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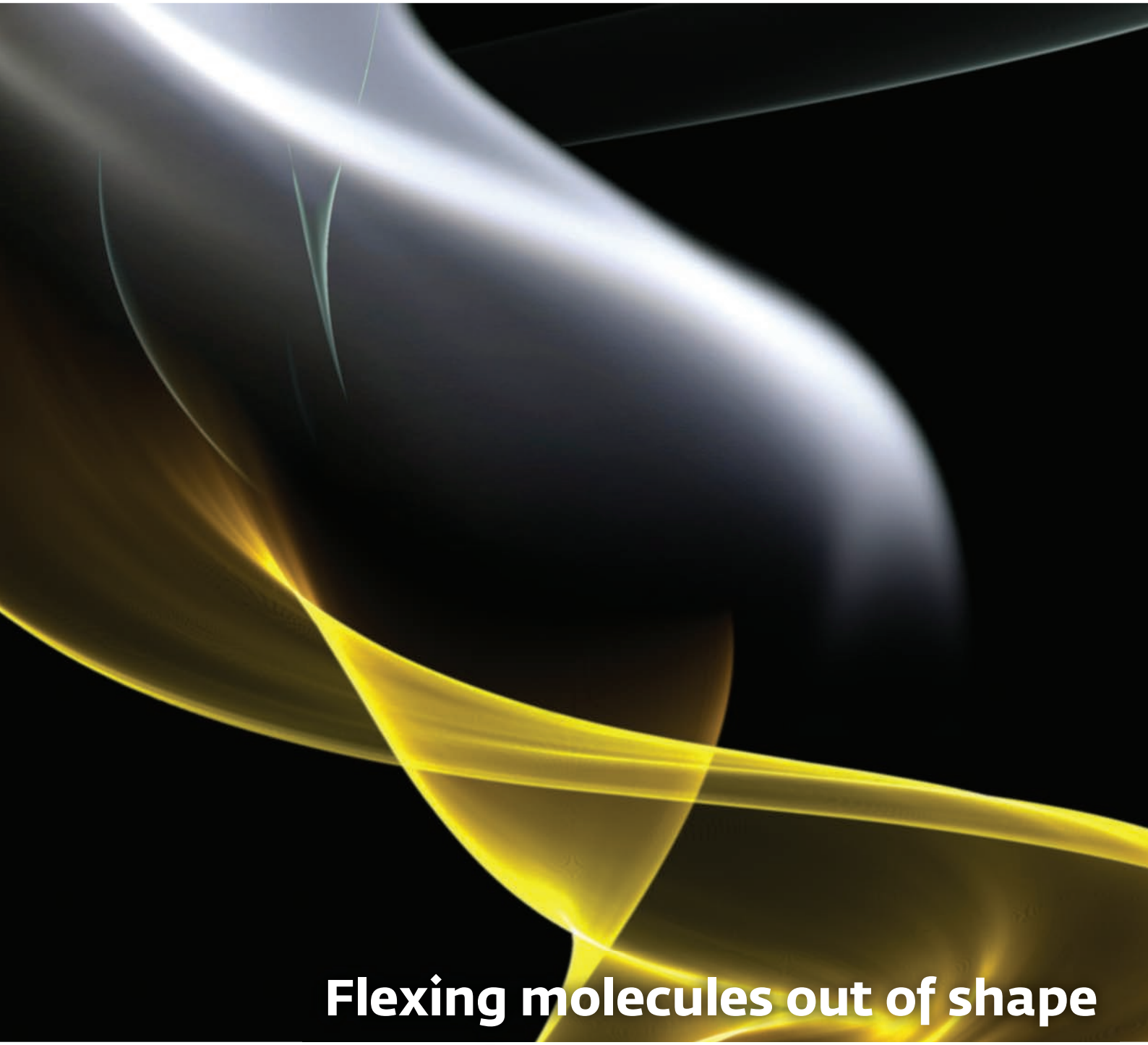

Flexing molecules out of shape

RIKEN

Physics

Discovering magnetic powers

Novel optical devices may result from the recent demonstration of the coupling of electric and magnetic fields in a light-absorbing material

For decades, scientists have studied a class of materials called 'multiferroics' in which static electric and magnetic structures are coupled to each other. This allows capabilities such as controlling magnetic order with electric fields instead of magnetic ones, making it easier to build devices such as sensors and computer memory.

The dynamic equivalent of this static coupling, or the linking of the electric and magnetic fields of excitations inside materials, would expand these capabilities even further. However, observations of dynamic coupling have been rare and coupling strengths weak. Now, researchers in Japan have observed strong cross-coupling of dynamic excitations in multiferroic materials called rare-earth perovskites[1]. The work has revealed optical properties in opto-electronic materials similar to those found in common dichroic glass (Fig.1), and may make possible new types of optical devices.

Figure 1: Dichroic glass used in jewelry produces different colors from light beams that travel along different paths. Similarly, rare-earth perovskite materials with dynamic cross-coupling between magnetic and electric fields have optical properties that depend on the direction of light.

Control via coupling

At the microscopic level, the electric and magnetic field structures inside any material are complicated. Small displacements of electrons from their equilibrium positions cause electric polarization and create associated electric fields. Similarly, electrons have either a 'spin up' or 'spin down' magnetic configuration that can produce magnetic fields, or dipoles. These electric and magnetic fields can be aligned randomly, or they can form complex, large-area structures useful for devices, explains Youtarou Takahashi from the Japan Science and Technology Agency and the RIKEN Advanced Science Institute, who led the team that observed the dynamic cross-coupling.

The microscopic electric fields in 'ferroelectric' materials, for example, are organized into domains containing millions of atoms. The fields inside a single domain point in the same direction, which can be set with an externally applied electric field. Since information can be stored in the domain orientations, scientists are studying ferroelectrics as candidates for next-generation, ultra-high-density storage. Similarly, microscopic domains in ferromagnets align into domains that can be controlled with an external magnet.

In most devices made from ferroelectric and ferromagnetic materials, like controls like: electric fields control electric

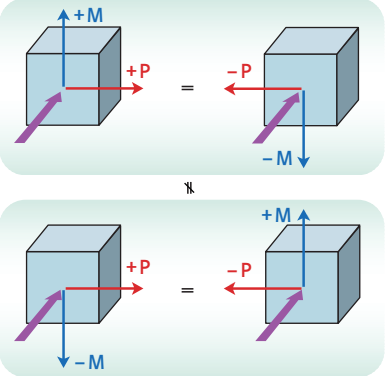

Figure 2: A schematic diagram of directional dichroism behavior. A rare-earth perovskite (black blocks) absorbs light (purple arrows). The internal magnetic (M) and electric (P) fields of the perovskite interact with the light according to their orientation relative to the light. As a result, the strength with which the perovskite absorbs light depends on the light's direction. Absorption strengths are equal for configurations connected by a '='.

domains, and magnetic fields control magnetic domains. In multiferroics, however, electric fields control magnetic structures and vice versa. This is useful because magnetic fields are more difficult to create and control at small scales than electric fields. The ability to move beyond static cross-coupling, and link the electric and magnetic field components of a time-varying excitation, could yield additional capabilities, such as control over the absorption of light and its direction.

Getting excited

Takahashi, along with colleagues from the University of Tokyo and the RIKEN Advanced Science Institute, observed strong, dynamic coupling by studying how rare-earth perovskite materials absorb light at terahertz frequencies. The microscopic magnetic field components, called spins, in these materials arrange spontaneously into a helix. Because light consists of oscillating electric and magnetic fields, its absorption can distort the material's atomic lattice.

Other researchers had previously observed that light absorption in rare-earth perovskites established a transient electric field that distorted the magnetic spin helix structure by modulating the interactions between neighboring spins. However, the reverse coupling did not exist—the magnetic distortion, or excitation, did not affect electric polarization—so the excitation was not mutually cross-coupled, Takahashi notes.

Takahashi and colleagues extended these results by changing the orientation of the incident light relative to the perovskite atomic lattice. They exploited the fact that rare-earth perovskites have an inherent electric field, or polarization, which results from a combination of their helical spin structure, and a 'spin–orbit' interaction that couples the orbital motion of electrons to electron spin. They found that, when they oriented the electric field of the incident light perpendicularly to the material's inherent electric field, a truly cross-coupled excitation resulted.

This cross-coupling resulted from the fact that the perovskite's inherent electric field was derived entirely from its helical spin structure: when it was affected by the light field, the spin structure was affected. And when the spin structure distorted, it in turn changed the electric field. The researchers confirmed the cross-coupled nature of the excitation by studying how absorption strength changed under different magnetic fields and varying incident light energy.

Switching backwards and forwards

Takahashi and his colleagues also demonstrated an immediate and remarkable consequence of this cross-coupled excitation: their rare-earth perovskite absorbed more of the light that passed through it in one direction than it did light passing through in the opposite direction. In a regular material, the absorption strength would be identical in each direction since only the strength of the electric polarization, internal to the material—not its direction—would affect absorption. When cross-coupling occurs, however, the directions of the absorbing material's internal electric and magnetic fields also matter. Because reversing the direction of light travel reverses at least one of these internal field directions, absorption will vary for different directions of travel (Fig. 2).

This so-called 'directional dichroism' effect, reminiscent of dichroic glass, could have applications to efficient optical switching of terahertz light signals in high-speed communication switches and optical circuits. This and other applications may represent the beginning of a new field. "I think that this research marks the beginning of magneto-electric optics, which will be based on a firm understanding of the microscopic mechanisms in magneto-electric materials," says Takahashi.

This nascent field will be helped, Takahashi continues, by the likelihood that cross-coupled excitations will turn out to be relatively common. Like the excitations observed here, they will probably be in the gigahertz-to-terahertz frequency regime, and will occur in materials that exhibit ferroelectric order derived from magnetic spin structure—possibly including many of the multiferroics that are already known to scientists.

