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The complex path to conductivity

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Mohamad Mahathir, former Prime Minister of Malaysia, awarded RIKEN Honorary Fellowship

On July 30, Tun Mahathir bin Mohamad, former prime minister of Malaysia, visited the RIKEN Wako campus to be awarded an Honorary Fellowship through the RIKEN program to recognize outstanding local and international achievements by individuals in a variety of fields. Mahathir is the second recipient of the honor. He was chosen for the award, "...in recognition of his profound understanding of science, his strong leadership in actively promoting science and technology policy, and his eminent political and diplomatic achievements in furthering prosperity in Asia and around the world," said RIKEN President Ryoji Noyori in his introductory remarks.

After accepting the award, Mahathir gave a strident and often hard-hitting speech, on topics ranging from Asia's place in the world to the moral responsibilities of scientists. The former physician, after acknowledging the crucial importance of scientific advances to the region and the world, spent considerable time during his talk cautioning those present against complacency and hubris: two dangers facing researchers who wield the enormous power of science.

He deplored the use of science in the development of instruments of war. "If we care to examine, we will find that every scientific discovery has been used to enhance the power to kill people," he claimed. "Every advance that we make in scientific knowledge—be it in chemistry, physics or biology—has been used to increase our capacity to kill. And we know that we have never hesitated to use these weapons to kill."

In his speech, Mahathir spoke on a subject that he has been addressing for much of his long career as a doctor, politician and statesman—the inequities between the rich nations of the West and the developing countries of the world. To ensure that the benefits of science are shared equitably with all the people of the world, he proposed forming an international body to oversee and license certain scientific research, an organization that would have jurisdiction over all countries.

Mahathir also urged scientists to use their knowledge and skills to address pressing issues confronting humankind, including overpopulation and drug addiction, as well as global warming and natural disasters. He said scientists should start by being aware of the dangers, and be sure to get their priorities right. "Today we know that we have only to determine what we want to produce, and if we provide sufficient money and scientific manpower for research and development we can achieve our objective," he said. "Truly, there are lots of things that can benefit from science for the betterment of human life."

He cited examples of projects that could be tackled immediately, including various ways to reduce the burning of fossil fuels and the environmental degradation that can result. Some technologies he mentioned were hybrid cars, as well as ways to harness wind and wave power, thermal differentials in the deep ocean, and the physical and geothermal power of volcanoes.

Water, he noted, is both a crucial resource and a source of contention in the world today. We could contribute to the alleviation of water-related conflict by transporting water by pipeline, as we do oil and gas. In this way, he said not only would we be able to provide drinking water, but enormous areas of arid land would become green as food crops are grown.

He asserted that Asia's role in the world should be in keeping with both its rising economic power and its culture. "Asia is an important player because the peoples of Asia have largely retained their moral values. Perhaps Asians are too conservative," he said. "But we need [to] temper progress with tradition."

Asians must seek to end the use of military force to resolve disputes, he said. "It is time that the solution to conflict is not through the determination of who is the winner. It is time to seek a solution that is in favor of both, in a win–win result. Rather than contest, there should be compulsory negotiation, arbitration

Pipelines conveying water from Malaysia to Singapore.

or judgment by third parties," he said.

Mahathir exhorted his listeners to "return to sanity, to resurrect moral values," while there is still time. "If this world and humanity are not to be destroyed by science then we need to agree on an international scientific code of ethics or morality," he warned.

"In the effort to regulate science and its applications, Asians must push for a no-war, no-loss solution," he continued. "Asia has a capacity in science equal to that of the West. Asia therefore has clout. We should use this clout to create a better world. A code governing scientific research and development...will achieve this."

The former Malaysian prime minister concluded his lecture with a warning: "Unless we realize this, the future of Asia, science and technology is bleak." ■

Tun Mahathir bin Mohamad was prime minister of Malaysia from 1981 to 2003. During his term in office he spearheaded the rapid modernization of the Malaysian economy, now one of the largest and most powerful in Southeast Asia. Along with the phenomenal economic growth, his policies virtually eradicated poverty, and put a host of social indicators such as literacy levels and infant mortality rates on a par with those of developed countries.

Mahathir is also known as an advocate of 'Asian values,' and as a vocal critic of the rich nations of the West.

Born in 1925, Mahathir studied medicine at the University of Malaya, and built a successful private practice in his home state of Kedah. He began his political career in 1946 at the age of 21, joining the nationalist United Malays National Organization (UMNO).

Long an admirer of Japan, Mahathir used this country's rapid postwar growth path as an example for his own nation, transforming Malaysia from an exporter of rubber and tin into a major manufacturer of electronics, steel and cars.

Mahathir is married to Tun Siti Hasmah bt Mohd Ali, also a physician. They have seven children.

A snapshot of RIKEN research to solve several serious environmental problems

RIKEN researchers are dedicated to improving knowledge about our world and bettering our lives—their activities range from exploring the cosmos to unraveling the intricate and complex processes that maintain our health. And, some RIKEN researchers are focused on solving serious environmental issues.

Recently, the push to discover novel genetic resources from the natural environment has been increasing worldwide. At RIKEN, young scientists are launching collaborative projects using a 'meta-omics approach' in their bid to discover novel biological resources. One group, for example, is using the termite symbiotic system to research bio-energy (Fig. 1). The group is hoping to conduct this work in partnership with other researchers from south-east Asian countries, other tropical nations, and Japan. Their aim is to establish a fundamental technology that will provide a bio-based energy and materials and improve the environment to achieve a sustainable society.

Another research group is focusing salty winds that contribute to damage caused by the accumulation of salt in soils, which is becoming a serious agricultural problem across Asia. Using heavy ion beam irradiation generated at the RIKEN ring cyclotron, the group, along with their colleagues from Tohoku University, has produced a novel, salt-resistant rice species (Fig. 2).

In collaboration with industry, another group has developed a novel process for extracting large quantities of a particular mucin (a type of protein) from several species of jellyfish that have become pests in Japan's coastal waters. One of the larger species can break set fishing nets after jamming them up (Fig. 3), while smaller species can clog water intakes at nuclear and conventional power plants. This substance, known as 'qniumucin' after a Japanese myth, can be used as a starting material for the production of designer mucins with multiple uses.

How we can realize Bio-based economy?

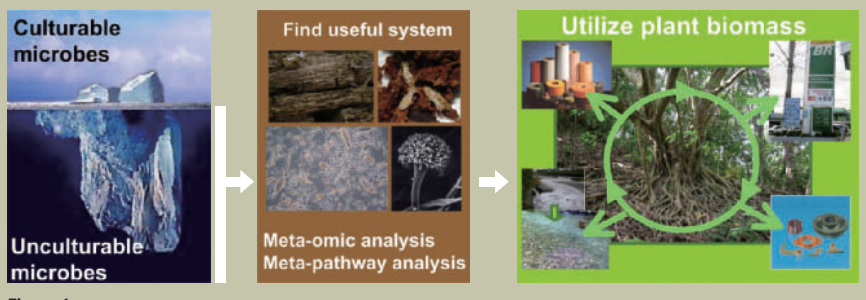


Figure 1

Figure 2

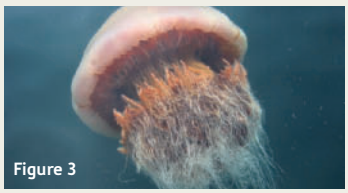


Figure 3

Playing tag highlights genetic disorder

Fluorescent and electrochemical labels help scientists detect genetic disorders that can cause cancer

A team of Japanese scientists led by Akimitsu Okamoto from the RIKEN Frontier Research System, Wako, has developed a new method for tagging a particular DNA base responsible for causing cancer.

Cytosine, a common DNA base, is reacted to add a methyl group to form methylcytosine during many biological processes. This process, known as methylation, is recognized as playing many important roles including gene regulation, DNA and protein stabilization, parental imprinting and X chromosome inactivation. Further, excessive methylation of cytosine has been shown to result in cancer. The development of simple techniques to detect methylcytosine is therefore of great interest to scientists.

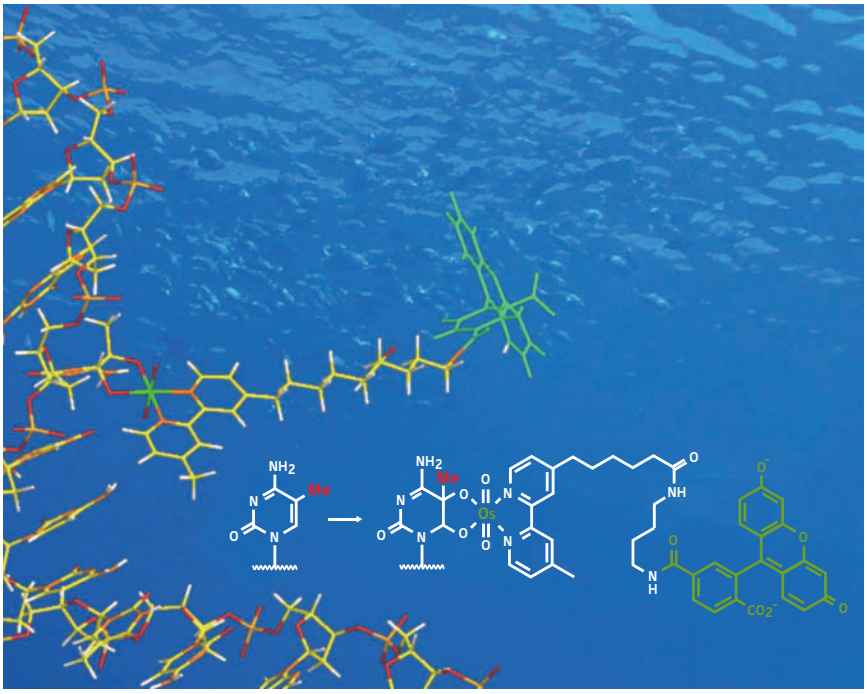


Figure 1: An illustration of methylcytosine labeled directly with a fluorescent tag.

