# RIKEN RESEARCH

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### Mud links cell polarity with cell division

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## How cells customize compounds

New laser-based imaging technology resolves a protein trafficking debate

A research team from RIKEN has developed and used high-speed, sensitive, live-imaging technology to help resolve a debate over how cells process the biochemical compounds they make, transport and secrete.

The work is significant because the preparation and delivery of such compounds is fundamental to the operation and communication of all cells and organisms. In addition, the new imaging technology the group developed can be applied to many other areas of interest such as tracking drug delivery and observing the invasion of cells by viruses.

Biologically active compounds in cells are typically constructed around a protein core that is assembled in a cluster of membranes called the endoplasmic reticulum. From there, the compounds pass into a second set of membranes known as the Golgi apparatus where the protein core is modified and customized for action by the addition of chemical groups, such as sugars and phosphates.

In higher organisms the Golgi apparatus resembles a stack of flattened bladders called cisternae (Fig. 1). Proteins from the endoplasmic reticulum enter at one end of the stack, the cis end, and move through the Golgi apparatus during processing. The finished compounds emerge from the other end, the trans end.

Until now, there has been a debate as to how this maturation process took place. One typical model suggests that each cisterna is a permanent structure and that proteins move from one cisterna to another during processing. An alternative is that new cisternae form at the Golgi entrance and move with their entire contents up the stack as they mature to break down and release the processed compounds at the exit.



Figure 1: An electron micrograph of a section through the Golgi apparatus of a higher plant. The cis side is the entrance, and the trans side, the exit.

As reported in *Nature*<sup>1</sup>, researchers from RIKEN's Discovery Research Institute in Wako were able to resolve this debate with a series of experiments using yeast. They chose yeast because unlike higher organisms the individual cisternae are not stacked together but independent of each other, scattered freely in the cell, and can be tracked easily. The researchers took pairs of membrane components-one associated with the early cis part of the processing and the other associated with a later stage-and labeled each with a different color fluorescent protein, one red and the other green.

With their new, live-imaging technology—a high-speed, confocal microscope linked to the latest, ultrasensitive cameras—the team can observe weakly fluorescent signals within living cells. So the researchers could detect and track their fluorescently labeled compounds, and use them to determine whether cisternae were either at the cis or trans stage or somewhere in between. In yeast, they found cisternae typically showed primarily red or green fluorescence confirming that cis and trans forms scatter independently through the cell.

The researchers then followed the progress of individual cisternae. They reasoned that if maturation occurred all within one cisterna, then the components associated with the membranes, hence the colors, should change over time. And that is exactly what they detected (Figs. 2 and 3). What's more, the color changes were always unidirectional—from red to green, or cis to trans-related membrane proteins, never the reverse. Cis-stage membrane proteins were not evident at the trans-stage.

But if that were so, the researchers argued, somehow the cis-stage membrane proteins would have to be moved out of the maturing cisternae after their job was done, and back to where the new cisternae were forming. The standard explanation for this involves



Figure 2: A yeast cisterna (white arrowhead) changes color over time as the proteins attached to the membranes change during processing. (red = cis: RFP-Sed5p; green = trans: Sec7p-GFP)

transportation in small membrane-bound bags called COPI vesicles.

In search of an answer, the research team examined a mutation which results in the formation of defective coats for COPI vesicles and prevents them from functioning properly. In yeast cells carrying this mutation the team detected



Figure 3: Typical graphs of the change in the relative fluorescence of red and green-tagged components (colored accordingly) in a cisterna over time.

that the speed of transition from cis to trans was more than three times slower, indicating that COPI vesicles are an important part of the maturation process. But as the mutation did not stop the process completely, other additional mechanisms are likely to be involved.

"We now want to look at the Golgi apparatus in higher organisms to see if our findings are also true for them," says project director Akihiko Nakano. "In future, we would like to use our technology to examine the dynamic events of how proteins are trafficked and sorted within cells."

Many more questions about Golgi apparatus processing remain to be answered, he commented. Why is it that different protein cargoes are processed at different rates, for instance, and how is this achieved? And, what mechanism ensures that the maturation process only runs one way?

The team hopes that further development of their technology in terms of speed and sensitivity will open further fields in cell biology for exploration.

 Matsuura-Tokita, K., Takeuchi, M., Ichihara,
 A., Mikuriya, K. & Nakano, A. Live imaging of yeast Golgi cisternal maturation. *Nature* 441, (1007–1010).

#### About the Author

Akihiko Nakano was born in 1952 in Hokkaido and received a Doctor of Science degree from the University of Tokyo in 1980. From 1980 to 1986, he worked as a research associate at the National Institute of Health also in Tokyo. From 1984 to 1986, he served as a post doctoral researcher at the University of California, Berkeley, and then returned to the National Institute of Health as a senior researcher. In 1998, he was appointed as a lecturer at the University of Tokyo, and became an associate professor in 1991. Since 1997, he has been serving as the Chief Scientist and Director of the Molecular Membrane Biology Laboratory at RIKEN's Discovery Research Institute in Wako. He is also a professor at the University of Tokyo Graduate School of Science.

http://www.riken.jp/engn/r-world/research/lab/ wako/membrane/



# Cellular scaffold plays dual role in cell division

A new spatiotemporal model of microtubule organization shows the exquisite levels at which the cell division process is controlled

Developmental biologists at RIKEN have determined a dual role for microtubules, the basic building blocks of the internal cellular scaffold, during the final stages of cell division or cytokinesis.

During cytokinesis, cells adopt an internal organization reminiscent of the earth's poles and equator. Spindles of microtubules connect the DNAcontaining chromosomes situated along the 'equator' with the area around both 'poles', the polar cortex. As the spindles pull the chromosomes away from the equator, the cell membrane inches inwards along the equator forming a cleavage furrow. This eventually splits the cell into two daughter cells.

Working with the worm *Caenorhabditis elegans*, a well-known model organism for studying animal development, Asako Sugimoto and Fumio Motegi from RIKEN's Center for Developmental Biology in Kobe, and colleagues from New York University in New York, USA, now propose a biphasic



Figure 1: Fluorescently labelled cells of the worm *C. elegans* showing the last phases of cell division (DNA is blue;  $\gamma$ -tubulin is green; aurora A-kinase is pink; E is early; M is mid; L is late).



Figure 2: Cytokinesis in *C. elegans*. a) The mitotic spindle and b) filamentous actin of the cytoskeleton. The contractile ring forms at the spindle equator while microtubule density is high.

model for the regulation of microtubule assembly during cytokinesis. Their model, presented in *Developmental Cell*<sup>1</sup>, explains cleavage furrow formation along the cell's equator.

