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Understanding the fly's sense of smell

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Biology

Old cells learn new tricks

As certain neurons within the hippocampus of the brain mature, their contributions to memory and perception change

The philosopher George Santayana famously remarked that "Those who cannot remember the past are condemned to repeat it." The hippocampus is essential to avoiding such mistakes, as this brain structure helps process memories in a manner that can usefully guide an organism's behavior.

The brain uses its ability to recall past actions to identify differences between highly similar yet distinct events, such as when you leave your keys in a different place than usual—a process called 'pattern separation'. The hippocampus also performs the opposite function—known as 'pattern completion'—in which it uses isolated pieces of information to reconstruct stored memories; looking at an old photo, for example, will cause the hippocampus to summon thoughts from the day the photo was taken.

Neuroscientists have generally believed that distinct segments of the hippocampus are responsible for pattern separation and completion. "These two functions have been thought to be opposing and competing processes," explains Toshiaki Nakashiba, a researcher with Susumu Tonegawa's team at the RIKEN-MIT Center for Neural Circuit Genetics in Cambridge, Massachusetts, USA. "Previous studies have indicated that the dentate gyrus is the anatomical location in the hippocampus for pattern separation, while the CA3 region handles pattern completion."

Tonegawa, Nakashiba and colleagues, however, have demonstrated that both processes are managed within the dentate gyrus, with specific contributions from two distinct subsets of neurons known as granule cells (GCs)[1].

Age discrimination

In some ways, the study benefited from a happy accident. The dentate gyrus is one of the only parts of the brain that replenishes neurons in adult life. At first, newly generated 'young GCs' are highly active, but gradually they settle down and become virtually indistinguishable from GCs formed before birth. The researchers developed genetically modified mice in which they could broadly inactivate, and re-activate, hippocampal GCs with a chemical agent that causes their synapses to stop working without harming the cells (Fig. 1). However, they were in for a surprise. "Unexpectedly, this mutant strain retained intact transmission from young GCs," says Nakashiba. "We didn't expect to see the selective blocking of synaptic transmission in 'old' granule cells, but this strain turned out to be a good model for studying the distinct roles of these cells in the dentate gyrus."

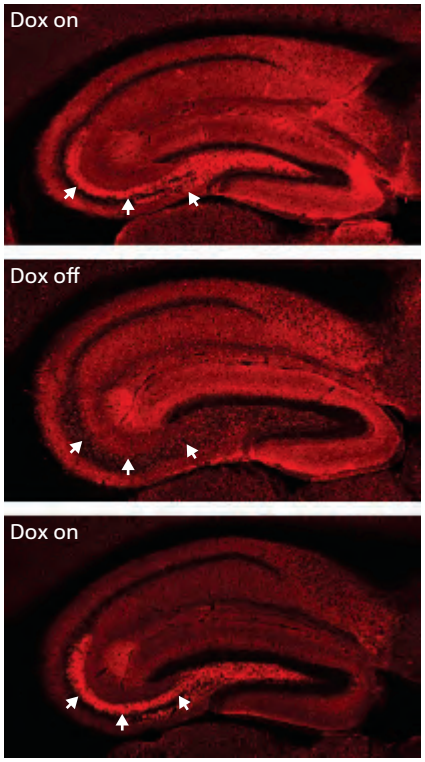


Figure 1: Fluorescently labeled VAMP2 protein (red) offers a useful indicator of synaptic activity. Granule cells in the dentate gyrus of the transgenic mice can successfully transmit signals to the CA3 region of the brain when treated with the chemical activator doxycycline (Dox) (top; arrows). Removal of Dox (middle) can inactivate this signaling, and be reactivated through the re-application of Dox (bottom).

Indeed, the subsequent observation of some unusual behavioral patterns in these mice led Nakashiba and his colleagues to design a series of tests that allowed them to characterize the relative contributions of these different generations of adult-born GCs to memory function.

In one set of experiments, the researchers tested pattern separation by training mice to associate a particular environment with a mildly painful shock. After several training blocks,

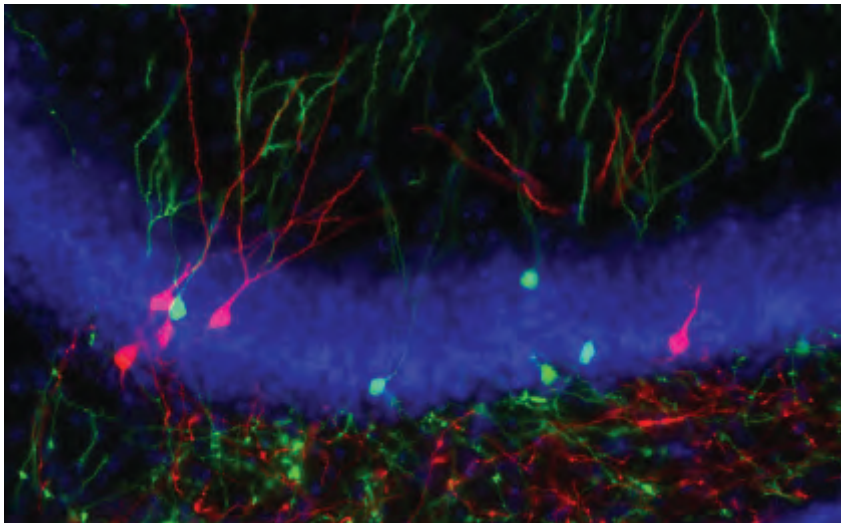


Figure 2: Granule cells within the dentate gyrus play distinct roles in memory formation and recall as they age (green, old granule cells; red, young granule cells).

wild-type mice learned to distinguish a shock chamber from a slightly different-looking chamber with no shock associated. Remarkably, mice with old GCs switched off not only achieved this discrimination, but did so faster, thus suggesting a primary role for young GCs in pattern separation.