Positively good tests needed

Although conventional methods to detect this compound have many advantages, they also have problems. Current methods cannot differentiate between cytosine and methylcytosine; they also destroy the DNA sample and are time-consuming. The latest technique by Okamoto and co-workers, published in the *Journal of the American Chemical Society,* is selective for methylcytosine, fast and allows easy detection[1].

Okamoto points out that there are, in fact, five key points to bear in mind when developing a new chemical assay for methylation detection. Firstly, techniques should take advantage of an easy-to-use form of chemistry, such as fluorescence or electrochemistry that is well established. Tests also need to produce results rapidly for them to be useful to patients in clinics. Next, any new assay should also give a positive result for methylcytosine and a negative result for cytosine. Ideally, being able to detect the exact location of the methylcytosine can provide further valuable information about the role of methylation each site. Lastly, techniques that do not damage the DNA sample avoid complications and errors during detection.

Since identifying the key features of a good assay, Okamoto's team dedicated two years to incorporating each of them into their work. Their technique takes advantage of the easy oxidation of methylcytosine and uses three, specially designed, components to enable detection. When the reaction takes place, the methylcytosine forms a stable complex with an oxidant, potassium osmate, and a rate-enhancing ligand. The ligand, a bipyridine derivative, can then react further to bond with a variety of fluorescent or electrochemical

tags allowing routine detection of the complex; therefore offering a test using straightforward chemistry (Fig. 1).

This conceptually new approach to detection also makes the grade by taking just six hours to complete. Importantly, the key complex only forms between the methylcytosine and the ligand. This leaves the cytosine in the sample untouched and allows a clear, 'positive test', distinction to be made. In addition, methylcytosines in single-stranded DNA efficiently formed the complex, whereas complexation of methylcytosines in a DNA duplex was suppressed. This result implies that the technique could be further developed to provide sequence-specific results giving detailed and accurate information of the methylated sites using untreated DNA samples.

Okamoto explains that there is still more work to be done. Currently, the information gained from the sequence-specific studies is limited as a consequence of the competing reaction with thymine, another DNA base. Also, the signal intensities and sensitivities are a little too weak to be useful on small sample sizes at this time.

Shifts in disease detection

Sequence-specific studies remain the focus of another, larger team in Okamoto's group. In a project extending over the past five years, this team has been developing tests to reveal an individual's general susceptibility to disease.

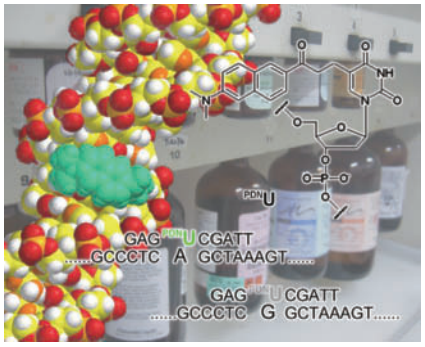


Figure 2: A graphical representation of the fluorescent DNA probe in action.

The most common type of variation in our genes is a single difference in one of the nucleotide building blocks of the DNA sequence, known as single nucleotide polymorphism (SNP—pronounced 'snip'). Scientists believe that it is these differences in SNPs that reveal susceptibility, and that their accurate analysis would play a key role in diagnostics. A new method to detect small changes in human genes could also lead the way in personalized medicine.

There are existing methods to detect SNPs, but their use is often limited by the need to identify large DNA sequences. However, this second project, uses derivatives of a fluorescent dye, known as PRODAN, to correctly identify SNPs quickly and efficiently[2].

PRODAN absorbs and emits light at different wavelengths depending on the polarity of its environment and when incorporated into DNA structures they can 'report back' differences in the microenvironment. Such differences would likely be the result of small changes in the DNA structure and allow detection of sequence variations (Fig. 2).

The researchers studied all combinations of DNA base matches and mismatches and observed the change between the wavelengths absorbed and emitted by the dyes. Only small differences were seen when the DNA base pairs were matched correctly, but large shifts were seen when there was a mismatch. "The use of this DNA probe makes it possible to judge the type of base located at a specific site on the target DNA, simply by mixing the DNA and the dye together. This method is a very powerful assay that does not require enzymes or time-consuming steps, and avoids errors," says Okamoto.

Following in the success of this second project, Okamoto and his team are now striving to improve their technique for methylation detection so it can be used routinely in clinics with standard fluorescence or electronic signal analyzers. Okamoto enthuses, "Because the total process finishes in a few hours, this technique may make it possible to design machines that automate a series of processes from purification of samples to analysis."

1. Tanaka, K., Tainaka, K., Kamei, T. & Okamoto, A. Direct labeling of 5-methylcytosine and its applications. *Journal of the American Chemical Society* **129**, 5612–5620 (2007).

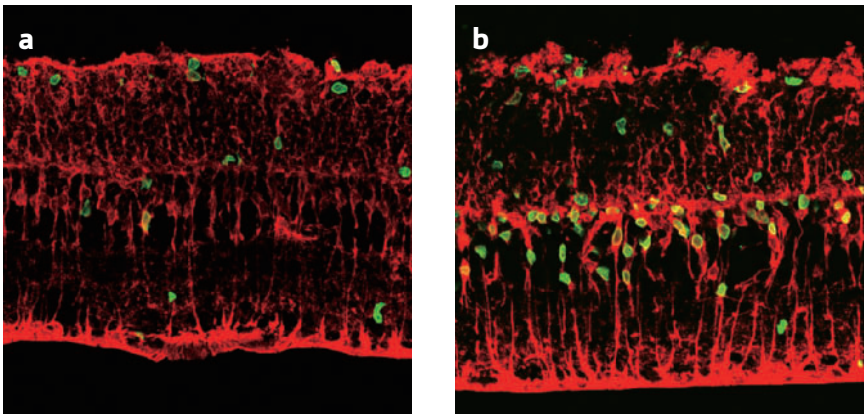
2. Tainaka, K., Tanaka, K., Ikeda, S., Nishiza, K., Unzai, T., Fujiwara, Y., Saito, I. & Okamoto, A. PRODAN-conjugated DNA: Synthesis and photochemical properties. *Journal of the American Chemical Society* **129**, 4776–4784 (2007).

About the researcher

Akimitsu Okamoto was born in Nagoya, Japan, in 1970. He graduated from the Faculty of Engineering, Kyoto University, in 1993, and obtained his PhD in 1998 from the same university. Afterwards he engaged in postdoctoral research at the Department of Chemistry, Massachusetts Institute of Technology, for a year. He returned to Japan as a research associate at the Department of Synthetic Chemistry and Biological Chemistry, Faculty of Engineering, Kyoto University, where he started his career in photochemistry and synthetic nucleic acid chemistry. He moved to the Frontier Research System, RIKEN, as an initiative research scientist in 2006. Since then, he has been the unit leader of the Okamoto Initiative Research Unit. His research focuses on the design, synthesis and physical properties of new, man-made biopolymers with various functions, and the design of unprecedented organic chemical systems for recognizing, transforming and visualizing a single component or atom in biopolymers of interest.

Stimulating retinal repair

Repairing damaged retinas is now a possibility



Journal of Neuroscience

Figure 1: Treatment of damaged retinas with Wnt3a significantly increases the amount of retinal regeneration as shown by the number of BrdU-positive proliferative cells (green). (a) The amount of regeneration that occurs naturally. (b) Retinal regeneration after Wnt3a treatment.

Japanese researchers from RIKEN and Kyoto University have demonstrated retinal regeneration in a mammalian model of retinal degeneration after stimulation of the Wnt signaling pathway. In addition to its better known roles in embryogenesis and development, this pathway also functions as a regulator of some adult stem cell populations.

The team's work may lead to new therapies for retinal diseases including the degenerative disease called retinitis pigmentosa, in which the rod and cone photoreceptor cells of the retina die off, leading to vision impairment and ultimately blindness.

Wnt stimulates regeneration *in vitro*

Previous research by the team, led by Masayo Takahashi at the RIKEN Center for Developmental Biology, Kobe, demonstrated that retinal support cells called Müller glia could de-differentiate, or revert to a cell type from earlier in its developmental pathway, to assume a neuronal fate, but the level of regeneration via this mechanism was very low, occurring in just a few cells.

Now, in an *in vitro* model of retinal damage, the team has found that retinal cell regeneration can be increased by as much as twenty-fold in the presence of the protein Wnt3a. Their findings are published in the *Journal of Neuroscience*[1].

The researchers initially performed experiments in cultured retinas isolated from rats, which can be used as a model for retinal damage. In these so-called explant cultures, the retina is cultured as a unit with no dissociation of retinal cells. After four days in culture, a small proportion of the Müller glial cells re-entered the cell cycle. Immunostaining of the cells further demonstrated that some of these cells were expressing proteins that were characteristic of neural stem cells, suggesting that the Müller glial cells were de-differentiating to neural progenitor cells. When they administered the protein Wnt3a, they found a significant increase in proliferation of these neuronal progenitors from the de-differentiated cells (Fig. 1).

"Newly generated cells constituted almost a layer of cells in the outer nuclear layer," says Takahashi. "We only observed several cells per field without Wnt treatment. Furthermore, the retinal neurons were regenerated all over the retina."

This process appears to involve the canonical Wnt signaling pathway, in which Wnt activation protects the β-catenin protein from degradation mediated by a glycogen synthase kinase complex, allowing it to accumulate in the nucleus where it regulates gene transcription (Fig. 2). A number of components of the pathway were shown to be present in the retina, including Wnt receptor and co-receptor proteins, glycogen synthase kinase and β-catenin. Treatment of the retinal explant cultures with Wnt3a caused accumulation of β-catenin in the nucleus and a subsequent increase in the expression of the cell cycle-regulating protein cyclin D1, a known target of the Wnt signaling pathway, compared to the levels of cyclin D1 in untreated cultures.