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ABOUT THE RESEARCHER

Youtarou Takahashi was born in Hokkaido, Japan, in 1978. He graduated from the Faculty of Sciences at Kyoto University in 2002, and obtained his PhD in 2007 from the University of Tokyo. He then joined the Japan Science and Technology Agency as a researcher on the Exploratory Research for Advanced Technology (ERATO) Tokura Multiferroics Project, and in 2011 became a lecturer at the University of Tokyo. His research focuses on the ultrafast dynamics of solids using optical spectroscopy. His current area of interest is the terahertz magnetoelectric dynamics of strongly correlated electron systems.

Accounting for missing particles

Measurements from high-energy collision experiments lead to a better understanding of why meson particles disappear

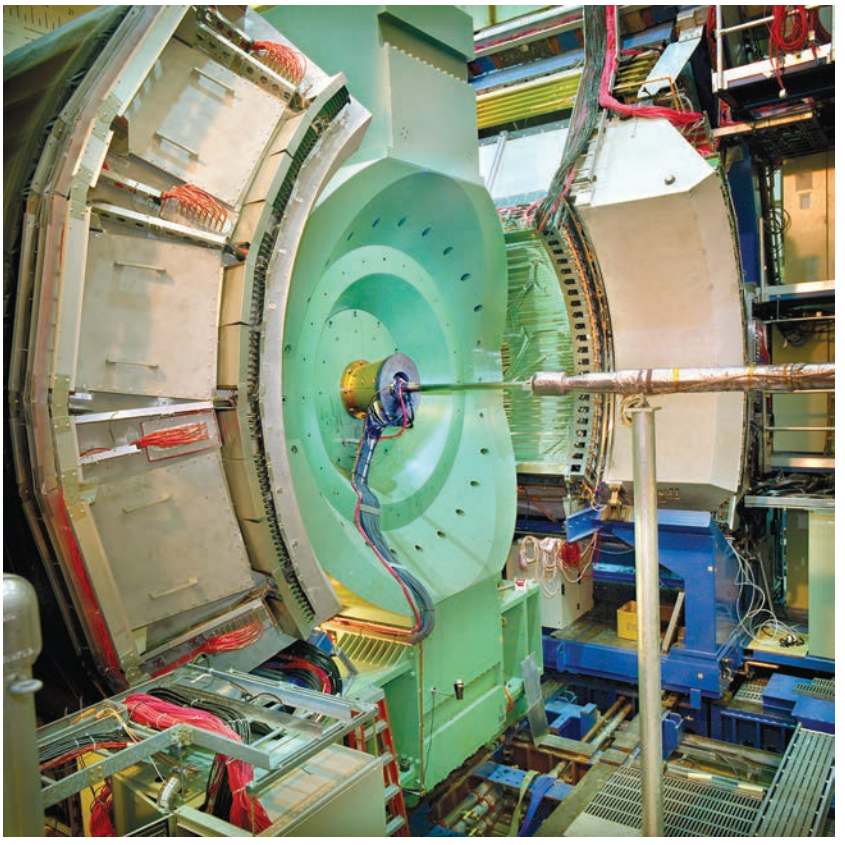

Figure 1: The PHENIX detector at the Relativistic Heavy Ion Collider measures the particles that emerge from high-energy collisions between nuclei.

For several years, physicists at the Relativistic Heavy Ion Collider (RHIC) at Brookhaven National Laboratory (BNL), USA, have studied an unusual state of matter called the quark–gluon plasma, which they believe mimics the hot, dense particle soup that existed immediately after the big bang. Now, the PHENIX collaboration at RHIC reports findings about a particle called the J/ψ meson that will help physicists distinguish the properties of the quark–gluon plasma (QGP) from those of normal matter[1].

To create a QGP, physicists crash gold nuclei together at close to the speed of light. This provides enough energy to break apart the protons and neutrons in the nuclei into their constituent quarks and gluons, which mediate the force between quarks. In this energetic mash up, a host of short-lived particles can form, including mesons, which are made up of a quark and an anti-quark.

When collisions of gold nuclei yield fewer J/ψ mesons than expected from theoretical predictions, it indicates that a QGP has formed. Suppressed meson production can occur because the QGP weakens the binding force between the two quarks in the J/ψ particle. The PHENIX collaboration's detector (Fig. 1) counts the number of J/ψ mesons created in collisions by detecting the electrons and muons—particles with the same charge, but more mass, than electrons—produced from J/ψ decays.

Effects other than the formation of the QGP, however, can also suppress the yield of J/ψ particles, which makes interpreting gold–gold collisions "ambiguous", says Yasuyuki Akiba, a scientist at the RIKEN BNL Research Center and a member of the PHENIX collaboration.

To isolate these other effects, the PHENIX team analyzed data taken in 2003 and 2008 from collisions between deuterium—a proton and neutron—and gold, since these collisions cannot form a QGP. Even in the absence of a QGP, the team found the production of J/ψ particles was more suppressed than expected at the highest relative velocities between the deuterium and the gold collisions. "Conventional models cannot describe the data," says Akiba.

The team thinks the unexplained suppression may be related to how the apparent density of gluons in the gold nuclei, which determines the rate of J/ψ production, varies with the speed of the deuterium.

More analysis is needed to determine whether this explanation is correct, but this work "gives a precise baseline that will be very useful for separating the quark–gluon plasma effects in gold–gold collisions," says Akiba. ■

1. Adare, A., Afanasiev. S., Aidala, C., Ajitanand, N.N., Akiba, Y., Al-Bataineh, H., Alexander, J. Angerami, A., Aoki, K., Apadula, N, *et al*. Cold nuclear matter effects on J/ψ yields as a function of rapidity and nuclear geometry in $d + A$ collisions at $\sqrt{s_{NN}}$ = 200 GeV. *Physical Review Letters* **107**, 142301 (2011).

Making better memories

Demonstration of a rare combination of electric and magnetic properties in a now readily producible material could improve electronic memory devices

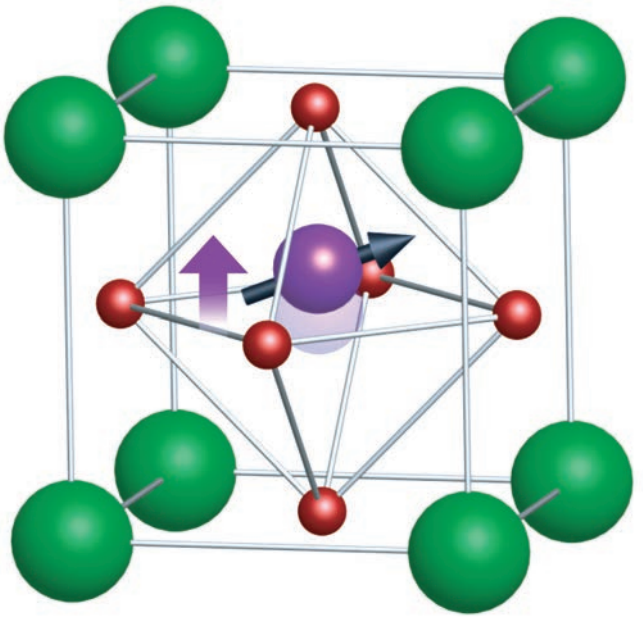

Figure 1: Strontium barium manganite's properties come from its manganese atoms (purple sphere). Spin (black arrow) endows the material with its magnetic properties, while the displacement of the ion from the center of the cubic lattice (purple arrow) makes it ferroelectric. Oxygen atoms are shown as red spheres and strontium or barium atoms are green.

An electric field can displace the cloud of electrons surrounding each atom of a solid. In an effect known as polarization, the cloud centers move away slightly from the positively charged nuclei, which radically changes the optical properties of the solid. Materials that can maintain this polarization, even when the external electric field is removed, are known as ferroelectrics and they could provide a novel route to higher-density memory devices.

"The function of ferroelectric materials is much expanded if they are also magnetic, and if there is a strong coupling between polarization and magnetization," explains Yasujiro Taguchi from the RIKEN Advanced Science Institute in Wako. Taguchi and his colleagues from RIKEN, and several other Japanese research institutes, recently demonstrated experimentally that the material strontium barium manganite ($(Sr,Ba)MnO_3$) has this rare combination of properties[1].

Previous experimental studies on $(Sr,Ba)MnO_3$ did not identify any signs of the ferroelectricity promised by theoretical simulations. The problem was an insufficient ratio of barium to strontium atoms: conventional crystal growth techniques had produced material with only a maximum ratio of 1:4. Taguchi and his colleagues therefore developed a new two-stage growth technique that enabled them to increase the barium content to 50%. By comparing the properties of crystals with different levels of barium content, they identified a transition to a ferroelectric state at a content ratio of between 40 and 45%.

Strontium barium manganite has a so-called perovskite crystal arrangement, which is characterized by a repeating cubic structure (Fig. 1). Manganese atoms are located at the center of the crystal and oxygen atoms are situated in the middle of each of the six sides. Either a strontium or a barium atom sits on each corner of the cube. The spin, or rotation, of an electron in the manganese ions makes the crystal magnetic. Ferroelectricity arises because the manganese ions are displaced slightly from the center of the cube. "Therefore the manganese ions are responsible for both polarization and magnetism and thus a strong coupling between the two emerges," explains Taguchi.

Materials that are both ferroelectric and have magnetic properties are called multiferroics. The multiferroic materials identified so far have either strong coupling between electricity and magnetism but small polarization, or large polarization with weak coupling. "We have now discovered a multiferroic material that has both [strong coupling and large polarization]," says Taguchi. "These properties are necessary requirements if multiferroic materials are to be applied to devices. One possible example is low-power-consumption memory devices." ■

1. Sakai, H., Fujioka, J., Fukuda, T., Okuyama, D., Hashizume, D., Kagawa, F., Nakao, H., Murakami, Y., Arima, T., Baron, A.Q.R., Taguchi, Y. & Tokura, Y. Displacement-type ferroelectricity with off-center magnetic ions in perovskite $Sr_{1-x}Ba_xMnO_3$. *Physical Review Letters* **107**, 137601 (2011).

