFs piece together, providing an understanding of the newly identified mechanism. They used strains of mice bred to lack compounds significant to the development of ILFs.

The researchers noticed that the numbers and size of ILFs in the gut paralleled the level of bacteria, increasing with bacterial colonization and decreasing with the use of antibiotics. Recently, they also discovered cells in adults similar to embryonic lymphoid tissue-inducer (LTi) cells essential to the development of immune centers, such as lymph nodes and Peyer's patches.

Fagarasan and her colleagues showed that these adult LTi cells could interact with underlying stromal cells in the gut to recruit the cellular components of ILFs—B cells and antigen-presenting dendritic cells (Fig. 1). But the adult LTi cells only did this effectively in the presence of bacterial cells which stimulate an immune response, partly through the production of tumor necrosis factor. So ILFs are only formed when bacteria are present. The researchers also demonstrated that functioning ILFs could transform typical B cells that make immunoglobulin M into those that produce IgA.

"If we can understand more about these LTi cells and their interactions," says Fagarasan, "it could provide us with the potential to manipulate the gut immune system." ■

1. Tsuji, M., Suzuki, K., Kitamura, H., Maruya, M., Kinoshita, K., Ivanov, I.I., Itoh, K., Littman, D.R. & Fagarasan, S. Requirement for lymphoid tissue-inducer cells in isolated follicle formation and T cell-independent Immunoglobulin A generation in the gut. *Immunity* **29**, 261–271 (2008).

Mapping disease progression

A protocol to form imaging molecules paves the way to new methods of detecting disease *in vivo*

A team of scientists from Japan has developed a new type of bio-label that can be used to detect and image unusually large molecules in experimental animals and non-human primates. The technique could lead to similar methods for being developed for use in humans.

Tracking diseases or monitoring disease progression in a patient is an important factor in deciding the best form of treatment. While biopsies—taking a small sample of tissue from a patient—remain standard hospital practice, more patient-friendly techniques are sought. Non-invasive techniques, such as imaging, can detect and monitor disease in the living body without the risks associated with surgery.

Now, Yasuyoshi Watanabe from the RIKEN Molecular Imaging Research Program, Kobe, as part of a large collaborative project with Koichi Fukase from Osaka University, has developed a new way of labeling biological molecules to make them suitable for imaging using the nuclear medicine technique of positron emission tomography (PET)[1].

"Previously, PET imaging methods have mostly focused on probing only low molecular weight compounds," explains Watanabe. He hopes to develop methods suitable for larger macro-molecules, such as peptides, nucleic acid sequences, glyco-conjugates and proteins that make up antibodies and drive his research.

When labeling macro-molecules it is important that biological activity is not lost; the antibody must continue to recognize and bind to an antigen—such as the surface molecules of specific cells including cancer cells, bacteria or viruses—and stimulate an immune response. As macro-molecules are often damaged or destroyed during the labeling process, the chemical protocol developed by Watanabe and colleagues uses only mild temperatures and aqueous solutions.

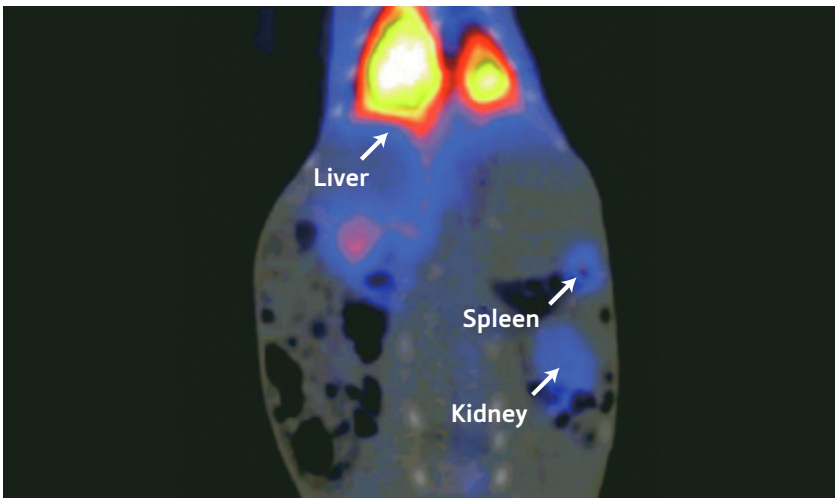


Figure 1: A picture of a new Gallium-containing imaging compound accumulating in several organs of a rabbit.

The researchers chose lysine, an amino acid residue, in the macromolecule as the group onto which the label would be attached. They attached the label, a small organic compound, specifically onto the lysine residue under the mild conditions. Next, they added Gallium, a radioisotope element, to form adducts with the label. The resulting derivatives, detectable using PET, were then tested for biological activity. Results obtained from rabbits showed that the label was easily detected and was found in the major organs of the rabbit as expected (Fig 1).

Watanabe and team are now investigating alternative strategies for labeling other macro-molecules, such as F-18, the radioisotope of fluorine, which is also widely used for PET imaging. Through continued research in this area the team hopes to develop better and more efficient ways to label molecules and extend the range of molecules that can be labeled. ■

1. Tanaka, K., Masuyama, T., Hasegawa, K., Tahara, T., Mizuma, H., Wada, Y., Watanabe, Y. & Fukase, K. A submicrogram-scale protocol for biomolecule-based PET imaging by rapid 6 π-azaelectrocyclization: visualization of sialic acid dependent circulatory residence of glycoproteins. ***Angewandte Chemie International Edition*** **47,** 102–105 (2007).

Global genetic risk for osteoarthritis

A gene mutation and susceptibility to arthritis are linked in two highly divergent ethnic groups

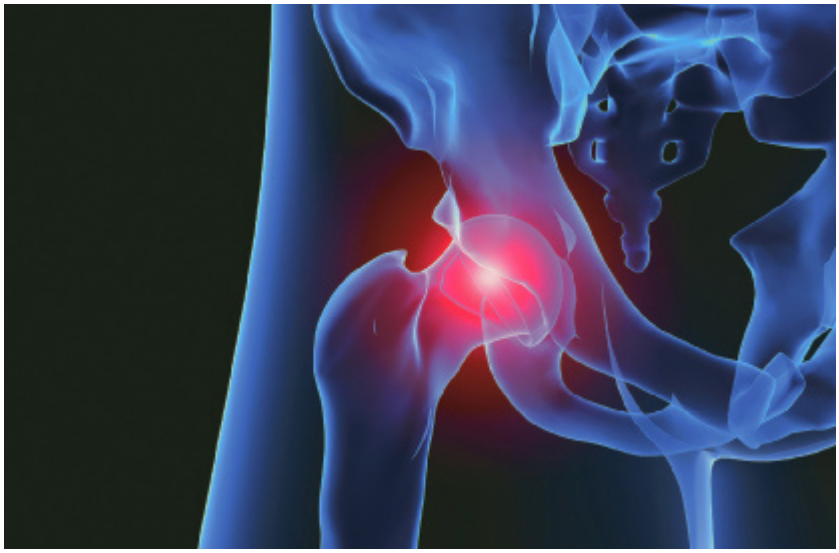


Figure 1: A pictorial representation of an inflamed hip as in OA.