Subsequent pattern separation experiments with more obviously different environments provided further support for this model. Mice with inactivated old GCs performed moderately worse at discrimination than wild-type counterparts; however, when the researchers used targeted irradiation to specifically kill off hippocampal young GCs, their performance suffered considerably.

Tonegawa's team also found compelling evidence that older GCs play a key role in pattern completion. In one test, they placed mice in a maze filled with opaque water, with four objects placed at different positions to provide orientation cues. Using those cues, wild-type mice and transgenic animals quickly learned to find an invisible platform submerged below water level at a fixed position in the maze.

Subsequent inactivation of old GCs did not notably impair the ability of transgenic mice to locate the platform, as long as all four cues were present. However, when the researchers reduced the number of cues to one, the treated animals took markedly longer than wild-type mice to find the correct spot. This, together with other experiments, suggests that the selective inactivation of old GCs considerably reduces the speed of pattern completion in the hippocampus.

Balance of power

This latter result is particularly surprising because neuroscientists have generally believed that pattern completion is performed in CA3, a region of the hippocampus that receives information from the dentate gyrus and which is characterized by extensive interconnection between its neurons. "This was believed to be a good network for associating multiple information sources, such as spatial location and contextual information, into a coherent representation," explains Nakashiba.

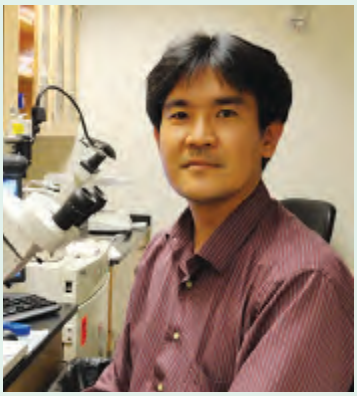
Instead, this process seems to be managed alongside pattern separation within the dentate gyrus (Fig. 2). The researchers raise the possibility that newly formed young GCs may be best-equipped to achieve the recognition of novel elements required for pattern separation, whereas older, more thoroughly integrated GCs are more likely to act as established sources of information for CA3 that facilitate memory recall through pattern completion.

Changes in cellular demographics could therefore have serious consequences. "Our data demonstrated that mice devoid of old neurons had enhanced pattern separation in some conditions, but were also defective in pattern completion," says Nakashiba. "This suggests that the balance between pattern separation and completion could be altered as a result of the loss of old neurons."

Tonegawa's group is now attempting to zoom in on the GC subsets that contribute most to these processes, and Nakashiba anticipates that the results of these studies could ultimately have important implications for understanding the neurological roots of cognitive deficits associated with disease, brain damage or old age.

1. Nakashiba, T., Cushman, J.D., Pelkey, K.A., Renaudineau, S., Buhl, D.L., McHugh, T.J., Barrera, V.R., Chittajallu, R., Iwamoto, K.S., McBain, C.J. *et al.* Young dentate granule cells mediate pattern separation, whereas old granule cells facilitate pattern completion. *Cell* **149,** 188–201 (2012).

ABOUT THE RESEARCHER



Toshiaki Nakashiba was born in Kanagawa, Japan, in 1971. He graduated from the Faculty of Sciences, Kyoto University in 1995, and in 2001 obtained his PhD from the same university in the field of developmental neurobiology, supervised by Dr Shigeyoshi Itohara. Nakashiba then joined the laboratory of Dr Susumu Tonegawa at the Center for Learning and Memory at the Massachusetts Institute of Technology (MIT) in Cambridge, USA, and in 2004 was promoted to the position of research scientist at the RIKEN-MIT Center for Neural Circuit Genetics. His research focuses on the role of hippocampal circuits in learning and memory processes, which he observes through behavioral experiments conducted on genetically modified mice.

Designing a dye you can count on

Chemists have a new tool for creating dyes with special optical properties that will prove invaluable to industrial and medical applications

Natural substances such as chlorophyll and the heme pigment of red blood cells contain colorful molecules known as porphyrins. They owe their exceptional visual characteristics to a 'macrocyclic' chemical structure that links several small rings together into a highly conjugated, aromatic framework. However, chemists who have synthesized porphyrin derivatives have sometimes found that this aromaticity—and any associated optical absorptions—simply disappears.