Using live imaging techniques for fluorescently labelled molecules, Sugimoto and colleagues studied the changes over time in density and location of different components of the cellular scaffold or cytoskeleton (Fig. 1). They first determined that prior to furrow formation, microtubules are enriched in the equatorial plane. All the while, filamentous actin, another component of the cytoskeleton starts forming a socalled contractile ring around the equator. As the microtubule density diminishes at the equator while increasing around the polar cortex, the contractile ring starts closing in (Fig. 2). "These observations combined with analyses using mutants and drugs revealed that the microtubules play two separate roles in the initiation of cytokinesis; one as an 'instigator' that localizes the contractile ring to the equator, and the other as a 'repressor' of the furrowing outside the equator," explains Sugimoto.

The team then embarked on a second round of experiments to reconcile these two seemingly contradictory roles of microtubules. Applying molecular biology technologies to manipulate the activities of particular control components of microtubule assembly, they discovered that control of this process gradually 'changes hands' from  $\gamma$ -tubulin, a microtubule nucleating protein, to a second control system characterized by an increased presence of the enzyme aurora-A kinase.

"This model of dual-roles of the cytoskeleton provides an attractive alternative to existing models representing the cell cleavage process in which single control systems fail to satisfactorily explain the different stages of cytokenesis," notes Sugimoto.

Motegi, F., Velarde N.V., Piano, F., & Sugimoto, A. Two phases of astral microtubule activity during cytokinesis in *C. elegans* embryos. *Developmental Cell* 10, 509–520 (2006).

# Getting genomic analysis off to a good start

A massive genomic research effort yields new insights into the structure of mammalian genes

The starting point for every gene's activity is its promoter, a stretch of DNA where specific proteins can bind to turn a gene on (or keep it turned off). Because of this, techniques for determining the locations of promoters are valuable tools for finding genes in a given region of the genome and for studying conditions under which those genes are active.

One such technique, known as 'CAGE', was recently described by Yoshihide Hayashizaki and his colleagues at the RIKEN Genomic Sciences Center in Yokohama. CAGE allows scientists to rapidly collect large numbers of short sequence 'tags' that can be used to identify transcription start sites (TSSs), and this data can in turn be used to zero in on promoters.

In new work described in the journal *Nature Genetics*<sup>1</sup>, Hayashizaki's group has collaborated with an international consortium of researchers, the RIKEN-directed FANTOM-3 project, to apply CAGE to the analysis of the mouse and human genomes, identifying hundreds of thousands of TSSs that could be used to locate likely promoters. According to Hayashizaki, the sheer quantity of data proved surprising. "The number of TSS was definitely much larger than the number of protein-coding genes and the number of reported, known promoters," he says.

Closer analysis of the data led to the identification of two major promoter classes. For 'narrow' promoters, transcription is initiated at very specific genomic sites, and the promoters show strong conservation between mice and humans. For 'broad' promoters, however, TSSs are scattered over much larger areas, and the promoters show greater evolutionary change between



species. Surprisingly, the narrow promoters, which contain specialized protein-binding sequences previously thought to be fundamental features of most mammalian promoters, proved to be much less common than the broad promoters that don't necessarily contain these sequences.

The data from this study has provided a valuable starting point for identifying important structural elements of different promoter types, data that could help scientists predict when individual genes are likely to become active and in which tissues or organs a given gene might be expressed. "This will allow a much more detailed understanding of the expression of genes," concludes Hayashizaki, "and will open new possibilities to modify their expression for biomedical applications."

Carninci, P., Sandelin, A., Lenhard, B., Katayama, S., Shimokawa, K., Ponjavic, J. *et al.* Genome-wide analysis of mammalian promoter architecture and evolution. *Nature Genetics* **38**, 626–635 (2006).

## How a fat cleaving enzyme works

Scientists solve the structure of an important fat cleaving enzyme and show how its ability to bind metal ions allows it to function

The fat molecule sphingomyelin is abundant in cell membranes throughout the body. Its breakdown by enzymes called sphingomyelinases is significant because one of its byproducts, ceramide, is an important signalling molecule in a variety of different cellular processes, as well as in many diseases including cancer and diabetes<sup>1</sup>.

In a report by scientists from the RIKEN SPring-8 Center in Harima and two other Japanese research institutes, the detailed atomic structure of one of these sphingomyelinases (Bc-SMase) has been determined—in this case from the bacterium *Bacillus cereus*. Knowledge gained from this structure should have direct application to humans because the enzyme in this bacterium has strong functional similarity to mammalian versions.

Bc-SMase can only work if it binds divalent ions such as  $Co^{2+}$  or  $Mg^{2+}$ , and to a much lesser extent  $Ca^{2+}$ . So to gain insight into the exact mechanism by which this enzyme binds these different ions and how they allow it to cleave sphingomyelin, Miyano and colleagues investigated at the atomic level the 3dimensional structure of Bc-SMase bound to one of these three types of ions. Their findings are reported in *The Journal of Biological Chemistry*<sup>2</sup>.

The team identified the three different structures by separately crystallizing Bc-SMase in a complex with each type of ion, and then they shot a beam of X-rays at the isolated crystals using the SPring-8 synchrotron facility. From the diffraction pattern of the X-rays that scattered after hitting the crystals, it was possible to determine the different structures of the enzyme as it bound to each different ion (Fig. 1).



The structure revealed to the scientists exactly how ion binding allowed the enzyme to interact catalytically with the sphingomyelin. It also showed that it bound Ca2+ slightly differently from  $\mathrm{Co}^{\scriptscriptstyle 2+}$  and  $\mathrm{Mg}^{\scriptscriptstyle 2+}\text{,}$  such that it was not able to as efficiently interact with the sphingomyelin, explaining why Ca2+ was a poorer co-factor for the enzyme. The research team also investigated a structurally unrelated portion of the protein from the ion-binding pocket and showed that it sits on the surface of the protein and allows it to bind cell membranes, which would bring it into proximity to the sphingomyelin.

Given the emerging importance of this class of enzymes, and its metabolic byproducts, in disease this structural information should go a long way in helping future research groups identify small molecules that can therapeutically target this class of enzymes.

- Sawai, H, Domae, N, & Okazaki, T. Current status and perspectives in ceramidetargeting molecular medicine. *Current Pharmaceutical Design* 11, 2479–87 (2005).
- Ago, H., Oda, M., Takahashi, M., Tsuge, H., Ochi, S., Katunuma, N., Miyano, M., & Sakurai, J. Structural basis of the sphingomyelin phosphodiesterase activity in neutral sphingomyelinase from *Bacillus cereus. Journal of Biological Chemistry* 281, 16157–16167 (2006).

