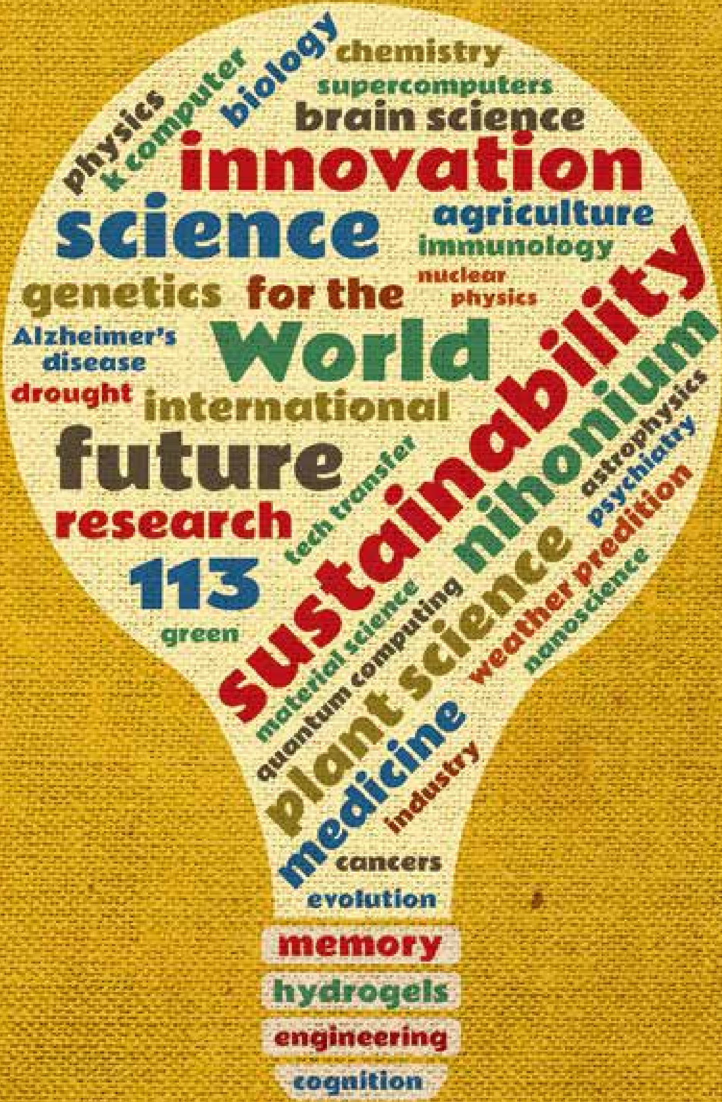
RIKEN

NATIONAL SCIENCE INSTITUTE of Japan



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RIKEN National Science Institute is Japan's most comprehensive institute for the natural sciences, conducting cutting-edge research in a wide range of scientific fields, including physics, chemistry, brain science, energy, medicine, nuclear physics, sustainable resources, computer science, plant science, genetics, nanoscience, developmental biology, electronics, artificial intelligence, and much more.

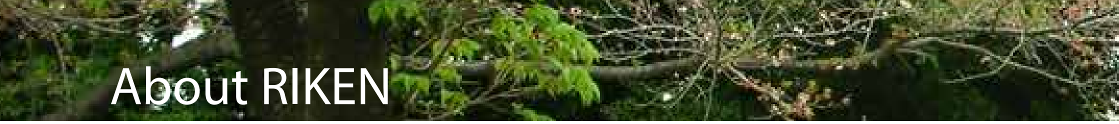
Message from President Hiroshi Matsumoto

This year marks the beginning of a new chapter in RIKEN's history, as we have embarked on a seven-year mid- to long-term plan that will run until 2025. Under this new plan, we have reorganized our life-science centers to encourage interdisciplinary collaboration, have set up a Cluster for Science and Technology Hub to ensure that RIKEN functions as an essential science and technology hub for Japan's academic community and its industry partners, and have established an Innovation Design Office that will help researchers envision how their research can contribute to society, particularly to sustainable development.

The new plan also calls for RIKEN to be a place where young researchers can commit themselves to long-term research projects and goals. However, working steadily on a challenge that will take years to complete is difficult with time restrictions. To address this issue, we are increasing the number of researchers with unlimited-term employment contracts that do not have a five- or ten-year limit.

Along with all the changes, we must not forget that our success depends on basic research. Along with increasing cross-discipline innovation and collaboration with industry, a major objective of the new plan is not new at all; we must continue to maintain our high quality basic research. These are the roots from which all our accomplishments can grow.

RIKEN is already a leading research institute in Japan, as is reflected by the consistency with which we publish in high-quality journals. However, the ultimate goal of these reforms is for us to be recognized as a top-tier scientific institute around the world. Although we still have some ways to go, we are making tangible progress, which will only increase in the years to come.



About RIKEN

BRIEF HISTORY

Key moments

RIKEN the Institute of Physical and Chemical Research, was founded in 1917 by prominent businessman and industrialist Eiichi Shibusawa along with leaders from various fields of research.

The initial years were rocky, but the third president, Masatoshi Okochi, strengthened the organization's foundation by creating a group of companies that commercialized RIKEN discoveries. In the prewar years, RIKEN contributed to scientific fields such as cosmic ray and cyclotron research, and also contributed to society through products such as vitamin A, piston rings, and a groundbreaking surface treatment for aluminum called alumite. However, the end of WWII marked a sudden end to an era of rapid expansion at RIKEN. The conglomerate created by Okochi was dissolved by the Occupation forces, and eventually reopened as a private company under the name KAKEN in 1948. Its leaders tried to make ends meet, but it was a difficult time. Things picked up in 1958 when it became a public corporation and changed its name back to RIKEN.

- 1917 - RIKEN is founded.
- 1948 - RIKEN becomes KAKEN Scientific Research Institute Ltd.
- 1958 - RIKEN becomes a public corporation.
- 2003 - RIKEN becomes an Independent Administrative Institution.
- 2016 - RIKEN is designated as one of three National Research and Development Institutes in Japan.
- 2017 - RIKEN celebrates its 100th anniversary.

In 1967, just as it celebrated its 50th anniversary, RIKEN relocated to a large state-owned land in the outskirts of Tokyo, and began to establish satellite institutions at other locations in Japan.

Modeled on the Max Planck Society in Germany, the satellite institutions were to be located across the country, each focusing on specific fields of research. Over the years, this vision has become reality, with the opening of multiple centers in Tsukuba, Sendai, Nagoya, Yokohama, and Kobe, and research expanding beyond physics and chemistry to numerous fields in the life sciences, computer sciences, and engineering.

National Research and Development Institute

In April 2015, RIKEN acquired a new status, this time as a National Research and Development Institute, and in 2016 was given new prestige as one of three Designated National Research and Development Institutes, just in time for the centennial celebration, which took place in 2017.

NEW PLAN, RENEWED FOCUS

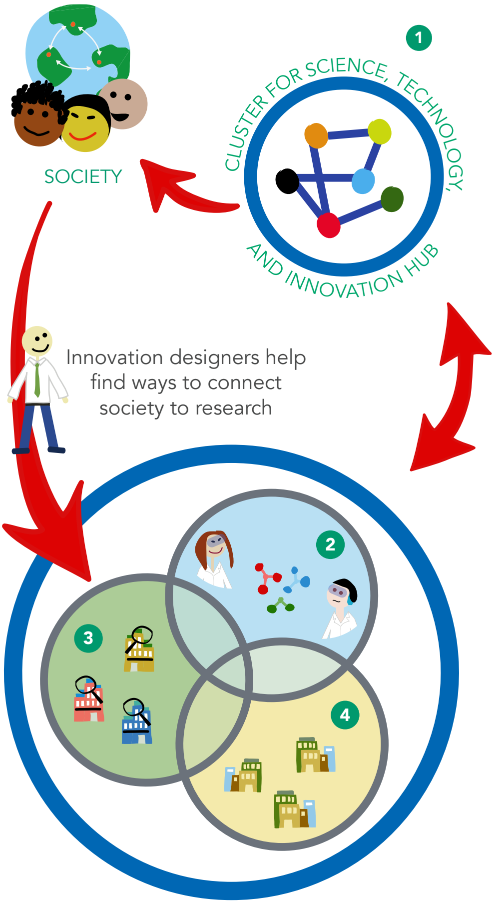
Organizational Philosophy

RIKEN has changed over the years, but its commitment to basic research remains the same. Now, under RIKEN's 4th mid- to long-term plan, research falls into four interactive and sometimes overlapping areas (see illustration): (1) Cluster for Science, Technology, and Innovation Hub (p. 38), (2) Cluster for Pioneering Research (p. 41), (3) Strategic Research Centers (p. 46), and (4) Research Infrastructure Centers (p. 48).

Future direction

Along with a renewed emphasis on society, the new plan incorporates RIKEN's desire to become an international hub that links research from around the world to appropriate industries—all for society's benefit. To facilitate this, the new plan includes an Innovation Design Office with three innovation designers—appointees who specialize in identifying real-world problems and communicating those needs to researchers, not only from a scientific perspective but also from the viewpoints of the social sciences and humanities.

Scan the QR code to watch an introduction to RIKEN.



Life Sciences

Life science research at RIKEN ranges from developmental biology and neuroscience to plant science and omics-based research. The common thread connecting these different disciplines is the desire to help society, whether it be by improving physical and mental health or by creating more durable plants and a more sustainable environment.

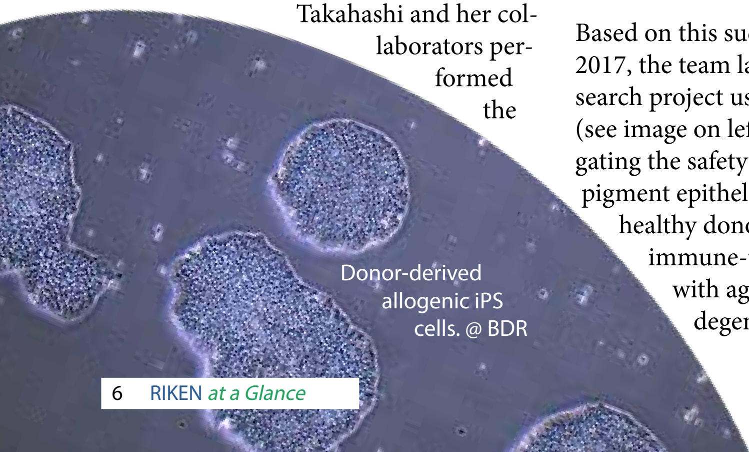
MEDICINE AND DISEASE

Regenerative medicine and iPS cells

Induced pluripotent stem cells (iPS cells or iPSCs) are stem cells created from mature cells of the body, such as skin cells. These stem cells can then be directed to mature into a desired cell type. Scientists hope to use iPS cells to help repair damaged tissues and organs. In 2013, researchers at the Center for Biosystems Dynamics Research (BDR) initiated the world's first clinical study using iPS cells in human patients. The treatment was for age-related macular degeneration—a leading cause of vision loss in older people. In 2014, Masayo Takahashi and her collaborators performed the first transplant of iPS-cell derived laboratory grown tissue into a human patient. This initial effort used autogenic iPS cells, meaning that they were derived from the same person who received the transplant. Since then, the group has made further advances using animal models. In 2017, they showed that mice who received iPS cell-derived retinal transplants could see light and use the visual experience to modify their behavior.

In 2016, the group began allogenic iPS-cell transplants in monkeys. They grew retinal pigment epithelial cells from iPS cells derived from one monkey and succeeded in transplanting them into another monkey without rejection.

Based on this success, in February of 2017, the team launched a clinical research project using allogenic iPS cells (see image on left). This study is investigating the safety of transplanting retinal pigment epithelial cells generated from healthy donor-derived iPS cells into immune-type matched patients with age-related macular degeneration. The team has



Donor-derived allogenic iPS cells. @ BDR

completed transplantation surgery in five patients as planned and is currently closely monitoring the patients for a one-year period.

Other RIKEN laboratories are leading the way towards growing different types of human tissue and organs in the laboratory. In 2016, BDR scientists reprogrammed iPS cells and successfully grew complex skin tissue—complete with hair follicles and sebaceous glands—in the laboratory. They were then able to implant these tissues into living mice, and the tissues formed proper connections with other organ systems such as nerves and muscle fibers (see image on right). In the future, this technique could be used for functional skin transplants in burn victims and other patients who require new skin, or even to combat hair loss. Importantly, the lab-grown skin exhibited sustainable hair cycles, indicating functional regeneration.