Takahashi and her colleagues also demonstrated that the Wnt signaling pathway was involved in the retinal regeneration process *in vivo*. Furthermore, the regeneration process could be stimulated with small molecule inhibitors of glycogen synthase kinase-3β, which normally blocks activation of the pathway, and conversely, is blocked by the application of Wnt3a inhibitor.

Next, the researchers showed that the regenerated cells migrated to the outer nuclear layer of the retina, where, in the presence of retinoic acid (a form of vitamin A), they observed differentiation into rod photoreceptor cells as evidenced

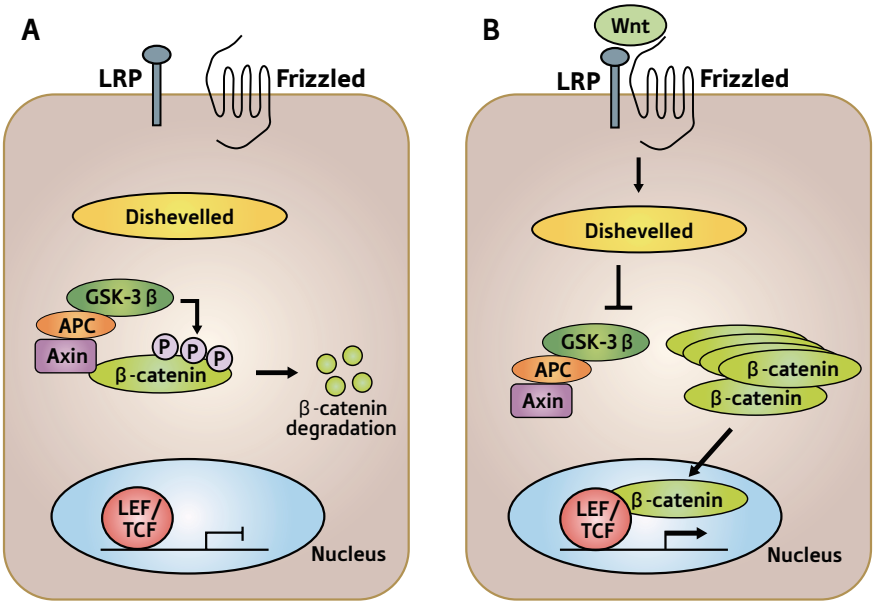


Figure 2: The Wnt signaling pathway activates gene transcription via β-catenin.
(a) In the absence of Wnt, a complex of proteins—including Axin, APC and glycogen synthase kinase-3 β—bind to β-catenin in the cell, marking it for destruction.
(b) Wnt binds to the cell surface receptors known as Frizzled and lipoprotein receptor-related protein (LRP), activating the so-called Dishevelled proteins, which inhibit the protein complex. This allows β-catenin to accumulate and cross into the nucleus where it interacts with transcription factors (LEF/TCF) to regulate the expression of specific genes.

by the appearance of cells expressing rhodopsin (Fig. 3).

Wnt-induced regeneration in a genetic model of degenerative disease

The team then isolated retinas from a strain of mice with a genetic defect that resembles the human disease retinitis pigmentosa. These mice exhibit a significant loss of photoreceptor cells within one month of birth. Treatment of these retinas with Wnt3a also resulted in the regeneration of retinal cells. This suggests that the Wnt/β-catenin signaling pathway contributes to central nervous system regeneration.

As the researchers had observed in the earlier experiments using retinal explant cultures from rats, a significant increase in cell proliferation was observed after Wnt3a treatment, and the de-differentiated neural progenitors migrated to the outer nuclear layer. But in retinas from mice already exhibiting advanced retinal degeneration, Wnt3a treatment had little or no effect, suggesting that the degree of degeneration prior to treatment affected the ability of the Wnt3a signaling pathway to stimulate repair processes.

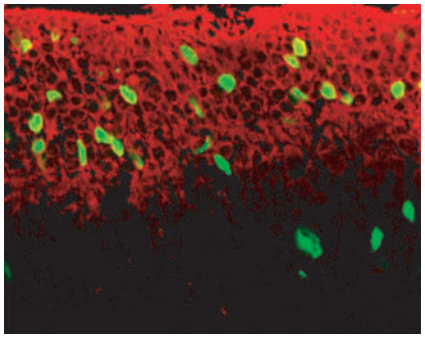


Figure 3: Photoreceptor cells expressing rhodopsin (green) can be seen after treatment of the retinal explant cultures with both Wnt3a and retinoic acid.

Differentiation of the neural progenitor cells into rhodopsin-positive photoreceptor cells was observed following treatment of the Wnt-treated cultures with retinoic acid. A similar result was observed after treatment of the cultures with valproic acid. This compound is an inhibitor of the enzyme histone deacetylase, which regulates expression of another protein involved in photoreceptor development, the transcription factor NeuroD.

Therapeutic possibility

Takahashi believes Wnt signaling may be a part of the natural restoration mechanism in the retina. However, more understanding of the pathway's role is required before the findings can be turned into therapeutic applications. Proof is also needed that the newly generated photoreceptors are incorporated into the retina, thus restoring its function.

The team's findings have therapeutic potential for reversing retinal degeneration and repairing damage. If the same regenerative effect can be stimulated in human retinas, small molecule drugs could be used to stimulate the Wnt signaling pathway *in situ*. Preliminary observations have shown regeneration potential in the primate retina.

"This is the first report to show the possibility of drug induced neural regeneration after damage in the central nervous system," says Takahashi. "If these newly generated neurons can form synapses and restore function, it will be applied to various diseases or conditions in the central nervous system that do not have therapies at all now." ■

1. Osakada, F., Ooto, S., Akagi, T., Mandai, M., Akaike, A. & Takahashi, M. Wnt signaling promotes regeneration in the retina of adult mammals. *Journal of Neuroscience* **27,** 4210–4219 (2007).

About the researcher

Masayo Takahashi received her MD from Kyoto University in 1986, and her PhD from the same institution in 1992. After serving as the assistant professor in the Department of Ophthalmology, Kyoto University Hospital, Japan, she moved to the Salk Institute, US, in 1996 where her research revealed that stem cells can be used as a tool for retinal therapy. She came back to Kyoto University Hospital in 1998, and since 2001 she has been an associate professor at the Translational Research Center, Kyoto University Hospital. She joined the RIKEN Center for Developmental Biology as a team leader of the retinal regeneration research team in 2006. Her clinical speciality is retinal diseases, especially macular diseases and retinal hereditary diseases. Her aim is to gain a deep understanding of these diseases and to develop retinal regeneration therapy.

It's all in the spin

Researchers show subtle fluctuations in electron spins are the origin of magnetism and superconductivity in a common oxide

Magnetism and superconductivity are material properties that generally exclude each other. The reason is that in a magnet, the electron spins—tiny magnets responsible for the material's magnetism—align in a common direction. On the other hand, superconductivity requires the pairing of electrons with opposing spins.

In that respect, sodium cobalt oxide, Na_xCoO_2, is unusual. It has a lattice structure with crystal planes formed by cobalt (Co) and oxygen (O) atoms. Along those planes it is ferromagnetic. However, when brought into contact with water, water molecules integrate into the material's crystal structure forming a slightly modified hydrated compound, $Na_xCoO_2 \cdot yH_2O$. And, this compound shows superconductivity along the CoO_2 planes at low temperatures.

However, a team of researchers from RIKEN's Discovery Research Institute in Wako, and colleagues from the universities of Chofu and Nagoya, now propose that magnetism and superconductivity in the non-hydrated and hydrated forms of Na_xCoO_2 actually share a common origin[1].

Typically, the origin of properties such as magnetism or superconductivity lies in the way electrons occupy the internal electronic states of a material. Like water filling an empty bucket, electrons in a material occupy all available electronic states beginning with the ones having the lowest electronic energy. Those electrons ending up at the 'top' of the bucket, also called the 'Fermi surface' (Fig. 1), are responsible for the electronic behavior of a material.

This Fermi surface can take quite complicated shapes. It can even consist of completely separate regions, particularly in crystals that are not symmetric in all directions. This is the case for Na_xCoO_2.

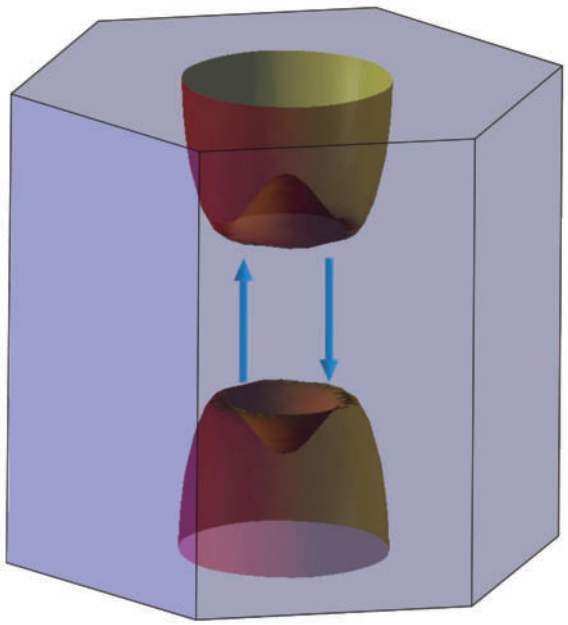


Figure 1: Fermi surface of Na_xCoO_2. The colored surface represents the maximum energy electrons can occupy in the crystal. The hexagonal outer structure is representative of the crystal symmetry itself. The gap between the disconnected areas of the Fermi surface can be bridged by electrons interacting with spin fluctuations (blue arrows).