# Color and light to illuminate biochemical pathways

A new fluorescent label for proteins to reveal greater molecular detail of biochemical pathways

A team of researchers from RIKEN and Hokkaido University have developed a fluorescent label for proteins with a large shift between the colors of light it absorbs and emits (Fig. 1). Their work should allow protein-protein interactions to be tracked more easily, thus revealing biochemical pathways in greater molecular detail.

The new tag can be used in conjunction with existing fluorescent labels in which the color shift is much smaller in the sensitive technique known as fluorescence cross-correlation spectroscopy. The idea is that while both labels can be excited by a single laser, each will fluoresce a different colour. So, two molecular species can be tracked simultaneously.

Fluorescent compounds absorb light at the specific wavelengths, or colors, which provide enough energy to boost electrons to higher energy levels. Light is emitted as the electrons fall back to their normal energy levels. But some energy is always lost as heat in the process, and so the wavelength of the light emitted is always longer, or less energetic, than that of the light absorbed. The difference is known as the Stokes shift.



Figure 1: Absorption (dotted line) and emission (full line) spectra of Keima, the new fluorescent protein label developed at the RIKEN Brain Science Institute.



Figure 2: The stony coral Montipora from which the violet-colored protein used as a basis for Keima was extracted.

Researchers from RIKEN's Brain Science Institute in Wako have worked with colleagues the Research Institute for Electronic Science at Hokkaido University in Sapporo to create the new fluorescent tag that has an absorption energy typical of labels already in use, but a Stokes shift larger than usual, so that its fluorescence is easy to distinguish.

As reported in *Nature Biotechnology*<sup>1</sup>, the team developed the label from a violet-colored protein found in the stony coral *Montipora* (Fig. 2) by changing its amino acid components and side chains at critical points until they generated a family of compounds that exhibited particular characteristics. The researchers have called the fluorescent protein Keima, after a Japanese chess piece that moves in the hopping manner of a knight.

The research team was able to demonstrate Keima's value by using it to follow protein-protein interactions. For instance, by attaching Keima and a cyan fluorescent protein either side of a protein sequence known to be cleaved by a particular enzyme, the researchers could study details of the interaction as the fragments with different colored fluorescent tags broke apart. They also tracked another interaction whereby two tagged compounds came together.

"This is a sensitive and quantitative technique for investigating proteinprotein interactions," says team leader Atsushi Miyawaki. "We are developing it to use in many systems. And pharmaceutical companies are interested in using it."

Kogure, T., Karasawa, S., Araki, T., Saito, K., Kinjo, M. & Miyawaki, A. A fluorescent variant of a protein from the stony coral *Montipora* facilitates dual-color singlelaser fluorescence cross correlation spectroscopy. *Nature Biotechnology* 24, 577–581 (2006).

# Placement of a new piece of the puzzle of cell division

Mud, an evolutionarily conserved protein, links cell polarity with cell division

Some cell types divide symmetrically, bestowing their contents equally upon two progeny. Other cell types divide asymmetrically, giving rise to two progeny that inherit unequal portions of parental cellular content. The choice of symmetry versus asymmetry is determined by the polarity of the cell, which influences the intracellular distribution of proteins, and by the position of the mitotic spindle, which effectively draws a line of division across a cell. Importantly, asymmetrical cell division is hardly the result of imprecision. In fact, the development of many biological systems, such as the neural system, depends on asymmetrical division. There are even indications that loss of asymmetry during cell division can result in a cancer-like state.

Previous work demonstrated that two Drosophila proteins, called Gai and Pins, influence cell polarity and the position of the mitotic spindle. However, the mechanism by which Gai and Pins regulate the cell division machinery was not completely understood. To tackle this question, Fumio Matsuzaki and colleagues at RIKEN's Center for Developmental Biology in Kobe searched for proteins linking Pins to the mitotic spindle, and identified the Mushroom body defect (Mud) protein as a Pin-interacting factor. Their work is reported in *Nature Cell Biology*<sup>1</sup>.

Images of dividing cells revealed that the cellular pattern of Mud localization correlates with the position of the mitotic spindle (Fig. 1). Analysis of cells lacking Pins demonstrated that Mud localization is influenced by Pins, and by components of the mitotic spindle itself. In cells expressing mutant forms of Mud, cell polarity was preserved, but mitotic spindle positioning was awry. These results highlight Mud as a factor essential for coupling cell polarity with mitotic spindle orientation. "This is the first time anyone has been able to show a general mechanism behind the coupling of cell polarity and axis of division," says Matsuzaki. Interestingly, Mud was required for mitotic spindle positioning in both symmetrically and asymmetrically dividing cell types.

The importance of the *Drosophila* Mud protein is suggested by its extensive evolutionary conservation. Both vertebrates and earthworms express Mud homologues, which interact with Pins homologues. Precisely how Mud couples cell polarity to mitotic spindle orientation remains to be investigated. However, these findings "may help us develop new insights into the means by which cells switch between proliferative and differentiative modes of division," notes Matsuzaki.

 Izumi, Y., Ohta, N., Hisata, K., Raabe, T. & Matsuzaki, F. *Drosophila* Pins-binding protein regulates spindle-polarity coupling and centrosome organization. *Nature Cell Biology* 8, 586–593 (2006).



Figure 1: Mud localization (red) regulates the orientation of mitotic spindles (green) in asymmetrically dividing wild-type *Drosophila* neuroblasts, or cells generating daughter cells that mature into nerve cells. DNA is blue.

## Thin membranes tough it out

Molecular sheet could find uses in filtration and fuel cells

A tough, flexible membrane just a few molecules thick has been grown to the size of a large postcard. Such thin sheets have never been grown this big before, and could find a range of uses in nanotechnology, the science of engineering at the molecular scale.

Permeable membranes can be used as filters, for example, while their elastic properties make them useful as sensors, rather like the tight skin of an eardrum.

Previous attempts to make such thin films have mostly been unsuccessful because they are simply too fragile. The thinnest membranes that can cover a significant area are generally several hundred nanometers (billionths of a metre) thick.

But Toyoki Kunitake and colleagues at RIKEN's Frontier Research System in Wako, have now developed a tough membrane just 35 nanometers thick, with an area of 16 cm<sup>2</sup>.



Figures 1a and 1b: These optical micrographs show how the nanomembrane can be sucked through the tiny tip of a pipette.



Figure 2: The thin film, supported by a wire loop, does not become brittle even when it dries out.