Over the last two years, the team has developed a new method for mass producing regenerated hair follicles. In 2018, animal testing of hair follicle regeneration began in conjunction with the RIKEN Program for Drug Discovery and Medical Technology Platforms, which as part of the Cluster for Science, Technology, and Innovation Hub, has bridged the gap between basic research and partners within industry.

These first steps toward creating living 3D tissue in the laboratory are truly groundbreaking. RIKEN is leading the way in this field that was considered science fiction just a few years ago, and which could ultimately create a world in which injured tissues are commonly replaced with tissue grown outside the body.

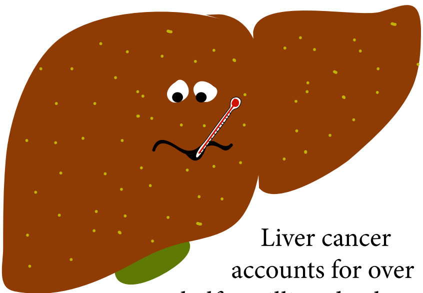
Bald mouse with functional and regenerative hair transplant derived from iPS cells @BDR

iPS cells can also be used to study disease development. In 2016, BDR scientists used iPS cells derived from patients with spinocerebellar ataxia, and grew three-dimensional mature Purkinje cells. They found that patient-derived cells became vulnerable when deprived of thyroid hormone. This new model system can be used to develop drug therapies for genetic disorders.

Cancer research

While iPS cells and regenerative medicine could be effective for some conditions, other illnesses need different approaches. In the case of cancer, RIKEN researchers are attacking the disease from all sides and working to improve diagnosis and develop new treatments, especially those that help prevent cancer from recurring.

In 2017, RIKEN scientists discovered how the spread of cancer in the liver might be prevented. Knowing that the surface of cancerous cells in the liver have excessive levels of fucosylated glycans, they searched and found an analog of the sugar fucose that prevented fucosylation. Tested in several lines of liver-cancer cells, they found that when fucosylation was blocked, the cancer could not invade other cells.



Liver cancer accounts for over half a million deaths per year, in large part because the rate of recurrence is high. Although chemotherapy can often eliminate most of the cancer, when liver-cancer stem cells survive, they can proliferate and lead to a relapse. In 2018, Soichi Kojima and colleagues at the Center for Integrative Medical Sciences (IMS) found that high expression of the MYCN gene is a biomarker for recurrence of liver cancer. They also found that the reason why acyclic retinoid—a derivative of vitamin A—is effective in preventing relapse, is because it acts to reduce MYCN expression in liver-cancer stem cells. Thus, MYCN is a good target for drug therapy.

In 2017, another IMS group was able to identify mutations and their associated biological signaling pathways that underlie the development of acute myeloid leukemia (AML), a disease that kills more than a quarter million people per year. By transplanting cells from people with AML into immune-deficient mice, they found that one of the most common mutations in AML can cause normal bone marrow to be transformed into AML cells. By blocking the abnormal signaling, they were able to illuminate AML in most of the mice.

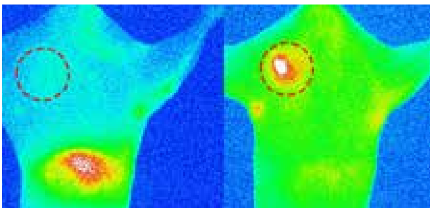
Another team of IMS scientists have developed a potential treatment for AML using WT1-expressing human artificial adjuvant vector cells. As of the summer 2018, this treatment is now part of a University of Tokyo Medical Hospital Phase-I clinical trial for patients with relapsed AML. To date, they have treated four patients and continue to monitor the effects.

In 2017, a team led by Hiroki Ueda at BDR developed a way to help reduce cancer relapse by making it easier to judge the effectiveness of anti-cancer drugs before they are tested in human clinical trials. The process uses a cocktail to visualize postmortem cancer metastasis of whole organs in 3D. The technique is extremely sensitive

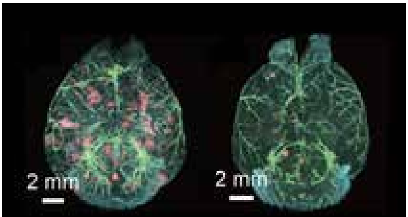
and can be used to detect individual cancer cells. Thus, it can be used to find dormant or drug-resistant cancerous cells, which will improve drug assessment and development (see image on right).

The optical clearing method used by Ueda and his team for looking at single-cell processes could be useful in regenerative medicine where events at the single-cell level are critical.

However, when doctors need to identify tumor locations in living organisms, tissue clearing is not an option. Researchers at BDR addressed this issue in 2017 by developing a way to attach extremely bright near-infrared fluorescent probes—called quantum dots—to antibodies. Because the near-infrared light can easily penetrate animal skin and tissues, tumor cells with known biomarkers can be imaged non-invasively (see image at bottom).



Near-infrared fluorescence images of breast tumors in mice (red circles). (left) Quantum dot injection. (right) Antibody-conjugated quantum dots specific for breast tumor cells correctly localized to tumor area. @BDR



Imaging of metastasized cancer in the mouse brain after treatment with two different anti-cancer drugs @BDR

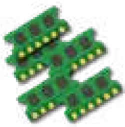
Immunology

Understanding how the immune system functions can help develop ways to fight off infection as well as combat hyperactive immune systems that are characteristic of autoimmune diseases. In 2017, scientists at IMS led by Sidonia Fagarasan have recently discovered that chronic activation of T cells, the immune system's enforcers, can deplete the body of essential amino acids, ultimately affecting mood and emotions through changes in brain activity.

Plasma B cells are another important type of cell in the immune system. Experiments conducted in 2018 by IMS researchers in collaboration with Osaka University revealed a mechanism through which B cells are transformed into plasma cells, allowing them to travel throughout the body and release antibodies in response to viruses. Understanding this process could allow scientists to create more potent vaccines for viral infections such as influenza.

BRAIN AND BODY

Learning and memory



Several laboratories at RIKEN are studying learning and memory using optogenetics. By inserting light-gated ion channels from algae or other species into specific neurons, scientists can excite or inhibit targeted neural circuitry with light.

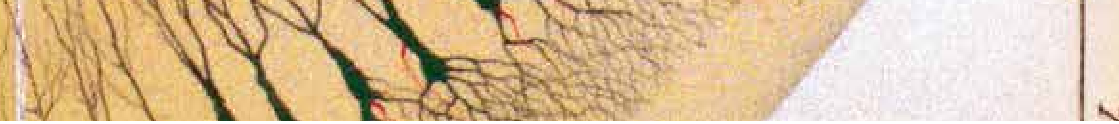
In 2015, scientists from the Center for Brain Science (CBS) and the Massachusetts Institute of Technology (MIT) used optogenetics to show that chronic stimulation of "happy" memories can reduce stress-induced depression in mice. In 2016, The CBS/MIT collaboration used optogenetics to retrieve "lost" memories in amnesiac mice and in mouse models of Alzheimer's disease. In another study, they identified a brain circuit devoted to memories of social encounters.

In 2017, the collaboration extended their research to long-term memory. They found long-term memory engram cells in the frontal cortex. Surprisingly, the cells were created at the same time as the initial memory, and then needed time to mature before activation would trigger the memories.

A recent 2018 study by Tom McHugh's lab at CBS found that memories of experience are not stored in hippocampal "place" cells as previously thought. These cells are critical for spacial memory, but the new study revealed the existence of "episodic" cells in the hippocampus that code for memories of experiences.

Other research at RIKEN focuses on different types of memory. One CBS laboratory has used optogenetics in mice to show that some forms of tactile memory require "top-down" feedback circuits from motor to sensory cortex. In another related study, the group showed that impaired memory consolidation resulting from sleep deprivation could be alleviated by stimulating a specific "top-down" circuit during non-REM sleep.

The Johansen lab at CBS uses optogenetics to study emotional learning. In 2016, they found a brain circuit that tempers emotional responses over time as context becomes predictable. In 2017 they found that flexible learning—being able to "unlearn" a learned behavior—involves two separate pathways, both originating in the same brain region and using the same neurotransmitter:



noradrenaline. In 2018, they found another set of paired neuronal circuits that facilitated/blocked fear extinction, this time both using the neurotransmitter dopamine. When danger is no longer associated with a situation, fear extinction is critical, and when prevented, the result can be phobias or post-traumatic stress. These neuronal circuits are therefore potential targets for drug therapies in these cases.

Cognitive and developmental disorders

Depression, Alzheimer's disease, autism spectrum disorders (ASD), and schizophrenia are just a few brain-related disorders that RIKEN scientists are tackling with animal models, genetic analysis, and electrophysiology.

In 2016, researchers at CBS used in vivo calcium imaging and transgenic mice to determine that the benefits of transcranial direct stimulation of the brain in treating depression are due to calcium surges from astrocytes. This

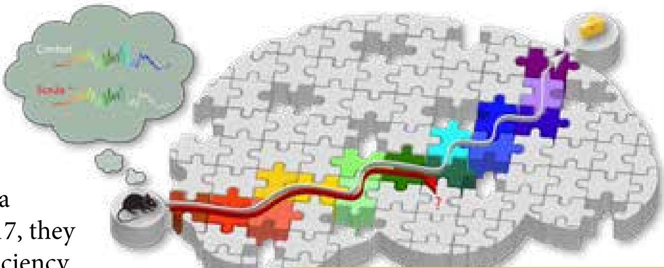
The mouse model for Alzheimer's disease with and without UTR gene deletion. The number of amyloid-beta plaques (green) was greatly reduced when the UTR gene was 70% deleted. @CBS

A 2018 CBS study links excessive serotonergic activity (right) to mitochondrial dysfunction (left) in a mouse model of bipolar disorder. Image: Milena Menezes Carvalho of RIKEN CBS.

discovery could place astrocytes as a major therapeutic target for depression and other neuropsychiatric diseases.

In 2018, CBS scientists discovered a link between serotonin, mitochondria, and bipolar disorder. In mouse models of bipolar disorder that have the ANT1 mutation, they found that mitochondrial dysfunction led to hyperexcitable serotonergic neurons in the dorsal raphe region of the brain.

In 2014, following 12 years of work, scientists at CBS developed an innovative model mouse that closely resembles the human form of Alzheimer's disease. Using these mice, a group of RIKEN researchers discovered a key protein called GnT-III whose elimination prevents the formation of amyloid-beta plaques, the hallmark of Alzheimer's disease. More recently, in 2018 the same lab has found a mutation that reduces amyloid-beta plaque formation (see image, p. 11).

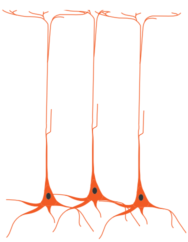


Disrupted memory replay in SCN2A+/- mice. The replayed sequences are incomplete (red line) and memory is only partially consolidated. @CBS

Another group at CBS has been studying ASD using a mouse model. In 2017, they linked serotonin deficiency to several ASD symptoms. By increasing serotonergic activity in the brain during development, they were able to improve the balance of brain activity and the mice socialized more normally.

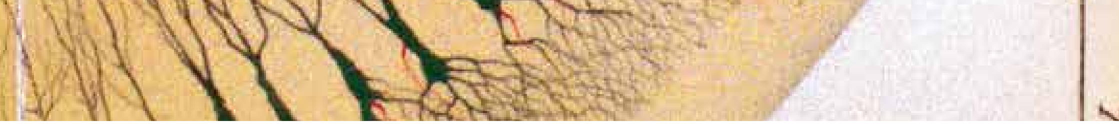
In 2018, McHugh's lab found that the mice with a deleted SCN2A gene have truncated memory replay in the hippocampus during sleep, which prevents full memory consolidation (see schematic at top). As this gene is associated with ASD and intellectual disability, the study provides insight into the mechanisms underlying these neurological disorders.

The most common cause of intellectual disability is Down syndrome. In 2018, McHugh's lab showed greater than normal inhibitory activity in the hippocampus of mouse models of the disease, supporting the hippocampus-inhibition theory of the syndrome.



CBS laboratories have also made recent discoveries related to schizophrenia. Using a mouse model of the disease, one study in 2018 found that prenatal lack of omega-3 and omega-6 fatty acids was linked to schizophrenic-like symptoms in offspring when they reached adulthood. The mechanism appears to be down-regulation of specific nuclear receptors, and drugs that increase activity at these receptors reduced schizophrenic-like symptoms in the mice.