An international team of scientists, including Shiro Ikegawa and colleagues at the RIKEN Center for Genomic Medicine (formerly the SNP Research Center) in Yokohama, has reported in the journal *Human Molecular Genetics*[1] a 'global' role for a specific variant, or polymorphism, of a gene in the susceptibility to osteoarthritis (OA). A large-scale statistical analysis of new data shows that mutation of a gene called *GDF5* (growth differentiation factor 5) and susceptibility to OA is wide-spread among European and Asian populations.

OA, also known as idiopathic degenerative arthritis, is the most common type of arthritis worldwide, affecting hundreds of millions of people every year. Like many human diseases, OA has several causes, including non-genetic (environment, trauma) factors; however, an underlying genetic component of OA has been clearly established by many studies.

Examining data from the UK and the Netherlands combined with three published European and Asian studies that were previously inconclusive, the researchers used a statistical analysis called meta-analysis to look for evidence of an association between the *GDF5* risk gene and susceptibility to OA. Meta-analysis combines data from several individual studies into a single dataset, which can increase the statistical power over that of the individual studies.

Analysis of the combined data—representing more than 11,000 individuals—revealed a significant association of the *GDF5* polymorphism and OA susceptibility. However, differences were noted in the risk of developing OA in the hip or the knee: European and Asia individuals in fact have a similar risk for knee OA. But the meta-analysis helped to reveal the significant risk for hip OA in Europeans.

Ikegawa's team has studied GDF5 for several years, initially linking the specific polymorphism in *GDF5* to OA in Asians, and producing mice with the *GDF5* mutation. The protein produced by the *GDF5* gene is normally involved in joint formation and especially important for development and regeneration of cartilage, the dense but pliable connective tissue on the surface of joints most susceptible to OA, such as the hip (Fig. 1).

Commenting on number of other genes that are known to be associated with genetic risk for OA, Ikegawa says: "In a strict sense, there are none. Only *GDF5* and asporin [a second gene Ikegawa's team previously linked to OA[2]] have definite functional data supporting the causality of OA, and replication in different ethnic groups." The paucity of other known genetic factors highlights the importance of the present study for estimating risk for OA. ■

1. Chapman, K., Takahashi, A., Meulenbelt, I., Watson, C., Rodriguez-Lopez, J., Egli, R., Tsezou, A., Malizos, K.N., Kloppenburg, M., Shi, D., *et al.* A meta-analysis of European and Asian cohorts reveals a global role of a functional SNP in the 5′ UTR of *GDF5* with osteoarthritis susceptibility. *Human Molecular Genetics* **17,** 1497–1504 (2008).
2. Nakamura, T., Shi, D., Tzetis, M., Rodriguez-Lopez, J., Miyamoto, Y., Tsezou, A., Gonzalez, A., Jiang, Q., Kamatani, N., Loughlin, J. & Ikegawa, S. Meta-analysis of association between the ASPN D-repeat and osteoarthritis. *Human Molecular Genetics* **14,** 1676–1681 (2007).

An international hub of diverse research

RIKEN SPring-8 Center, Harima

> "With the addition of the XFEL installation, the SPring-8 campus will become a world-class center of excellence for photon science."
>
> **Tetsuya Ishikawa**
> **Director, SPring-8**

Harima Institute
www.harima.riken.go.jp/eng
Guide for submitting research proposals
user.spring8.or.jp/1_3_review_p_e.jsp

Designed and built jointly by RIKEN and the Japan Atomic Research Institute, the 'Super Photon ring-8 GeV' (SPring-8) synchrotron facility, opened in 1997 and managed by the Japan Synchrotron Radiation Research Institute (JASRI), is one of the most important of the large-scale facilities available at RIKEN.

In 2008 scientists at SPring-8 accelerated their research activities using the world's brightest synchrotron radiation source, unearthing the secrets of systems normally invisible to the eye. The diverse topics that came under the spotlight at SPring-8 in 2008 include the development of a novel method for the analysis of metal nanoparticles in application to reliable hydrogen storage, the detailed observation of rewriteable DVDs, elucidation of a more precise physical structure for an enzyme implicated in Alzheimer's disease, and investigation of the molecular details associated with the control of DNA replication.

Built to encircle Mount Miharakuriyama at the Harima Science Garden City in Hyogo Prefecture, west of Kobe, the ring itself is 1,436 meters in circumference and supports a maximum of 62 beamlines, 50 of which are currently operational, and seven of which are operated by RIKEN through its SPring-8 Center under the auspices of the RIKEN Harima Institute.

Many of the other beamlines are available for public use, providing a range of light sources from hard X-rays (300 keV) to vacuum ultraviolet light (300 eV), all at the highest brilliance currently available in the world. High-energy gamma rays (1.5–2.9 GeV) and infrared sources are also available. Every year, about 14,000 researchers visit the facility, conducting in total more than 2,000 experiments.

Top-level research outcomes cannot be achieved without effective collaboration, and the trend toward joint research was further consolidated in 2008. For example, academics and private companies reached an agreement in the past year to build the first joint beam, which will be used for the research and development of innovative large-molecule materials. SPring-8 has also been a key tool for the Japanese Government's large-scale initiatives, such as the nanotechnology support project.

International partnerships have been developed through researcher exchanges and agreements among institutions over the past few years. Individual foreign researchers are also encouraged to come and work at SPring-8, with research proposals being assessed twice yearly by a Proposal Review Committee according to published criteria. Non-proprietary projects on a public beamline can be conducted at minimal cost for foreign nationals affiliated with organizations outside Japan, involving only the fixed fees required to cover wear and tear.