The researchers studied the theoretical electron interaction between the disconnected parts of the Fermi surface and found that electrons can jump between these 'islands'. This is made possible by so-called 'spin fluctuations'—tiny changes in the way electron spins are aligned with each other. Through these synchronized tilts in their spins, electrons can gather just the right amount of energy to bridge the gaps at the Fermi surface. This electron interaction is crucial to mediate the material's electronic properties and, according to Ryotaro Arita from the RIKEN team, "provides the necessary incentive for the electrons to create either ferromagnetism or superconductivity".

Such a common origin for both phenomena in Na_xCoO_2 is quite rare, although Arita is convinced that if proven experimentally, this might lead to the discovery of other superconducting materials with disconnected Fermi surfaces. ■

1. Kuroki, K., Ohkubo, S., Nojima, T., Arita, R., Onari, S. & Tanaka, Y. Unified origin for the 3D magnetism and superconductivity in Na_xCoO_2. *Physical Review Letters* **98**, 136401 (2007).

Electron theory solves heavy problem

Unusual properties of lithium vanadate explained

Today's high-tech devices would not exist without a good theory to predict how electrons move through semiconductor crystals. But gaps remain in the theory—some insulating materials are erroneously predicted to conduct electricity, for example. Resolving these problems could lead to a more robust theory that enables new breakthroughs in electronics.

As part of this effort, a RIKEN researcher and his colleagues have developed a new theoretical method for predicting how electrons will behave at very low temperatures, called the projective quantum Monte Carlo (PQMC) method, and used it to solve a puzzle about the unusual electrical conductivity, heat capacity and magnetic properties of a material called lithium vanadate (LiV_2O_4) (Fig. 1)[1].

In a single atom, electrons can only occupy certain energy levels, known as orbitals. But in a crystal made up of trillions of atoms these orbitals smear into bands, each representing a range of energies available to the electrons. In semiconductors, electrons must acquire enough energy to hop into the lowest unoccupied band before they start to flow.

In certain materials, there is a magnetic attraction between the electrons flowing through the conduction band and those which remain trapped on the stationary atoms. This can slow the conduction electrons down, and make the trapped electrons, known as 'heavy fermions', behave as if they were much heavier than normal. Lithium vanadate is the first material where electrons residing in a lower orbital, called 3d, are responsible for heavy fermion behavior that appears below about -240 ˚C.

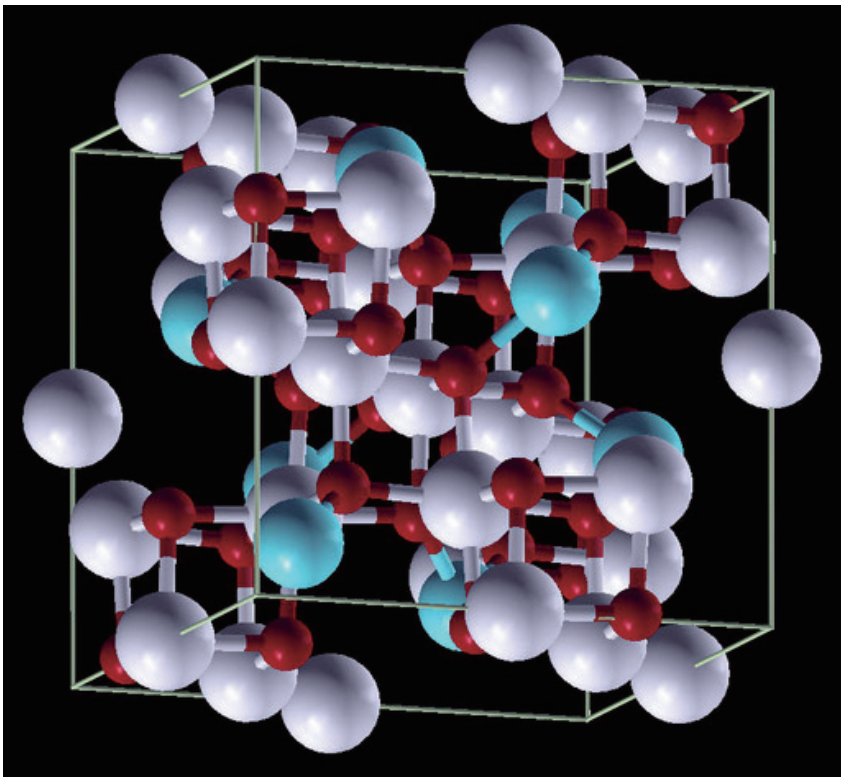


Figure 1: The crystal structure of lithium vanadate (LiV_2O_4) (Li, blue; V, white; O, red).

Despite the chilly conditions, there has been hot debate about exactly how this works. Now Ryotaro Arita, of RIKEN's Discovery Research Institute in Wako, and his colleagues believe they have the answer. The team has combined two established ways of calculating how electrons spread around atoms, and used PQMC to extrapolate the case to very low temperatures.

Their calculations show that the orbitals around the vanadium atoms are subdivided into a lower energy band (a_{1g}) where electrons remain tethered to their parent atoms, while those in an upper level (e_g) effectively form a conduction band. The lower band acts as a Mott insulator: such materials do not conduct electricity because the mutual repulsion between neighboring electrons forces them to stick by their parent atoms. This makes the a_{1g} band primarily responsible for the heavy fermion effects seen in LiV_2O_4.

The team now hopes to refine their theory further to explain other anomalous behavior in metals, insulators and semiconductors, says Arita. ■

1. Arita, R., Held, K., Lukoyanov, A. V. & Anisimov V. I. Doped Mott insulator as the origin of heavy-fermion behavior in LiV_2O_4. *Physical Review Letters* **98**, 166402 (2007).

Electrons on the edge are fractal

Understanding a material's transition from a metallic to an insulating state hinges on the fractal nature of electrons

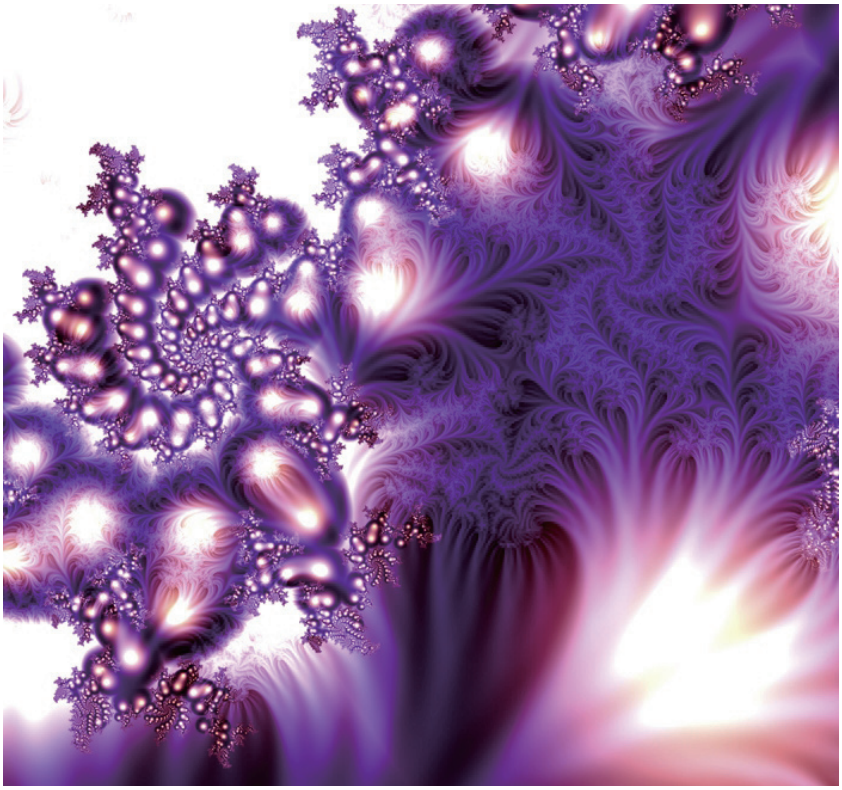


Figure 1: The beauty of fractals. The fractal nature of the electron wave function is shown to strongly influence the transition of two-dimensional materials from a metallic to an insulating state.

A team of researchers from RIKEN's Discovery Research Institute, Wako, and the US universities of Chicago and Santa Barbara has elucidated the role played by electrons in the transition of a two-dimensional disordered material from an insulating to a metallic state.

Most materials are either in a conducting state (that is, they are metallic) or an insulating state. However, some materials can suddenly switch from being a conductor of electric current to an insulator and vice versa, for example through the application of pressure, illumination with light or other means. This process is known to physicists as metal–insulator transition and originates in the way electrons are spread throughout a material. If the electrons are tightly bound at fixed locations and cannot move, the material is in an insulating state. In the metallic state, the electrons are spread widely throughout the material and can move freely from one end to the other.

At the transition from a metallic to an insulating state, characteristics of the electrons change rapidly and the electron distribution becomes fractal. This means that the electrons assume patterns that are self-replicating—the same structural motif repeats itself from a small localized scale to a large global scale (Fig. 1).

Now, the Japanese and US research team has studied metal–insulator transitions occurring in a plane. They demonstrated that the so-called conformal field theories (CFTs)—a powerful mathematical tool—are ideally suited for investigating these planar systems. "CFTs should give us an ultimate theoretical description of metal–insulator transitions in two dimensions," explains RIKEN's Akira Furusaki, a member of the team. The team's findings, obtained from applying CFT principles, have now been published in the journal *Physical Review Letters*[1].

In particular, the researchers evaluated the fractal nature of the electrons at the center of the two-dimensional plane, and at its borders and corners. They found the properties of the electrons are quite different at the borders and corners compared with those at the center. More importantly, the researchers demonstrate that these different properties at the borders and corners are fundamentally linked to each other.

"These findings are only a first step towards pinning down which CFT models describe the metal–insulator transitions," explains Furusaki. More studies will be necessary to explore the capabilities of the CFTs. This will not only increase our understanding of metal–insulator transitions, but also of other related disordered systems such as turbulence in air or water. ■

1. Obuse, H., Subramaniam, A. R., Furusaki, A., Gruzberg, I. A. & Ludwig, A. W. W. Multifractality and conformal invariance at 2D metal-insulator transition in the spin-orbit symmetry class. *Physical Review Letters* **98**, 156802 (2007).