In an earlier study, CBS researchers hypothesized that genetic factors in schizophrenia affect neuron function. They grew neurons from iPS cells that came from patients with schizophrenia, and which were lacking a region on chromosome 22. Their study connected one of the missing genes in that region to abnormal differentiation of neurons and an imbalance between the number of neurons and astrocytes in the schizophrenic brain.



Sleep and circadian rhythms

RIKEN researchers are also actively studying factors that affect sleep and circadian rhythms. In 2016, scientists at BDR led by Ueda found seven new genes in mice that regulate sleep duration. These genes could become targets for drugs that treat sleep disorders or certain psychiatric disorders that occur with sleep dysfunction.

These discoveries were possible thanks to a new technique for generating mouse lines with different mutations. Using this technique, in 2016 his team found a region on the Cry1 gene that regulates the duration of the circadian rhythm in mice. In 2017, they identified a molecular mechanism that keeps the circadian clock from being affected by changes in temperature even though it runs on enzymatic activity that normally speeds up or slows down when the temperature changes.

Most recently, in 2018 the group has discovered two genes (Chrm1 and Chrm3) that are essential for REM sleep (when we dream) and regulate its duration.

Also in 2018, researchers at CBS discovered a peripheral circadian clock in the choroid plexus that can affect the main clock in the suprachiasmatic nucleus. This clock can fine-tune the suprachiasmatic clock via the Bmal1 clock gene and might be important for proper sleep.

Growth and Development

Basic research into morphogenesis—the process through which organisms change their shapes during development—is critical for the budding field of organogenesis. Recent research at BDR has uncovered mechanisms involved in the fundamental morphogenetic processes of cell-cell adhesion and tissue folding, both of which involve microtubules.

Poor cell-cell adhesion can contribute to the invasiveness of cancer cells. In 2017, a BDR group discovered a process through which poor adhesion in colon carcinoma cells can be reversed through microtubule polymerizing inhibitors. Also in 2017, a group at BDR discovered that the protein Patronin plays a key role in reorganizing microtubule networks, allowing 2D epithelial sheets in Drosophila (fruit flies) to fold into 3D structures (see image below).

Late stage dorsal folding in a Drosophila embryo @BDR

Other BDR scientists have developed a method of statistical analysis that allows reconstruction of organ morphogenesis from as few as 10 cells. Using their new technique, the group mapped the early stages of brain development in chickens, finding that mature morphology was attained through positional rearrangement of existing cells rather than new cell growth (see image on the right).

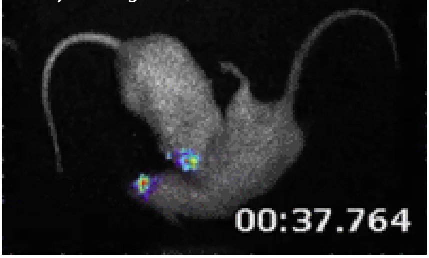
Morphological changes in the chick forebrain @BDR

New non-invasive brain science technology

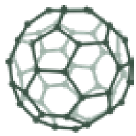
Discoveries are preceded by advances in technology and innovative new methodologies. In the last few years, RIKEN scientists have made several breakthroughs that could direct the course of research for years to come.

Optogenetics is a useful tool for studying brain circuitry, but until now is has only been useful in animals, has required implanted optical fibers, and has been limited to surface brain regions.

A still from a movie demonstrating bioluminescence in the brains of two freely moving rats @CBS.



In 2018, a CBS team led by McHugh succeeded in combining optogenetics and nanotechnology to overcome these issues. By injecting nanoparticles that convert near-infrared light to blue light into the brain, they were able to activate optogenetically tagged cells by applying near-infrared light from outside the head. This opens the door for the development of noninvasive optogenetic technologies.



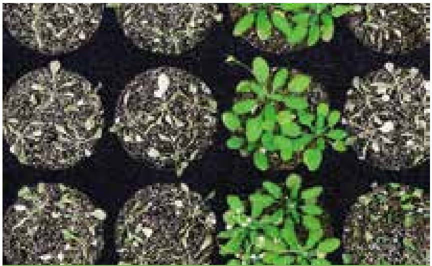
In 2018, the lab of Atsushi Miyawaki at CBS developed another type of non-invasive technology. By successfully mutating the enzyme luciferase, this team took bioluminescent molecules such as those found in fireflies and modified them to make bioluminescent signals that are a thousand times brighter. When these molecules were introduced into the brains of mice or marmosets, individual neurons could be monitored from outside the head, simply based on the strong luminescence signal (see image to the left).

AGRICULTURE AND THE ENVIRONMENT

Drought and high temperatures

Drought has always been a problem for farmers, but increasing populations and unpredictable climate change have made it a much bigger concern in recent years. While RIKEN researchers cannot change the weather, they are working on ways to mitigate the problem by developing ways to help plants survive periods without water.

In 2017, scientists at the Center for Sustainable Resource Science (CSRS) collaborated with the International Center for Tropical Agriculture in Colombia and the Japanese International Research Center for Agricultural Sciences to develop a transgenic rice plant that yielded more seeds and had more biomass than wild-type rice when grown in real drought field conditions in Colombia. The higher yield was related to their greater water content, greater use of light for photosynthesis, and greater amount of chlorophyll in the leaves (see image at bottom).



Treatment with acetic acid (vinegar) protects plants from drought @CSRS

Also in 2017, a CSRS group led by Motoaki Seki found a completely different way to assist plants during drought. The team studied mutant Arabidopsis plants that were strongly resistant to drought. They found that the resistance was related to greater production of acetic acid, the main ingredient of vinegar. Tests showed that treating wild-type Arabidopsis (see image at top), rice, wheat, and maize with acetic acid protected the plants from drought. In a recent follow-up study in 2018, the team was able to make a drought resistant

Field performance of unmodified Curinga rice (left) and a promising transgenic strain (right) that yielded more rice @CSRS transgenic plant that produces its own extra acetic acid only when water is scarce.

Other laboratories at CSRS are focused on understanding how plants regulate water retention. In 2018, a group led by Kazuo Shinozaki discovered a peptide phytohormone that detects drought in the soil and then travels to the leaves where it helps to close pores and keep water inside the plant. Another group studied a receptor that recognizes compounds found in smoke. Without it, plants leak water through the damaged protective layer covering the leaf surface, and through larger-than-normal pores. These findings provide targets for further research aimed at improving water retention during drought.

Similar to drought, extreme temperatures also threaten plants and our ability to produce agricultural crops. A 2018 study by Kazuki Saito at CSRS identified a previously unknown gene that is activated by extreme heat. Without the HIL1 gene, excessive heat destabilizes chloroplast membranes, which proves fatal over time. This gene could be a target for boosting protective responses in response to global warming.

Salt stress and poor soil

Plants also have ways to protect themselves from other types of

environmental stress, and RIKEN scientists are studying them in the hope to develop more resilient crops. One of the most common issues facing crops is salt stress. When soil is too salty, it dehydrates plants by drawing their water out and also poisons them with excess sodium.

In 2017, Seki's group found that ethanol can increase tolerance to salt stress in Arabidopsis and in rice by reducing toxic elements called reactive oxygen species—the same types of harmful molecules we try to eliminate when we eat foods that contain antioxidants. Like the drought protection afforded by acetic acid, this could be a simpler, safer, and more universal approach to salt-stress protection than making many different genetically modified plants.

In 2018, the group also found a gene for a plant peptide that naturally protects plants from salt stress, probably by

combating the accumulation of excess sodium. The team was able to make synthetic pieces of the peptide that could confer the same protection, indicating the potential for treating different plant species with supplements made from synthetic peptide fragments (see image).

Plant treated with peptide fragment (bottom) is more tolerant to salt stress than control @CSRS

Pollution and Phytoremediation

Contaminated water is a global concern affecting developed and developing countries alike. Not only is it dangerous if left untreated, decontaminating polluted water typically requires fossil fuels and a tremendous amount of energy. As an alternative to these typical processes, phytoremediation is a method that uses photosynthesizing organisms to clean up soil or water contamination.

15 LIFE ON LAND

In 2017, a CSRS group showed that the moss *Funaria hygrometrica* can tolerate and absorb a high amount of lead from water. Analysis revealed that this is possible because the moss's cell walls contain polygalacturonic acid, a compound also found in some fruits when they become ripe.

14 LIFE BELOW WATER

Cell-wall extracts could also absorb lead, and the researchers are currently evaluating the safety of using this moss and working with industry to develop effective ways to practically apply these findings to real-world situation such as acid mine wastewater.

CSRS has also been researching ways to remediate soil that has been contaminated by nuclear accidents, similar to what happened after the 2011 earthquake/tsunami in Japan. In 2017, a CSRS lab identified methyl cysteinate as a cesium accumulator in *Arabidopsis* that binds to cesium on the roots or inside plant cells. A valuable metal, cesium can be dangerous when radioactive and identifying cesium accumulators will help design ways to use plants to extract it from soil.

This discovery follows another from the same lab in 2015, which identified a compound that actually blocks cesium uptake by binding to it in the soil. This is ideal for preventing radioactive cesium in the soil from entering the food chain.

INTERVIEW WITH EXECUTIVE DIRECTOR MOTOKO KOTANI

What does RIKEN look for in a scientist?

What kind of researcher are we looking for at RIKEN, and why?

Kotani: Researchers at RIKEN are ambitious and eager to pioneer new areas of research. But they are also people who understand that the research they conduct should, in some sense, contribute to society. This can be in the form of creating new value for society through innovation, or by making scientific discoveries that allow humanity to advance go beyond what is currently known.

Recognizing the importance of our research, in 2017 RIKEN was given the prestigious status of Designated National Research and Development Institute. To fulfill the new missions that we have been charged with by the government under this status, we provide scientists with a rich research environment and opportunities to interact with other scientists across disciplinary boundaries. We are very much aware of the special responsibility that we have been given along with the new status.

Why is diversity in researchers important?

Kotani: More diversity provides a wider range of perspectives and is therefore a source of dynamism. New ideas are born from daily intersections, leading to unexpected connections or discoveries. Science is always a frontier, so it is no longer science when the dynamism fails.

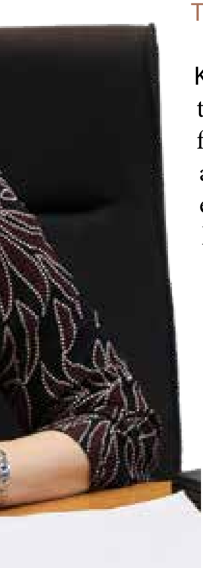
Specifically, why is it important to have an international workforce?

Kotani: In the modern world, great research is almost by its very nature international. At RIKEN, we are always looking for the most outstanding and driven researchers, and that means looking for the best people from around the world. For us, this is important, and we provide an attractive environment to encourage people to come to RIKEN and conduct their research with us. And of course, a positive side-effect of having an international workforce is that when researchers move on to other institutes, they bring their networks and fondness for RIKEN with them, and this stimulates collaborative work between RIKEN and other institutes overseas.

We are looking for people who are philosophers as well as scientists. Why is this important?

Kotani: Since the premise of science is that it creates social value, it is clear that scientists must consider the significance of their research. I believe it is important that they have their own philosophies that allow them to link the research they do to the scientific and historical contexts within which they work.

What else should scientists consider when designing their research projects?



Kotani: Sustainable development is a critical issue for all of humanity, and the Sustainable Development Goals set by the United Nations are a useful framework. The problems we confront are complex and global in nature, and they cannot be solved by researchers from any specific discipline. Rather, they must be tackled by all-out efforts incorporating interdisciplinary knowledge. While this requires some top-down direction, we are certainly looking for researchers who are conscious of these goals and the importance of using science, technology, and innovation to reach them.

Scan QR code to see and hear what it's like to work at RIKEN

Come to RIKEN

PROGRAMS FOR SCIENTISTS

Special postdoctoral researchers program

In the Special Postdoctoral Researchers (SPDR) program, young and creative scientists are given the opportunity to be involved in autonomous and independent research under the direction of their host laboratory's primary investigator. The program helps promising young scientists to establish global careers with three years of funding. A generous remuneration package is supplemented with an annual research budget of 1 million yen (about US $8,000) allocated to the host laboratory.

Bo Thomsen, SPDR Fellow

This program is open to researchers in mathematical sciences, physics, chemistry, biology, medical science or engineering who have a doctoral degree and fewer than five years of postdoctoral experience. This is one of RIKEN's initiatives aimed at opening our facilities and resources to the world and creating a stimulating research environment that places our organization at the forefront of global science and technology.