In addition to forging domestic and international collaborations, RIKEN's pursuit of more effective, powerful light is far from over. Not only is SPring-8 constantly being upgraded, RIKEN and JASRI are also constructing the new X-ray Free Electron Laser (XFEL) at a dedicated site adjacent to SPring-8. Designated as a key technology of national importance by the Japanese Government, the XFEL output is generated using a beam of freely moving electrons rather than by excitement of bound atomic or molecular states as is the case with conventional lasers. This technology promises radiation a billion times brighter than existing X-ray sources, along with pulse periods 1,000 times shorter, and will allow real-time observations of objects with atomic-level resolution. The XFEL source will also facilitate, for example, the analysis of proteins without the need to crystallize the proteins in advance. The new linear XFEL facility is scheduled for completion in 2010, although a prototype XFEL source has already been installed. Like SPring-8, this 'dream light source' will be made available for shared public use.

"With the addition of the XFEL installation, the SPring-8 campus will become a world-class center of excellence for photon science," says Tetsuya Ishikawa, Director of the RIKEN SPring-8 Center.

Modeling a complex future

RIKEN Next-Generation Supercomputer Research and Development Center, Kobe

Many of the most important issues facing society at the beginning of the twenty-first century are staggeringly complex, ranging from climate change and the development of renewable energies, to personalized medicine and food security. One way to conquer these challenges is to carry out realistic simulations of possible scenarios for each situation using ever more powerful computers. RIKEN is at the forefront of this field with the Next-Generation Supercomputer project, which aims to develop the fastest computer in the world.

Designated by the Japanese Government as a key technology of national importance, the Next-Generation Supercomputer project was launched in 2006 with a budget of $1.15 billion and is scheduled for completion in 2012. The project, which is being undertaken by RIKEN in partnership with Japanese industry, universities and the government, involves the construction of the computer and its associated research and development center on Port Island, an artificial island built on reclaimed land in Kobe Harbor, close to Kobe International Airport.

When completed, the Next-Generation Supercomputer will be able to perform 10 quadrillion numerical operations per second, making it more than 250 times faster than the Earth Simulator in Yokohama completed in 2002, and about 10 times faster than the world's fastest supercomputer. It will allow fine-tuned simulations to be conducted to elucidate phenomena such as the complex interactions among the thousands of genes in the human body, and the role of gravity in the formation of galaxies and planets.

The detailed design of the supercomputer will likely be finalized in fiscal 2009, after which the project will enter its most critical phase—the development and evaluation of prototype central processing units (CPUs). The new supercomputer, which has been designed to consume less energy and space than its predecessors, will house tens of thousands of CPUs and allow a wide range of simulations to be performed.

With ever-intensifying competition surrounding the design and construction of supercomputers, the success of the project will largely hinge on the development of distinctive software applications and platforms. "We need to be well-positioned to generate research outcomes soon after the supercomputer is completed," says Tadashi Watanabe, Project Leader of the RIKEN Next-Generation Supercomputer Research and Development Center in Wako.

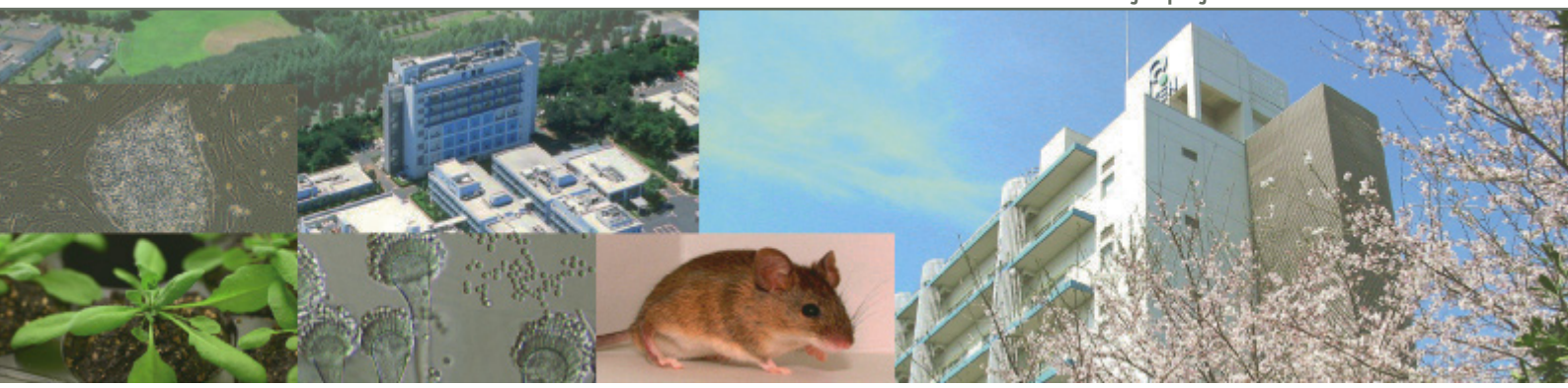
Accordingly, RIKEN is accelerating development of application software to maximize the capabilities of the computer. Given the large investment in the project, Watanabe stresses that "We intend to use every second of machine operation." The computer itself will be designed for general-purpose use, but the Japanese Government has identified life sciences and nanotechnology as the mainstay 'Grand Challenge Applications'. On top of this, RIKEN is leading the development of 'Next-Generation Integrated Simulation of Living Matter' for the simulation of everything from molecules to organs in the human body.

Japan's ongoing commitment to developing major computer systems has led to many innovations with a global reach. Not only will the Next-Generation Supercomputer project continue this trend, but it will also be integrated with a layered network of supercomputers distributed across Japan, providing access to scientists and engineers in universities, research institutions and industry across the country. The supercomputer will also be made available for collaborations with overseas scientists.

> "We intend to use every second of machine operation."

Tadashi Watanabe
Project Leader, NSC

NSC
www.nsc.riken.jp/index-eng.html



Stewarding the future of life sciences

RIKEN BioResource Center, Tsukuba

> "We are constructing networks with Asian institutions to elevate Asia's presence in the international scientific community."

Yuichi Obata
Director, BRC

BioResource Centre
www.brc.riken.go.jp/inf/en
National Bioresource Project
www.nbrp.jp

Modern medical, agricultural and biological research depends heavily on model organisms and standard genetic materials for testing, analysis and genetic engineering. These resources are to biology what purified elements and compounds are to chemistry and materials science—they make controlled experimentation possible.

Established in 2001, the RIKEN BioResource Center (BRC) at the Tsukuba Institute has grown to be one of the world's most important repositories and distribution centers of such biological materials.