Metal complexes take shape

Researchers provide a detailed insight into the change in structure of a metal complex when exposed to light

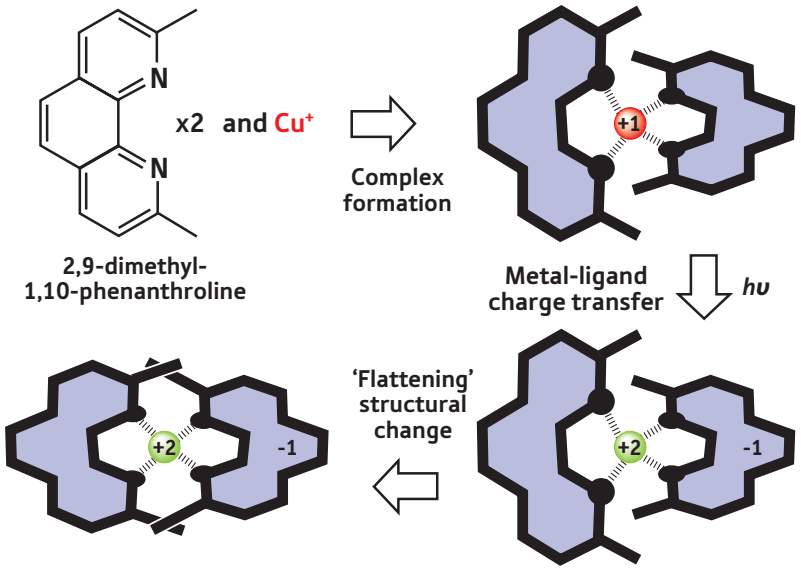


Figure 1: Formation and structural dynamics of a metal-ligand complex.
Two 2,9-dimethyl-1,10-phenanthroline molecules bind to a copper(I) ion (red) to form a metal-ligand complex. In the lowest energy state (known as the 'ground' state), the two organic ligands are oriented perpendicular to one another; the four nitrogen atoms forming a tetrahedron with the copper ion at its center. When the complex absorbs visible light, higher energy 'excited' states are formed, which involve the transfer of an electron from the copper(I) ion to the ligands, resulting in the oxidation of singly charged copper(I) to doubly charged copper(II). This electronic change of the copper ion leads to a structural reorganization in which the complex flattens, although does not become completely planar.

Compounds made up of organic molecules bound to metal ions—often referred to as 'metal-ligand complexes'—are an important class of chemical substances. Certain copper complexes are used by some plants for photosynthesis, and are also promising candidates for solar cell applications.

The number of electrons associated with a given metal ion (oxidation state) often determines the structure of metal-ligand complexes because it strongly influences how the organic ligands are arranged. This phenomenon is observed in copper complexes, where the structure depends on whether the metal ion is in the +1 or +2 oxidation state; referred to as Cu(I) and Cu(II), respectively.

The molecule 2,9-dimethyl-1,10-phenanthroline forms a complex with Cu(I) ions (Fig. 1). Interestingly, by shining visible light on this complex, the copper ion can be changed into the +2 oxidation state through a process known as metal-ligand charge transfer, in which an electron jumps from the metal to the ligands. This reorganizes the initially perpendicular organic ligands to give a flattened—but not completely planar—structure.

Although this kind of photo-induced structural change is widely known, there is not a well-developed understanding of how it occurs. As Tahei Tahara from RIKEN's Discovery Research Institute in Wako points out, "our knowledge of the photochemical dynamics of metal-ligand complexes is limited in comparison with what we know about organic compounds."

Now, by studying the fluorescence of the copper complex, Tahara and co-workers have developed a detailed description of how these structural changes happen. This was done using ultrafast time-resolved spectroscopy experiments in which the Cu(I) complex was illuminated with visible light. The resulting fluorescence emitted from the complex was monitored over very short (femtosecond) time-scales.

The results, reported in the *Journal of the American Chemical Society*[1], show that the Cu(I) complex is converted into a higher energy excited state in which the copper ion is oxidized to the +2 state, but retains the original structure in which the ligands are perpendicular to one another. After what Tahara describes as, "an unexpected waiting time," this complex finally distorts into the 'flattened' structure (Fig. 1).

The finite wating time before the structural change suggests a potential energy profile for these structural changes that contradicts the present theoretical understanding of the dynamics of metal-ligand complexes. Therefore, this study not only sheds new light on the fundamental question of how metal-ligand complexes change shape in real time, but could have implications for practical applications that use these materials. ■

1. Iwamura, M., Takeuchi, S. & Tahara, T. Real-time observation of the photoinduced structural change of bis(2,9-dimethyl-1,10-phenanthroline)copper(I) by femtosecond fluorescence spectroscopy: A realistic potential curve of the Jahn–Teller distortion. *Journal of the American Chemical Society* **129**, 5248–5256 (2007).

Breaking the frustration

The crystal structure of an oxide material is directly coupled to its 'frustrated' magnetic structure

Researchers from the RIKEN SPring-8 Center in Harima, the Japan Atomic Energy Agency and the universities of Tokyo and Virginia have discovered how changes to the crystal structure of the oxide material $HgCr_2O_4$ correlate to its magnetic state.

$HgCr_2O_4$ has an intriguing crystal structure where all relevant atoms are arranged in tetrahedra (Fig. 1). When the interaction between the magnetic atoms at the corners of these tetrahedra is antiferromagnetic, a magnetic state with a zero net 'moment' is expected to occur—that is, there should be as many magnetic arrows pointing upwards as downwards. However, the geometry of the tetrahedra means that no perfectly homogeneous distribution of the moments is possible. This is known as 'geometrically frustrated magnetism'.

To break the frustration, the system compensates for the uneven distribution of magnetic moments by distorting the crystal lattice (Fig. 1a). However, in response to an increasing external magnetic field, the magnetic moments realign and there is a stepwise reduction in crystal distortion (Fig. 1b). Once all magnetic moments are forced to point in the same direction, a perfectly symmetric crystal structure is assumed (Fig. 1c).

As reported in the journal *Nature Physics*[1], the research team studied the behavior of this material as they applied a slowly increasing magnetic field. They confirmed that the external magnetic field eventually breaks the zero magnetization of the sample and causes the magnetic spins to align along the external field—evidenced by sudden jumps in the sample magnetization followed by plateaus with constant magnetization.

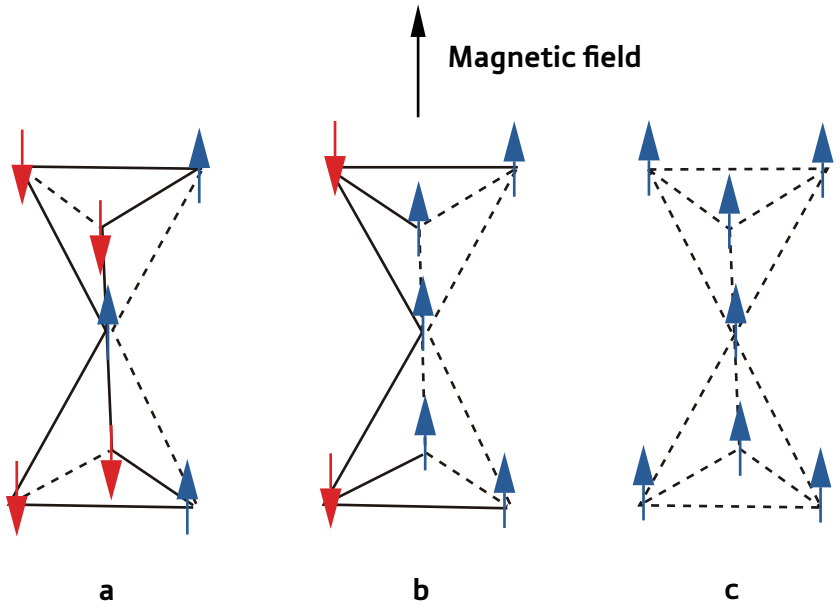


Figure 1: Breaking the frustration in $HgCr_2O_4$. (a) In low magnetic fields the material shows an antiferromagnetism for which the system compensates via a number of shortened atomic bonds (solid lines) compared with the symmetric, undistorted case (dashed lines). (b) & (c) As the magnetic field is increased, the magnetic moments align increasingly along the external field, while the structure assumes a less distorted configuration.

Unlike other materials, $HgCr_2O_4$ is uniquely suited for this type of study, as these changes occur in magnetic fields small enough to be generated in experiments. Therefore, "the observation of magnetization plateaus in this compound over a wide range of magnetic fields is novel and a manifestation of the geometrical frustration," explains Koichi Katsumata from the RIKEN team.

Importantly, the researchers studied for the first time the simultaneous evolution of the material's crystal structure and found that as the magnetization jumps between the different plateaus, the crystal structure becomes less distorted (Fig. 1). Katsumata is therefore confident that this study "has unveiled the origin of some of the intriguing properties of geometrically frustrated magnets." In particular, the results allow the validation and refinement of theoretical models describing the interaction between magnetism and crystal structure not only in this compound, but also in related systems. ■

1. Matsuda, M., Ueda, H., Kikkawa, A., Tanaka, Y., Katsumata, K., Narumi, Y., Inami, T., Ueda, Y. & Lee, S.-H. Spin-lattice instability to a fractional magnetization state in the spinel $HgCr_2O_4$. *Nature Physics* **3**, 397–400 (2007).

Pinpointing genetic lesions of autism

New work links autism with defects in the sequence of a gene expressed in the brain

A recent study establishes a causative relationship between a single gene and susceptibility to autism, a relatively prevalent neurological disorder characterized by impaired social and communicative behavior. Much work indicates that a strong genetic component underlies autism susceptibility. Although genetic mapping studies identified an autism susceptibility region on human chromosome 7, whether specific genes located within this region are associated with autism is not known.