Now, a research team led by Atsuya Muranaka and Masanobu Uchiyama at the RIKEN Advanced Science Institute, Wako, reports a new way to manipulate the peculiar aromatic properties of macrocycles[1]. The team has found that the aromaticity of a porphyrin-type molecule called hemiporphyrazine can be switched on and off by altering the compound's electron count. This creates a dye with tunable optical absorption of near-infrared light—a type of radiation critical to applications involving organic solar cells and photodynamic cancer therapies.

Conjugated molecules exhibit aromatic properties only when their number of so-called 'pi' electrons is a multiple of the formula $4n+2$, where n is an integer. For example, porphyrin rings with 18 pi-electrons are stable and can share electrons aromatically, making them responsive to light. But a porphyrin with 20 pi-electrons readily gives up two electrons and returns to the favored aromatic state.

Hemiporphyrazines, however, are an unusual kind of macrocycle: their particular combination of carbon and nitrogen double bonds produces a non-aromatic structure that is thermally stable with 20 pi-electrons. Despite the promising material characteristics of these porphyrin analogues, their non-aromatic nature currently limits their usefulness. "From a theoretical point of view, it seems easy to take hemiporphyrazines down to 18 pi-electrons," notes Muranaka. "But so far, no one has succeeded in doing this experimentally."

The researchers solved this problem by putting four hydroxyl (OH) atoms into hemiporphyrazine to facilitate a redox reaction (Fig. 1). Mixing this compound with a strong oxidizing reagent caused two OH units to lose an electron and turn into double-bonded oxygen atoms, transforming hemiporphyrazine into an aromatic 18 pi-electron system. Consequently, the dye displayed intense near-infrared optical absorption peaks where none existed before.

The team reverted its hemiporphyrazine to 20 pi-electrons by mixing it with a reducing agent. This reversible system is sure to interest developers of 'on-demand' opto-electronic materials. Muranaka says that the next step is to prepare a 22 pi-electron hemiporphyrazine—a new aromatic species that quantum calculations predict would have similar or stronger near-infrared absorption bands. ■

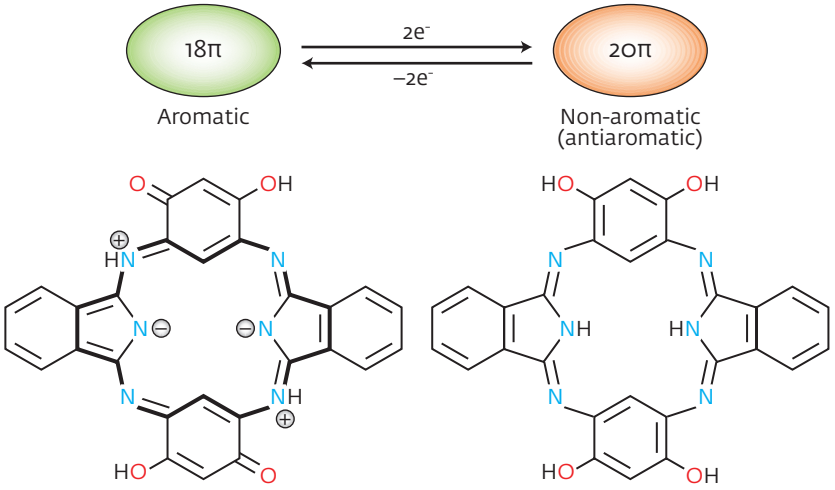


Figure 1: Adding hydroxyl atoms (OH) to a conjugated dye called hemiporphyrazine (bottom structures) enables a redox switching reaction between aromatic (left) and non-aromatic (right) states, setting the stage for 'on-demand' absorption of near-infrared light.

1. Muranaka, A., Ohira, S., Hashizume, D., Koshino, H., Kyotani, F., Hirayama, M. & Uchiyama, M. [18]/[20]π hemiporphyrazine: a redox switchable near-infrared dye. *Journal of the American Chemical Society* **134,** 190–193 (2012).

Illuminating lassos for cellular insights

Real-time monitoring of RNA splicing in living cells moves a step closer with the development of a novel fluorescent probe

Numerous biological processes depend on molecules called lariat RNAs (LaRNAs). These lasso-shaped structures form in the cell during RNA splicing. During this process, transcribed RNA strands convert to messenger RNA before undergoing translation into proteins. A way to quickly and efficiently characterize these molecules in living cells is now available, thanks to a method developed by a research team led by Hiroshi Abe of the RIKEN Advanced Science Institute, Wako[1]. The method identifies LaRNAs using molecular pairs called reduction-triggered fluorescent (REFT) probes. When in close proximity to LaRNAs, these probes react and generate a fluorescent signal.

In contrast to earlier approaches to identify elusive LaRNAs, Abe and his team adopted a simple, non-enzymatic strategy. They exploited RNA strands to make a template of a reaction between the probe components, consisting of a fluorescent dye precursor and a reducing agent called triphenyl phosphine (Fig. 1). To position the probes, they attached the precursor and the triphenyl phosphine to separate DNA strands and then paired them with the complementary RNA template. In an open linear template, the REFT components were too far apart to react. However, the circular loop of LaRNA templates brought the reacting species close enough to facilitate the fluorescence-inducing reaction.