Operating under the principles of 'Trust', 'Sustainability' and 'Leadership', the BRC strives to provide the best bioresources for life sciences research in Japan and abroad. The center's distinguished position partly lies in its capacity to handle a wide range of living strains in five major categories: experimental animals (mice), experimental plants (*Arabidopsis*), cell lines of human and animal origin, genetic materials, and microorganisms.

The BRC has been the core of the Japanese Government's National BioResource Project since its launch in 2002, and plays a key role in the support of international communities such as the Federation of International Mouse Resources and the Asian Mouse Mutagenesis and Resource Association.

The BRC also serves as a center of development for new resources and tools to be used in key research areas using the BRC's resources, and provides support for research groups involved in animal development, plant physiology and the development of mouse mutants. One of the latest additions is the integrated database called the 'Systematic Consolidation of *Arabidopsis* and other Botanical Resources' (SABRE).

As part of the ongoing development of the BRC in the past year, three research teams and one research unit were transferred to the center from the RIKEN Yokohama Institute. The BRC became the repository for lines of human induced pluripotent stem (iPS) cells, developed by Shinya Yamanaka at Kyoto University. Subsequently, the distribution of cell lines to nonprofit academic institutions began in March 2009. A mouse iPS cell line was also made available a year earlier.

Highlights of a fruitful year include the establishment of cell lines that produce functional red blood cells from mouse embryonic stem cells by BRC scientists at the Cell Engineering Division, which runs the 'RIKEN Cell Bank'. In other work, multiple teams joined forces to develop a high-speed congenic mouse derivation system that halved the generation turnover of mice to an average of 44 days.

The newly established Technology and Development Team for Mouse Phenotype Analysis also opened the Japan Mouse Clinic in 2008. This facility carries out thorough phenotyping of mouse mutants using a platform of more than 400 test items based on the pathogenetic understanding of human diseases.

With the advancement of life sciences in recent years, bioresources have undergone rapid expansions in number and volume, making it difficult for these resources to be managed effectively by a single country. The BRC is actively running training courses to encourage best practice, and is increasing efforts to foster international alliances. One of the latest examples is an agreement between the BRC and Taiwan's National Yang Ming University in December 2008 toward the development of a joint graduate program.

"Asia still lags behind the US and Europe. We are constructing networks with Asian institutions to elevate Asia's presence in the international scientific community," says Yuichi Obata, Director of the BRC.

International invitation programs

Beyond borders—striving toward internationalization

Increasing scientific knowledge while promoting international cooperation and understanding are among the core principles of RIKEN. Whether a doctoral candidate or an experienced researcher, there are many opportunities—and no national boundaries—at RIKEN.

RIKEN is renowned for its genuine commitment to internationalization and strives to provide the best and most exciting opportunities for young non-Japanese scientists in the crucially important early stages of their careers. One manifestation of this support comes in the shape of RIKEN-funded programs for those wishing to join RIKEN in the fields of physics, chemistry, biology, medical science or engineering for both short and long terms; and while RIKEN may not be able to help with all the difficulties foreign researchers will face in their daily life in Japan, it can at least guarantee a scientific experience that is second to none.

For Doctoral Candidates
International Program Associate (IPA)

www.riken.jp/engn/r-world/riken/organ/ipa.html

RIKEN offers students 35 years or younger the opportunity to complete their doctoral studies as an International Program Associate (IPA) under the supervision of a senior RIKEN scientist. Applicants should be non-Japanese nationals who are, or are soon to be, holders of a master's degree and who have enrolled as a doctoral candidate at a university that has signed (or shows a willingness to sign) a cooperative agreement with RIKEN under the Joint Graduate School Program.

The funding for the IPA position extends for a maximum of three years (four years in the case of a PhD in medicine) and covers daily living expenses, housing costs and one return trip between RIKEN and the researcher's home country.

The RIKEN researchers in charge of supervising successful applicants must also hold concurrent positions as visiting faculty at a collaborating Japanese or overseas university. RIKEN has thus far accepted 40 IPAs and intends to increase the number of IPAs to 100 per year by 2012, including 60 from Japanese universities and 40 from abroad.

IPA Research Examples

- Experimental and theoretical studies of electron transport through molecules
- Cell-recognizable matrix engineering for regenerative medicine
- X-ray diffraction studies of Fe(II) complexes in different spin states
- Characterization of regulatory interaction between the pre-replication complex and nuclear pore formation in human cells
- Synthesis and catalysis of novel organo–rare-earth-metal complexes
- Investigation of the collective properties of neutron-rich Ne and Mg isotopes
- Development of advanced computational fluid dynamics (CFD) technology based on volume computer-aided design (VCAD) and application to the preservation of cultural relics

For Postdoctoral Researchers
Foreign Postdoctoral Researcher (FPR) Program

www.riken.jp/fpr

The Foreign Postdoctoral Researcher (FPR) program is an opportunity for young, non-Japanese postdoctoral researchers to contribute to the outstanding achievements of RIKEN's ongoing projects. Working under the direction of a laboratory head, successful applicants will have the chance to bring their creative and original ideas to life. The experience of innovation at RIKEN is expected to set the stage for the researcher to become an internationally recognized scientist in the future.

The FPR program is one of RIKEN's initiatives aimed at creating an invigorating, borderless research environment that will place RIKEN at the forefront of global science and technology.

Applicants should be in possession of a doctoral degree by the starting date, and will usually have less than five years' postdoctoral research experience. The contract is for one year in the first instance, and may be renewed for up to three years. In addition to generous remuneration, an annual research budget of one million yen will be provided. RIKEN will provide guidance on research activity and administrative procedures. There are currently close to 20 FPRs, and RIKEN will accept and maintain up to 50 FPRs per year by 2012.

FPR Research Examples

- Studies on the non-perturbative aspects of string theory and the matrix model
- Characterization of charge density wave crystals by scattering and photoemission spectroscopy (PES) using soft X-rays
- Synthesis of oligosaccharyl donors for creation of glycoproteins using biosynthetic machinery
- Determination of cellular and molecular mechanisms of synapse formation in the zebrafish nervous system
- Investigation of eukaryotic aminopeptidase enzymes under environmental stress
- Nano-Raman spectroscopy of thermo-mechanical and electrical stress in advanced electronic devices and sensors

For Leaders in their Fields
Initiative Research Unit (IRU) Program

www.riken.jp/r-world/research/research/iru/IRU.pdf

Successful world-class researchers often only reach full stride in their 30s and 40s. RIKEN offers the Initiative Research Unit (IRU) program to help ambitious young scientists fully realize their potential creativity by offering a high degree of independence and flexibility.