Twist-and-glow molecules aid rapid gas detection

Fast and sensitive detection and identification of air-borne gases is now possible using a newly developed sensor

In an emergency such as a factory fire, ascertaining which gases are present in the air is critical to preventing or minimizing poisoning. This requires gas sensors that react quickly and provide a visual signal. However, many existing detection systems work for only one gas, or they use a chemical reaction that is too slow to respond in emergency situations.

Now, Takashi Uemura of Kyoto University and colleagues at several other Japanese institutes, including the RIKEN SPring-8 Center, have created a gas sensor that works rapidly, emits a clear fluorescent signal, and detects different gases[1]. Most importantly, the new sensor can distinguish between gases with similar chemical and physical properties.

Uemura and colleagues' sensor contains so-called 'flexible porous coordination polymers' coupled with fluorescent reporter molecules that change structure, and therefore emit signals, according to different gases present in the air.

"We thought that the incorporation of functional polymers into flexible porous coordination matrices would show unique dynamic properties," says Uemura. He and his colleagues therefore inserted a fluorescent reporter molecule into the coordination polymer, whereupon the whole combined structure twisted out of shape.

In this normal and twisted state, the fluorescent light from the reporter is quite dim and green. Once gas molecules are introduced, the structure begins to return to its original shape, and the fluorescence returns, brightening as the gas pressure intensifies. For example, the fluorescence changes from green to blue when the molecule adsorbs carbon dioxide.

Figure 1: In an emergency situation, rapid detection and identification of air-borne gases is critical to effective decision making by response personnel.

By this method, the sensor allows regular monitoring of both the type of gas and its concentration in the air. Crucially, the fluorescent response begins within seconds upon interaction with the gas and is complete within minutes, allowing emergency responders to make decisions quickly (Fig. 1).

In addition to these attributes, this is the first such detection system shown to work for gases with almost identical physical properties, the team notes. "Physical properties, such as size, shape, and boiling points, are very similar between carbon dioxide and acetylene, for example, so it is difficult to distinguish between them," explains Uemura. "Our material has carboxylate sites in the pore, and these sites can bind to acetylene more strongly than carbon dioxide.

"This unique cooperative change of host and guest could allow us to design new advanced materials," he adds. By investigating different flexible host structures and other 'guest' reporter molecules, the researchers believe they could create gas detection systems for a variety of different gases and other applications in the future. ■

1. Yanai, N., Kitayama, K., Hijikata, Y., Sato, H., Matsuda, R., Kubota, Y., Takata, M., Mizuno, M., Uemura, T. & Kitagawa, S. Gas detection by structural variations of fluorescent guest molecules in a flexible porous coordination polymer. *Nature Materials* **10**, 787–793 (2011).

Economizing chemistry, atom by atom

Industrial chemistry is set to improve from novel rare-earth metal catalysts that reduce waste and improve aromatic bond-forming reactions

In chemistry, downsizing can have positive attributes. Reducing the number of steps and reagents in synthetic reactions, for example, enables chemists to boost their productivity while reducing their environmental footprint. This type of 'atom economy' could soon improve, thanks to a new rare-earth metal catalyst developed by Zhaomin Hou and colleagues at the RIKEN Advanced Science Institute, Wako[1]. Their catalyst makes it simpler to modify aromatic carbon–hydrogen (C–H) bonds with silicon-bearing silyl ligands—a reaction step critical to pharmaceutical and materials science manufacturers alike.

Silicon, which is less electronegative than carbon or hydrogen atoms, can significantly alter the electronic characteristics of an organic molecule. Replacing the hydrogen atoms of an aromatic C–H group with silyl groups has emerged as an important strategy in industrial-scale chemical synthesis because these substituents can tune molecular reactivity, enabling construction of elaborate chemical frameworks.

Chemists normally use transition metals such as platinum or rhodium to catalyze aromatic silylation reactions. But to achieve high conversions, these catalysts need to be mixed with additional hydrogen acceptor reagents, which can generate unwanted waste products, including alkanes.

Hou and colleagues have pioneered studies into rare-earth metals, such as scandium, which have different catalytic properties to transition metals. Recently, they found that 'half-sandwich' scandium complexes, bonded on one side by a flat organic ring, showed unique activity and selectivity in the presence of carbon double bonds[2]. This made investigations of unsaturated aromatic molecules a natural next step.

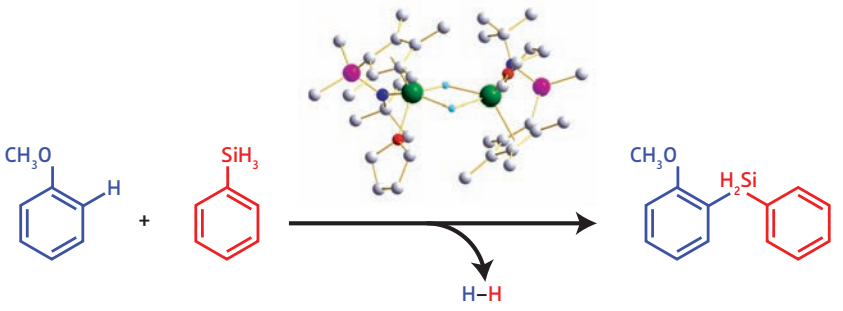

Figure 1: A scandium catalyst (green spheres, center) can catalyze the addition of a phenylsilane (orange structure) to anisole (blue structure) to give cleaner products, using fewer reagents, than achieved previously.

When the researchers mixed a methoxy–benzene compound called anisole with the half-sandwich scandium catalyst and a phenylsilane, they found that the silyl group substituted onto the aromatic ring with excellent selectivity and yields (Fig. 1). Furthermore, the catalyst did not require hydrogen acceptor reagents, and generated only H_2 gas as a by-product. Hou notes that this reaction is highly advantageous in terms of atom economy.

X-ray and spectroscopic measurements revealed that the working form of the catalyst, which contained a pair of 'bridging' hydrogen atoms, activated the reaction by coordinating the anisole's methoxy group to the rare-earth metal. According to Hou, this relatively strong interaction directs silylation to occur almost exclusively at the position adjacent to the methoxy unit on the aromatic ring—a 'regioselectivity' that outshines that of transition metal catalysts, whose weak oxygen–metal interactions often produce an undesirable mix of silylation isomers.

The team will continue to explore new approaches to improving catalytic sustainability and selectivity by tapping into the extraordinary properties of rare-earth metals. ■

1. Oyamada, J., Nishiura, M. & Hou, Z. Scandium-catalyzed silylation of aromatic C–H bonds. *Angewandte Chemie International Edition* **50**, 10720–10723 (2011).
2. Takimoto, M., Usami, S. & Hou, Z. Scandium-catalyzed regio- and stereospecific methylalumination of silyloxy/alkoxy-substituted alkynes and alkenes. *Journal of the American Chemical Society* **131**, 18266–18268 (2009).

Resolving controversy at the water's edge

High-level spectroscopy and computer simulations of specially diluted liquids reveal the long-debated structure of air–water interfaces

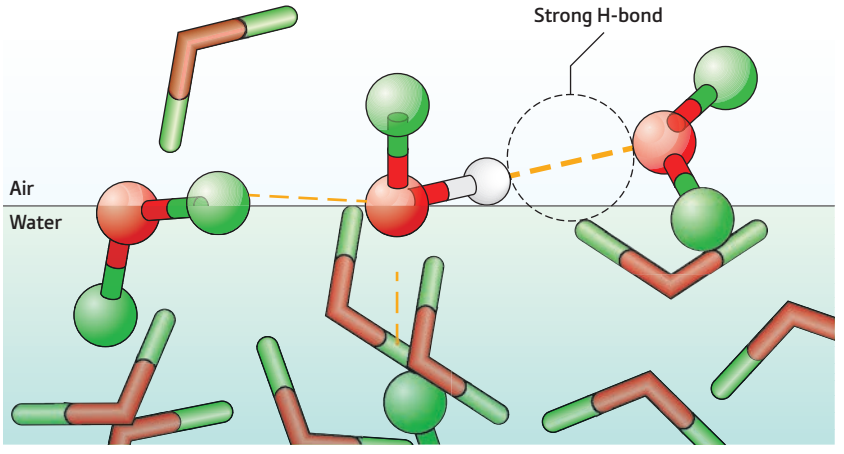

Figure 1: A 'snapshot' from a molecular dynamic simulation reveals that water molecules align at air–water interfaces as coordinated pairs linked by hydrogen bonds.

Water (H_2O) has a simple composition, but its dizzyingly interconnected hydrogen-bonded networks make structural characterizations challenging. In particular, the organization of water surfaces—a region critical to processes in cell biology and atmospheric chemistry—has caused profound disagreements among scientists. Now, Tahei Tahara and colleagues from the RIKEN Advanced Science Institute in Wako, in collaboration with researchers in Japan and Europe, have uncovered the presence of strongly bonded water pairs at the air–water interface[1], rather than previously hypothesized 'ice-like' surface structures.

Observing surface water molecules, just a few monolayers thick, requires special experimental techniques that prevent interference by more plentiful bulk particles. One such approach is called vibrational sum frequency generation (VSFG), a laser-based method that selectively vibrates interfacial molecules. Previous VSFG measurements of surface water showed two vibrations that resemble signals recorded from bulk ice and liquid water states. Some scientists have proposed that these vibrations correspond to a partially disordered mix of liquid and four-coordinated ice-like surface structures—a theory at odds with thermodynamic evidence.