"The SPDR program allows for me a great degree of freedom to conduct my research in computational modeling of proton transfer in membrane proteins," says Bo Thomsen, from Denmark, who is doing his postdoctoral research in the Theoretical Molecular Science Laboratory. "The environment at RIKEN promotes interactions between researchers both within and outside your field of research through internal symposia, workshops, and social gatherings. Furthermore, the generous funding allows for maintaining and developing a strong national and international network. RIKEN's SPDR program provides me with an ideal stepping stone on the way toward senior research positions."

Qualified candidates of all nationalities are welcome to apply.

International Program Associates Program

Shruti Bhagat, IPA Fellow

RIKEN offers non-Japanese PhD candidates at participating universities the chance to undertake their doctoral studies in Japan under the supervision of a senior RIKEN scientist. Each year RIKEN accepts about 100 students as International Program Associates (IPAs). Students enrolled, or about to enroll, in a PhD at one of the many Japanese and overseas universities participating in RIKEN's Joint Graduate School program are eligible to apply.

As of March 2018, we had IPAs from 45 universities in Asia and Europe studying at RIKEN. They included students from Peking University in China, Seoul National University in South Korea, USM in Malaysia, Liverpool University in the United Kingdom, and ETH Zurich in Switzerland.

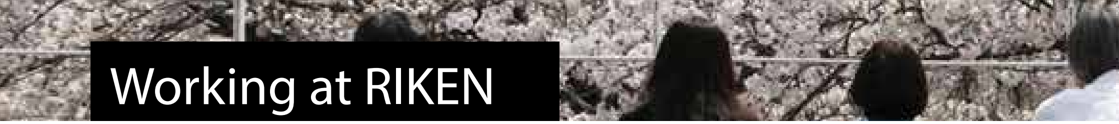
Associates receive living expenses, a housing allowance and round-trip airfare, as well as the benefit of international collaboration in their research and the chance to experience a new culture.

"RIKEN is possibly the best place in the world to study the regulation of transcription and its impact on disease," says Shruti Bhagat from India, "and as a member of the IPA program, I have been able to learn something new every day."

"RIKEN provides a unique research experience which encourages international and local collaborations, along with ample opportunities to learn from world experts through continuous seminars and workshops. These aspects combined create a multidisciplinary environment which is crucial for the development of young researchers."

Hakubi Fellows Program

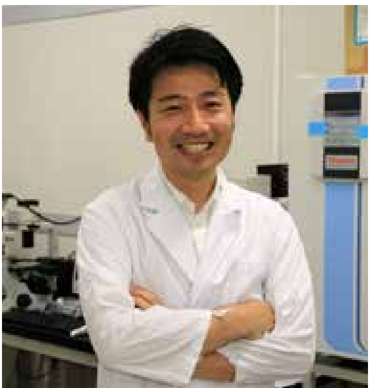
The RIKEN Hakubi Fellows Program offers junior laboratory leader positions for research by exceptional individuals. Fellows are given the opportunity to independently engage in creative and ambitious research in natural and mathematical sciences,



including research areas bordering the humanities and social sciences, and are provided with a generous salary and research support. Laboratories established under the program can operate for up to seven years.

An important goal of the RIKEN Hakubi Fellows Program is to foster stimulating interactions among outstanding researchers with diverse backgrounds and to create an intellectual hub of scientists with different disciplines within and beyond RIKEN. The word hakubi, which literally means "white brow," comes from the nickname of Ma Liang, an exceptional official featured in the *Three Kingdoms*, who was said to have white strands of hair in his eyebrows.

Hirofumi Shintaku, whose lab was established in April 2018, is studying new techniques for genetic sequencing within cells. He says, "My research began from the study of fluid dynamics and transport phenomena in very small confined spaces like those within cells. In my previous work I developed a microfluidic system that enables high-throughput sequencing of cytoplasmic and nuclear RNA of single cells, and I am grateful for being accepted into the Hakubi program as it will allow me to use this system to look at the regulation of gene expression involving RNA localization and transport in single cells."



Hirofumi Shintaku, Hakubi Fellow

In addition to our state-of-the-art research facilities and open research environment, we aim to provide a comfortable and congenial environment for researchers and their families from around the world. A wide range of programs, services, and welfare benefits are available to all RIKEN employees, regardless of gender or nationality.

SCHOOLS/VISITING SCHOLARS

Summer Programs

The CBS Summer Program is an opportunity for undergraduate and graduate students, as well as postdoctoral researchers, to study brain science in Japan in either a two-month laboratory internship at a CBS laboratory, or an intensive one-week lecture course given by distinguished international scientists.

The RIKEN IMS International Summer Program (RISP) aims to provide PhD students and young postdoctoral

CBS Summer School participants

researchers from around the world with the opportunity to learn about cutting-edge research in immunology and genomic medicine. It takes place over one week at the IMS facility in Yokohama and includes presentations from internationally distinguished scientists and each participant.

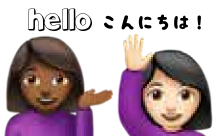
Other schools

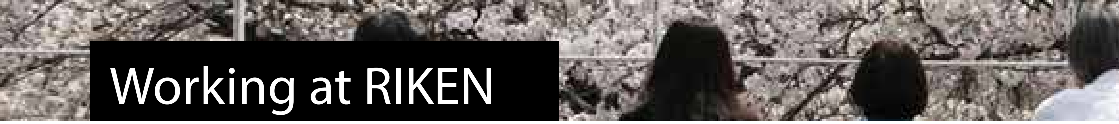
The Nishina School offers select students from Peking University, Seoul National University, The University of Hong Kong, and several Japanese universities, the opportunity to acquire hands-on experience in theoretical and experimental nuclear physics in a two-week summer school at the Nishina Center for Accelerator-Based Science (RNC).

WORKING ENVIRONMENT

English is OK!

Many of RIKEN's laboratories are completely bilingual with Japanese and non-Japanese scientists and technical staff working side by side to achieve common goals, and most scientific seminars are given in English. RIKEN also offers a bilingual administrative environment that provides needed information in a timely fashion in both Japanese and English. RIKEN also provides introductory Japanese lessons for those who don't speak any Japanese. Rest assured, you will be able to succeed in your research and enjoy life in Japan even if you don't speak the language when you arrive.





In addition, all full-time RIKEN employees are members of the RIKEN Employee Mutual Aid Society which sponsors a wide range of employee club activities and events, both cultural and sports-related.

Help staff and housing

Friendly bilingual staff are on-hand at the major RIKEN campuses to provide information and support to help researchers deal with healthcare, housing, childcare and schooling, and the practical issues of daily life.

The main Wako campus has both single and family apartments while other RIKEN campuses have a range of accommodation available, either on or off campus. For long-term stays, we can provide introductions to local real estate agencies and, when necessary, assist with procedures.

Family care and support

To help researchers focus on their work without having to worry about bringing their children off-campus, daycare programs are available for infants, toddlers and preschool aged children at the Wako, Yokohama and Kobe campuses. RIKEN offers special leave, in addition to its regular paid leave, for caring for sick children or other family members.

RIKEN is a strong advocate of gender equality and has Personal Support Coordinators who provide individualized guidance on RIKEN's support programs and services related to pregnancy, childbirth, childcare, and the care of sick or elderly family members.

WORKFORCE AND DIVERSITY

20%
INTERNATIONAL
(21% of new hires in 2017)

1900+
SCIENTISTS

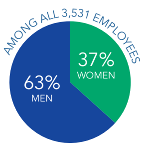
Includes all scientists directly employed by RIKEN

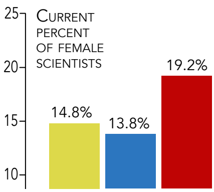
International Diversity

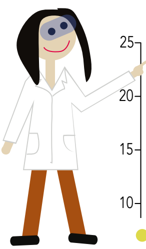
RIKEN employed 3,531individuals in 2017, a figure that has remained relatively constant over recent years. Among the nearly 2,000 scientists employed by RIKEN, roughly 20% come from outside Japan.

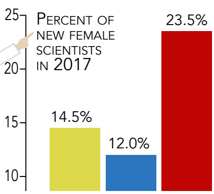
Gender Diversity

RIKEN is also making strong efforts to increase the number of women in research and management positions. In Japan, women are generally underrepresented in the world of science and technology, but RIKEN has shown leadership in this area by implementing a variety of programs to encourage the recruitment and retention of female scientists and staff.





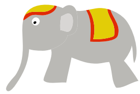




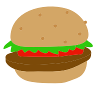
780+
INTERNATIONAL FACULTY AND STAFF

40%
EAST ASIA

27%
EUROPE

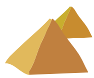


11%
SOUTHEAST ASIA



9%
THE AMERICAS

8%
SOUTH ASIA



3%
MIDDLE EAST + AFRICA

2%
OCEANIA

Includes scientists, visiting scholars, students, technicians, and administrative staff

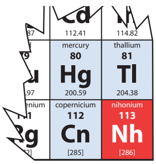
All data as of Oct. 2017

Physical Science & Engineering

RIKEN was originally known in English as the Institute for Physical and Chemical Research, and reflecting this, the institute has a long tradition of excellence in fundamental physics and chemistry. In 2015, that work was rewarded when the International Union of Pure and Applied Chemistry announced that a RIKEN-led team had officially discovered nihonium, with chemical symbol Nh—the first chemical element to be discovered in Asia. This work goes back to the seminal research conducted by RIKEN including the construction of the first cyclotron built outside of the United States.

NUCLEAR PHYSICS

THE DISCOVERY OF NIHONIUM



In 2004, a group headed by Kosuke Morita of the RNC used the center's linear accelerator to successfully bombard zinc ions into a bismuth layer, creating a new element with atomic number 113. Two more atoms were created, in 2005 and 2012, and the group was granted discovery rights and the right to propose the name for the new element. Today, the group has upgraded its detector and is fast on the trail of element 119, the next undiscovered element on the periodic table. In 2017 they succeeding in producing and accelerating a vanadium beam, which will be crucial to the effort, and the new GARIS-II detector—a key element of the experiments—has been completed.

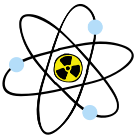
EXOTIC NUCLEI

In addition to their work on new elements, scientists from RNC are working with partners around the world to study exotic atomic nuclei, contributing to a better understanding of how the universe began and how it is composed at the nuclear level. In 2017, physicists announced that they had used the RI Beam Factory to create 73 new exotic nuclei, adding new species to the 7,000 that are hypothesized to be able to exist. Scientists at RNC continue to search for the "island of stability"—a realm where we can find longer-lived nuclei than

(left) The Supremes Star on the Hollywood Walk of Fame. (right) Zinc plaque on the Nihonium "walk of fame" that runs from the Wako city train station to RIKEN (see the final nihonium plaque on page 1).

those in the area currently explored, and are also looking at the feasibility of using the center's heavy ion beam to transmute troublesome nuclear waste into more easily managed isotopes.

Antimatter



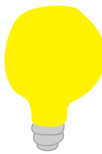
One of the key questions in physics today is why there is so little antimatter in our universe. In 2010, members of an international collaboration including RIKEN managed to trap antihydrogen atoms for 1,000 seconds, and now they are able to store it almost indefinitely, raising the hope of being able to do advanced research on antimatter. In 2017, an international collaboration led by Stefan Ulmer of the Cluster for Pioneering Research (CPR) used sophisticated equipment at CERN's Antiproton Decelerator in Europe to measure the magnetic moment of the antiproton, improving upon the precision of the previous best measurement

Penning trap that captures antiprotons @ CPR

by a factor of more than 3,000 (see image at bottom). In 2015 the same collaboration took the world's most precise measurement of the difference between the charge-to-mass ratios of the proton and antiproton, finding them to be the same to within 69 parts per trillion.

LIGHT, MAGNETISM, AND SPACE

Photonics



In photonics—the study of light—RIKEN scientists are working to see things that were previously invisible. One avenue of research is to develop lasers and other light devices with ever more powerful and rapid pulses, with the aim to develop attosecond lasers that will be able to look at the positions of individual electrons within materials. In 2018, RIKEN researches generated short, high-peak-intensity laser pulses with a wavelength of 3.3 micrometers, bringing science closer to the possibility of seeing the dance of individual electrons.