The membrane is made from a mixture of zirconium oxide and various carbon-based polymers. Combining these ingredients in just the right proportions produces a sheet that is surprisingly strong yet incredibly thin, they report in the journal Nature Materials<sup>1</sup>. "And we can make much bigger sheets, if a larger apparatus is available," says Kunitake. The team found that when the membrane was floating in a pool of alcohol, it was flexible enough to be sucked into the tip of a tiny pipette, folding up like a wellpacked parachute as it passed through a hole some 30,000 times smaller than the sheet itself (Fig. 1).

One previous problem with thin films is that they usually become brittle when allowed to stand in air rather than in a protective bath of solvent. But the team's membrane retained its strength for several months even when it was hung out to dry (Fig. 2). In a final feat of strength, the dry film was placed over the end of a glass tube and used to support a column of alcohol that weighed about 70,000 times more than the film itself. The membrane was slightly permeable, allowing one drop of the liquid to seep through every ten seconds or so.

The scientists say this is a good sign that their sheet could be useful as a separation membrane, allowing certain molecules through while keeping others back. This process is also crucial to developing more efficient fuel cells, an environmentally friendly source of electricity that relies on the steady flow of charged ions from one chamber to another.

Vendamme, R., Onoue, S-Y., Nakao, A. & Kunitake, T. Robust free-standing nanomembranes of organic/inorganic interpenetrating networks. *Nature Materials* 5, 494–501 (2006).

# Novel genetic link found for familial degenerative hip arthritis

Genetic detectives link a type of devastating hip arthritis to novel chromosome location

Moving freely by walking is a remarkable ability almost all of us enjoy. But disease can claim victim the ability to walk, especially as we age. Degenerative arthritis of the hip joint (hip OA), for example, can cause extreme pain, inactivity and complete crippling. The causes of hip OA vary, but some types of the disease are found clustered in families, which strongly indicates a genetic cause.

In *The American Journal of Human Genetics*<sup>1</sup>, Shiro Ikegawa and colleagues at RIKEN's SNP Research Center, in Yokohama, describe evidence from a large Japanese family for a genetic cause of a new type of familial hip OA. The new information may help unravel the cause of this and other types of hip OA—a collection of diseases that affects thousands of people, especially of French and Japanese descent.

The new study is akin to a detective story and the search for the cause of an elusive menace. The menace is hip OA. The investigators are detectives seeking medical information that might provide a clue about a genetic link to hip OA. One difficulty is that not all types of hip arthritis are the same. Many types of



Figure 2: The graph indicates the family tree of the disease, with affected individuals in black and unaffected siblings and relatives in white. Males are represented by squares and females by circles.

hip inflammation occur; there are even different types of hip arthritis.

But some forms of hip OA have a clear genetic component, which is determined by the frequency of hip OA in immediate family members and the 'dominant' appearance—like hair color—of the disease. Ikegawa and colleagues found such evidence in one patient and her family (Fig. 1 and 2). "An elderly Japanese woman had been seeing a doctor, one of the co-authors," says Ikegawa. "One day she was asked about her family. It was a start."

A detailed family history revealed a genetic link to crippling hip OA, usually beginning in adolescence and worsening over time, often requiring surgical hip-joint replacement. Painstakingly, Ikegawa and colleagues spent two years working to find that the affected members of the Japanese family almost certainly have a single mutation on chromosome 13 that is responsible for the disease.

"This is the starting point for identifying a [new] hip OA gene, which could lead to innovative treatment," says Ikegawa. Although hip OA is not yet cured, the cause of this devastating disease may now be closer at hand through the work of science detectives like Ikegawa and his group.

 Mabuchi, A., Nakamura, S., Takatori, Y. & Ikegawa, S. Familial osteoarthritis of the hip joint associated with acetabular dysplasia maps to chromosome 13q. *The American Journal of Human Genetics* 79, 163–168 (2006).



Figure 1: An X-ray (autoradiograph) of diseased hips (left) that were replaced by surgery with artificial, metal joints (right).

## Seeking the full story on spin

The origins of the fundamental properties of particles in the core of atoms continue to puzzle scientists

Protons and neutrons, commonly referred to as nucleons, are fundamental particles of nature. Together with the electron they comprise most of the atoms that form the world we live in.

Unlike electrons, nucleons consist of even smaller subparticles, the quarks. Typically, it is the properties of quarks that determine nucleon properties. However, scientists are puzzled by a physical property of quarks known as spin. A concept from quantum physics, spin can be loosely compared to an intrinsic rotation of particles. What vexes scientists is simply that nucleon spin does not add up by counting only the contributions from the quark spins.

A team of RIKEN researchers, as part of a large international collaboration known as PHENIX, is on the hunt for a possible explanation. The general belief is that, at least in part, another species of particle within nucleons—the gluons could be responsible.

To confirm this, the PHENIX team conducted experiments at the Brookhaven National Laboratory in the USA which operates a high-energy particle accelerator ideally suited for this task. "We used one of the most sensitive ways to measure gluon spin in a proton," explains Yasuyuki Akiba from RIKEN's team. The experiments involve protons that collide at extremely high energies. As a result, a large number of new particles are produced. "About 500 Terabytes, or about 100 000 DVDs, of data are created annually," says Akiba.

Key to these measurements is the exact alignment of the proton spins. This is achieved with a 'snake' magnet (Fig. 1) whose rotating magnetic field causes the random proton spins to align as the beam of the high-energy particle accelerator passes through the magnet.



Figure 1: One of the 'snake' magnets that is necessary to produce high-quality proton beams.

"Design of the magnet was challenging due to the severe limitations on the length of the equipment," explains Masahiro Okamura from RIKEN who built the magnet. While the gluon spin has been measured previously, the improved beam polarization achieved by the new snake magnet led to more precise results. Their findings are published in *Physical Review D*<sup>1</sup>.

Now confident that gluons contribute to some of the nucleon spin, but not enough to explain all of it, the research team continues the search for contributions from more exotic particles within the proton. Initial experiments, using further refinements, have recently been reported in *Physical Review Letters*<sup>2</sup>. With the final explanation of the nucleon spin eluding scientists, international efforts like the PHENIX collaboration will be required to solve this intriguing fundamental problem.

- Adler, S. S., Afanasiev, S., Aidala, C., Ajitanand, N.N., Akiba, Y., Al-Jamel, A., *et al.* Improved measurement of double helicity asymmetry in inclusive midrapidity π° production for polarized *p* + *p* collisions at √*s* = 200 GeV. *Physical Review D* 73, 091102(R) (2006).
- Bai, M. Roser, T., Ahrens, L., Alekseev,
  I.G., Alessi, J., Beebe-Wang, J., *et al.* Polarized proton collisions at 205 GeV at RHIC. *Physical Review Letters* **96**, 174801 (2006).