Other VSFG experiments, however, have suggested that the two vibrations arise from one structure undergoing coupling interactions. To resolve this dispute, Tahara and colleagues turned to heterodyne-detected VSFG (HD-VSFG), a high-level spectroscopic method that detects how the phase of the vibrational signals shifts with respect to the incident laser beam—information that can pinpoint molecular orientation at interfaces.

The researchers then employed a trick using isotopes to account for coupling effects of water molecules: they added the deuterium (D)-bearing compounds HOD and D_2O to pure water. By gradually diluting the number of oxygen–hydrogen (OH) bonds in the liquid, these isotopes suppress the interactions between the vibrational modes that normally occur. The remaining 'stretching' vibrations that extend and contract OH bonds then provide clear information about the interfacial water structure.

The team's experiments revealed that as the isotopic dilution progressed, the two OH bands merged into a single peak, which is clear evidence of vibrational coupling within a single structure. After performing molecular dynamic simulations and comparing the results to the HD-VSFG data, a new picture emerged of the air–water interface (Fig. 1): the low-frequency OH vibrations were due to tightly joined pairs of liquid water molecules.

"We were wondering what kind of structure can have strong hydrogen-bonds other than ice at water surfaces," says Tahara. "When our experiments and [co-author] Morita's simulation answered the question, rather than surprise I felt that 'This is it!' because its structure is quite reasonable." ■

1. Nihonyanagi, S., Ishiyama, T., Lee, T.-K., Yamaguchi, S., Bonn, M., Morita, A. & Tahara, T. Unified molecular view of air/water interface based on experimental and theoretical $\chi^{(2)}$ spectra of isotopically diluted water surface. *Journal of the American Chemical Society* **133**, 16875–16880 (2011).

Decoding DNA's annotations

A chemical probe that can differentiate between chemical tags adorning DNA could provide insights into how nature switches genes on and off

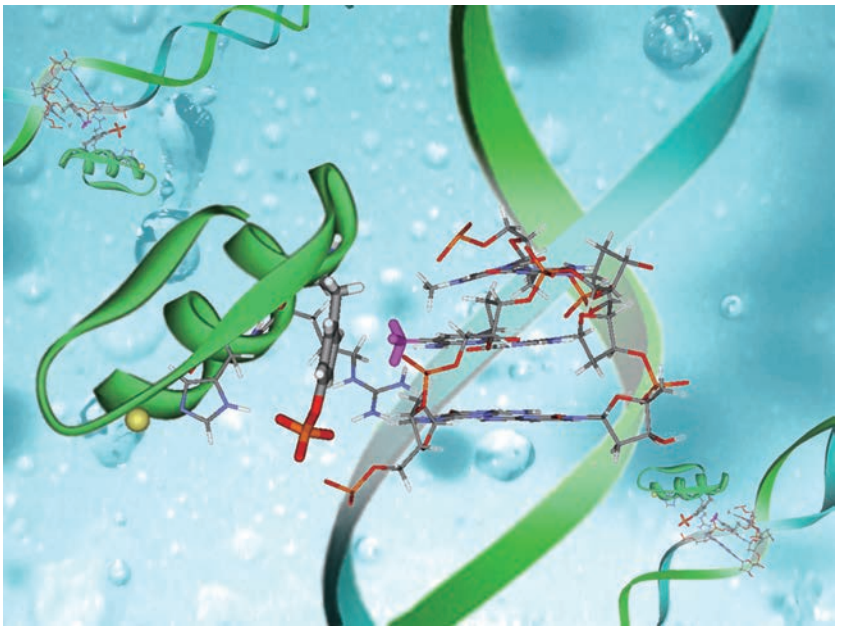

Figure 1: The Sp1 peptide probe (left) binds a DNA strand (right) and reveals the presence of an epigenetic marker that is a methyl group (purple).

In the currently hot research area known as 'epigenetics', researchers are discovering that offspring inherit much more from their parents than just their genes. Individuals also inherit detailed instructions on how to use the genetic sequence coded in their DNA via small chemical, or epigenetic, markers that decorate DNA strands. The markers can activate some genes and switch off others. Epigeneticists are racing to decode the roles of different markers; but, first, they must develop the ability to read them. A new chemical probe, developed by a research team led by Akimitsu Okamoto at the RIKEN Advanced Science Institute, Wako, is showing promise as an analytical tool to assist this quest[1].

The team's probe can differentiate between two epigenetic markers—methyl and hydroxymethyl markers—that differ by the presence of a single oxygen atom. Methyl groups, one of the first epigenetic markers discovered, are known to inactivate gene expression; 'demethylation', or removal of a methyl group from the DNA, allows gene expression to restart.

"We know the mechanism of DNA methylation, but nobody knows the mechanism of DNA demethylation," Okamoto explains. One possibility is that the body converts the methyl marker into a hydroxymethyl group, as the first step in the process of removing it, in preparation to reactivate a gene. However, current tests cannot distinguish between the two epigenetic markers, preventing that theory from being tested.

The chemical probe developed by Okamoto and colleagues is based on a peptide called Sp1, which is known to bind to DNA. The researchers previously modified the structure of Sp1 so that it adheres strongly only to DNA strands incorporating a methyl marker (Fig. 1). They then showed that if the peptide binds to a DNA strand, it reveals the presence of the methyl group[2].

In their latest study, the researchers showed that modified Sp1 will not bind to DNA when the methyl group is converted to a hydroxymethyl—thereby allowing them to tell the two groups apart. The extra oxygen atom in the hydroxymethyl group disrupts the interaction between the peptide and the DNA, so the two cease to adhere together.

Okamoto and his colleagues are now planning to modify the peptide to detect an even wider range of epigenetic markers, which will allow the study of their role in gene expression. "Our next step is to develop the methods for effective sequencing and detection of DNA containing cytosine, 5-methylcytosine, 5-hydroxymethylcytosine, 5-formylcytosine, and 5-carboxycytosine," Okamoto says. ■

1. Nomura, A., Sugizaki, K., Yanagisawa, H. & Okamoto, A. Discrimination between 5-hydroxymethlcytosine and 5-methylcytosine by a chemically designed peptide. *Chemical Communications* **47**, 8277–8279 (2011).
2. Nomura, A. & Okamoto, A. Phosphopeptides designed for 5-methylcytosine recognition. *Biochemistry* **50**, 3376–3385 (2011).

Giant cell reveals metabolic secrets

Clarification of metabolite regulation and distribution in a large, freshwater algal cell illuminates important aspects of general cell metabolism

Figure 1: The freshwater alga *Chara australis*, which has giant cells ideal for cell biology studies.

Chemical reactions within the cell produce intermediate and end products in the form of small molecules called metabolites. Using an approach called metabolomics, a research team led by Kazuki Saito of the RIKEN Plant Science Center, Yokohama and Tsuruoka, has elucidated the localization and dynamics of 125 metabolites within a single giant cell of the freshwater alga *Chara australis*[1]. The team's findings provide important insights into the fundamental processes of cells in general.

Metabolites play important roles in the regulation of critical biological processes, such as growth, differentiation, and, in the case of so-called 'secondary metabolites', chemical defense. "Metabolomics is the systematic study of these unique chemical footprints, and involves identifying and characterizing the many metabolites found in a cell, tissue, organ or organism, as well as their production, distribution and dynamics," explains Saito.

Because the enzymes involved in producing and converting different metabolites are often localized within subcellular structures called organelles, biologists generally assumed that metabolites are also highly compartmentalized within the cell, but none had demonstrated this comprehensively.

"Understanding the compartmentalization and dynamics of metabolites within single organelles represents an enormous technical challenge, not least because of the tiny size of these structures in most cells," says Saito.

He and his colleagues therefore turned to *C. australis* as a model system (Fig. 1). This species has a particular cell type, called an internodal cell, which can grow to a length of around 20 centimeters. Because of theirs large size and volume, internodal cells are widely used to study various aspects of cell biology, including membrane physiology. The researchers purified single vacuoles, a type of organelle, from these cells. They then used a battery of sophisticated metabolomic techniques to determine the localization and dynamics of metabolites in the vacuole and other cellular fractions collectively known as the cytoplasm.

Focusing on phosphate compounds, Saito and colleagues detected 125 known metabolites, and showed that they fluctuated independently in the vacuole and cytoplasm under various light conditions. They therefore concluded that metabolites are spatially regulated within the cell, moving between the vacuole and the cytoplasm according to conditions. "Ours is the first study to confirm specific compartmentalization of comprehensive metabolites in a single vacuole from a single cell," notes Saito.

Using a specialized microinjection technique, they researchers also observed metabolite transport across the membrane surrounding the vacuole. This suggested to them that the vacuolar membrane plays an important role in regulating transport of metabolites in and out of the vacuole. ■

1. Oikawa, A., Matsuda, F., Kikuyama, M., Mimura, T. & Saito, K. Metabolomics of a single vacuole reveals metabolic dynamism in an alga *Chara australis*. *Plant Physiology* **157**, 544-555 (2011).

Keeping an eye on the Japanese genome

A particular type of age-related macular degeneration in the Japanese population is linked to four regions of the genome

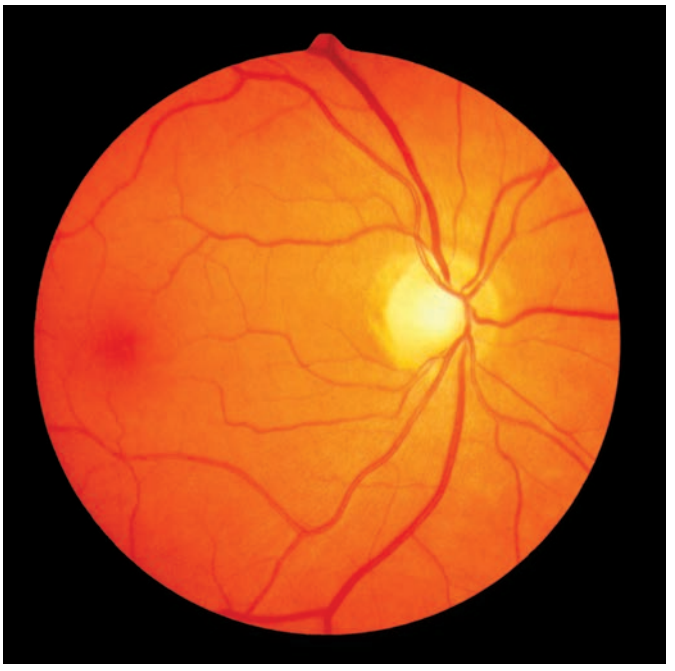

Figure 1: A photograph of a healthy eye. AMD-affected eyes have dark spots that lead to severe visual impairment in the elderly of developed countries.