In 2014, scientists from the SPring-8 Center (RSC) in Harima used the powerful x-rays of the SACLA free-electron x-ray laser to determine the structure of a key part of the photosynthesis mechanism, and in 2017 a group performed experiments, in collaboration with partners from around the world, demonstrating a phenomenon called "superradiance,"—which involves the collective excitation of atomic nuclei—that had been predicted by Robert H. Dicke in 1954.

Young visitors at the Nishina Center learning about the elements on RIKEN Open Day @RNC

Scientists at the Center for Advanced Photonics (RAP) are also working to develop lasers that operate in the terahertz range—a long neglected portion of the electromagnetic spectrum that will allow explosives and illicit drugs to be imaged within luggage, making security checks more rigorous. In 2018, RIKEN scientists developed nonlinear optical materials that can convert terahertz light to higher frequency infrared light, which can be detected more efficiently.

Spintronics

Scientists led by Yoshinori Tokura at the Center for Emergent Matter Science (CEMS) have been instrumental in paving the way toward devices that use a property of electrons known as "spin" rather than charge, allowing for much more efficient electronic devices that would not produce heat in the way that electricity does. In 2015, researchers in Tokura's group demonstrated the existence of stable skyrmions—tiny magnetic vortexes in materials that could be manipulated to create low-power memory devices—at room temperature, and in 2017, RIKEN scientists found that magnetic domains on the surface of a special material called a "topological conductor"—which conducts electricity on the surface but not in the bulk of the material—can be manipulated using a magnetic tip. Both of these discoveries should help pave the way to spintronic devices based on magnetic rather than electrical manipulation.

Looking to the Stars

RIKEN is also active in the area of astrophysics. In 2017, researchers from RIKEN and the Max Planck Institute for Astrophysics used computer models to show, through an analysis of radioactive elements, that the supernova of Cassiopeia A, a roughly 340-year-old gas remnant of a nearby explosion, may have been initiated and powered by neutrinos escaping from the neutron star left behind at the origin of the explosion.

Also in 2017, using data from the recent neutron star merger, a RIKEN research and colleagues were able to put a hard lower limit on the radius of super-dense neutron stars, finding that they must be at least 10.7 kilometers in radius.

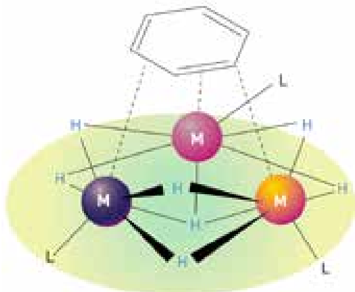
CHEMISTRY

Greener fuel

CSRS scientists led by Zhaomin Hou made the news in 2014 for "breaking benzene"—unlinking the difficult-to-break carbon-carbon bonds in aromatic compounds found in petroleum and biomass, a process that is important for the production of fuels and other valuable chemicals from natural resources.

In the chemical industry, the cleavage of these bonds requires the use of high-temperature solid catalysts, usually giving rise to a mixture of products, and the mechanisms are still poorly understood. CSRS scientists used a metallic complex called trinuclear titanium hydride to accomplish the task at relatively mild temperatures and in a highly selective way (see image to the right).

In 2017, they showed that they could use this method to create a low-energy chemical procedure with the potential to strip nitrogen-containing impurities from crude oil and help to make the petroleum industry more environmentally friendly. In addition, taking a cue from denitrifying microbes, CSRS scientists announced in 2018 that they had developed a catalyst that can create harmless nitrogen gas from nitrites—a common pollutant from fertilizers.



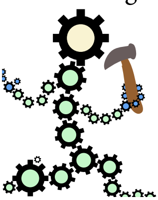
A hexagonal benzene molecule bound to a multinuclear hydride @CSRS

ENGINEERING

Revolutionary photovoltaic cells and materials

Scientists at CEMS have been on the leading edge of organic solar cells, which could have new applications different from silicon-based materials. In 2015, researchers developed a polymer with a particular molecular orientation, providing an energy efficiency of 9%, approaching the 15% that is usually considered the threshold at which these new cells will become competitive. Using that film, but replacing the glass substrate with a flexible material, in 2017 another group from CEMS created an ultra-thin, super-durable flexible solar cell that can be attached to a fabric and washed without losing its ability to generate electricity. They hope to use this to create clothes that can monitor the health of the person wearing them (see image to the right).

RIKEN scientists are also actively working with hydrogels—a type of polymer that is made up mostly of water but which, due to its chemical structure, adopts interesting properties. In 2015, a group at CEMS created a hydrogel that lengthens and contracts, like a muscle, in response to rises and falls in temperature. They were able to shape the gel in such a way that, when placed in a water tank, it could actually wade through the water. They also created a tiny film that responds to minute changes in humidity, actually leaping into the air in response to the presence of small amounts of water in the air, and developed a material that, despite being quite strong, can also "repair" itself by recreating bonds when reassembled after breakage.



Wearable, washable solar cells @ CEMS

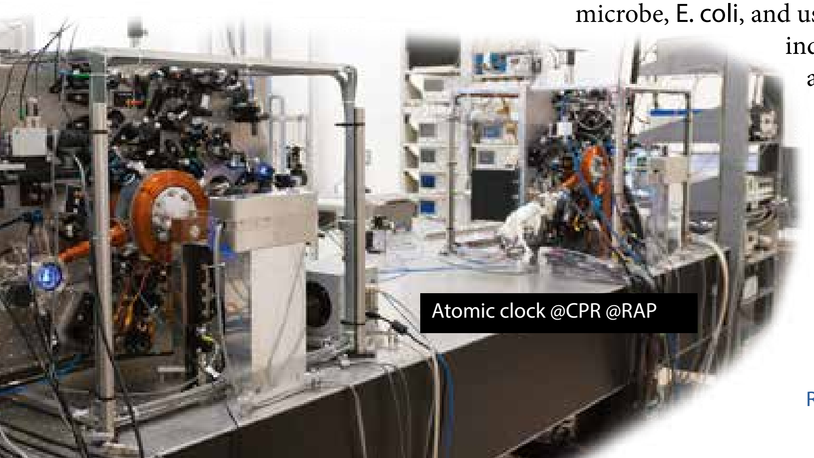
In 2017, a team from CEMS has also made a thin stretchable polymer that can be applied on human skin for long periods without triggering irritation, thanks to a structure that allows air to pass through it. They succeeded in monitoring muscle activity with a device on this material, pointing to the possibility of using this for medical monitoring of patients.

In research published in 2017 in another area—colors—scientists from CPR and RAP have taken clues from nature—butterflies—and peacocks—to

make materials whose color can be fine-tuned so that the shape of the material, rather than a pigment, can be used to create a range of colors.

An atomic clock

A team led by Hidetoshi Katori from CPR and RAP, and who also has a lab at the University of Tokyo, has built a pair of optical lattice clocks that can keep time with incredible precision (see image below). While a typical quartz watch can vary by about 15 seconds every month, these clocks will only go out of sync by a second in around 16 billion years—more than the universe has existed so far. Using it, scientists plan to open the era of "relativistic geodesy," where the shape of the earth can be precisely measured by clocks going faster or slower following Einstein's theory of relativity. Using a dedicated optic fiber, in 2016 they successfully measured the altitude difference between two clocks set at the RIKEN Wako campus and the University of Tokyo—15 kilometers apart—with a precision of just 5 centimeters.



Atomic clock @CPR @RAP

Robots

Robot @ CBS

As part of a project that uses our understanding of the human brain to create new technologies that contribute to vehicle operation and rehabilitation for stroke victims, scientists from CBS have developed a robot that learns to walk using a programmed desire to keep its motion sensors from moving abruptly. Unlike other walking robots, it walks at a very high efficiency, with a gait that approaches that of people (see image above).

Bioengineering

Engineering is more than just machines, however, as scientists are working actively on biological systems as well. In 2017, researchers from CSRS genetically reprogrammed a common microbe, E. coli, and used it to produce industrially important maleic acid from feedstock rather than from crude oil, which is the typical method used in industry.

Physical Sciences & Engineering

Looking at the very small

The SACLA x-ray free electron laser in Harima allows us to look at the world on the smallest scale. Despite being just 700 meters in length it produces laser beams with a wavelength under 1 angstrom, the shortest in the world. These pulses are being used to see how bonds between atoms are formed to create molecules, and thus helping to answer fundamental questions about how matter is put together. Using the instrument, scientists have shown how photons initiate a cascade that pushes protons out of a cell, creating an electric charge difference that is subsequently used to power the cell's activities.

A range of techniques are being developed by RIKEN scientists. For example, in 2018, researchers from RSC, which operates SACLA, created a new technique called hard x-ray spectro-ptychography, which allows them to observe the oxidation process at the nanoscale, achieving a level of detail never realized before. They used the technique to analyze car exhaust.

Even smaller-scale facilities can contribute to research breakthroughs. In 2018, using a tabletop light source, scientists from RAP led by Katsumi Midorikawa achieved a peak power of 2.6 gigawatts, emitting attosecond pulses that will be able to look at rapid processes such as the forming and breaking of molecular bonds.

Tiny worlds

RIKEN scientists have achieved other technical challenges. In 2015, researchers made the smallest nanocrystal in the world—a crystal made up of just 19 atoms, in a discovery that could help the creation of biopharmaceuticals and biosensors. In another achievement that could help life science research, scientists built a flexible microfluid chip made of glass that weighed just 3.6 milligrams.

Looking at single cells

One of the hot topics in biology today is the analysis of single cells. At RIKEN, a number of groups are working on this. A group working on big data analysis has come up with new methods for looking at RNA expression in individual cells, allowing us to understand how genes are expressed not just in the individual as a whole but by different cells in different situations and different points of time. Scientists from BDR have also created a system that allows the molecules found in a single living cell of even organelles of the cell to be extracted and analyzed, allowing for an understanding of how molecules move throughout cells.

Computer Science & Mathematics

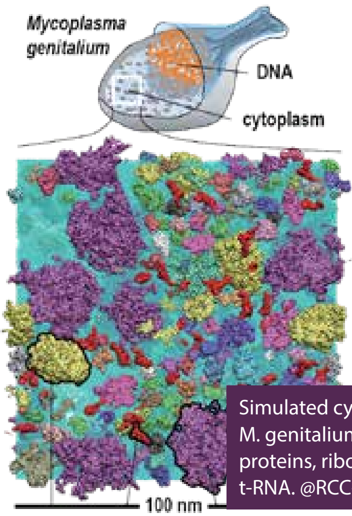
RIKEN has been at the forefront of supercomputing for decades. More recently, we have opened two new strategic research centers, and scientists have begun to explore theoretical mathematical approaches and their application in scientific fields such as parallel computing and artificial intelligence. Together with a strength in modeling complex systems, RIKEN is already making breakthroughs in these new endeavors.

SUPERCOMPUTERS AND AI

Next-generation supercomputing

The K computer, which was operated by the RIKEN Center for Computational Science (R-CCS) until 2019, performed some of the world's most complex simulations. In June 2018, RIKEN and Fujitsu began testing the advanced chips for the next supercomputer—dubbed Fugaku, and completed the design in April 2019. The new supercomputer will be put to good use in areas such as drug development, material analysis, and fundamental physics, as well as in new areas such as artificial intelligence and big data analysis.

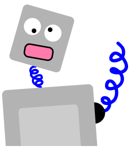
Scientists from the R-CCS used the K computer to perform simulations in a wide range of important fields. For example, computer simulations were used as part of a system that predicts torrential rain in an area of western Japan. Further, in 2018, a group led by Hirofumi Tomita used a climate model of how aerosols—dust and other small particles—interact inside clouds to show why, contrary to previous belief, increasing the amount of aerosols in the air does not always lead to increased precipitation.



Simulated cytoplasm of M. genitalium containing proteins, ribosomes, and t-RNA. @RCC-S @BDR

Simulation-based research is being used in other areas of our lives. In 2016, a group led by Yuji Sugita showed that the behaviors of proteins and other molecules in the cytoplasm of Mycoplasma genitalium are more complex than what was previously believed. The dynamics and stability of these macromolecules are determined not only by specific interactions but also by non-specific interactions, which were not previously regarded as important (see image on previous page).

Artificial intelligence

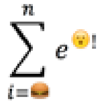


With the establishment of the Center for Advanced Intelligence Project (AIP) in 2016, RIKEN expanded into the world of artificial intelligence research, another area that involves the development of new mathematical tools. The AIP was established as part of the government's plan to strengthen Japan's research in this crucial area. The center is focusing on areas such as "deep learning," in which machines go beyond performing simple operations and begin to recognize patterns, particularly when they only have limited information. Deep learning can also be applied to finding solutions to critical social problems such as infrastructure maintenance.