## Nguyen Dinh Dang Embracing art and science

#### A Vietnamese nuclear physicist at RIKEN is also an accomplished painter

Art has always been important to Nguyen Dinh Dang. He began learning to draw at just five years old and soon became an outstanding student. Blessed with artistic talent and an unfaltering passion, Dang could have become a professional painter. However, restrictions on artistic work and the difficulty in making a living as a painter in the war-time Vietnam led him to pursue a career in science. But, art remained a lifelong interest. Even the Vietnam War and a lack of materials didn't dampen this native of Hanoi's passion for painting.

"Many people claim themselves painters, but the most difficult and beautiful thing is the mystery of the universe. Only few people can comprehend this," says Dang, who is now an Accelerator Research Scientist at RIKEN's Nishina Center for Accelerator-Based Science in Wako.

Good at mathematics and physics, Dang was among the students who topped the entrance exams to Vietnam's national universities in 1975, and got the state scholarship to study abroad. He chose to enroll in 1976 in one of the world's best institutions for studying basic sciences — the Moscow State University.

Dang recalls he visited excellent fine-art museums, and devoted himself to painting on vacations during his time in Moscow. Academically, he earned two doctoral degrees: a PhD and a Doctor of Physics and Mathematics Sciences at the Moscow State University.

Dang spent his postdoc in Germany and Italy in the early 1990s. While in Italy, Dang was surprised to receive a letter asking him to apply for a scholarship in Japan. He realized later that this was the result of a recommendation by his former PhD supervisor Vadim Soloviev, a renowned physicist at the Joint Institute for Nuclear Research in Dubna, Russia.

Returning home from Italy, Dang organized Vietnam's first large-scale international conference in nuclear physics in spring 1994. There he met Akito Arima, the then president of RIKEN and prominent nuclear theorist. "Dang is multi-lingual, presents opinions clearly and has a firm grasp of physics," Arima recalls.

#### Studying the behaviors of nature's building blocks

Many physicists, including Dang, are investigating how atomic nuclei behave under unusual conditions. A nucleus consists of protons and neutrons, and forms the core of an atom. Nuclei are stable when protons and neutrons have the right balance. But nuclei easily become unstable when they have large deformations, or many more neutrons than protons. They even heat up at high excitation energies. Although the properties of stable nuclei have been well-studied, those of nuclei under extreme conditions largely remain a mystery. Further unveiling the structure of these nuclei could provide a better understanding of how the universe was created.

One of the important features of nuclei is 'giant resonance'. It is an oscillation, which involves many nucleons, at a certain frequency around the equilibrium shape of the nucleus. Depending on the type of oscillations, the status of giant resonances differs. "By studying these properties we can learn a lot about nuclei," Dang says.

The most prominent giant resonance is a collective oscillation of all protons against all neutrons in a nucleus. This type of resonance, called 'giant dipole resonance' (GDR), was discovered about 70 years ago in photonuclear reactions. Dang has been studying nuclear GDR since the early 1980s and building his expertise in different countries.



**Figure 1:** The photoabsorption cross section of GDR has a typical bell shape, whose width depends on temperature. In 2003, compared to their 1998 predictions (green line), Dang and Arima achieved theoretical results (red) much closer to experimental systematic (data points) for the GDR width.

#### Helping end a three-decade debate

Arriving in Japan in 1994, Dang took up a 10-month fellowship at Tokyo University's Institute for Nuclear Study. Meanwhile, Arima asked him to work at RIKEN, where he moved in 1995, to tackle a controversial issue related to a giant resonance called the Gamow-Teller resonance. This resonance is created by neutrons that spin upwards (or downwards) as they oscillate against protons that spin downwards (or upwards), and plays a key role in neutrino physics and astrophysics since it affects the initial dynamics of a collapsing supernova.

The controversial issue was that experimental observations showed only about 60% of the strength of the resonance that was predicted theoretically. Researchers around the world were divided between two explanations for this discrepancy. Arima was a vocal supporter of the simpler explanation, which does not involve non-nucleonic degrees of freedom, but had a limited influence on the debate.

In 1997 researchers at the Research Center for Nuclear Physics in Osaka succeeded in producing definitive experimental results that supported Arima's theory. Concurrently, Dang proposed a new model that combined RIKEN's cutting-edge computer

power with a microscopic approach. The results of his theoretical calculations neatly described the experimental data<sup>1</sup>. The three-decade debate was almost over, as Arima's group became closer to fully explaining the gap.

Dang then began to focus on his long-term interest in the GDR in nuclei that heat up as they are formed in heavy-ion fusion or other reactions. Scientists are puzzled because, while at moderate temperature the width of GDR extracted from

these 'hot nuclei' increases with temperature, it stops expanding when the temperature reaches a certain value. Despite many attempts, physicists have failed to offer a consistent description of the phenomenon.



**Figure 2:** "In my mind, I am always a small child to my parents, who are old and weak but their love for me and each other is so immense that they are associated with the image of the ocean in winter," Dang says. He won the title 'Fine-Work Artist' at the 41st annual exhibition of the Individual Artist Association for this painting.

In 1998, Dang and Arima proposed a new model to clearly explain the thermal behavior of GDR. The results of their calculations described well where the width expands and where it saturates<sup>2</sup> (Fig. 1). In 2003, they elaborated on their theory and became the first to show an important effect of the nuclear superconducting property that provided a more comprehensive explanation of the phenomenon<sup>3</sup>. Encouraged by the success in the study of hot nuclei and GDR, Dang has been applying the model to other types of resonances.

#### **Blessed with an artistic life**

In addition to enhancing his stellar scientific career, the move to Japan gave Dang great opportunities to hone his artistic skills. "Only in Japan I could establish a life that includes painting regularly," he says. In 1995, he resumed painting after a four-year break, and has since held a number of solo and joint exhibitions. He says once he gets an idea, he spends nights and weekends painting.

For the past two decades, Dang's painting has shifted from impressionism to surrealism, whose most eminent representative, Salvador Dali, remains one of Dang's favorite masters. "Surrealism

> is the way I can express my ability the best," he says. In one recent painting titled 'Winter Ocean', he painted himself along with his mother giving a piece of banana to his father (Fig. 2). The two couples in the background are also his parents in their Parisian student days. Dang was twice named as a 'Fine-Work Artist' at the exhibition of the Individual Artist Association held annually in Tokyo. In November, Dang plans to hold a group exhibition with 12 Japanese artists in Hanoi.