The IRU program currently consists of eight research units, led by both Japanese and foreign mid-career scientists, and is managed as part of the RIKEN Advanced Science Institute in Wako.

Applicants should hold a doctoral degree in a natural science, and have a proven track record of experience and achievement including the ability to design and implement an ambitious research plan and manage a small research unit. The full-time position carries a one-year contract in the first instance, but is renewable for up to five years. Each unit is provided an annual grant of about 50 million yen, which covers the leader's annual salary of around 10 million yen as well as research and personnel expenses. Each unit also receives a start-up subsidy in the first year of up to 10 million yen for establishing a laboratory. The leader will have access to RIKEN's common equipment and facilities as well as the freedom to select research and technical staff, and to apply for competitive grants.

Details of the programs available for non-Japanese researchers can be found at: www.riken.jp/engn/r-world/research/research For further information, contact the RIKEN Global Relations Office (e-mail: gro-pr@riken.jp).

RIKEN contributing to society

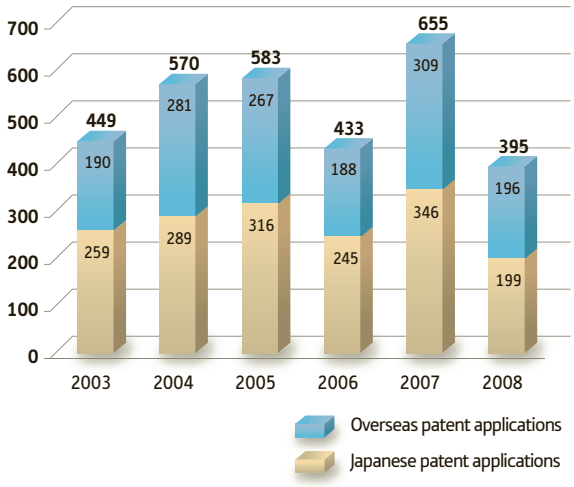
Technology Transfer

In addition to communicating its achievements through the publishing of research papers, RIKEN also makes many patent applications each year for discoveries and inventions with discernible commercial value in order to secure legal protection for its research successes. The RIKEN technology transfer portfolio is managed by the Center for Intellectual Property Strategies (CIPS), which acts as a conduit between RIKEN and the business 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. It also provides active support for venture capital companies—numbering 25 as of April 2009—established by RIKEN scientists in developing practical applications for their research achievements.

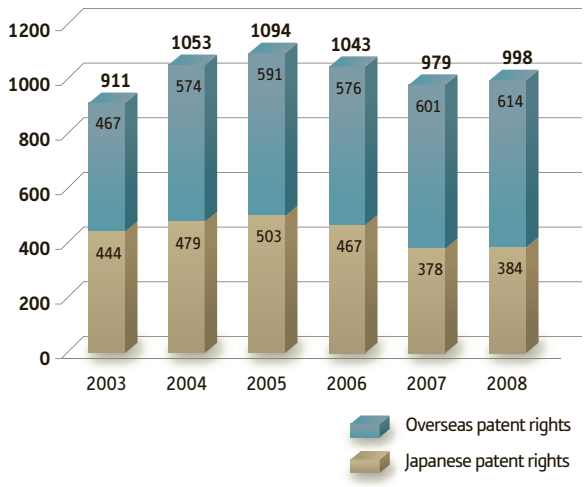
RIKEN patent activity in 2008

RIKEN registered a total of 998 patents in fiscal 2008–2009, representing an increase of 1.94% on the previous year. Almost two-thirds of these patents were registered outside Japan. In addition, 395 patent applications—evenly split between foreign and domestic filings—were made in the same period. Management of existing patents and licenses held by RIKEN and its collaborators yielded revenue of $806,000 in fiscal 2008. RIKEN also actively pursues opportunities for filing patents in foreign countries for inventions already covered by patents in Japan.

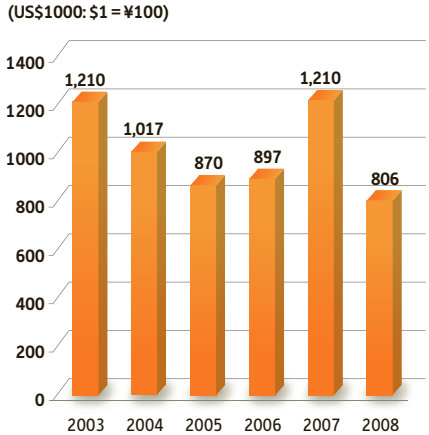
Patent applications



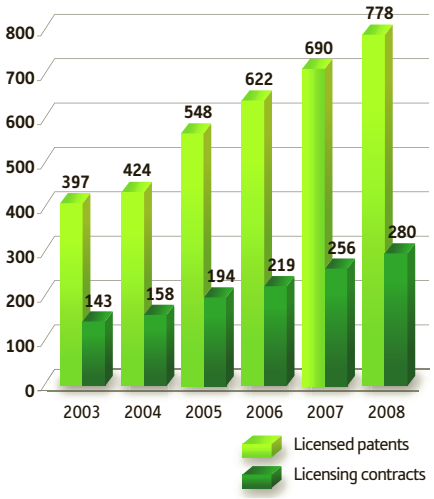
Patent registrations



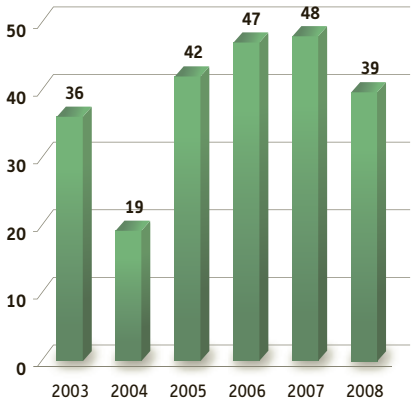
Patent income



Licensing contracts



New patent licenses



Facts and figures

RIKEN ANNUAL REPORT 2008–2009

Charting the future course of RIKEN

RIKEN Governance

The Board of Executive Directors is the supreme policy-making body at RIKEN and is composed of the president and the executive directors. The administration of affairs at the campus institute level is the domain of institute directors, who oversee and manage the operations of an entire RIKEN campus. Within each RIKEN campus, individual research centers and institutes are managed by a center director who exercises strong leadership in the strategic management of the research center or institute.