In 2018, AIP scientists with colleagues from the University of Tokyo used artificial intelligence to develop a new method for sorting cells—a normally painstaking process. This finding could help make diagnosing cancer easier. The method, which does not use images, is called "ghost cytometry." Researchers from AIP have also used artificial intelligence to search for molecules with specific attributes, by generating molecular models and using complex calculations to predict their physical properties.

MATHEMATICS AND THEORY

Exploring new mathematical approaches



Scientists at the Interdisciplinary Theoretical and Mathematical Sciences Program (iTHEMS), are exploring the role of mathematics in science and going beyond disciplinary boundaries. Currently, most mathematics used in theoretical science were created more than 100 years ago. Scientists at iTHEMS are exploring newer abstract frameworks to see if they can be used to solve problems in natural science or yield as yet unknown mathematical connections among phenomena in physics, biology, and other areas.

In 2017, a group of biologists and mathematicians from iTHEMS and other RIKEN centers used computer simulations to show how random movements allow the color-sensing cells in the eyes of a fish to come to the proper arrangement. In 2018, scientists from iTHEMS and RNC used the powerful K computer to predict the existence of a new exotic particle, called the "di-Omega particle," which is composed of six quarks, rather than three.

NATIONAL SHARED-USE LARGE-SCALE FACILITIES

SUPERCOMPUTING

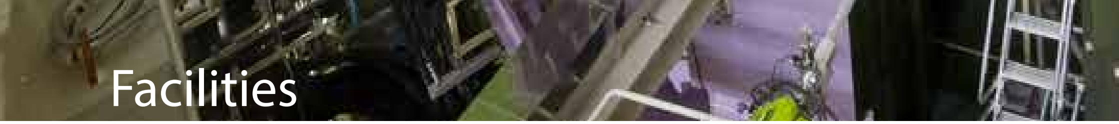
The RIKEN Center for Computational Science (R-CCS) in Kobe is Japan's leading supercomputing center. The K computer, which operated from 2011 to 2019, became the first supercomputer in the world to achieve a LINPACK performance rating of 10 petaflops. It held on to the top spot in the Graph500 ranking—which gauges the ability of computers to perform data-intensive operations—for seven consecutive periods. During the seven years when it was open for use by outside users, it was used as a platform not only for basic research but also for commercial applications. RIKEN is currently engaged in the development of a new more powerful supercomputer, named Fugaku, which

Supercomputer Fugaku
(富岳) @ R-CCS

is slated to go into operation in a few years. The supercomputer Fugaku will be used to help resolve social challenges in areas such as health and longevity, disaster prevention, weather forecasting, energy conservation, clean energy, material design, and manufacturing processes. It will also be used in AI and data science research.

SPRING-8 AND SACLA

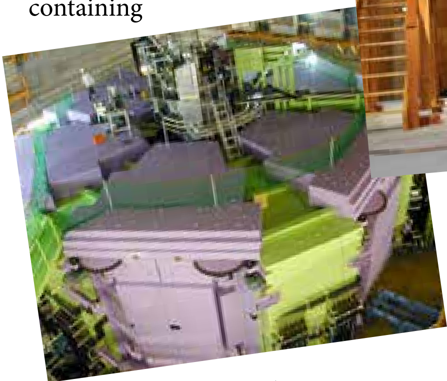
The RIKEN SPring-8 Center in Harima is responsible for managing two large-scale facilities: SPring-8 and SACLA. SPring-8 is a synchrotron radiation facility and SACLA is an x-ray free electron laser facility. SPring-8 celebrated its twentieth anniversary of user operation in 2017. These two powerful tools help researchers in both academia and industry to conduct advanced research in materials science, spectroscopic analysis, earth and planetary science, life science, environmental science, and industrial applications. SACLA produces laser beams of light with very short wavelengths that are a billion times brighter and have a pulse width a thousand times shorter than the light available from SPring-8. This make it an ideal instrument for observing ultrafast phenomena and small molecular structures.



OTHER FACILITIES

Radioactive Isotope Beam Factory

The Radioactive Isotope Beam Factory (RIBF) at RNC in Wako is RIKEN's next-generation heavy-ion research facility. It provides researchers with the most intense ion beams in the world. At its heart lies a superconducting ring cyclotron—the world's largest—measuring 18 meters in diameter and weighing 8,300 tons, nearly as much as the Eiffel Tower. Recent upgrades to the facility allow for the generation of intense beams containing about 4,000 unstable nuclei, which range from hydrogen to uranium, making it possible to probe beyond the limits of the known nuclei. The facility is also used for heavy-ion breeding, allowing the efficient creation of new plant varieties.



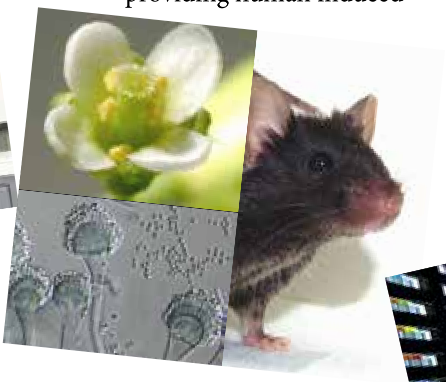
Life Science Technology Platform

RIKEN has a rich set of advanced facilities used for research in medicine and other areas of life sciences. The NMR facility in Yokohama—one of the world's largest—operates 13 nuclear magnetic resonance spectrometers, which are used for three-dimensional structural analysis of proteins and other molecules. In addition to medicine, these tools are being used to promote technological innovation. The Genome Network Analysis Service, also in Yokohama, offers gene expression analysis and genomic sequencing using high-throughput next-generation sequencers. Further, the molecular imaging facility in Kobe, equipped with microPET scanners and cyclotrons for producing PET-scanner tracers, as well

as MRI and CT facilities, provides a human resource development program for analyzing the dynamics of various molecules in the body.

BioResource Research Center

The BioResource Research Center (BRC) in Tsukuba, established in 2001, has quickly developed into one of the world's most important repositories and distribution centers of biological resources for life science research. The center's reputation derives from its capacity to handle a wide range of living strains of experimental animals and plants, cell lines of human and animal origins, genetic materials, microorganisms and the associated bioinformatics. The center is particularly notable for providing human induced



pluripotent stem (iPS) cells to researchers. Visit their website to find if there are resources that will be valuable in your research.

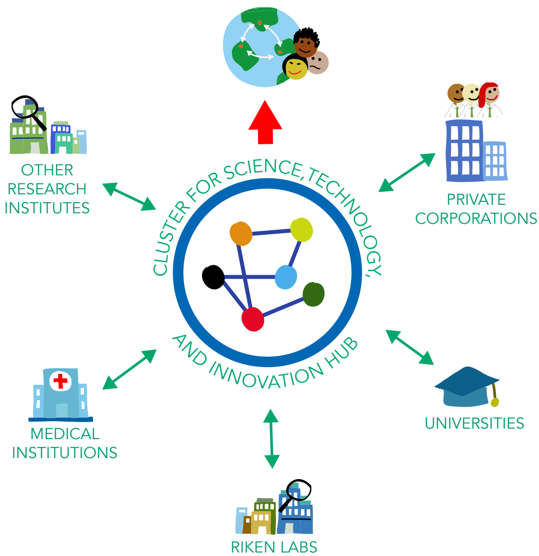
Head Office for Information Systems and Cybersecurity

The mission of this office is to provide IT support to the entire institute, and it is currently working on a strategy to develop IT systems that will encourage the maximization of research results by leveraging information systems to allow researchers to concentrate on what is most important—their research. In addition, it works closely with RIKEN researchers on research and development in informatics—incorporating information science, information processing, information systems, and computer science—and data science, which are essential for collaborations spanning all of RIKEN, as well as those between RIKEN centers and research groups, including interdisciplinary undertakings. The Office manages a number of supercomputers that are used by researchers both inside and outside RIKEN.

CLUSTER FOR STI HUB

Innovation at RIKEN

It is very much in RIKEN's blood to bring the products of its basic research into applications that can benefit society. This was well articulated by the third president of RIKEN, Masatoshi Okochi, who insisted that the fruits of research be returned to society, and went as far as to create a group of companies—known as the RIKEN Konzern—that were dedicated to commercializing the inventions made in RIKEN's laboratories. At its peak, the Konzern had 63 companies under its umbrella.



The Cluster for Science, Technology, and Innovation Hub is a group of programs through which RIKEN collaborates with other institutes, universities, local governments, and industries around the world to facilitate tech transfer and bring innovations to society.

Today, RIKEN has a dedicated organization—the Cluster for Science, Technology, and Innovation (STI) Hub—which focuses on creating collaborations with universities and private companies and on translating research breakthroughs into innovation. A number of programs within the Cluster look at specific areas of science—drug discovery, preventive medicine and diagnosis, healthy living, and artificial intelligence and big data—and the labs work to translate discoveries at RIKEN into real-world technologies.

Starting in April 2018 a new experiment has been launched to further stimulate innovation. Work is now being carried out to lay the foundation for the establishment of a private sector company that will be tasked with managing RIKEN's intellectual property and finding appropriate partners to commercialize research findings.

Running together

The innovative "Baton Zone" is one of the key programs in which scientists and industry work together.

Programs in the Cluster for STI Hub

- PREVENTIVE MEDICINE AND DIAGNOSIS INNOVATION PROGRAM
- MEDICAL SCIENCE INNOVATION HUB PROGRAM
- DRUG DISCOVERY AND MEDICAL TECHNOLOGY PLATFORM PROGRAM
- COMPASS TO HEALTHY LIFE RESEARCH-COMPLEX PROGRAM
- INDUSTRIAL CO-CREATION PROGRAM
- BATON-ZONE PROGRAM

The name, taken from the analogy of a relay runner passing the baton to the next runner, indicates how the program involves a handing on of knowledge from one partner to another. The program's goal is to transfer scientific achievements into commercial products through partnerships with private companies.

Laboratories within the Baton Zone Program, which are staffed by a mixture of RIKEN and industry researchers to tackle specific challenges, focus on diverse areas including vaccines, plant breeding, organ preservation, and hydrogen energy storage.

Another important part of RIKEN's collaborations is the RIKEN Venture System. Under it, we contribute to industrial technology and people's everyday lives by using the new knowledge and new technologies that arise in the course of research at RIKEN in basic natural science. Some of the companies that have been established under the system are Photon-Labo, which is working in the field of nondestructive measurement of infrastructure such as tunnels using a laser system, and Cykinso, which sells test kits that allow customers to gain an understanding of their intestinal flora. As of 2018, 47 companies have been certificated as RIKEN Venture and 16 RIKEN Venture companies are currently operating.

RIKEN VENTURE certification mark

TARGETED PROGRAMS

Within the Cluster for Science, Technology, and Innovation Hub there are five research programs that are working to link basic research to innovation in key parts of society.

Drug discovery

The RIKEN Program for Drug Discovery and Medical Technology Platforms assists the identification of new treatments for cancer and other diseases by promoting collaboration within RIKEN on the development of innovative pharmaceuticals and medical technologies. The Program is involved in all phases of development from the discovery of promising drug targets to the identification of potential lead compounds such as small molecules and antibodies. It supports the acquisition of intellectual property rights to drugs and technologies that can then be brought to the development phase. The program also provides support for translational research and the transfer of potential drug candidates to preclinical and clinical phases of drug development.

Personalized medicine

Personalized medicine is a new paradigm that represents a shift from statistical abstraction of the patients toward the view that each patient is unique. This is a new scientific as well as social challenge. As a pillar of RIKEN's efforts to rise to this challenge, the Medical Sciences Innovation Hub Program (MIH) is developing a new biomedical science based on the pure description of diseases using multi-omics data. Scientists there have applied the Markov chain model, which is a well-known tool for modeling the temporal properties of many phenomena to describe changes in individual conditions during the life course. Data is being gathered from patients with immune disorders, cancer and developmental disorders.

Preventative medicine

Disease prevention is more effective when signs or symptoms of disease are detected early. Research groups in the RIKEN Preventive Medicine and Diagnosis Innovation Program deploy a broad range of research resources in physics, chemistry, engineering, biology, and medical science to develop and establish more efficient detection technologies. They are working on the discovery of new biomarkers, the development of detection technology for clinical practice, and the development of diagnostic kits. The Program interfaces between the scientific advances made at RIKEN and colleagues in medical institutions, companies and research organizations, ensuring that scientific breakthroughs are effectively translated into clinical practice.