Dang says it's not important to explain the literal context of any artwork. But feeling matters everything. "In the creative process of both art and science, the most important thing is intuition. You feel something intuitively. You cannot explain how it comes to you," he says.

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#### About the researcher

Nguyen Dinh Dang was born in 1958 in Hanoi, and graduated from the Moscow State University in 1982. He received his PhD in nuclear physics in 1985, and his doctor of physics and mathematics sciences in 1990 at the same university. He came to Japan in 1994 as a research fellow of the Nishina Memorial Foundation and joined RIKEN in 1995. Currently, he's an Accelerator Research Scientist at RIKEN's Heavy-Ion Nuclear Physics Laboratory, Nishina Center for Accelerator-Based Science. Dang is also serving as a senior scientist at the Institute for Nuclear Science and Techniques of the Vietnamese Atomic Energy Commission, where he got his permanent position in 1982. Dang is a member of the Fine-Arts Association of Vietnam and Japan's Individual-Artist Association. He also speaks fluently Vietnamese, English, Russian, and French. His personal website is http:// rarfaxp.riken.go.jp/~dang/

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## **Completing superstring theory —the ultimate theory of matter**

#### Hikaru Kawai

#### **Chief Scientist**

Theoretical Physics Laboratory Sub Nuclear System Research Division Nishina Center for Accelerator Based Science RIKEN Wako Institute

What is matter? What is force? What is space-time? In the near future, the answers to these long-asked questions may be found in the ultimate superstring theory. When completed, this theory alone will provide a clearcut explanation for all the phenomena in nature, even providing solutions to the riddle of the birth of the universe. "I had expected that superstring theory would have been completed slightly earlier, but it will not take long to reach the goal," says Hikaru Kawai, chief researcher in the Theoretical Physics Laboratory at the Sub Nuclear System **Research Division of RIKEN's Nishina Center for Accelerator-Based Science. He** is now working to complete superstring theory using a matrix model.



#### What is the ultimate theory?

"When I was a fifth-grade student in elementary school, I stumbled upon a book on my father's bookshelf titled 'Evolution of Physics' by Albert Einstein and Leopold Infeld, translated into Japanese in the Iwanami Shinsho Series. Although I could not understand what was written in the book, I was deeply impressed by the power of physics to solve various problems solely by means of thought." Thus aspiring to be a physicist, Kawai is now working to complete the 'ultimate theory' that could not be perfected by Einstein, although he had been dreaming of doing so all his life.

In physics, research into matter at increasingly smaller scales has been undertaken essentially in pursuit of a theory that will provide a unified explanation for the nature of elementary particles, which represent the smallest units of matter, and the forces exerted between elementary particles. At the end of the 1970s, the theory was almost completed, and later at the beginning of the 1980s, experiments confirmed the theory. At present, this theory is known as the 'standard model.'

"To date, there has been no experimental data demonstrating that the standard model is wrong. However, the model has two major drawbacks."

One concerns the necessity to substitute several tens of parameters, including the electron mass and the gravitational constant, into the equation. The standard model does not enable theoretical derivation of values for the electron mass, the gravitational constant and other parameters.

Another concerns the inability to explain clearly how gravitational forces work in the world of elementary particles. In addition to gravitational forces, there are three forces in nature: electromagnetic forces, the strong force,





and the weak force. Although these three forces have been explained in a unified fashion by the standard model, gravitational forces are the only type of force that cannot be successfully incorporated into the standard model.

"To unify gravitational forces with the other three types of forces and to derive values for the several tens of parameters essential to the standard model from a formula having absolutely no parameters —that's the ultimate theory we have been pursuing. The most promising candidate for the ultimate theory is 'superstring theory' (Fig. 1)."

#### From a 'point' to a 'string'

The major difference between the standard model and superstring theory resides in the fact that the smallest unit of matter is assumed to be a point of zero size in the standard model and a stretchable string in superstring theory (Fig. 2). What is meant by a shift from a point to a string?

For example, different points can approach each other infinitely closely, in which situation the gravity value is calculated to be infinite—an unrealistic solution. This infinity issue prevents the standard model from incorporating gravitational forces successfully. "An extended string obviates the necessity for assuming a situation that produces an infinite value. Hence, gravitational forces can be naturalistically incorporated into the ultimate theory."

However, superstring theory involves a major drawback. Our universe is fourdimensional space-time, comprising the three dimensions of space and the one dimension of time, and superstring theory cannot be described without mathematical contradiction unless tendimensional space-time is assumed. For this reason, superstring theory has long been neglected due to its inability to explain the real universe, and has been studied by only a few researchers.

#### **Evolution of superstring theory**

In 1984, the situation changed dramatically. It was found that an assumption known as 'space-time compactification' to round off the excess six of the ten dimensions would enable the derivation of something like the fourdimensional space-time shown by the standard model from superstring theory.

"In those days, I was a student at Cornell University in the U.S. I speedily organized a study group and began research into superstring theory. Researchers were all obsessed because they felt they their own work might soon be forestalled by someone completing the theory before them unless they speeded up their research."

However, this first boom settled down after a few years. Because it had been impossible to accurately formulate



superstring theory, there were wide variations in the number of dimensions and methodology for compactification, resulting in the derivation of a very large number of space-times with various dimensions. For example, many fourdimensional space-times were derived by compactifying six dimensions, each of which appears to be similar to, but somewhat different from, the fourdimensional space-time shown by the standard model.

A clue to solving this problem started to emerge in 1995, when the second boom started. Relationships between the various space-times derived from superstring theory began to be clarified. The individual space-times appear distinct from each other because they are all viewing the one theory from different aspects.

Furthermore, M-theory emerged in splendid style. In M-theory, the minimum unit of matter is taken to be a two-dimensional membrane, rather than a one-dimensional string. The theory is eleven-dimensional, having an extra dimension. As such, M-theory was increasingly expected to unify the variety of space-times derived from superstring theory. Because of the additional dimension, however, the theory is more difficult to formulate accurately than before. "Most recently, an increasing number of researchers think that M-theory represents no more than the ultimate state of the string."

### Completing superstring theory using a matrix model

Now that the second boom has passed, research into superstring theory seems to have stagnated somewhat. Can we expect the arrival of a third boom that will lead to the completion of superstring theory?

"I believe that superstring theory will be completed in the near future," says Kawai with confidence. How is he planning to complete the theory?