Performance assessments using these probe-linked DNA strands, which could bind different portions of the LaRNAs, showed that a fluorescent signal was emitted only when the reacting components could access the target at the lasso junction. "This offers a high signal-to-background ratio during the detection," says Abe. His team also demonstrated that bigger LaRNA loops increased the accessibility of the probes, enhancing the fluorescent response. Furthermore, splicing reactions carried out *in vitro* revealed that the probes did not hinder the function of associated catalysts and LaRNA production in cells.

Abe and colleagues compared their REFT system with the conventional fluorescence resonance energy transfer (FRET) approach, which also relies on probes that fluoresce when next to each other. Without any optimization, the REFT probes outperformed the FRET probes in distinguishing LaRNAs from similar structures. "Our probes recognize the unusual secondary structure of the [lassos] whereas conventional methods can only be applied to linear RNA structures," explains Abe. He adds that the flexible RNA molecules can adopt various geometries that strongly resemble the lariat architecture causing FRET to produce false positive results.

The team is currently planning to use the REFT probes to image RNA. "An important application of our system is the real-time monitoring of splicing in living cells," says Abe. ■

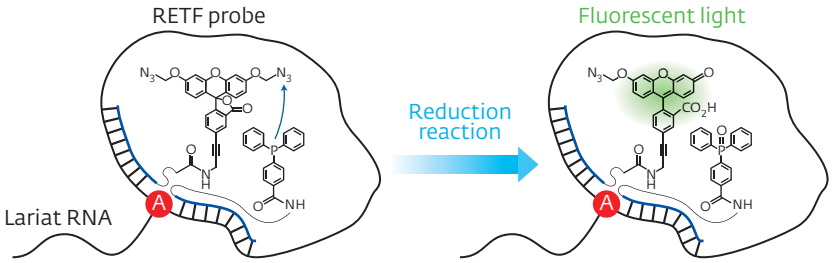


Figure 1: Schematic representation of the reduction reaction between the dye precursor and triphenyl phosphine within the lasso structure of an LaRNA molecule. When these probes meet at the junction (A), fluorescent light is emitted, effectively tagging the molecule.

1. Furukawa, K., Abe, H., Tamura, Y., Yoshimoto, R., Yoshida, M., Tsuneda, S. & Ito, Y. Fluorescence detection of intron lariat RNA with reduction-triggered fluorescent probes. *Angewandte Chemie International Edition* **50,** 12020–12023 (2011).

Revealing the stars of brain adaptability

Star-shaped brain cells called astrocytes are found to bridge the gap between global brain activity and localized circuits

Global network activity in the brain modulates local neural circuitry via calcium signaling in non-neuronal cells called astrocytes (Fig. 1), according to research led by Hajime Hirase of the RIKEN Brain Science Institute[1]. The finding clarifies the link between two important processes in the brain.

Activity in large-scale brain networks is thought to modulate changes in neuronal connectivity, so-called 'synaptic plasticity', in the cerebral cortex. The neurotransmitter acetylcholine regulates global brain activity associated with attention and awareness, and is involved in plasticity.

To investigate how these processes are linked, Hirase and his colleagues simultaneously stimulated the whiskers of mice and the nucleus basalis of Meynert (NBM), a basal forebrain structure containing neurons that synthesize acetylcholine and project widely to the cortex. Using electrodes and an imaging technique called two-photon microscopy, performed through a 'cranial window', they monitored the responses of cells in the barrel cortex, which receives inputs from the whiskers.

Recordings from the electrodes showed that repeated co-stimulation of the whiskers and NBM induced plasticity in the barrel cortex. This plasticity depended on two types of receptors—muscarinic acetylcholine receptors (mAChRs) and *N*-methyl-D-aspartic acid receptors (NMDARs). Two-photon imaging microscopy further revealed that activation of the mAChRs during co-stimulation elevated the concentration of calcium ions within astrocytes of the barrel cortex.

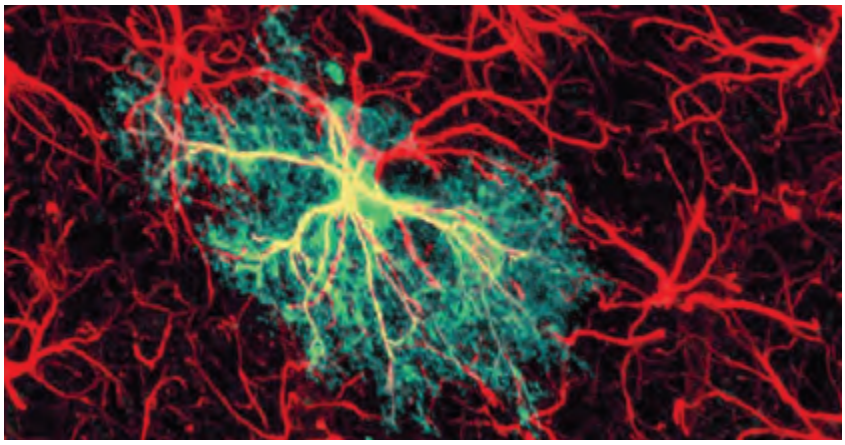


Figure 1: Astrocytes are star-shaped cells with numerous fine projections that ensheath synapses in the brain.