A team led by Teiichi Furuichi, a scientist at RIKEN's Brain Science Institute in Wako, sought to determine whether *CADPS2*, a gene within this region, influences autism susceptibility. This work by Tetsushi Sadakata, a researcher of his team, and his colleagues was published in a recent issue of the *Journal of Clinical Investigation*[1].

CADPS2 (also called *CAPS2*) encodes a protein that regulates the trafficking and release, or exocytosis, of vesicles containing cargo such as neurotrophic factors, which influence brain cell maturation and survival. To determine whether the absence of *CADPS2* influences autism development, the researchers generated mice carrying a disrupted version of *CADPS2*.

The mutant mice exhibited normal visual, auditory, olfactory and motor function, all of which are normal in autistic patients. However, like autistic humans, CADPS2-deficient mice engaged in fewer social interactions with other mice, displayed heightened anxiety and reduced exploration in unfamiliar environments, and were hyperactive even in familiar surroundings.

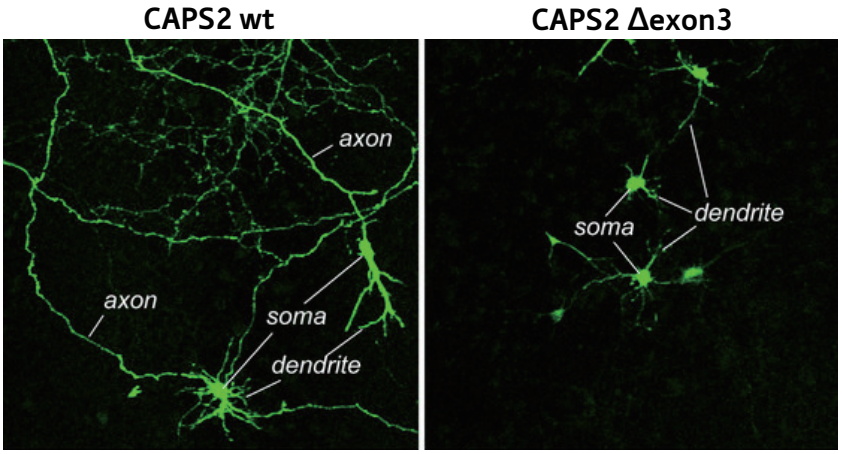


Figure 1: Normal CAPS2 protein (CAPS2 wt) is transported through the axon of neocortical neurons (left), whereas shorter protein (CAPS2 Δexon3) is not (right).

Absence of *CADPS2* resulted in cellular defects mirroring those frequently observed in the brains of autistic patients, such as reduced development and impaired survival of certain varieties of brain cells including some GABAergic interneurons and cerebellar Purkinje cells. Provision of brain-derived neurotrophic factor (BDNF), a protein found in CADPS2-associated vesicles in normal mice, rectified these cellular abnormalities.

Notably, some autistic but no healthy patients expressed a mutated shorter version of *CADPS2*. Like full-length CADPS2, this mutant CADPS2 protein promoted the secretion of BDNF. However, only full-length CADPS2 bound to the dynactin complex, which regulates the transport of vesicles through the axon, a specific region within brain cells. Accordingly, full-length but not mutant CADPS2 was found within the axons of brain cells (Fig. 1).

Not all autistic patients examined in the study exhibited mutations in *CADPS2*, and the cause why the shorter CADPS2 is produced remains unknown. Nevertheless, these findings highlight a specific gene that might contribute to the development and/or pathology of autism.

"These results provide a clue that might aid in the development of early diagnostic tests for autism and therapies effective in treating autism," says Furuichi. ■

1. Sadakata, T., Washida, M., Iwayama, Y., Shoji, S., Sato, Y., Ohkura, T., Katoh-Semba, R., Nakajima, M., Sekine, Y., Tanaka, M., *et al.* Autistic-like phenotypes in *Cadps2*-knockout mice and aberrant CADPS2 splicing in autistic patients. *Journal of Clinical Investigation* **117**, 931–943 (2007).

Heading in the right direction

Researchers find a gene controlling embryo orientation

Developmental biologists from RIKEN working with Japanese and Canadian colleagues have located an important gene that regulates the establishment of the head-to-tail or anterior-to-posterior (A–P) axis in mice. The future development of the whole embryo is orientated to this point of reference.

The A–P axis appears before the emergence of the three primary germ layers of body tissue during the process known as gastrulation, when the primitive ball of cells called the blastula folds in on itself to form the more complex, layered structure of the gastrula. Before gastrulation, there are only two types of tissue—epiblast from which the animal proper develops and visceral endoderm (VE) that forms all of the support structures such as blood vessels and nutrient cells.

The establishment of the A–P axis involves interplay between the VE cells and the underlying epiblast. In particular, a group of VE cells furthest from where embryonic structure attaches to the uterus migrates to close to where the head will develop in the epiblast. At the same time VE cells near the posterior end of the axis switch on a gene, *Wnt*, that produces a compound necessary to initiate gastrulation. In contrast, the VE cells at the head end or anterior visceral endoderm (AVE) produce compounds which block *Wnt*.

Earlier work has shown that the developmental gene known as *Otx2* is critical in the generation and function of the AVE. In mutants lacking *Otx2* there is no migration of VE cells to form the AVE and a key antagonist to *Wnt* is not produced. But the factors that regulated *Otx2* were unknown.

Chris 73

Figure 1: The pufferfish, *Takifugu rubripes*, has similar genes and compounds to mice controlling the establishment of the A–P axis.

In a recent paper in the *Proceedings of the National Academy of Sciences*[1], the researchers from RIKEN's Center for Developmental Biology in Kobe and their colleagues describe how they used carefully engineered transgenic mice to demonstrate the critical role of the transcription factor *Foxa2* in regulating *Otx2*. In laboratory studies, they also showed that the Foxa2 protein is needed for the production of at least two *Wnt* antagonists. Through these actions *Foxa2* controls the establishment of the A–P axis.

Similar genes and compounds also exist in the pufferfish, *fugu* (Fig. 1). In fact, the group found, the *fugu* equivalent of *Foxa2* can actually work in mice. According to the researchers, this shows how tightly the whole regulatory system has been conserved in the evolution of higher vertebrates from the bony fishes. ■

1. Kimura-Yoshida, C., Tian, E., Nakano, H., Amazaki, S., Shimokawa, K., Rossant, J., Aizawa, S. & Matsuo, I. Crucial roles of *Foxa2* in mouse anterior–posterior axis polarization via the regulation of anterior visceral endoderm-specific genes. *Proceedings of the National Academy of Sciences USA* **104**, 5919–5924 (2007).

Embryos back to front

Several protein interactions help to establish the front and back sides of an embryo

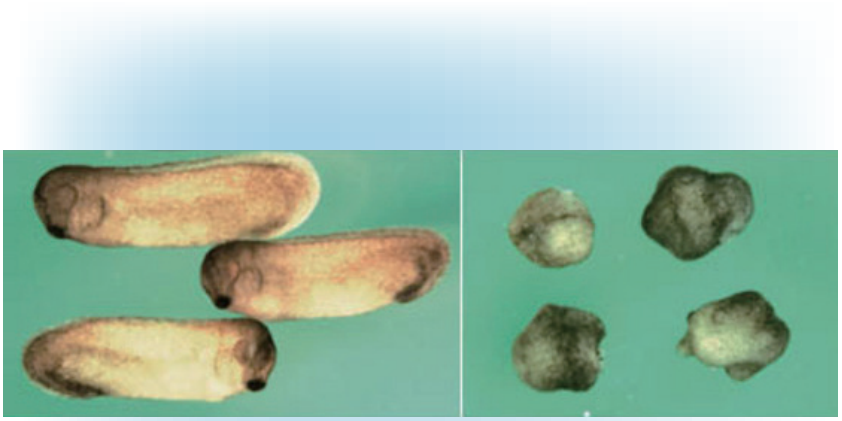
An important stage in the early development of an embryo is the formation of the dorsal–ventral axis, which distinguishes the front (ventral) side of the animal from the back (dorsal). RIKEN researchers at the Center for Developmental Biology in Kobe are identifying the genes and proteins that contribute to this process in *Xenopus laevis*, the African clawed frog.

Before the dorsal–ventral axis becomes established, the embryo is essentially a symmetrical sphere. The first signs that the symmetry is broken are uneven distributions in a complex network of proteins called the Wnt signaling pathway. However the differences in Wnt activity are too small to induce such a dramatic polarization, implying that other factors may amplify the effect.

The researchers found that XTsh3, a protein produced by the so-called Teashirt (Tsh) gene family, was strongly expressed in dorsal areas of the embryo[1]. "In *Xenopus*, it is easy to see gene functions by RNA injection into embryos," says team leader Yoshiki Sasai. "XTsh3 injection induced dorsalization of the embryos." Furthermore, when XTsh3 activity was deliberately inhibited, the dorsal axis didn't form at all (Fig. 1).

The activity of XTsh3 was found to be strongly related to levels of a protein called β-catenin, which has a crucial role in Wnt signaling. β-catenin accumulates in the cell nucleus and activates target genes that contribute further to the dorsal development.

"XTsh3 is an essential amplifier of Wnt signaling, which is activated on the dorsal side soon after insemination," says Sasai. However the formation of the dorsal axis doesn't occur until several hours later. In future Sasai would like to investigate the specific timings of each event. "One of our favorite hypotheses is that XTsh3 may be involved in the persisting memory of Wnt activation on the dorsal side."



EMBO/European Molecular Biology Organization

Figure 1: *Xenopus* embryos grown under normal conditions (left) and with inhibition of the XTsh3 protein (right).

XTsh3 may have even more functions that the team has not yet discovered, because the molecule has the potential to bind with DNA. For example, the high levels of XTsh3 in the nervous system may contribute to development of the spinal cord once the dorsal–ventral axis is established.