In making decisions, RIKEN strives to strike a balance between top-down and bottom-up initiatives to realize optimal scientific governance. The advisory functions of the president in decision-making are reinforced as follows.

The **Research Priority Committee** is composed of experts from both within and outside RIKEN and discusses the overall direction of research activities for RIKEN with a view toward the future. This committee advises the president and the Executive Board on the prioritizing of research subjects and areas that are deemed the most important, and ways to implement the systems necessary for carrying out research and resource allocation.

The **Institute and Center Director Committee** is composed of the institute directors and center directors at the five constituent RIKEN campuses. This group provides a forum for directors responsible for research at RIKEN to exchange information and opinions, and to share common knowledge on research and management at RIKEN.

The **RIKEN Science Council** is an advisory body whose remit is to examine suggestions made on the research fields that should be studied and the policies required for promoting research with a long-term yet broad perspective from the stance of scientists and to advise the RIKEN President.

Evaluating Performance

RIKEN undertakes self-evaluation based on national guidelines for organizations, research themes and the performance of individual scientists. In carrying out this important work, RIKEN is guided by the RIKEN Advisory Council and the individual Center and Institute Advisory Councils.

The **RIKEN Advisory Council (RAC)** is composed of world-famous scientists from various research fields of domestic and international repute as well as individuals with managerial experience in research institutes. The RAC provides suggestions on both general research activities and the management of the research institutes at RIKEN. The RAC evaluations inform the creation of future plans for RIKEN research activities and provide guidance on improving management structures. For example, the results of the 6th RAC evaluation, conducted in June 2006, were used in the formulation of the second mid-term plan. A copy of the RAC report may be found online at:
www.riken.jp/engn/r-world/info/report/rac/pdf/6report.pdf

The most recent appraisal of RIKEN was carried out by the 7th RAC in April 2009. The council was charged with 1) evaluating RIKEN's responses to the 6th RAC proposals outlined in the document "RIKEN: Leading Japanese Science to Global Pre-Eminence", 2) proposing a management policy to realize the goals of the second mid-term plan, and 3) evaluating RIKEN's collaborations within its own institutes and centers and with external institutions. The resultant RAC proposals are to be submitted to the RIKEN Executive Board to further promote these collaborative efforts.

The **Center and Institute Advisory Councils** are bodies set up within the individual research centers and institutions at RIKEN to receive management evaluation and advice from eminent domestic and international scientists in their respective fields of research. The closer integration of the roles of these advisory councils and the RAC began with tabling of shared consultation plans by the president to the 7th RAC evaluation in April 2009. It is intended that moves will be made toward realizing a common overall appraisal for RIKEN by tying the work of the individual advisory councils with that of the RAC such that the results of advisory council evaluations are reflected in the overall evaluation of RIKEN.

Members of the RIKEN Advisory Council

RAC core members

Dr Zach W. Hall
Chair
(Neuroscience)
Emeritus Vice Chancellor, University of California, San Francisco
Former Director, National Institute of Neurological Disorders and Stroke
Founding President, California Institute for Regenerative Medicine

Dr Hiroo Imura
Vice-Chair
(Medicine, Endocrinology)
Chairman, Foundation for Biomedical Research and Innovation
Principal Fellow (Chair), Center for Research and Development Strategy, Japan Science and Technology Agency

Dr Yuan Tseh Lee
Vice-Chair
(Chemistry)
President Emeritus and Distinguished Resarch Fellow, Academia Sinica

Dr Howard Alper
(Chemistry)
Distinguished University Professor, University of Ottawa
Chair, Government of Canada Science, Technology and Innovation Council

Dr Teruhiko Beppu
(Applied Microbiology)
Professor, Advanced Research Institute for the Sciences and Humanities, Nihon University

Dr Colin Blakemore
(Neuroscience)
Professor, Department of Physiology, Anatomy and Genetics, University of Oxford

Dr Rita R. Colwell
(Oceanography)
Distinguished University Professor, Center for Bioinformatics and Computational Biology, University of Maryland

Dr Mitiko Go
(Bioinformatics)
Executive Director, Research Organization of Information Systems

Dr Toshiaki Ikoma
(Electronics)
Adviser, Canon Inc.

Dr Biao Jiang
(Chemistry)
Director, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences

Dr Paul Kienle
(Physics)
Professor Emeritus, Department of Physics, Munich University of Technology

Dr Karin Markides
(Chemistry)
President, Chalmers University of Technology

Dr Hans L. R. Wigzell
(Medicine, Immunology)
Director, Center for Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet

Dr Rainer E. Metternich
Absentee Participant
(Drug Discovery)
Vice President, Basic Research and Site Head, W.P., Biomedical Research Administration Dept., Merck Research Laboratories

RAC members and Advisory Council chairs

Dr Allan Bradley
(CLAC/Genetics)
Director, Wellcome Trust Sanger Institute

Dr Max D. Cooper
(RCAI/Medicine)
Professor, Department of Pathology and Laboratory Medicine, Emory University

Dr Hidetoshi Fukuyama
(ASI/Basic Solid State Science)
Professor, Department of Applied Physics, Faculty of Science, Tokyo University of Science

Dr Sydney Gales
(RNC/Nuclear Physics)
Director, Grand Accelerateur National D'Ions Lourds

Dr Sten Grillner
(BSI/Neuroscience)
Professor, Nobel Institute for Neurophysiology, Karolinska Institutet

Dr Wilhelm Gruissem
(PSC/Plant Biotechnology)
Professor, ETH Zurich, Institute of Plant Sciences

Dr Jean-Louis Guenét
(BRC/Veterinary Medicine, Mouse Genetics)
Director, Unité de Génétique des Mammifères, Institut Pasteur

Dr Jerome Hastings
(RSAC/Applied Physics)
Professor, Photon Science, SLAC National Accelerator Laboratory

Dr Bengt Långström
(CMIS/Biochemistry)
Professor, Department of Biochemistry and Organic Chemistry, Uppsala University

Dr Mark Lathrop
(GSC/Gene Science)
Director General, Center National de Genotypage