"Superstring theory can be developed without mathematical contradiction, even in the context of two dimensions or less. Because we are living in a fourdimensional world, superstring theory, which assumes two dimensions, is a 'toy theory' that cannot explain reality. Around 1990, however, it was found that the two-dimensional setting would enable completion of superstring theory thanks to the mathematical simplicity. The idea that emerged at that time was a model based on a matrix, which is taught even in highschool mathematics."

Kawai encountered the matrix model when he was a student at graduate school. In 1984, while in his 20s, he received the Nishina Prize for his prominent achievements in research into the standard model using a matrix model.

"Using the matrix model, the behavior of the string can be expressed very closely. Although some researchers say that ten-dimensional superstring

### Figure 2: A moving string as the minimum unit of matter

At present, the electron and quark are considered to represent the smallest units of matter. The standard model assumes that a point is the smallest unit, whereas superstring theory assumes a string. The string turns into a quark after entering one mode of vibration and an electron after entering another mode.

theory cannot be completed with our currently-available knowledge of mathematics, I do not think there is any relationship between the essentials of physics and mathematical complexity. A slight improvement in the II B matrix model we have discovered (Fig. 3) would result in the completion of superstring theory. The formula thus established would be understandable even by high-school students."

Then, can the rightness of the completed superstring theory be demonstrated? "Deriving accurate values for the several tens of parameters essential for the standard model from a formula with no parameters would be sufficient to demonstrate the theory. However, to demonstrate experimentally the existence of strings, an enormous level of energy-say 1015 times higher than the level achievable using current accelerators—is required. Because the energy generated by accelerators has been increasing about 10-fold every decade, strings may be visible in 150 years time-in the mid-22nd century-though this may be an optimistic prospect."

### The 50th universe that produced human beings

Capable of explaining all the phenomena in nature, superstring theory is expected to solve the riddles concerning the birth and evolution of the universe. In the midst of the second boom of research into superstring

$$S = \frac{1}{g^2} \left\{ -\frac{1}{4} \sum_{\mu,\nu} \operatorname{Tr} \left[ (A_{\mu}, A_{\nu})^2 - \frac{1}{2} \operatorname{Tr} \left( \overline{\Psi} \Gamma^{\mu} \left[ (A_{\mu}, \Psi) \right] \right) \right\}$$

Figure 3: II B matrix model discovered by Kawai and his group

theory, a unique idea called the 'brain world' was proposed, which assumes our four-dimensional universe to be enclosed like a membrane in the tendimensional world. However, Kawai clearly denies this idea, saying, "I do not believe it, although it is one possibility."

Kawai has proposed a 'cyclic universe theory' jointly with Masao Ninomiya and Masafuni Fukuma, who are physicists at Kyoto University.

"Capable of explaining

all the phenomina in

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in the near future."

The currently widelyaccepted theory of the birth of the universe assumes that the universe was of sub-micron sizethe size of an elementary particle-just after its birth, and soon underwent a rapid expansion known

as inflation to grow into the big-bang universe, or a fireball of macroscopic size between one millimeter and one meter (Fig. 1). "Although inflation may actually have occurred, a special premise is essential for that to be true. As a researcher into elementary particle theories, I cannot accept this passively."

Available observations of the present universe make it certain that the bigbang universe measured between one millimeter and one meter. If inflation did not occur, then how did the bigbang universe become as large as to be visibly perceivable? This question is answered by the cyclic universe theory.

After expansion, when the density of matter becomes high, the universe enters

a stage of contraction due to gravity, finally converging to a single point. This is called the 'big crunch'. In the traditional theory, it is considered that the universe will become extinct once the big crunch has occurred. It should be noted, however, that according to superstring theory, the big crunch is followed by another big bang and the universe begins expanding again.

"It is thought that the universe may

have been repeating cycles of contraction and expansion-the big crunch and the big bang-repeatedly. theory will be completed Furthermore, the bigbang universe grows about four times larger with every cycle. Some

> 50 cycles of expansion and contraction should result in a size for the big-bang universe of between one millimeter and one meter."

> According to the cyclic universe theory, the lifespan of the universe increases about eight times with every cycle of expansion and contraction. The age of the present universe is estimated to be about 13.7 billion years, and the lifespan of the one-generation-older universe is estimated to be about 3 to 4 billion years, which seems too short for intelligent life to come into being. It is likely that we human beings are able to exist because the universe has had a long lifespan through repeated cycles of expansion and contraction. However,

Kawai says, "the cyclic universe theory is no more than a tentative assumption, and I do not insist that it is right."

We are living in the most exciting era of physics, one in which superstring theory is about to be completed to dramatically contribute to solving the riddle of the universe and clarifying the reason for the existence of human beings. It is hoped that in the near future Kawai's laboratory will announce revolutionary progress that will go down in the history of physics. 

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#### About the researcher

Hikaru Kawai was born in 1955, and graduated from the University of Tokyo's Department of Physics in 1978. In 1983, he earned his doctorate in physics from the same university. In 1982, he became a postdoctoral research associate at Cornell University and then an assistant professor in 1984. In 1988, Kawai was appointed as an assistant professor at the University of Tokyo's Department of Physics and a professor at the current High Energy Accelerator Research Organization (KEK) in 1993. In 2001, he became the chief scientist at the Theoretical Physics Laboratory, RIKEN's Nishina Center for Accelerator-Based Science. He has been concurrently serving as a professor of the Graduate School of Science, Kyoto University, since 1999.

### Molecular Imaging Program is ready for full-scale operation

An agreement was concluded between RIKEN and the City of Kobe in July to collaborate in the promotion of a new research program, the Molecular Imaging Program, which is to be based at the Kobe Medical Industry Development Project, and which was launched earlier this year, 2006. The agreement will take the Program one step closer to full-scale operation.

The Program aims to accelerate the drug design process using a novel method involving the analysis of the molecular dynamics of drugs in vivo utilizing molecular imaging, an important technology used in positron emission tomography. With the unprecedented advantage of domestic access to two cyclotrons, the Program hopes to capitalize on one of Japan's main strengths—chemical synthesizing technology —to develop methodologies for the creation of novel PET tracers more efficiently than ever before possible. Newly devised PET tracers will be evaluated for their efficiency in the delivery of a drug to its target prior to permitting supply for practical use. One of the most important characteristics of the Program is its use of primates for in vivo experimentation.

The Program, located in the Kobe Medical Industry Project district, will collaborate with both the RIKEN Center for Developmental Biology in the promotion of generic research, and with the Foundation for Biomedical Research and Innovation in carrying out clinical trial assessment, and endeavor to cultivate research talent experienced in academic, industrial and public collaboration on a national level. The Program's facilities are currently under construction, and expected to be completed within the year. The Program is expected to go into full swing in January, and planning to organize an international symposium to take place thereafter at a yet undetermined time.