Age-related macular degeneration (AMD) is a common disease that can result in blindness. It is caused by cell death in the eye's retina, which is partly responsible for transforming visual stimuli into electrical signals to the brain. Asian populations tend to exhibit a particular type of the disease, called exudative AMD, which includes changes in the blood vessels of the eye. Caucasians, however, tend to exhibit AMD without these vascular abnormalities. Now, a research team led by Michiaki Kubo at the RIKEN Center for Genomic Medicine in Yokohama has identified four genomic areas that increase the risk for exudative AMD in Japanese individuals[1].

The researchers searched for genomic regions linked to exudative AMD by investigating single-nucleotide changes in the human genome. They compared the frequencies of 500,000 single-nucleotide changes between individuals with exudative AMD and normal, or control (Fig. 1), individuals. Other research groups had previously performed this kind of genome-wide association study (GWAS) in Caucasian populations, but not in the Japanese.

Kubo and colleagues began by performing a GWAS on 800 Japanese individuals with exudative AMD and 3,000 Japanese controls; they identified two genomic regions previously linked to AMD in Caucasians. This suggested to the researchers that the mechanisms underlying AMD in both populations are likely to be similar.

In a 'replication study' using 700 patients and 15,000 controls, the researchers then carefully examined 77 additional genomic areas that showed potential as candidate exudative AMD-associated regions in their initial GWAS. The replication study yielded two additional genomic regions that were linked to exudative AMD. One of these—on chromosome 4—covered four nearby genes, so the researchers were unable to pinpoint with certainty which of the genes were responsible for the disease risk. However, another region—on chromosome 8—was linked to the gene called *TNFRSF10A*, which encodes a receptor expressed in the eye that modulates inflammation and cell death.

The variant of the gene that Kubo and colleagues linked to exudative AMD seemed to regulate the expression of the receptor. "We are next planning to investigate exactly how the signaling pathway initiated by this receptor would affect the development of exudative AMD," explain Kubo and Satoshi Arakawa, the study's first author.

The identification of these genomic regions that are linked to exudative AMD could aid in the development of new therapies. "Our results will also help in the construction of risk prediction models for exudative AMD," say Kubo and Arakawa. ■

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Expanding the genomic map

A large-scale study of East Asian individuals reveals a number of previously overlooked genetic variants with potential roles in a number of metabolic diseases

Figure 1: Newly identified genetic variants could provide useful biomarkers for predicting and treating metabolic disorders in East Asian individuals.

Broad, population-based investigations known as genome-wide association studies (GWAS) are now a standard tool for helping scientists to pinpoint genetic variations that can contribute to disease risk or pathology. However, most of the studies performed to date have focused predominantly on populations of European ancestry, and therefore ignore or overlook risk markers that specifically predominate among other ethnic groups. A recent GWAS from a large team of scientists based in Korea and Japan, including Yukinori Okada of the RIKEN Center for Genomic Medicine in Yokohama, has addressed this inequity by specifically seeking out factors that might contribute to metabolic disease in East Asians[1] (Fig. 1).

In a GWAS, scientists analyze genomic data from large numbers of people who manifest a particular condition or trait of interest. They do this by seeking out small sequence changes known as single-nucleotide polymorphisms, or SNPs, that show a strong statistical association with the presence or absence of that particular trait.

In an earlier study, Okada and colleagues analyzed more than 14,000 Japanese individuals and found several previously unidentified loci of interest[2]. This time, they performed an initial analysis in over 12,000 Korean individuals, and then replicated apparent 'hits' in a far larger group of over 30,000 individuals from Japan, Korea and China. This increased scale gave the researchers the ability to identify rare but meaningful associations with greater confidence.

They focused on finding genetic variants associated with imbalances in blood sugar, cholesterol and other indicators of metabolic function. "The recent rise of prevalence of metabolic diseases like diabetes, hyperlipidemia and chronic renal disease is a serious medical problem," says Okada, "and these types of studies have been mainly conducted in European populations, but there are few studies on Asians."

The team's investigation uncovered 33 SNPs associated with metabolic function, 10 of which were previously unidentified. One of these SNPs was closely linked with variability in blood sugar levels, although the same SNP showed no significant association with this metabolic trait in a northern European cohort. The researchers also identified a segment of chromosome 12 that appears to affect multiple metabolic phenotypes in both Europeans and East Asians; however, the specific sequence variations associated with these traits differ between the two populations.

Collectively, these data highlight the importance of expanding the breadth of GWAS analyses to cover the full spectrum of ethnic diversity. Okada and colleagues are planning to embark on an even larger-scale GWAS of East Asian populations in the near future. ■

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2. Kamatani, Y., Matsuda, K., Okada, Y., Kubo, M., Hosono, N., Daigo, Y., Nakamura, Y. & Kamatani, N. Genome-wide association study of hematological and biochemical traits in a Japanese population. *Nature Genetics* **42**, 210–215 (2010).

Holding back immunity

A 'gatekeeper' protein plays a critical role in helping immune cells to sound a warning after encountering signs of tumor growth or infection

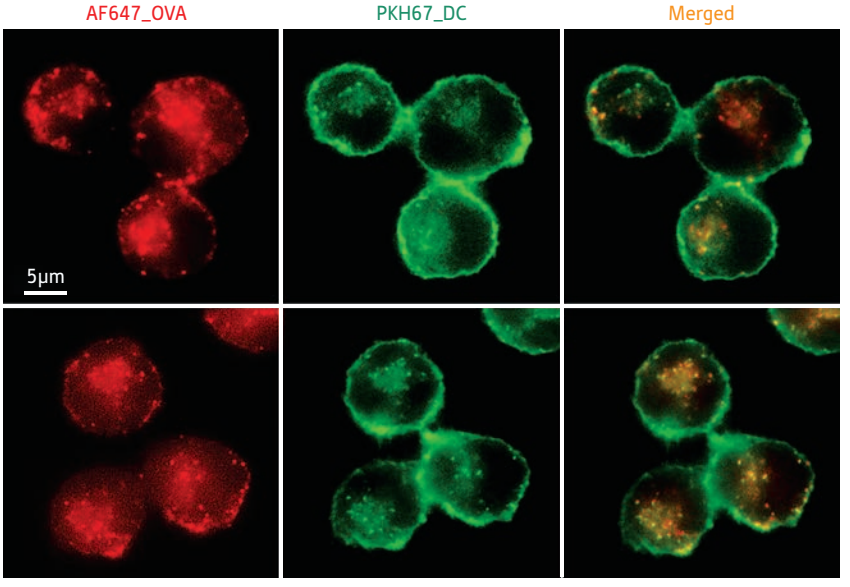

Figure 1: Compared to untreated dendritic cells (top), cells treated with an HSP90 inhibitor (radicicol) (bottom) tend to retain a larger percentage of the antigen ovalbumin (red; left) within membrane bound endosomes (green; middle). Endosomes are labeled with a stain that marks the membrane protein PKH67.

When the body's own cells turn into ticking time bombs, as in cases of viral infection or cancerous transformation, a mechanism known as 'cross-presentation' enables the immune system's dendritic cells (DCs) to sound the alarm.

"Dendritic cells first internalize cancerous or virus-infected cells through a mechanism called phagocytosis, and then process cellular antigens into short peptides," explains Heiichiro Udono of the RIKEN Center for Allergy and Immunology in Yokohama. DCs subsequently present these fragments to killer T cells, which seek out and destroy other affected cells. Phagocytosed molecules travel within sealed membrane bubbles called endosomes, and new work from Udono and his colleagues has revealed insights into how these antigens are released into the cytosol prior to cross-presentation[1].

Udono's team focused on heat-shock protein 90 (HSP90), a molecule that previous studies have linked to cross-presentation. HSP90 comes in two forms, α and β, which perform overlapping roles. Mice need at least one of these proteins to live. Udono and colleagues succeeded in generating healthy mice that exclusively lack HSP90α. They found that, although HSP90β appears to make some contribution, the loss of HSP90α had a striking effect on antigen processing. DCs isolated from these mice showed defects in their capacity for cross-presentation, and failed to activate killer T cells efficiently following exposure to ovalbumin, a model antigen.

HSP90α-deficient DCs proved perfectly capable of internalizing ovalbumin within endosomes; however, they generally failed to release this antigen into the cytosol. The researchers noted a similar effect after treating genetically normal DCs with a chemical that inhibits HSP90α (Fig. 1), confirming the central role of this protein in endosomal release.

Udono and colleagues further demonstrated the extent of these defects by injecting HSP90α-deficient mice with cytochrome *c*, a protein that selectively eliminates a subpopulation of DCs after being taken up and released into the cytosol. Strikingly, cytochrome *c* treatment had a dramatically reduced effect on DCs from mutant mice relative to their wild-type counterparts. "This is the most sensitive *in vivo* assay to show antigen translocation to the cytosol," says Udono. "This phenomenon was absent in HSP90α knockout mice, which makes me confident that our finding is important and has physiological relevance."