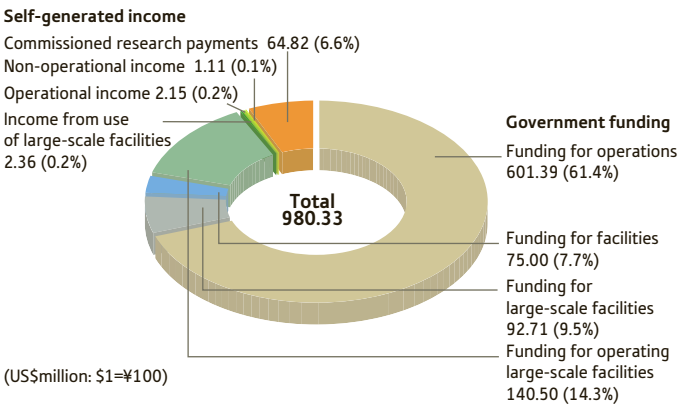
Dr Austin Smith
(CDB/Stem Cell Biology)
Medical Research Council Professor and Director, Wellcome Trust Centre for Stem Cell Research and Institute for Stem Cell Biology, University of Cambridge

Diversity of funding streams

RIKEN Budget

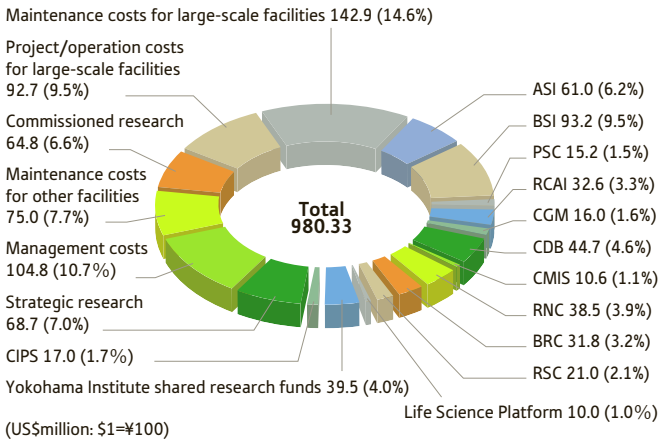
The Japanese Government remains the primary financial supporter of RIKEN, and in common with other Independent Administrative Institutions, RIKEN is responsible for deciding how to distribute its funds for operations. However, while the government grants broad latitude on how the funding should be used by RIKEN, it continues to monitor and scrutinize spending closely. The government funding for facilities is used by RIKEN to acquire tangible assets, such as the purchase of land and the construction of buildings. Costs for the maintenance and development of SPring-8, XFEL and the Next-Generation Supercomputer are shared with the government under a legal proviso that guarantees the use of such advanced facilities for the benefit of the public. In an effort to diversify its revenue stream, RIKEN works hard to obtain funding from other sources, as summarized below.

Income



(US$million: $1=¥100)

Expenditure

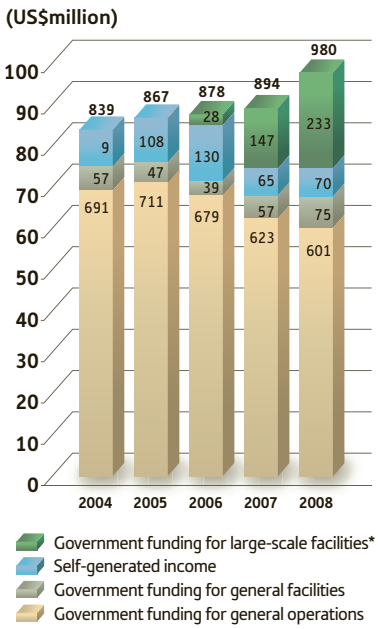


(US$million: $1=¥100)

External funds

RIKEN also acquired funds from various government bodies, including the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT), as well as public and private organizations in fiscal 2008–2009.

Recent budget profile



Acquisition of external funds

Category		FY2006	FY2007	FY2008
				US$million
1. Competitive funds	Grants-in-Aid for Scientific Research	26.34	32.66	37.28
	Grants-in-Aid for Scientific Research (Ministry of Health, Labour and Welfare, and Ministry of Environment)	0.38	1.57	0.82
	Special Coordination Funds for the Promotion of Science and Technology	3.28	1.84	0.37
	Projects funded by organizations that fund science and technology	12.28	12.25	17.11
	Basic Research Programs (Japan Science and Technology Agency)	5.44	22.13	29.25
	Other publicly supported projects	3.54	4.39	3.93
Sub-total		**51.26**	**74.84**	**88.76**
2. Non-competitive funds	Government commissioned research	101.36	43.37	36.82
	Government-related commissioned research	2.61	3.30	2.38
	Government grants	0.90	1.18	1.71
	Private grants	1.15	0.97	2.23
	Contributions	2.67	2.22	1.67
Sub-total		**108.70**	**51.04**	**44.80**
Total		**159.96**	**125.89**	**133.56**

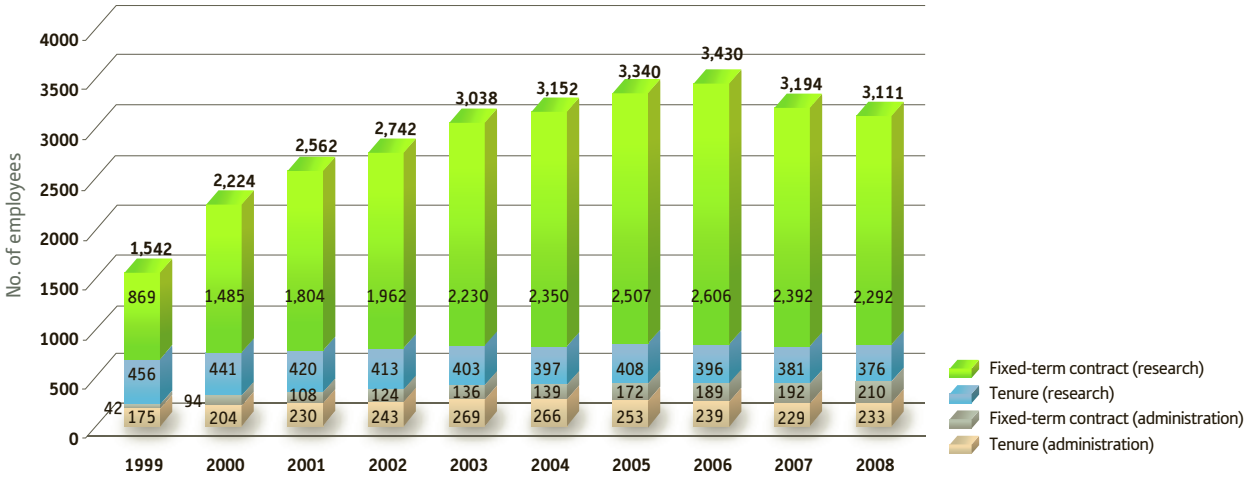
*Large-scale facilities include: SPring-8, XFEL and the Next-Generation Supercomputer.