Healthy lives and communities

The Compass to Healthy Life Research Complex Program was established to create a platform that will bring together a range of research players to investigate diverse aspects of human health, in order to develop an integrated system for looking at individual health including novel methodologies to quantitatively measure the extent of health (precision health), and to develop best-matched solutions for the maximization of individual health. This program also supports the startup of new healthcare businesses based on the precision health model.

Using AI for better health

Diseases are typically tackled by identifying a cause and then targeting that cause. However, there are many disorders that have multiple factors associated with them, and the result is a combinatorial explosion. To overcome

this, the MIH is working to develop an information geometry based reasoning technology that consists of multidimensional descriptors for multi-omics data and dimensionality reduction technology. These technologies will be applied to the development of personalized prediction algorithms for multifactorial disorders. Developed technologies will be available for medical institutions and industry.

Another new development in 2018 was the establishment of the Industrial Co-creation Program, which aims to solve challenges through large-scale collaborations between RIKEN and industrial partners. The earliest is a partnership between RIKEN and DAIKIN, an air conditioner manufacturer, to work to reduce the burden of fatigue by conducting research related to the indoors environment, where many people in advanced society spend much of their time.

Tech transfer

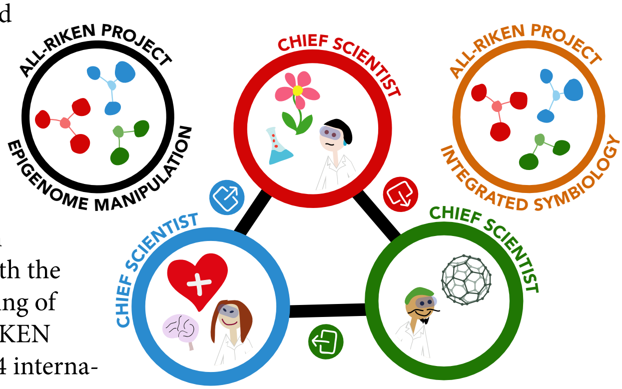
In addition to these programs and laboratories, RIKEN is active in sharing its discoveries with the world through the licensing of technologies. In 2017, RIKEN has 505 domestic and 674 international patents in areas ranging from physics to medicine. A special section on our website allows potential partners to search for technologies that might fit their needs.

CLUSTER FOR PIONEERING RESEARCH

Smashing boundaries

One of the unique aspects of RIKEN as an institute is the way in which scientists are encouraged to interact between disciplinary boundaries and organizational borders, and to take the lead in pioneering new areas of science.

One of the pillars of RIKEN's reorganization under our Fourth Mid-to Long-Term Plan was the establishment of a new organization—the CPR—which is dedicated to encouraging



CPR forms the core of RIKEN's curiosity-driven cross disciplinary system. Chief Scientist Laboratories interact to pioneer emerging research fields and help plan future research strategies. CPR also manages two cross-organizational projects.

Innovation and collaboration

RIKEN researchers to work together across institutional boundaries and to take the challenge of opening up new fields. The Chief Scientist laboratories working in CPR are able to pursue their research from a long-term perspective while interacting with scientists from both CPR and other centers across RIKEN.

In fact, when President Hiroshi Matsumoto took the reins at RIKEN in April 2015, one of the things that he said surprised him was how low the barriers are between laboratories and disciplines compared to the situation in universities. Indeed, interdisciplinary collaboration—coupled with a strategy to use such collaboration to pioneer new fields—has always been part of RIKEN's DNA.

Research Groups

In addition to the interdisciplinary nature of the Chief Scientist laboratories, several of RIKEN's current strategic research centers have been deliberately organized with a multidisciplinary mission. CSRS brings together researchers in plant science, chemical biology, catalytic chemistry, and biomass engineering, and provides them with the latest technology in data science, artificial intelligence, and genomic analysis to contribute to achieving a number of the Sustainable Development Goals adopted by the United Nations. At CEMS, specialists in physics, chemistry, and electronics are collaborating to a create a new generation of highly energy efficient devices and to contribute to the birth of quantum computing.

Further, in the iTHEMS program, researchers from mathematics, physics, computational science, and life sciences are working together to find new applications for mathematical models. This is a milestone, as it has brought the study of mathematics back to RIKEN after a hiatus of just about a hundred years, following the death of RIKEN's first president, Dairoku Kikuchi—a mathematician.

Based on this multidisciplinary structure, a number of events are held each year in which scientists from different fields, nationalities, and positions can come together to share their results and discuss how they can collaborate to help answer the scientific questions and social needs in line with RIKEN's mission. These events include the Interdisciplinary Exchange Evening, held a few times each year, and Discovery Evening, a venue for young scientists, as well as the Summer School for junior scientists and the reporting session for researchers working on grants awarded under RIKEN's competitive interdisciplinary program.

INTERNATIONAL RESEARCH PARTNERS

Partnerships and Agreements

As RIKEN continues to grow, so does its network of collaborators at research institutions around the world. RIKEN actively supports research collaborations and the exchange of researchers, students and staff with universities and institutions all across the globe. RIKEN has 15 overseas joint research centers (see list on p. 42) and is partners with over 40 countries around the world. Partnerships include General Collaborative Agreements and Memorandums of Understanding (MoUs).

270 Research collaborations & MOUs (2017)

RIKEN Facility Office at RAL (UK: Rutherford Appleton Laboratory)

KFU-RIKEN (Russia: Kazan Federal University)

RIKEN-MPG (Germany: Max Planck Society)

RIKEN-Tsinghua (China: Tsingua University)

RIKEN-XJTU (China: Xi'an Jiaotong University)

RIKEN-SJTU (China: Shanghai Jiao Tong University)

SIOM-RIKEN (China: Shanghai Institute of Optics and Fine Mechanics)

RIKEN-KRIBB (Korea Institute of Bioscience and Biotechnology)

NCTU-RIKEN (Taiwan: National Chiao University)

RIKEN-BNL (USA: Brookhaven National Laboratory)

RIKEN-MIT (USA: Massachusetts Institute of Technology)

USM-RIKEN (Malaysia: Universiti Sains Malaysia)

NTU-RIKEN (Singapore: Nanyang Technical University)

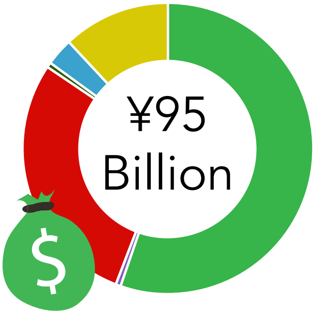
RIKEN-NCBS (India: National Centre for Biological Sciences)

RIKEN-JNCASR-IISc (India: Jawaharlal Nehru Center for Advanced Scientific Research & the Indian Institute of Science)

Signing ceremony for a joint collaboration between RIKEN, Zhejiang Hangzhou Future Sci-Tech City, and ZIIT, Sept. 2018

Budget, research output, and patents

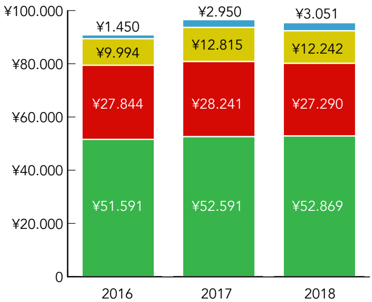
FY2018 YEAR-END REVENUE



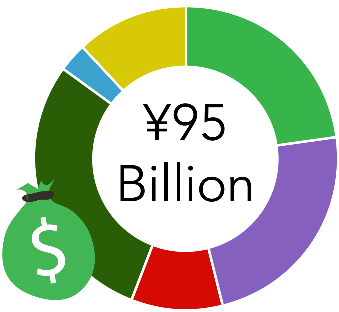
- Government funding for operations (¥52.869)
- Operational and non-operational income (¥0.665)
- Government subsidies for large-scale facilities (¥27.290)
- Income from shred use of large-scaled facilities (¥0.401)
- Subsidy for Advanced Integrated Intelligence Platform project (¥3.051)
- Commissioned projects income (¥11.176)

YEAR-END REVENUE OVER TIME

- Government funding for operations
- Government subsidies for large-scale facilities
- Self-generated income
- Subsidy for Advanced Integrated Intelligence Platform project

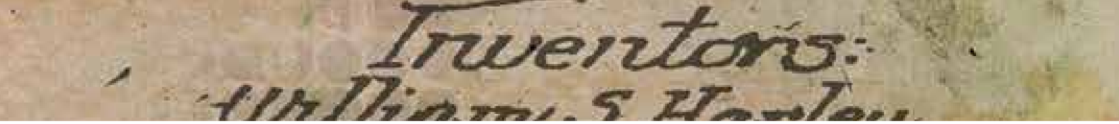


FY2018 YEAR-END EXPENDITURES



- Research projects (¥21.960)
- Research infrastructure management (¥22.296)
- Personnel and administration (¥9.277)
- Operation and construction of large-scale facilities (¥27.691)
- Advanced Integrated Intelligence Platform (¥3.051)
- Commissioned research (¥11.176)

All values given in billion yen (1 billion yen is approximately 9 million US dollars)



RESEARCH OUTPUT

RIKEN SCIENTISTS PUBLISHED 2672 PAPERS IN 2017

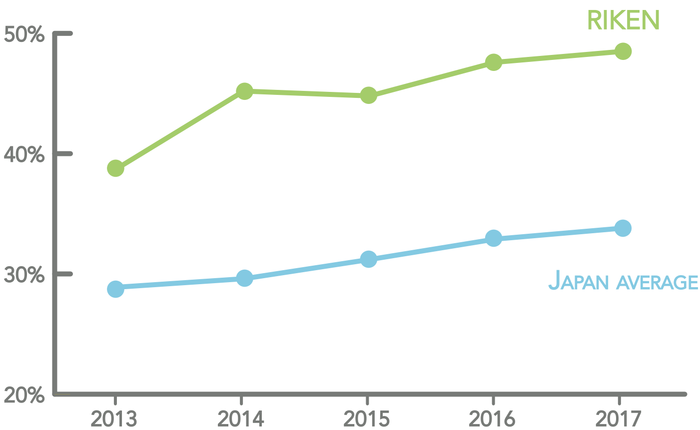
BY CITATION BASED ON ALL PAPERS PUBLISHED WORLDWIDE IN 2016

24% OF RIKEN PAPERS RANKED IN THE TOP 10%

4% RANKED IN THE TOP 1%

SUCCESSFUL INTERNATIONAL COLLABORATIONS CONTINUE TO RISE

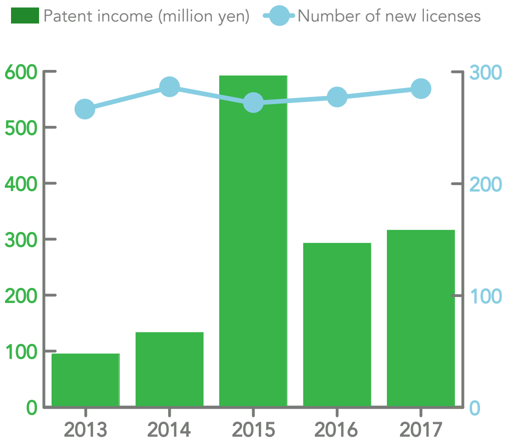
PERCENTAGE OF INTERNATIONALLY CO-AUTHORED PAPERS



Data collected from InCites by Clarivate Analytics on Sep 4, 2018

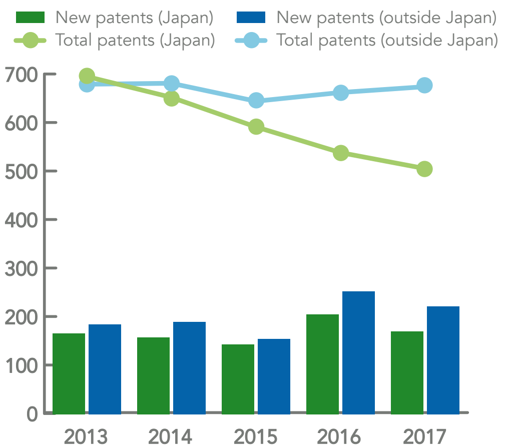
PATENTS

RIKEN EARNED 317 MILLION YEN FROM PATENTS IN 2017



In addition to publishing research results in top-level journals, RIKEN also actively encourages scientists to patent their discoveries and protect RIKEN's intellectual property portfolio to ensure that industry can use it to improve people's lives. Some of our recently licensed technologies include a high-tech blood pressure monitor, new varieties of Japanese cherry blossom trees, and a safe and environmentally friendly line of pesticides.