The researchers repeated these experiments in mutant mice lacking the receptor that controls the release of calcium ions in astrocytes. Since co-stimulation of whiskers and NBM did not induce plasticity in the mutants, Hirase and colleagues concluded that calcium signaling in astrocytes acts as a 'gate' linking the changes in global brain state induced by acetylcholine to activity in local cortical circuits.

Furthermore, the researchers found that stimulation of the NBM led to an increase in the extracellular concentration of the amino acid D-serine in the normal, but not the mutant, mice. D-serine is secreted by astrocytes and activates NMDARs. Hirase's team had previously shown that astrocytes are electrically silent in living rodents even in the presence of neural activity[2]. The new findings showed that the biochemical, as opposed to electrical, activation of astrocytes induces them to release the transmitter that modulates synaptic plasticity in the neuronal circuitry.

"Our study is probably the first to show that calcium signaling in astrocytes is related to neuronal circuit plasticity in living animals," says Hirase. "We are now studying if this type of calcium signaling occurs in all parts of an astrocyte or is restricted to some parts of the cell." ■

1. Takata, N., Mishima, T., Hisatsune, C., Nagai, T., Ebisui, E., Mikoshiba, K. & Hirase, H. Astrocyte calcium signaling transforms cholinergic modulation to cortical plasticity *in vivo*. *The Journal of Neuroscience* **31,** 18155–18165 (2011).
2. Mishima, T. & Hirase, H. *In vivo* intracellular recording suggests that gray matter astrocytes in mature cerebral cortex and hippocampus are electrophysiologically homogeneous. *The Journal of Neuroscience* **30,** 3093–3100 (2010).

Periodic organization that runs deep and wide

Confirmation of repeated patterns of neurons indicates a stereotypical organization throughout the brain's cerebral cortex

Neurons are arranged in periodic patterns that repeat over large distances in two areas of the cerebral cortex, suggesting that the entire cerebral cortex has a stereotyped organization, reports a team of researchers led by Toshihiko Hosoya of the RIKEN Brain Science Institute[1]. The entire cortex has a stereotypical layered structure with the same cell types arranged in the same way, but how neurons are organized in the other orientation—parallel to the brain's surface—is poorly understood.

Hosoya and his colleagues therefore examined layer V (5) of the mouse cortex, which contains two classes of large pyramidal neurons that look identical but differ in the connections they form. One projects axons straight down to regions beneath the cortex; the other projects to the cortex on the opposite side of the brain.

First, the researchers examined expression of the *id2* gene in cells of the visual cortex, because these cells form clusters in that part of the brain. They found that *id2* is expressed in nearly all cells that project axons downward, but not in those that cross over. Hosoya and colleagues verified this by visualizing the connections of cells using fluorescent cholera toxin, which binds to cell membranes and travels along the axons.

Further examination of gene expression patterns in tissue slices revealed that the cells are arranged in clusters aligned perpendicular to the brain's surface, and that the clusters are organized in a regular pattern, with the same basic unit repeating every thirty micrometers (Fig. 1). They also observed the same pattern in layer V of the somatosensory cortex, suggesting that this organization is common to all other areas.

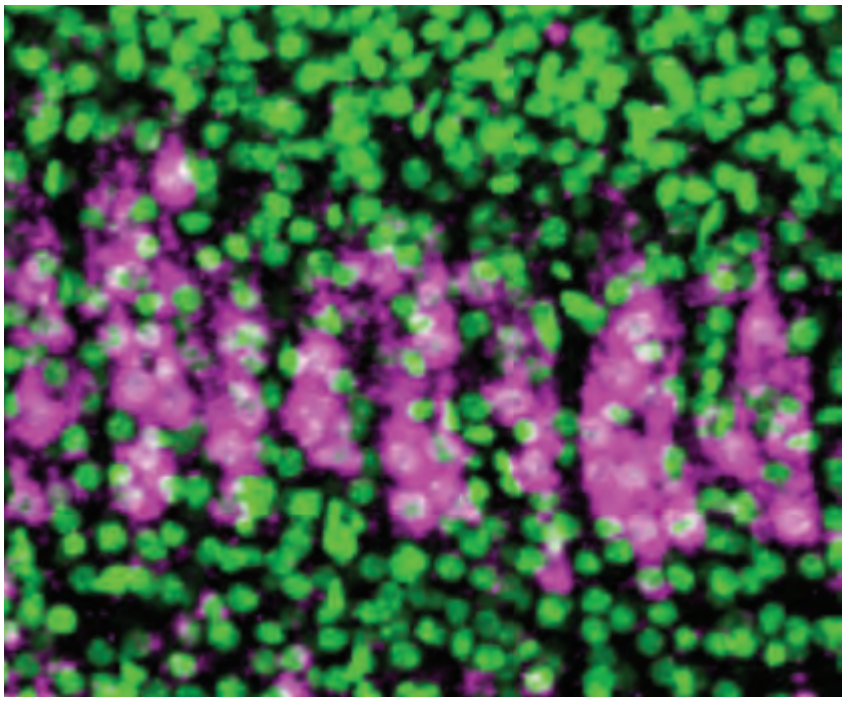


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Figure 1: In the mouse visual cortex, neurons expressing id2 mRNA (magenta) are found in regularly repeating clusters.