Accordingly, Udono believes that molecules that modulate HSP90 activity might help clinicians to boost a patient's immune counterattack against infection or cancer. "If we can control the expression levels of HSP90 and other heat shock proteins," he says, "it could be of great benefit to human health." ■

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TAISEI MUSHIRODA

Laboratory Head, Laboratory for Pharmacogenetics
Research Group for Pharmacogenomics
RIKEN Center for Genomic Medicine

Advancing personalized medicine: tailoring drugs to fit a patient's genetic predisposition

Drugs are not equally effective on all patients. A treatment that is dramatically effective on some patients can be ineffective on others. Drugs can also have serious side effects; in the worst case, a drug used to treat a disease can produce a fatal outcome. By examining genetic differences among individuals and administering drugs on the basis of such findings, the impact of side effects can be reduced. Taisei Mushiroda, the Laboratory Head of the Research Group for Pharmacogenomics at the RIKEN Center for Genomic Medicine, is making advances in personalized medicine with research into how drugs can be tailored to a patient's genetic information through the analysis of single nucleotide polymorphisms (SNPs).

Preventing fatal side effects using genetic information

Anticancer agents, while effective in only 25% of patients (Fig. 1), have severe side effects that aggravate many patients. In 2001, a study on the efficacy rates of a broad range of drugs was published in the US. According to the paper, the efficacy rate of analgesics was about 80%, whereas rates for cancer or Alzheimer's disease drug treatments were low at 20–30%. This is because conventional medicine involves uniformly prescribed drugs for different patients, without taking into account their personal dispositions or genetic characteristics.

Side effects from drugs cause severe discomfort to millions of patients worldwide. A survey shows that in the US, about two million patients experience serious side effects annually. "Japan's population is about two-fifths of the US, so approximately 800 thousand Japanese suffer side effects from drugs each year," explains Mushiroda. "The effectiveness and side effects of drugs differ among individuals. If it were possible to predict before administration whether side effects would occur, and prescribe a drug matched to the individual, the number of patients who suffer side effects would decrease."

Pharmacogenomics combines the fields of pharmacology, the study of drug action, with genomics, the study of an organism's genomes. According to Mushiroda, pharmacology has two goals: "One goal is to develop new drugs; the other is to find how to use existing drugs appropriately. While new drug development is the task for pharmaceutical companies, we are focusing on existing drugs. We aim to make personalized medicine a reality, and thereby improve the quality of life for each patient by using genetic information to prescribe drugs 'tailored' to the characteristics of the individual."

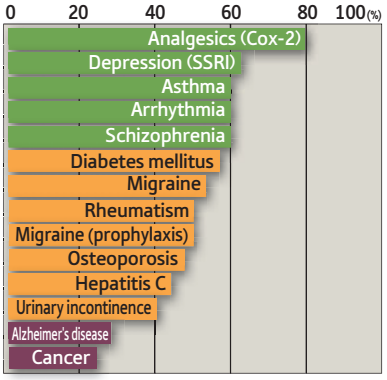


Figure 1: Drug effectiveness on common diseases

Not all drugs are equally effective in all patients. Some types of drugs, such as analgesics, are effective on almost all patients, whereas other types, such as anticancer agents, are effective only on 25% of patients. In working towards the realization of personalized medicine, it is important to develop ways of using genetic information to prescribe to patients the most suitable drugs in light of their genetic risk to side effects.

Mushiroda and his team are currently focusing on the side effect known as drug rash. A type of eczema that occurs due to reactions to medication, drug rash is characterized by inflammation of the skin and mucosa, which in more severe cases can lead to fever and inflammation of the internal organs. Drug rash is difficult to treat, with about 10% of patients experiencing fatal complications. Another negative aspect of drug rash resides in the likelihood that symptoms will not ameliorate even when medication is discontinued. After onset, there is no easy way to remedy the condition.

"We are promoting research with a focus on genetic information in order to develop a method for predicting the risk of side effects. Provided that the patient is known to be predisposed to drug rash, it is possible to avoid risk by refraining from using the respective drug or by reducing its dose."

Identifying the single nucleotide polymorphism (SNP) that plays a key role in drug rash

Japan's Ministry of Health, Labor and Welfare announced that the gout treatment allopurinol, the antiepileptic drug carbamazepine and the analgesic, anti-inflammatory, antipyretic drug loxoprofen hold the highest incidences of serious drug rash.

"The data we collected showed that the great majority of drug rash cases were caused by carbamazepine. We therefore proceeded to clarify the relationship between carbamazepine and drug rash, using Genome-Wide Association Study (GWAS). We divided our study population into two groups: those who experienced side effects and those who did not. We performed a comprehensive analysis of single nucleotide polymorphisms (SNPs) on the genome to statistically extract SNPs that are significantly associated with drug rash. The gene involved in drug rash was then identified from among those positioned near the SNPs (Fig. 2)."

Strands of DNA carry genetic information in the sequenced arrangement of the four bases A (adenine), T (thymine), G (guanine) and C (cytosine). Consisting of some three billion base pairs, the human genome carries the complete genetic information of a human being. Although there is more than 99% base sequence homology in all people, the remaining 1% of base sequences differ individually. "These differences are SNPs. It is estimated that more than 10 million SNPs are present in the human genome. They are associated with the appearance and constitution of the individual, and even with how drugs work and what side effects develop."

Discovery of the drug rash-associated gene

Figure 3 shows a Manhattan plot for the results of a GWAS conducted by Mushiroda. The horizontal axis indicates each SNP's chromosomal location while the vertical axis indicates the degree of SNP association with drug rash. About 500 thousand SNPs are plotted, and the SNPs positioned higher on the horizontal axis have a more reliable association

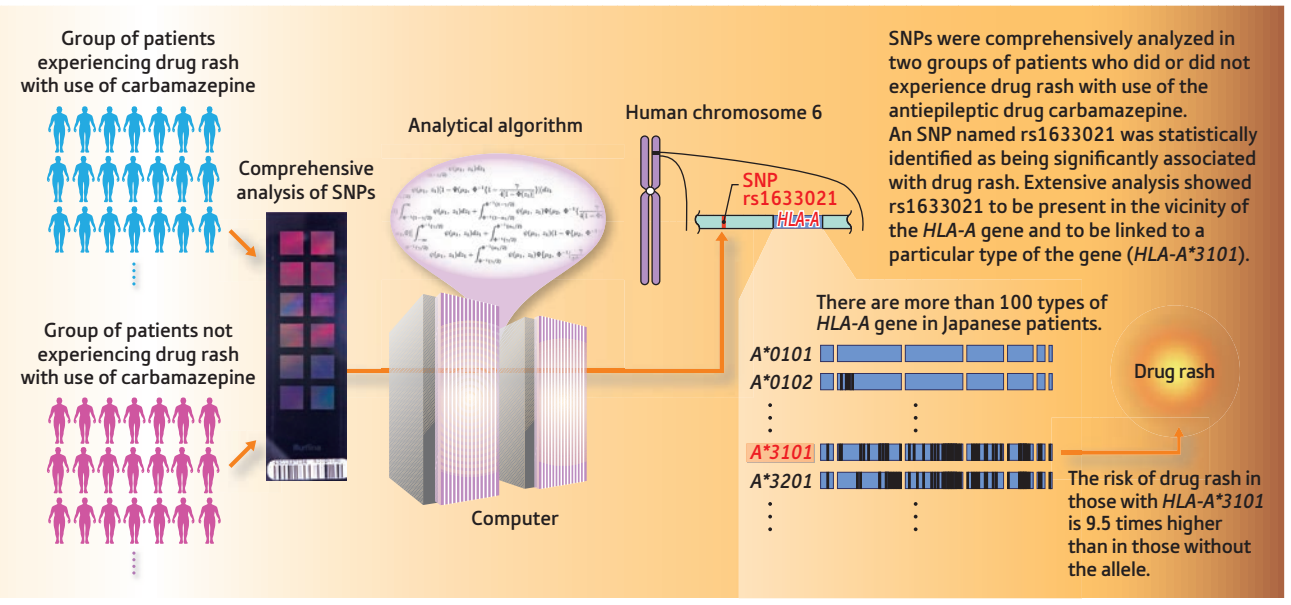


Figure 2: GWAS identification of genes associated with drug rash

with drug rash. Mushiroda explains, "This Manhattan plot shows that an SNP named rs1633021, on human chromosome number 6 (Chr6), is prominent at a high position. Extensive analysis located this SNP in the vicinity of the gene called *HLA-A*." The *HLA-A* gene works in the production of the human leukocyte antigen (HLA), a protein involved in immunity, and is known to occur in about 100 different types (base sequence patterns) in Japanese patients. "When we examined all types of the gene one by one, a type named *HLA-A*3101* was found to be associated with drug rash in Japanese patients (Fig. 2). The risk of drug rash in persons with this allele is 9.5 times higher than in those without this type."

According to Mushiroda, it is reasonable to use the limiting phrase "in Japanese patients."

"This is because the positions and ratios of SNPs vary depending on ancestral origins," he explains. Even if some SNPs are found to be associated with drug rash in a population other than Japanese, for example in Americans, it is necessary to re-examine which SNP is associated with the side effects in the Japanese population, because the positions and ratios of SNPs differ between the two population groups.

"For example, a paper published in 2004 concluded that type *HLA-B*1502* can be used as a biomarker for carbamazepine-induced drug rash in the Han Chinese in Taiwan. The risk of contracting drug rash in persons with *HLA-B*1502* is 2,500 times higher than in those without this type." In the US, with this finding in mind, the drug label of carbamazepine was revised to include the statement that patients with *HLA-B*1502* are at increased genetic risk to drug rash and are therefore more predisposed to side effects of the drug, and were advised to first undergo testing for the presence or absence of *HLA-B*1502* before initiating treatment. In this case, patients with *HLA-B*1502* refers to patients of Chinese ancestry. This type of gene is rarely found in Japanese patients.