RIKEN FILED 393 NEW PATENTS IN 2017



Plants developed using heavy ion beams to generate advantageous mutations @ RIBF @RNC

STRATEGIC RESEARCH CENTERS

Center for Advanced Intelligence Project (AIP)

The AIP was launched in April 2016. Our center aims to achieve scientific breakthroughs and to contribute to the welfare of society and humanity by developing innovative technologies. We also conduct research on ethical, legal, and social issues caused by the spread of AI technology and develop human resources. (p. 34)

Center for Advanced Photonics (RAP)

RAP is working to make the invisible visible by pushing the possibilities of light to the extreme. Attosecond (10-18 seconds) lasers will make it possible to see the motion of electrons, super-resolution microscopes are making the nanoworld visible, metamaterials are allowing us to manipulate the spectrum, and terahertz light will open up new undreamt of technologies. At RAP, we focus not simply on making discoveries that are applauded by the research community, but rather on contributing to society through practical applications. (pp. 28, 30-32).

Center for Biosystems Dynamics Research (BDR)

BDR aims to elucidate the biological functions that unfold within an organism during its life by viewing the lifecycle from birth to death as a dynamic process involving the establishment, maintenance, and breakdown of a balanced and interlinked system of molecules, cells, and organs. BDR scientists carry out research to observe, manipulate, and model biological phenomena that take place on multiple scales—from molecular to whole-body—throughout the lifecycle of multicellular organisms, including development, growth, maturation, aging, and regeneration stages. The BDR also aims to apply its findings to regenerative medicine and the development of diagnostics, thereby contributing to the extension of healthy life expectancies, which is a critical issue for Japan and many societies with aging populations. (pp. 6-9, 13-14, 32-33)

Center for Brain Science (CBS)

Scientists at CBS are on a mission to advance basic research into the functions of the brain and the mind—from the levels of single-cells and whole bodies all the way to societal systems—and develop innovative technologies in the process. Research at CBS is multi-disciplinary and we focus on four themes: (1) High-level cognitive functions of the human brain: How do we reflect on ourselves, make inferences, and predict what others are thinking? (2) Universal biological principles: Hierarchical studies based on animal models to understand brain functions and brain-body interactions; (3) Data-driven research led by theoretical and technological advances: Using big data to develop new theories and improved AI systems; (4) Tackling the global challenge of brain disease: Developing diagnostic and therapeutic methods for neuropsychiatric disorders. (pp. 10-14, 22-23, 31)

Center Emergent Matter Science (CEMS)

Working towards a sustainable society, scientists at CEMS are developing fundamental science and technology to reduce energy consumption for information processing as well as the environmental burden for energy production. We use condensed-matter physics, supramolecular chemistry, and quantum information electronics to generate novel materials and devices. New properties emerge in materials or molecular assemblies fabricated from interactions between large numbers of component electrons, atoms, or molecules on a nanoscale level. These new materials and properties can be used for technologies such as highly efficient energy-conversion devices and low-power-consumption electronics. (pp. 28, 30, 42)

Interdisciplinary Theoretical and Mathematical Sciences Program (iTHEMS)

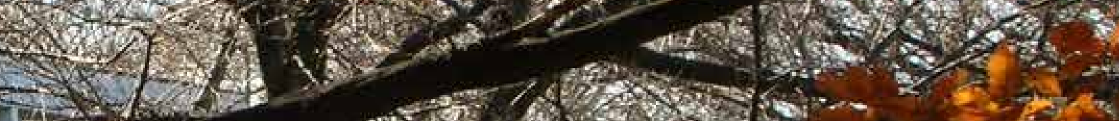
The goal of the iTHEMS program is to function as an international center that brings together researchers in theoretical, mathematical, and computational science and use mathematical methods to unravel mysteries of the Universe, matter, and life, as well as to solve key problems in modern society. Additionally, iTHEMS aims to develop an ideal environment for young researchers to make major breakthroughs by offering interdisciplinary and in-residence schools, workshops featuring leading-edge researchers in fundamental science, industry-academia partnership lectures for learning about how mathematics is being used by companies and society, and daily interactions among theoretical, mathematical, and computational scientists. (pp. 34, 42)

Center Integrative Medical Sciences (IMS)

At the IMS, we aim to the pathogenesis of human diseases and establish new therapies by conducting cutting-edge research on the human genome and immune function. To that end, we have established four Divisions: (1) the Division of Genomic Medicine, (2) the Division of Human Immunology, (3) the Division of Disease Systems Biology, and (4) the Division of Cancer Immunology. IMS' research is based on the concept of disease as a dynamic body system interacting with environmental stresses. We will create a research platform to clarify the processes that maintain or disrupt body homeostasis and to transfer that knowledge into the creation of new therapies and medicines. (pp. 8-9, 22-23)

Nishina Center for Accelerator-Based Science (RNC)

RNC on the Wako campus is a world-leading accelerator facility for theoretical and experimental nuclear physics research. It is named after Yoshio Nishina



who constructed Japan's first (and the world's second) cyclotron at RIKEN in 1937. The Nishina Center was established in 2006 to promote research into the origin of matter by investigating the nature of nuclei and their constituents, elementary particles. That year, the Radioactive Isotope Beam Factory (RIBF), with its world's first superconducting ring cyclotron and superconducting radioactive isotope beam separator started full-scale operation. The Nishina Center collaborates with researchers around the world. (pp. 23, 26, 28, 34, 36, 46)

Center for Sustainable Resource Science (CSRS)

Since its establishment in 2013, CSRS has been a leader in creating a sustainable society through transdisciplinary integration of plant science, chemical biology, and catalytic chemistry. Using the Sustainable Development Goals (SDGs) adopted by the United Nations in 2015 and the agreement of the COP21 on achieving zero greenhouse gas emissions as guidelines, we are promoting five flagship projects: (1) Innovative Plant Biotechnology, (2) Metabolic Genome Engineering, (3) Innovative Catalysts, (4) Leading-edge Polymers, and (5) Advanced Research and Technology Platforms. The goal of the CSRS is to create a future world where people can live healthy and prosperous lives. To achieve this, we carry out problem-solving research and contribute to a sustainable society based on the concept of developing manufacturing methods with reduced environmental impact. (pp. 15-17, 29, 31, 42)

RESEARCH INFRASTRUCTURE CENTERS

BioResource Research Center (BRC)

The BRC in Tsukuba was established in 2001 and has quickly developed into one of the world's most important repositories and distribution centers of biological resources for life-science research. The center's reputation derives from its capacity to handle a wide range of living strains of experimental animals and plants, cell lines of human and animal origins, genetic materials, microorganisms, and the associated bioinformatics. We are particularly notable for providing human induced pluripotent stem (iPS) cells to researchers. Please visit our website to find if there are resources that will be valuable in your research. (p. 37)

RIKEN Center for Computational Science (R-CCS)

The R-CCS is the leading research center in high performance computing and computational science in Japan, soon to be operating the supercomputer Fugaku. Our objectives are to investigate "the Science of (high performance) computing, by computing, and for computing," and promote the core competence of the research in a concrete fashion as open source software. Additonally, we collaborate with many other global leadership centers. Our previous

supercomputer (the K computer) was open for public operation between the fall of 2012 and the summer of 2019, producing multitudes of world-leading scientific and engineering results, not only for academia, but also for industry. Following its success, we began developing the supercomputer Fugaku in April 2014, with which we aim to achieve orders of magnitude increases in our capabilities as well as better ease of use and synergy with other IT ecosystems such as big data and artificial intelligence. Fugaku is expected to commence operations sometime around 2021 and serve as a keystone for solving some of the most important scientific and social problems facing the world. (pp. 33, 35)

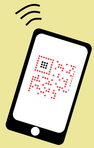
SPring-8 Center (RSC)

The primary mission of the RSC is to maintain stable and reliable operation of the large-scale research facilities—SPring-8 and SACLA—by providing brilliant X-rays for researchers at universities, research institutes, and industries. We develop state-of-the-art technologies for the production and utilization of brilliant X-rays and creates new science through the synergistic use of the two facilities. We also develop analysis tools for cryo-electron microscopy and high-performance NMR, which complements synchrotron radiation. (pp. 27-28, 32, 35-36)

Thank you for reading about RIKEN!

Although RIKEN publishes more than 2000 research papers every year, we cannot hope to cover all of them in this booklet.

If you are interested in keeping up to date on current research throughout the year, or learning more about specific laboratories, please check out our website and follow us on social media.



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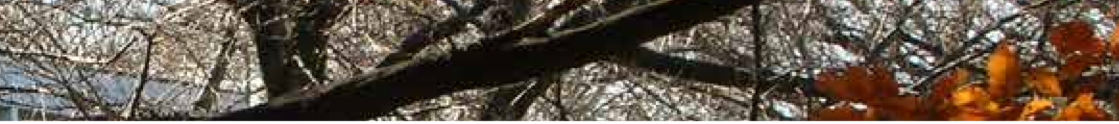
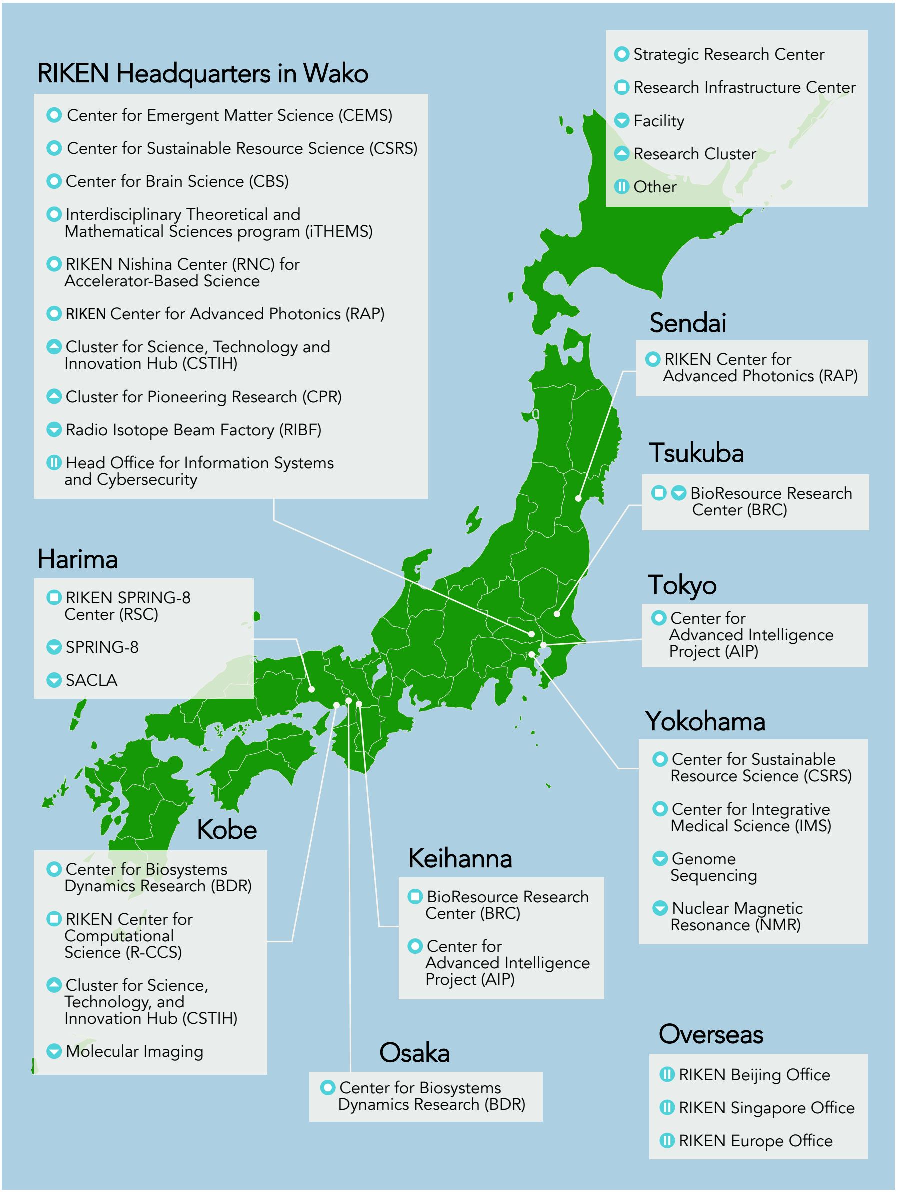


RIKEN ACROSS JAPAN / OVERSEAS OFFICES



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