By generating a strain of mutant mice expressing green fluorescent protein in the progenitor cells that produce the cells in layer V during brain development, Hosoya and his colleagues investigated the embryonic origin of these cells. This revealed that each cluster contains neurons that are produced by different progenitor cells.

Finally, the researchers showed that the regular pattern persists in the adult visual cortex, and that neurons in each cluster show the same activity patterns in response to visual stimulation. "Our preliminary data suggest that at least several other areas in the cortex have the same structure," says Hosoya. "It's likely that the entire cortex has the same organization, and I expect that the human cortex has the same structure." ■

1. Maruoka, H., Kubota, K., Kurokawa, R., Tsuruno, S. & Hosoya, T. Periodic organization of a major subtype of pyramidal neurons in neocortical layer V. *The Journal of Neuroscience* **31,** 18522–18542 (2011).

Hamlet sets the stage for neuronal development

A genetic 'reset switch' enables a signaling pathway to induce multiple developmental outcomes for olfactory neurons

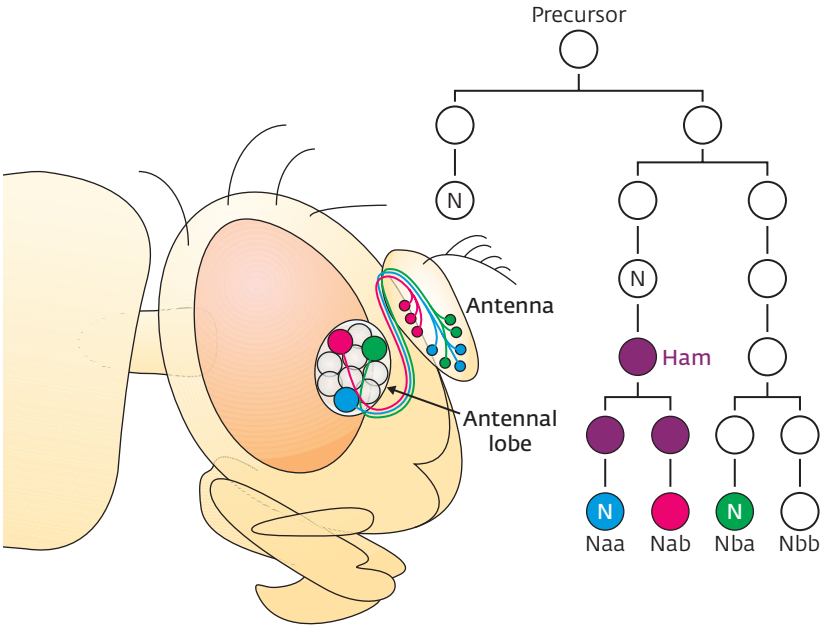

Figure 1: Interplay between Notch signaling and Hamlet activity gives rise to diverse olfactory receptor neurons (ORNs), each with distinct structures and subsets of olfactory receptors (left). The precursor cell (right) divides to yield two daughter cells, one of which undergoes Notch (N)-mediated gene activation. Hamlet (Ham) subsequently resets Notch's genetic effects, and the absence or subsequent restoration of Notch signaling determines which type of ORN (Naa or Nab) will result from differentiation.

Within the nervous system, a handful of signaling pathways modulate development of a cornucopia of different neuronal subtypes. "Even small alterations in neuron differentiation pathways can disrupt subsequent circuit organization and catalyze the genesis of neurological disorders," explains Adrian Moore of the RIKEN Brain Science Institute in Wako.

Recent work from Moore's team, which includes Keita Endo of the University of Tokyo, has revealed mechanisms governing this complexity in the fruit fly olfactory system[1]. Within the antennae—the fly equivalent of the nose—it was known that cells called neuronal precursors undergo multiple rounds of 'asymmetric division', wherein each resulting daughter cell follows a distinct developmental path, yielding different combinations of olfactory receptor neurons (ORNs). Moore's team showed specifically that ORN precursors undergo two rounds of division, yielding four different cellular subtypes, three of which will typically mature into ORNs.

Earlier work from Endo showed that the activation or suppression of signaling by the Notch protein helps differentiate these cellular fates[2], but other factors were clearly involved. Their joint research demonstrated that a second protein, Hamlet, modulates the effects of Notch.

"This [process] provides an important foundation for all future studies of odorant receptor expression and axon targeting control on the olfactory system," says Moore. The researchers found that presence or absence of Notch and Hamlet activity plays a central role in establishing the identity of these subtypes, and this in turn determines both the connections formed by the resulting ORNs as well as the subset of olfactory receptor proteins that will be expressed (Fig. 1).

Moore and Endo's study also revealed a surprising mode of action for Hamlet. Chromosomal DNA is wrapped around clusters of protein, and chemical changes to those proteins profoundly alter local gene activity—a mechanism called 'epigenetic regulation'. They found that Hamlet selectively deactivates genes activated by Notch by triggering such changes. This means that immature ORNs produced by division of a Notch-activated cell can essentially be 'reset' by Hamlet. The ultimate developmental fate of those cells is then determined, in part, by whether or not they subsequently undergo a new round of Notch activation.