Relationship between drug rash caused by the antiepileptic drug carbamazepine and the *HLA-A*3101* gene

Mushiroda and his colleagues conducted a study on Japanese epileptic patients undergoing treatment with carbamazepine. Of the sixty-one patients who experienced drug rash, 37 (about 61%) were found to have the *HLA-A*3101* gene. In contrast, of the 376 patients who did not experience drug rash, 329 (about 88%) were found to lack *HLA-A*3101*.

"Reportedly, about 3% of Japanese patients experience drug rash when taking carbamazepine. About 60% of those have *HLA-A*3101*. It is therefore recommended that 60% of 3% (about 2%) of Japanese epileptic patients take antiepileptic drugs other than carbamazepine. In this way, the incidence of drug rash can be reduced by 2%," says Mushiroda. However, as this association was only discovered in 2010, further evidence must be presented before it can be useful in a clinical setting.

Relationship between drug rash caused by HIV antiretroviral drug nevirapine and the *HLA-B*3505* type gene

A collaborative study of Thai HIV patients by Mushiroda's team and Thailand's Mahidol University in 2009 identified an SNP that can serve as a biomarker of drug

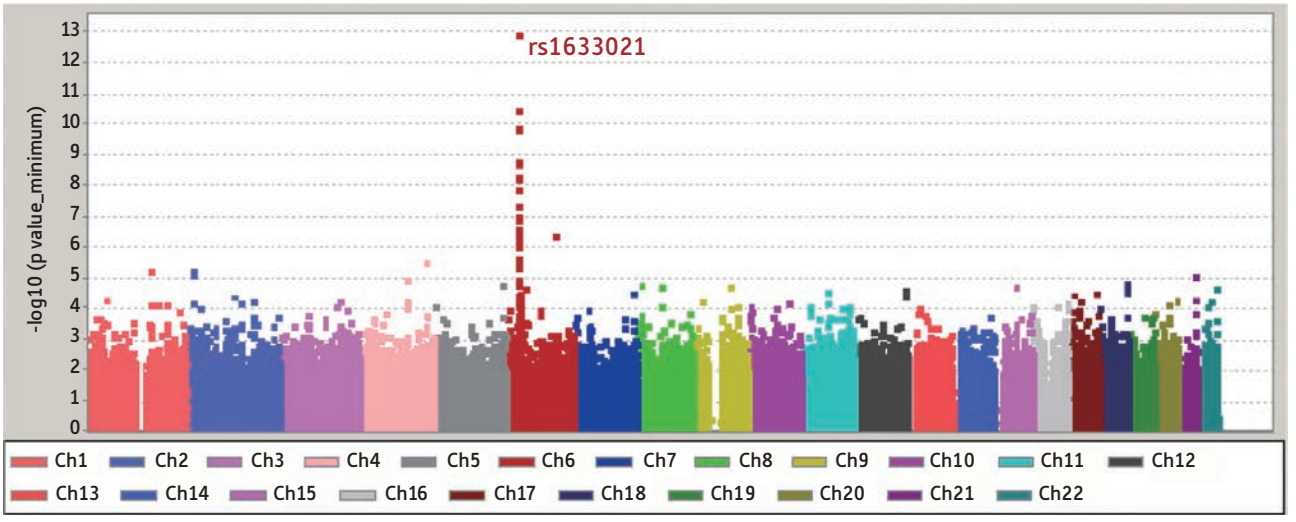


Figure 3: Manhattan plot of GWAS for carbamazepine-induced drug rash

This plot identifies which SNPs of the 500,000 found on human chromosomes are associated with carbamazepine-induced drug rash. Each dot corresponds to one SNP, and the SNPs positioned higher on the vertical axis have a more reliable association with this side effect. The plot shows that the chromosome 6 SNPs bear the most reliable association with carbamazepine-induced drug rash.

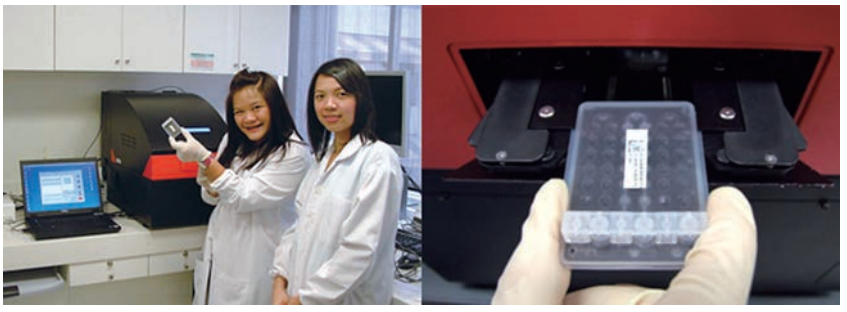


Figure 4: The TPSA-003 genotype analysis system

RIKEN and Thailand's Mahidol University are jointly conducting clinical research to demonstrate the feasibility of antiretroviral therapy for HIV infection based on personal genetic information. Developed through collaborative efforts with RIKEN, Toppan Printing Co. Ltd. and RIKEN Genesis Co. Ltd., the TPSA-003 genotype analysis system enables SNP genotyping in one hour. (Photo courtesy of Toppan Printing Co. Ltd.)

rash caused by the antiretroviral drug, nevirapine. Mushiroda says, "About 20% of patients who received nevirapine experienced drug rash. This is much higher than the aforementioned 3% incidence of carbamazepine-induced drug rash in Japanese patients. Even more problematic is the fact that generic forms of nevirapine are widely used in Thailand with government approval."

Examination of SNPs identified an *HLA-B* allele named *HLA-B*3505* which was found to be associated with nevirapine-induced drug rash. "In this study, of the 143 patients who experienced drug rash, 28 (20%) were found to have *HLA-B*3505*, whereas of the 181 patients who did not experience drug rash, 179 (99%) did not have the type," explains Mushiroda. "The risk of drug rash was thus about 22 times higher in those with *HLA-B*3505* than in those without."

Personalized medicine expected to find clinical applications in 1 or 2 years

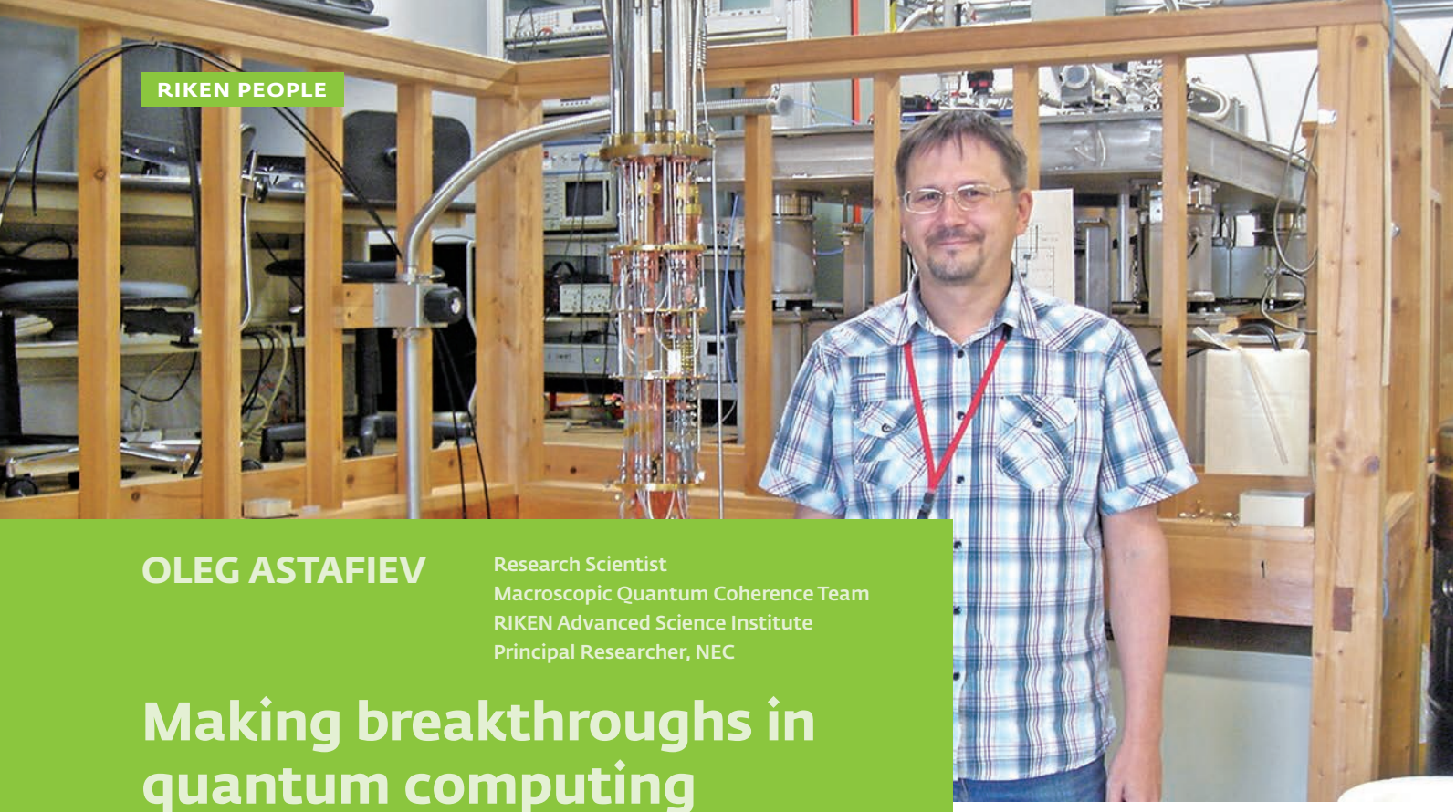
The next step after identifying the associated SNP is to determine its applicability in the clinical setting. It is also necessary to verify that SNP diagnosis is effective in both therapeutic and cost-benefit aspects. In ongoing prospective clinical research of nevirapine, it has been estimated that SNP diagnosis would cut annual medical expenditures by about US$60,000 (about ¥5 million) per hospital. This next phase will be necessary for successful application of the new system to the antiepileptic drug carbamazepine.