### The increasing visibility of RIKEN's female researchers

The RIKEN Discovery Research Institute's Aiko Takamine, a student from the University of Tokyo, is the first recipient of the L'OREAL-UNESCO for Women in Science Japanese Fellowship, an award that supports young female scientists working in material or life sciences. The prize acknowledged Dr. Takamine's development of an rf ion guide that aims at the study of proton and neutron distributions in unstable nuclei.

Takamine is not the only women at RIKEN to gain attention recently. In 2005, fifteen women were awarded various prizes by organizations within and outside of Japan. In fact, the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT) commended the activities two RIKEN women, and another was honored by the Society of Japanese Women Scientists.



Akiko Takamine (left side) and other two winners

"I think I was able to earn the award thanks to the better research environment at RIKEN, including RIKEN's excellent staff and world-class facilities," said Takamine about winning the Women in Science fellowship. "The machine we have developed will be incorporated into one of the principal facilities of RIKEN RI-beam factory. I hope that I would continue my research as a member of RIKEN."

#### Yokohama Science Salon

The third Science Salon was held on July 20 at RIKEN Yokohama Institute. At this annual event, eminent guests from within RIKEN and outside, and from science and other fields, give talks on a wide range of important and interesting subjects. People living in Yokohama and from companies nearby are also welcomed to the campus for this event.



Shuji Nakamura (furthest on the right), talking with participants after the lecture

The guest speaker was Shuji Nakamura, a materials scientist at the University of California, Santa Barbara (UCSB). Nakamura is famous for having invented blue LEDs, during his time in a Japanese company before he moved to UCSB. In Japan, the remuneration awarded to inventors is very low, and so Nakamura decided to take his employer to court over the amount he received for this major invention.

Nakamura said that Japanese researchers need to be more aware of their own rights when they make inventions and that by starting venture companies they could not only make more money themselves, but also bring long-term benefits to the country as a whole. The audience of 200 listened with great interest. In particular there were several good questions about researchers' lifestyles. Afterwards people commented that, "I found out about the differences in the American and Japanese research environments," and "It was a stimulating talk."

#### Summer Party 2006 at the Wako Institute

The annual RIKEN Summer Party was held on July 7, with the aim of promoting friendship between

people at RIKEN and everyone who works with the institute to provide support for its foreign researchers. Guests were invited from Wako city, Saitama prefecture, local schools and hospitals, and the various embassies in Tokyo. July 7 is also the date of the Tanabata festival, when Japanese people traditionally write their wishes on small pieces of paper and hang these on bamboo trees, and at the party this year there was a large and beautifully decorated bamboo tree on display.

The party was buffet-style, and more than 400 people were in attendance. RIKEN President Ryoji Noyori could be seen talking with some of RIKEN's young researchers from overseas, embassy staff, and the mayor of Wako, Minoru Nogi. A number of foreign ladies were wearing colorful yukata, summer kimonos. The room was filled with the sounds of cheerful conversation in English, French, and Chinese, as well as Japanese, and everyone seemed to enjoy the pleasant atmosphere.



## Stepping into the future—Japan's cyclotron, Part II

For the past few decades, researchers at RIKEN have aimed to create a world-leading, massive cyclotron facility. Their unflagging endeavor will come to fruition next year

RIKEN's fourth cyclotron supported Japan's research on nuclear physics for 24 years until its closure in 1990. But, soon after its launch in 1966, its successor was already within the sights of researchers.

The fourth cyclotron, equipped with a magnet pole of 160 centimeters in diameter, came to the fore in the mid-1970s when nuclear physicists were paying greater attention to heavy ions. Although it was Japan's first cyclotron to accelerate heavy ions, its capacity was limited to a lighter group of heavy ions, and the energies produced were low.

Worldwide researchers were experiencing similar problems to RIKEN, so they began building the nextgeneration accelerators capable of handling heavier ions with higher energies from the mid-1970s through the 1980s. At RIKEN, a team led by Hiromichi Kamitsubo pursued an idea to combine two injectors with a separated sector cyclotron, called a ring cyclotron; the aim was to accelerate all the atomic elements from proton to uranium in the periodic table.

Development of the ring cyclotron system was a huge project in both size and expense. So RIKEN proceeded step-by-step by first building RIken LineAC (RILAC)—an injector that is a linear accelerator. Then in 1975, RIKEN started to research the design of the ring cyclotron and requested, in 1979, a total of 13.5 billion yen from the government. But due to the hefty amount, the funds came only after tough negotiations with government officials. RIKEN won the budget in 1980.

The ring cyclotron has four sector-form magnets placed like a ring so it can focus high-energy beams better than a conventional cyclotron.

The two injectors are used to accelerate particles before putting them into the ring cyclotron. One is RILAC and the other is an azimuthally varying field (AVF) cyclotron designed to accelerate lighter ions. Combining the injectors with the ring cyclotron led to the efficient generation of high-energy beams.

RILAC was completed in 1981 to become the world's first frequency-variable, heavy-ion linear accelerator (linac). The ring cyclotron began operation in 1987 and the AVF cyclotron in 1989. This equipment is a set of RIKEN's fifth generation cyclotron facility.

Later, key devices were developed and added at the accelerator's facility. An example is the RIKEN Projectilefragment Separator (RIPS), the world's first fully fledged machine to produce high-energy radioactive isotope (RI)



Cyclotron researchers get together to celebrate the completion of the first ring cyclotron.

beams in combination with the ring cyclotron. This paved the way for deeper insights into nuclear structure research and nuclear astrophysics.

Researchers have been using heavy-ion beams for various other fields of research, including the investigation of the effect of such beams for on cancer cells as well as the creation of plant mutations.

RIKEN researchers also became the first in 2004 to discover the element with atomic number 113, the heaviestever created, by using RILAC and a novel nuclei separator, called the gas-filled recoil separator (GARIS).

In recognition of the increasing importance into radioactive isotopes, in 1995 RIKEN researchers embarked on an ambitious plan to create a massive RI Beam Factory at the site of the '160 cm cyclotron', which had already been shutdown. They aim to produce 3,000 kinds of RI beams for all the atomic elements using heavy ions up to uranium accelerated at much higher energies than before. In addition to existing cyclotrons and other devices, the RI Beam Factory will house two additional room-temperature ring cyclotrons and the world's most powerful superconducting ring cyclotron. Stepping into unexplored fields of nuclear physics, the researchers plan to obtain the first beam with uranium ions by the end of this year.



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