Building a better research environment

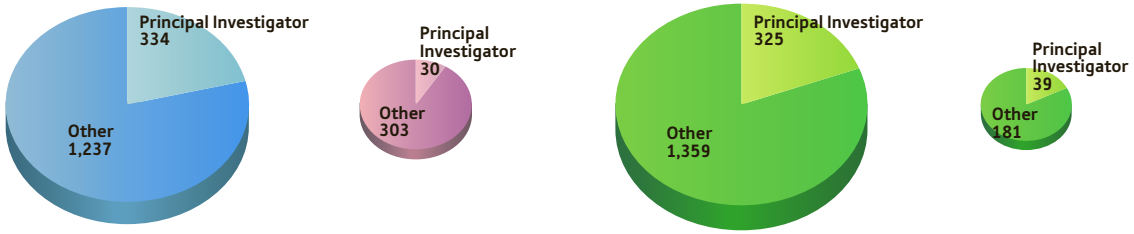
RIKEN personnel

RIKEN maintains a two-track approach to the recruitment of staff: a tenured employment system under which staff are employed until mandatory retirement at the age of 60, and a system of fixed-term contracts specific to the type of work undertaken. Tenured employment is generally offered to personnel involved in curiosity-driven research in laboratories headed by chief scientists, and to those contributing to the development of technology as part of ongoing research and accumulation of knowledge. Fixed-term contracts are generally offered to personnel appointed to work in research centers on projects of predetermined, finite duration.

Employment Status of RIKEN Personnel (as of March 31, 2009)



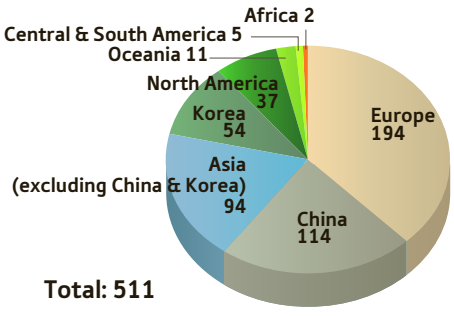
Research Staff Employed by RIKEN (as of March 31, 2009)



Diversity at RIKEN

By attracting the most talented scientists from Japan and abroad, RIKEN actively promotes a research environment that fosters the very best of international research. Diversity among personnel is a vital factor contributing to RIKEN's success, and RIKEN has set ambitious targets for increasing the number of female and non-Japanese scientists undertaking research at its many institutions and research centers as part of the second mid-term plan announced in 2008.

International researchers by country of origin
(including visiting researchers, 2008)



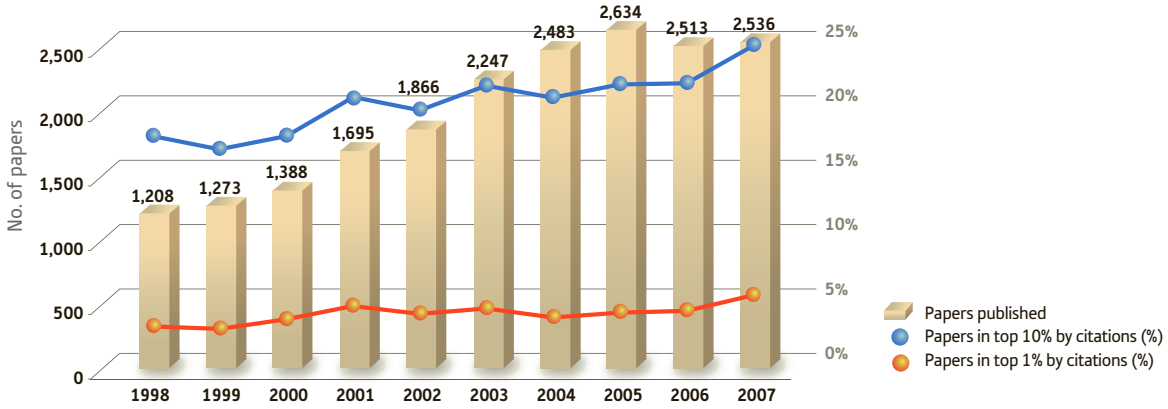
World-class research at RIKEN

Continued Improvement in Quality and Quantity of Publications in 2008

The 2008–2009 fiscal year saw RIKEN maintain its position as one of the world's premier research organizations. In 2008 a total of 2,896 primary papers were published by RIKEN researchers. Absolute productivity was higher than in 2007, and the proportion of papers rated among the 10% and 1% most highly cited papers in the world also continued to increase.

Primary Papers Published by RIKEN Researchers and Status of Citations

(Thomson ISI Expanded Science Citation Index, November 2008)



Raising the international profile of RIKEN

RIKEN RESEARCH

Showcasing the best of RIKEN's research activities to the global community and building RIKEN as a global brand are at the heart of RIKEN's science communication strategy. Key components of this strategy are the RIKEN RESEARCH website—published in Japanese and English—and the associated English-language monthly magazine distributed both in conventional print format and as a free download from the RIKEN RESEARCH website. Together these make the very best of research emanating from RIKEN available in a format that is accessible to specialists and non-specialists alike. Since its inception in 2006, the RIKEN RESEARCH website has established itself as the face of RIKEN for the international community. In 2008–2009 the website was accessed by visitors from 163 different territories, and the popularity of the site is expected to rise further following the recent introduction of a radically redesigned second-generation site offering improved usability and visitor experience. Over the same period, issues of the RIKEN RESEARCH monthly print magazine containing 188 of the best research highlights selected from the entire portfolio of RIKEN RESEARCH were distributed to individual scientists and top-flight universities and research institutions around the world. By combining traditional media with the latest electronic media in innovative ways, RIKEN continues to raise its profile in the international community.

RIKEN RESEARCH
English: www.rikenresearch.riken.jp
Japanese: www.rikenresearch.riken.jp/japan

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www.riken.jp

RIKEN, Japan's flagship research organization, conducts basic and applied experimental research in a wide range of science and technology fields including physics, chemistry, medical science, biology and engineering. Initially established as a private research foundation in Tokyo in 1917, RIKEN became an independent administrative institution in 2003.

For further information on the research presented in this publication or to arrange an interview with a researcher, please contact:
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www.rikenresearch.riken.jp

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