Abnormal Wnt activation is also known to cause certain types of colon cancer in mammals. Four Tsh family genes are known in humans, but the roles of the genes are still to be investigated. It is also not known how far Tsh's functions are conserved across species. Studies on the *Drosophila* fruit fly have shown a possible role of Tsh in Wnt signaling, but so far no link between Tsh activity and axis formation. ■

1. Onai, T., Matsuo-Takasaki, M., Inomata, H., Aramaki, T., Matsumura, M., Yakura, R., Sasai, N. & Sasai, Y. XTsh3 is an essential enhancing factor of canonical Wnt signaling in *Xenopus* axial determination. *The EMBO Journal* **26**, 2350–2360 (2007).

The birth of reproduction

Researchers find key to how DNA replication begins

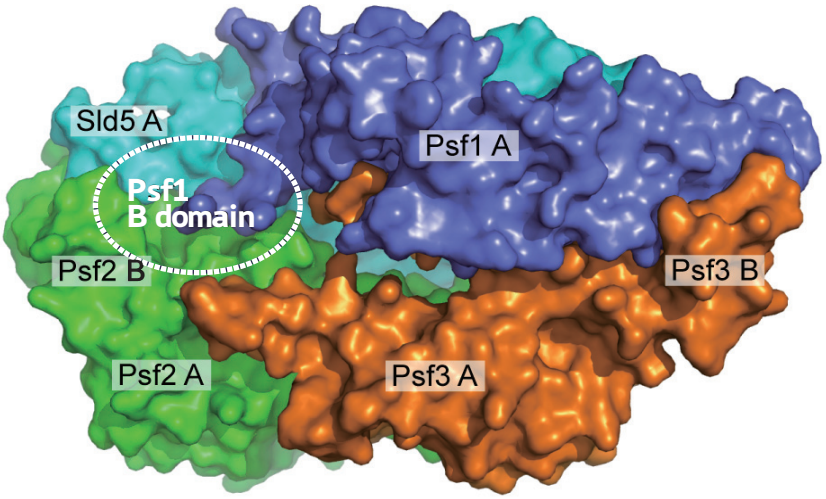
A team of Japanese molecular biologists has determined the structure of a protein complex that plays a key role in the initiation of one of the most fundamental of biological processes: the replication of DNA. The structure suggests how the complex functions, they say.

During replication, the double-stranded, helical DNA molecule is unraveled into two single strands each of which serves as a template for synthesizing a new and complementary strand of genetic material. The complete process generates two identical double-strands of DNA.

Previous studies have provided evidence that the so-called GINS complex, a macromolecular protein complex, is an important component of the molecular machinery that splits the two strands of helical DNA apart, creating what is known as a replication fork.

In a recent paper in *Nature Structural & Molecular Biology*[1], researchers from RIKEN's Discovery Research Institute in Wako and from Osaka University describe how they determined the crystal structure of the four subunits comprising the GINS complex and demonstrated how they fit together. Subsequent biochemical analyses in which crucial parts of some subunits were removed or altered systematically allowed the team to infer the roles of the subunits.

The four protein subunits—Sld5, Psf1, Psf2 and Psf3—are of similar size, each about 200 amino acids long. The team's crystallographic work showed that the subunits pack together into a two-layered trapezoid structure, with Sld5 and Psf1 on one level above Psf2 and Psf3, respectively, on the other (Fig. 1). Each subunit includes two domains, A and B, through which they interact and link to each other.



Nature Structural & Molecular Biology

Figure 1: A model of the GINS complex showing how the subunits fit together and highlighting the critical B domain of Psf1.

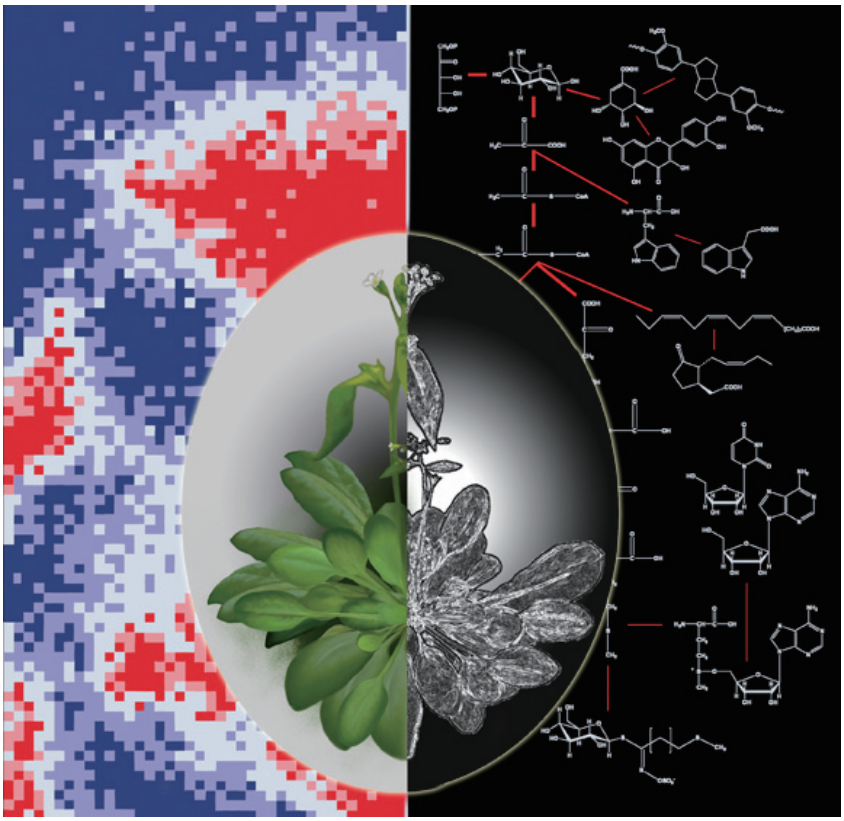
The team's biochemical analyses demonstrated that Psf1 is the most critical to the operation of the GINS complex. Its B domain must remain intact and in position for the complex to retain its full activity. While altering the B domain of Psf1's horizontal partner Sld5 loosens the tightness with which the complex is bound and can reduce activity; loss of the B domain of Psf1 has no effect on stability of the complex but inhibits its activity completely.

The research team suggests that while the other three subunits provide a tightly bound platform to support Psf1, it is the B domain of Psf1 that interacts with and organizes other proteins to initiate the DNA replication process. In future, the group hopes to determine which protein actually binds to GINS, with the aim of eventually initiating DNA replication *in vitro*. ■

1. Kamada, K., Kubota, Y., Arata, T., Shindo, Y. & Hanaoka, F. Structure of the human GINS complex and its assembly and functional interface in replication initiation. *Nature Structural and Molecular Biology* **14**, 388–396 (2007).

Vegetable matters

Researchers identify genes controlling health-giving compounds in common food crops



Romy Klausnitzer, RIKEN Plant Science Center

Figure 1: Integrative omics studies using model plants (e.g. *Arabidopsis thaliana* (center)) give us a wider perspective on plant metabolism, leading to elucidation of gene function and regulatory mechanisms.

Japanese scientists have identified genes controlling the production of important compounds, known as glucosinolates, produced in food crops. Vegetable plants from the family Brassicaceae, such as cabbage, broccoli and cauliflower, produce glucosinolates, which are useful in human health and to the environment. They are anti-carcinogenic with antioxidant properties and offer a natural defense against crop pests, potentially reducing the need for synthetic pesticides.

The biosynthesis of glucosinolates was poorly understood until the research team, led by Masami Yokota Hirai and Kazuki Saito from RIKEN's Plant Science Center in Yokohama, used an 'omics-based approach', combining transcriptome and metabolome data to describe this process[1]. The transcriptome includes all transcribed genes in certain conditions, and the metabolome comprises all the end products of gene expression. Integrating these sets of information gives a more complete picture of the biosynthetic pathway under study (Fig. 1).

According to Hirai and Saito, the omics-based approach can be used to comprehensively identify a set of genes involved in a particular metabolic pathway—it can be a powerful tool used to distinguish the most important gene of many that may encode a particular transcription factor. A transcription factor is a protein that controls when and where those genes are expressed.

The researchers revealed that long-chain, or aliphatic, glucosinolate biosynthesis is associated with two uncharacterized transcription factor genes, *Myb28* and *Myb29*, by comparing the condition-independent transcriptome data with condition-specific information—a procedure called transcriptome coexpression analysis. *Myb28* is a master transcription factor controlling many genes and *Myb29* is an accessory. In the model plant *Arabidopsis*, the team then overexpressed *Myb28* and found a huge increase in the production of glucosinolates; and in a mutant lacking *Myb28*, they found a decrease in production. The team later renamed these genes *Production of Methionine-Derived Glucosinolate (PMG) 1* and *2*.

This is the first report of genes regulating the aliphatic glucosinolate biosynthetic pathway. It shows that transcriptome coexpression analysis is highly versatile and suitable for comprehensively identifying genes involved in plant metabolism. A greater understanding of metabolic systems will lead to subsequent biotechnological applications.

"We eat Brassicaceae vegetables daily," says Hirai. "By over-expressing *PMG1* or controlling the expression of its orthologs in these vegetables, we can develop physiologically functional vegetables with higher amount of glucosinolates." This could be useful in human nutrition. These genes are promising targets for the genetic engineering of glucosinolate production, possibly on an industrial scale. ■

1. Hirai, M.Y., Sugiyama, K., Sawada, Y., Tohge, T., Obayashi, T., Suzuki, A., Araki, R., Sakurai, N., Suzuki, H., Aoki, K. *et al.* Omics-based identification of *Arabidopsis* Myb transcription factors regulating aliphatic glucosinolate biosynthesis. *Proceedings of the National Academy of Sciences USA* **104**, 6478–6483 (2007).