Moore and colleagues also observed that, beyond simply switching off active Notch genes, Hamlet may define subsets of target genes that can subsequently be reactivated by Notch signaling. "The modifications induced by Hamlet may help establish cell fate by marking gene promoters for use later during differentiation," says Moore. "This could prove fundamental to understanding the process of neuronal diversification." ■

1. Endo, K., Karim, M.R., Taniguchi, H., Krejci, A., Kinameri, E., Siebert, M., Ito, K., Bray, S.J. & Moore, A.W. Chromatin modification of Notch targets in olfactory receptor neuron diversification. *Nature Neuroscience* **15,** 224–233 (2011).
2. Endo, K., Aoki, T., Yoda, Y., Kimura, K. & Hama, C. Notch signal organizes the *Drosophila* olfactory circuitry by diversifying the sensory neuronal lineages. *Nature Neuroscience* **10,** 153–160 (2007).

A genetic alternative to fertilizer

A plant transporter gene triggered in nitrogen-starved environments could be engineered to reduce the need for nitrogen fertilizers

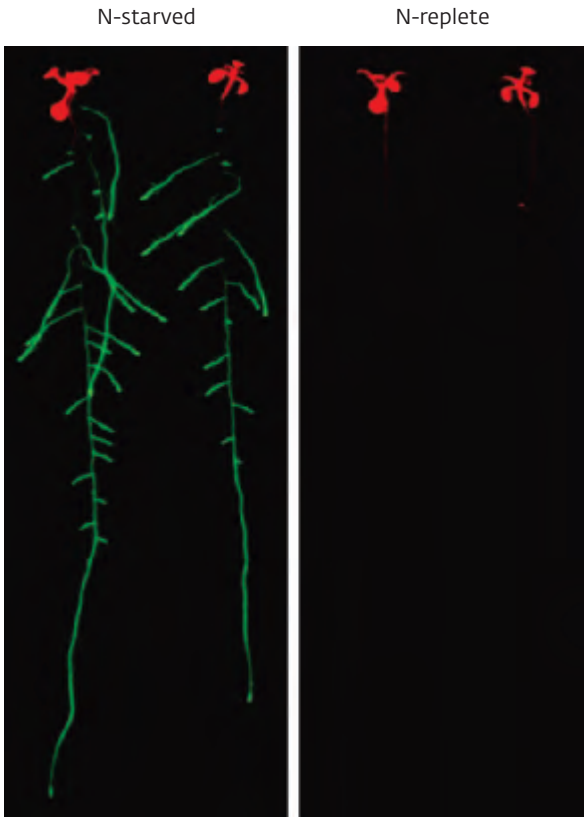

Figure 1: Green fluorescence indicates activation of the *NRT2.4* transporter gene in *Arabidopsis* roots when nitrogen is scarce (left) but not when the soil is replete with this nutrient (right).

Several studies have shown that a lack of nitrogen in soils adversely affects crop yields. The modern use of nitrogen fertilizers has improved yields to meet expanding global food demand, but in some cases up to 50% of the nitrogen in fertilizers reaches surrounding water bodies in the form of nitrate, causing pollution. As the use of nitrogen fertilizers is rapidly increasing worldwide each year, there is a fundamental need to understand how plants absorb nitrate, and how this absorption can be improved in crops.

In *Arabidopsis* plants, nitrogen starvation triggers expression of the nitrate transporter gene known as *NRT2.4*, which allows the plants to absorb trace amounts of nitrate for survival. Now, Takatoshi Kiba and colleagues at the RIKEN Plant Science Center in Yokohama, together with scientists from France and the UK, have gained insight into how *NRT2.4* works to benefit nitrogen-starved plants[1].

"Although nitrogen is one of the most important nutrients for plant growth and productivity, how plants sense and respond to levels of nitrogen in soils is not well understood," explains Kiba. "This is why we started the study focusing on the *NRT2.4* gene."

Using green fluorescent proteins and reporter enzymes to help pinpoint the location and presence of the gene, Kiba and his team found a pattern of *NRT2.4* expression in the roots and shoots of *Arabidopsis* seedlings (Fig. 1).

The researchers worked with 10-day-old *Arabidopsis* seedlings, each weighing around 1 milligram, and measured the tiny amounts of nitrate absorbed by the plants. "Detection of nitrate influx at very low concentration was the main challenge of this work," explains Kiba. "To obtain valid data, we had to improve the precision of the assay and measurement methods." They prepared their samples very carefully in assays before measuring nitrate levels with high-performance liquid chromatography and an automated N/C analyzer-mass spectrometer.

The improved precision paid off, because the team's results revealed that the *NRT2.4* gene is crucial in increasing nitrate absorption by *Arabidopsis* plants at very low concentrations. However, not all plants are equal. "Our preliminary investigation suggests that some domesticated crop plants do not have any mechanism equivalent to *NRT2.4* in *Arabidopsis*," Kiba explains. "It is possible that domesticated plants have lost such a mechanism because it is not necessary in a fertilized environment."