Before SNP genotyping can be firmly established in medical practice, however, a quick and accurate method to examine SNPs at the lowest cost is needed. In collaboration with Toppan Printing Co. Ltd. and RIKEN Genesis Co. Ltd., Mushiroda's team have developed the TPSA-003 genotype analysis system which can help to deliver more economical SNP genotyping (Fig. 4). The system provides results automatically in just one hour, simply by placing a single drop of untreated blood in the dedicated container and inserting the sample in the machine. "This is a groundbreaking machine. The conventional method involves the complex process of separating leukocytes from the blood sample, extracting the DNA from the leukocytes and applying the DNA to the machine to analyze SNPs. Conventionally, DNA extraction alone requires at least half a day even when undertaken by a highly skilled person. With the new system, the same task, including SNP genotyping, is completed in 60 minutes. This means that an accurate diagnosis can be obtained while the patient stays in the waiting room. Quick diagnosis is a big advantage for the patient as well."

Thanks to prospective clinical research and development of the fully automated SNP analyzer, SNP genotyping for nevirapine has undergone a major advance toward practical use. Over the next one or two years, the examination is scheduled for use in actual treatment in Thailand. Personalized medicine has at last entered the stage of practical application. Mushiroda is confident about the future applications for SNP genotyping. "I want to bring SNP genotyping into clinical use in Japan as soon as possible by applying the research design used in our joint research in Thailand. The most important thing is to feed back our research achievements to the patients themselves."

ABOUT THE RESEARCHER

Taisei Mushiroda is currently Head of the Laboratory for Pharmacogenetics at the RIKEN Center for Genomic Medicine. He graduated from the Graduate School of Pharmaceutical Sciences, Kanazawa University in 1988 and then joined Hokuriku Seiyaku Co. Ltd. (now Abbott Japan), where he spent 15 years undertaking pre-clinical and clinical pharmacokinetic studies in drug discovery and development. He earned his PhD from Hokkaido University in 2000 under the direction of Dr Tetsuya Kamataki. He joined RIKEN in 2003 and commenced research into the identification of SNPs and genes associated with drug responses. His current research focuses on integrating genomic information and drug responses of patients to establish "personalized medicine" that aims to provide the right drug at the appropriate dose for each individual patient.



OLEG ASTAFIEV

Research Scientist
Macroscopic Quantum Coherence Team
RIKEN Advanced Science Institute
Principal Researcher, NEC

Making breakthroughs in quantum computing

What do you do at RIKEN?

I work on RIKEN projects in the field of quantum computing in the Macroscopic Quantum Coherence Team led by Dr Jaw-Shen Tsai, under the umbrella of the RIKEN Advanced Science Institute. The group is based at the NEC Green Innovation Research Laboratories in Tsukuba, a purpose-built science city about 90km northeast of Tokyo.

How and when did you join RIKEN?

Prior to joining my current group, I was working at Tokyo University in the field of mesoscopic physics with semiconducting quantum dots. Through my research, I encountered the work of RIKEN's Tsai group, and they were already familiar with my own work at Tokyo University. Due to this prior connection, the transfer from Tokyo University to working for RIKEN at Tsukuba was smooth and natural, and I was able to continue research in quantum mechanics on slightly different systems.

What attracted you to RIKEN?

A key reason for joining RIKEN was because it allows me to pursue my dream of working on superconducting quantum systems. The research environment at RIKEN is of a very high standard and we have everything we need in terms of equipment and facilities to produce excellent results. Furthermore, funding is generous and allows us to procure the latest equipment and support necessary for top-level research. Additionally, working at an internationally renowned institution like RIKEN means that we have frequent opportunities to travel and participate in scientific meetings around the world.

Please tell us about your research at RIKEN.

The Macroscopic Quantum Coherence Team initially worked on the superconductivity of nanostructures, and at the time I joined, the group had just commenced a project on quantum computation. The work is related to very fundamental physics, and it is extremely exciting. The basic element for quantum computers is a quantum bit (qubit) which we fabricate on a micron-to-nanometer size superconducting circuit. In addition to quantum computing, the qubit can be considered as an artificial quantum system or atom. Such artificial quantum systems can be used for many different applications. Particularly, they allow the creation of fully controllable quantum electronics devices with some new properties. We have demonstrated a series of fundamental quantum optical phenomena on the new basis of the artificial atoms. Our results have been recognized by the scientific community and have been published in highly ranked scientific journals such as *Nature*, *Science* and *Physical Review Letters*.

What have been the highlights of your time at RIKEN so far?

I am extremely happy to be working at RIKEN. Discovering fundamentally new things which have never been described before is one of the most exciting parts of scientific work. My work has been twice recognized with awards from RIKEN – once for my studies on the decoherence of qubits, and again for demonstrating the lasing effect on artificial atoms. I am very grateful for this high evaluation of my work.

What would you say to other people considering joining RIKEN?

I would highly recommend RIKEN as a place to work as it offers great opportunities to carry out top-level research. For foreigners, RIKEN offers an excellent chance to participate in science in Japan. The institute also does its best to help foreigners with their daily life and involve them in different cultural activities, which makes life in Japan very interesting and enjoyable.

CONTACT INFORMATION

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Elias James Corey appointed RIKEN Honorary Fellow

Elias James Corey, Sheldon Emery Research Professor of Harvard University, was awarded the title of RIKEN Honorary Fellow on December 6, 2011. The title of RIKEN Honorary Fellow is conferred upon persons without a RIKEN affiliation who have achieved eminence on a global scale. Other RIKEN Honorary Fellows include Leo Esaki, laureate of the 1973 Nobel Prize in Physics, former Malaysian Prime Minister Mahathir bin Mohamad, and Yuan T. Lee, laureate of the 1986 Nobel Prize in Chemistry, and most recently, David Baltimore, President Emeritus and Millikan Professor of Biology at the California Institute of Technology (Caltech) and laureate of the 1975 Nobel Prize in Physiology or Medicine.

Corey was awarded the 1990 Nobel Prize in Chemistry for his development of the theory and methodology of organic synthesis. He has received numerous awards including the Japan Prize in 1989 and the Priestley Medal in 2004. In 1988, he was awarded the National Medal of Science by the president of the United States, and in 1989 he was decorated with the Order of the Rising Sun, Gold and Silver Star by the Japanese government. In addition to his remarkable achievements, Corey has devoted much of his life to teaching, and many of his former students now play important roles in academic and industrial fields. RIKEN President Ryoji Noyori spent a year as a postdoctoral fellow with Corey's laboratory at Harvard University.

Prior to the award ceremony, several principal investigators in the field of chemistry showcased RIKEN's chemistry research to Corey, followed by a discussion joined by President Noyori, and Exective Directors Maki Kawai and Kenji Oeda. After the award ceremony, Corey was given a tour of the RIKEN Wako campus where he was introduced to Kosuke Morita, who discovered element 113 at RIKEN's Radioactive Isotope Beam Factory, and to Atsushi Miyawaki, head of the Laboratory for Cell Function Dynamics, who attracted public attention in 2010 for his research on a new reagent that makes biological tissue samples transparent without diminishing fluorescence. Corey praised the researchers' discoveries as well as RIKEN's cutting-edge facilities and high-quality research.

Nobel laureate Elias James Corey is appointed RIKEN Honorary Fellow by RIKEN President Ryoji Noyori

Corey also gave a special lecture titled "Some Reflections on 60 Years of Teaching and Research" on December 5 at the Japan Academy in Tokyo where he is an Honorary Member. The lecture was co-sponsored by the Japan Academy and RIKEN, and was attended by around 200 people eager to hear Corey talk about his life and work. ■

RIKEN ion beam technology used to create brewing yeast

Heavy ion beams produced by the RIKEN Ring Cyclotron at the RI Beam Factory have played a key part in the alcoholic beverage-brewing process. The Radiation Biology Team at the RIKEN Nishina Center for Accelerator-Based Science, in collaboration with the Saitama Industrial Technology Center and the Saitama Sake and Shochu Makers Association, have used the ion beams to produce a new brewing yeast. The yeast is now being used to produce several brands of sake by local brewers in Saitama prefecture, in a distinct example of RIKEN technology's practical applications in industry.

Three types of Japanese sake called 'Nishina Homare' produced using a new brewing yeast

Three types of sake brewed using the new yeast were produced at three breweries in Saitama, and entered the market in November 2011. They are collectively known as 'Nishina Homare' ('in honor of Nishina'), named after Yoshio Nishina, the father of nuclear physics in Japan and one of RIKEN's most eminent scientists.

Ion beams also have applications in the generation of new plant varieties. As heavy ion beams induce mutagenesis—a process which results in a mutation—more rapidly than other breeding techniques, they are capable of generating new varieties in plants within just a few years. Using this technique, which was pioneered in Japan, Radiation Biology Team leader Tomoko Abe has already developed a number of new plant varieties, including dahlias, petunias, dianthus, salt-resistant rice and high-yield rice. The most recent variety developed by Abe's team is a new type of cherry blossom that can bloom all year round. ■

RIKEN in 2012: Becoming a more visible presence in society

The New Year opened at RIKEN with words of greeting from President Ryoji Noyori. Noting that Japan will need to make radical efforts to recover and rebuild after the devastation of the Great East Japan Earthquake, President Noyori emphasized how important it will be for RIKEN to contribute to these efforts. RIKEN will need to become a more visible presence within society, he said, and to achieve this, it must focus on research areas and topics that will make the most effective use of RIKEN's considerable resources and talents, while at the same time maintaining its commitment to basic research. ■

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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.

RIKEN RESEARCH is a website (www.rikenresearch.riken.jp) and print publication intended to highlight the best research being published by RIKEN (www.riken.jp). It is written for a broad scientific audience and policy makers interested in science and aims to raise global awareness of RIKEN and its research.

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