International Nuclear Physics Conference (INPC2007)

The 2007 International Nuclear Physics Conference was held at the Tokyo International Forum on June 3–8.

In this conference, a series of seven public lectures for the Centennial Celebration of Hideki Yukawa were included. Yukawa was a prominent Japanese physicist who discovered the origin of the nuclear force, and was Japan's first Nobel laureate.

In his speech at the opening ceremony the Emperor commented on RIKEN. "At RIKEN, Dr Yoshio Nishina, who inspired and nurtured the two Nobel Laureates Dr Yukawa and Dr Tomonaga, built Japan's first cyclotron. After the war the cyclotron was sunk in the sea, and one can imagine the disappointment of Dr Nishina. But the needs for such facilities are clear, and international cooperation in this field will in the future become ever more important."

The conference's plenary sessions included discussions on fundamental nuclear interaction, neutrino physics, quark–gluon plasma, hadron structure, the structure of the nucleus, nuclear reactions, nuclear astrophysics, applications, and new facilities. Some speakers discussed overviews of research from a historical viewpoint. Nuclear physics started with Yukawa's meson theory, and now embraces a great range of phenomena, from the particles that make up the nucleus to the structure of stars. In the future, this will be advanced by experiments with high-energy radioactive isotope beams and other developments. A talk by the director of the RIKEN Nishina Center, Yasushige Yano, attracted special attention as it presented exciting results from the Radioactive Isotope Beam Factory (RIBF), including data of a new isotope, which was discovered on the RIBF's first day of operation.

The International Union of Pure and Applied Physics (IUPAP) awarded the IUPAP Young Scientist Prize to three young scientists from around the world, including Kimiko Sekiguchi from RIKEN, for her work on three-nucleon force effects. Two recipients shared the Young Scientist Award donated by the journal *Nuclear Physics A*, and Takao Sakaguchi of Brookhaven National Laboratory in the USA was awarded a prize for the best poster.

Nobelist Tonegawa named first RIKEN Fellow

The first recipient of the title of RIKEN Fellow is Susumu Tonegawa, a professor at the Massachusetts Institute of Technology, an Investigator of the Howard Hughes Medical Institute, and the 1987 Nobel laureate in Physiology or Medicine.

The presentation ceremony was held July 6 at the RIKEN Okouchi Hall in Wako. Tonegawa gave a commemorative lecture: 'Yesterday, Today and Tomorrow'.

RIKEN established the new title to honor scientists both inside and outside RIKEN, who have made outstanding achievements in the natural sciences and shown superior discernment on a global scale. Recipients will be asked to advise on the management of RIKEN and offer insights on ways to stimulate the institution and otherwise contribute to its development.

RIKEN, Fujitsu researchers take on shogi

RIKEN and a subsidiary of Fujitsu have begun a collaborative research project on the brain activity of people while playing shogi.

The project, undertaken by RIKEN and Fujitsu in cooperation with the Japan Shogi Association, aims to elucidate the information-processing mechanism of the brain as it analyses the pieces on the shogi board. Cerebellar activities as the player goes through decision-making processes will be monitored using functional magnetic resonance imaging. The team expects this research to help extend an understanding of the mechanism of intuitive thought, which is believed to be unique to humans.

Their research will be publicized on the Fujitsu 'island' in 'Second life.com'—an interactive virtual-reality website.

The second RCAI International Summer Program (RISP 2007)

The second RIKEN Research Center for Allergy and Immunology (RCAI) International Summer Program (RISP 2007) was held in Yokohama July 20–27. Forty-three graduate students and postdoctoral fellows from 16 countries participated in RISP 2007. During the first part of the program, held for four days at RCAI, participants gave poster and oral presentations and there was a series of lectures by invited speakers from RCAI, various Japanese universities and from abroad. The second part of the program was the joint RCAI/Japanese Society for Immunology (JSI) meeting 'Development and Maintenance of the Immune System' held at Pacifico Yokohama. Fifteen of the participants stayed on at RCAI for an additional week-long laboratory internship from July 30 to August 3.

The research interests of the participants were quite varied, although T cell development and regulatory T cells were a major focus. Everyone who attended the sessions was very impressed by the high quality of the oral presentations and by the insightful questions asked during these presentations by participants and the invited lecturers. The lectures provided an overview of the immune system ranging from molecular analysis of antigen receptor signaling to whole-animal studies. Each lecturer incorporated introductory material pertinent to their topic as well as recent highlights from his or her own research.

Several of the lecturers invited to speak in the first part of the program also gave talks during the second part of the meeting, providing continuity in the material covered. Many new topics were also introduced, thus further increasing the breadth of the immunology coverage available to the RISP participants. Awards for the best RISP posters were presented at a reception on the first evening of the RCAI/JSI meeting. Toward the end of the reception, all the participants gathered as a group and their spokesman, Omar Duramad, a graduate student from the University of Texas, MD Anderson Cancer Center, expressed their deep appreciation to the organizers for inviting them to RISP 2007, and for an exceptional experience. The success of this unique program is due to the efforts of the Organizing Committee, chaired by Tomohiro Kurosaki, the RISP Secretariat who made sure everything went smoothly, and in particular to the efforts of the outstanding participants. Planning is already underway for the next RISP, tentatively scheduled for June 2008.

Paving the way for young researchers

The RIKEN unique postdoctoral program at RIKEN encourages promising young scientists to exercise their creativity and become independent

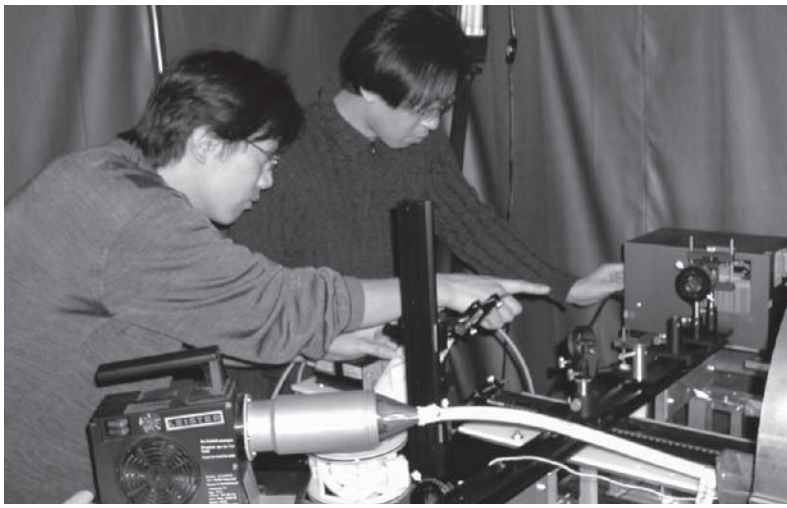


Figure 1: Young researchers who won a position at RIKEN under the Special Postdoctoral Researchers Program are actively challenging basic research.

Fostering young researchers is crucial for Japan to become the nation underpinned by innovative science and technology that its longtime slogan boasts. To achieve this goal, in 1989 the then Science and Technology Agency (now the Ministry of Education, Culture, Sports, Science and Technology) joined hands with RIKEN and inaugurated the Special Postdoctoral Researchers Program to support young researchers.

The new program is unusually attractive; it provides young postdoctoral researchers, or post-docs, with a high-profile workplace at RIKEN laboratories where they can actively engage in original research under comfortable conditions (Fig. 1).

In the late 1990s, Japan was behind the USA and Europe in supporting young researchers. Many researchers at RIKEN and elsewhere thought that a lot of PhD graduates fresh out of college had to work for low wages until they were hired by universities on tenure; and they were also forced to spend much time on non-research activities on behalf of senior faculty members. These researchers add that Japan lacked an environment where young scientists could exercise their creativity.

The RIKEN Special Postdoctoral Researchers Program was expected to break with the rigid employment structure in Japan. At first, the program, supported by the Science and Technology Agency, accepted only 25 post-docs, but RIKEN gradually increased the budget and capacity. The number totaled 82 in 1996, when the government's ambitious plan to produce 10,000 post-docs was launched under the '1st Science and Technology Basic Plan'. The program is basically a one-year contract but can be renewed for a maximum of three years, and also offers as much as ¥487,000 ($4,060) per month as a 'reward', in addition to ¥1.3 million ($10,800) to cover annual research expenses.

The program's good reputation spread by word of mouth among young scientists, increasing the number of applicants from 78 in 1989 to 280 in 1996. By 2003, the number reached almost 400. RIKEN assumed full responsibility for the program in 2005.

The RIKEN ambitions to reach out to young researchers extended beyond research students. RIKEN was well aware of the importance of technicians who support very difficult experiments, so it established another program in 1993 to foster highly skillful 'super technicians'.

In 1996, RIKEN also created a unique program called the Junior Research Associate (JRA) system, which targeted masters graduates enrolled in PhD courses. Successful applicants became part-time staffers at RIKEN. And although their rewards were much lower than the Special Postdoctoral Researchers Program, it helped raise the motivation of many students compelled to work part time in order to cover living costs while training to be a working scientist.

In 2001, RIKEN established what is now known as the Initiative Research Program, the purpose of which is to provide an opportunity for young researchers to organize and manage their own research unit. A unit usually consists of several researchers and technical assistants. It is hoped that, with this experience, unit leaders will sharpen their skills to become future leaders in the scientific research community.

The Program is now part of the Frontier Research System, and currently consists of seven units. These units are tackling novel themes such as elucidating the link between stress imposed on the endoplasmic reticulum and human diseases, designing photo-functional nucleic acids and proteins, and synthesizing functional oligomers.

This year RIKEN set up another program, known as 'Foreign Postdoctoral Researcher' (FPR), for young non-Japanese scientists who have demonstrated creative and innovative ideas, and who can be expected to become internationally active in the future. RIKEN is now accepting applications for FY2008 (http://www.riken.jp/engn/r-world/info/recruit/071005/index.html).

www.rikenresearch.riken.jp

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

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