Introducing the *NRT2.4* gene to crops may improve nitrogen uptake efficiency in the future. Kiba notes that "this could eventually enable us to reduce nitrogen fertilizer use and to conduct sustainable agriculture easily." ■

1. Kiba, T., Feria-Bourrellier, A.-B., Lafouge, F., Lezhneva, L., Boutet-Mercey, S., Orsel, M., Bréhaut, V., Miller, A., Daniel-Vedele, F., Sakakibara, H. & Krapp, A. The *Arabidopsis* nitrate transporter *NRT2.4* plays a double role in roots and shoots of nitrogen-starved plants. *The Plant Cell* **24,** 245-258 (2012).

Reacting to changing circumstances

An analysis of a subset of immune cells reveals how these cells rally defenses against infection while keeping potentially harmful inflammatory reactions in check

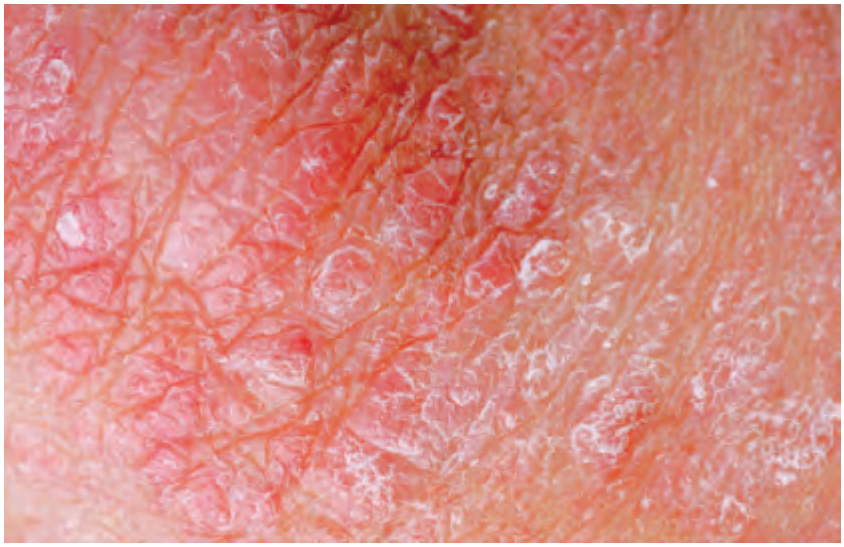

Figure 1: In autoimmune conditions such as the skin condition psoriasis, the immune system attacks tissues in the body, with painful consequences for patients.

T cells represent a significant component of the 'muscle' in the immune system, promoting aggressive action against perceived threats or restraining fellow immune cells from launching an unhealthy autoimmune response (Fig. 1). Dendritic cells (DCs) help to manage these cells, presenting bits of antigen to T cells in a context that allows them to react appropriately.

As with everything in the immune system, however, the biological details are considerably more complex. "DCs consist of heterogeneous subsets, including conventional DCs (cDCs) and plasmacytoid DCs (pDCs)," explains Katsuaki Sato of the RIKEN Research Center for Allergy and Immunology in Yokohama, "and the precise functional role of each DC subset in immune responses remains unclear." Sato is especially interested in pDCs, as the experimental data obtained to date have done little to clarify their behavior within the body.

Sato and his colleagues from Japan and France recently published a detailed analysis of pDC function, achieved by selectively obliterating this cell population in mice[1]. To do this, the team inserted a toxin gene into the gene encoding Siglec-H, a protein uniquely expressed by pDCs; by chemically activating this fatal factor, the researchers could rapidly eliminate Siglec-H-producing cells. As an added benefit, this insertion effectively knocked out Siglec-H expression, revealing the functional contributions of this protein in otherwise normal pDCs.

pDCs express a protein called toll-like receptor 9 (TLR9), which responds particularly to the presence of pathogens such as viruses and bacteria. The researchers determined that pDCs generate various inflammatory signals in response to TLR9 activation, but that the levels of these signals are normally modulated by the inhibitory action of Siglec-H, which appears to be a key regulatory molecule in these cells.

Their experiments confirmed a central role for pDCs in responding to infection, driving both the inflammatory response pathway as well as the production of pathogen-destroying cytotoxic T lymphocytes. However, pDCs also appear to make an important contribution to the process of 'peripheral tolerance', which holds the immune system in check and prevents it from overreacting to non-threatening antigens. Specifically, pDC signals inhibited the production of antigen-specific helper T cells, which activate other immune cells, and favored the formation of regulatory T cells, which help to restrain the immune response.

These latter findings were somewhat surprising, and Sato hopes to delve further into their implications for human health in future studies. "We have a plan to analyze the role of pDCs and their regulation in the control of autoimmune disease," he says. ■

1. Takagi, H., Fukaya, T., Eizumi, K., Sato, Y., Sato, K., Shibazaki, A., Otsuka, H., Hijikata, A., Watanabe, T., Ohara, O. *et al*. Plasmacytoid dendritic cells are crucial for the initiation of inflammation and T cell immunity *in vivo*. *Immunity* **35,** 958–971 (2011).

On the scent of olfactory control

Gene mapping reveals the architecture that controls the expression of the genes responsible for our sense of smell

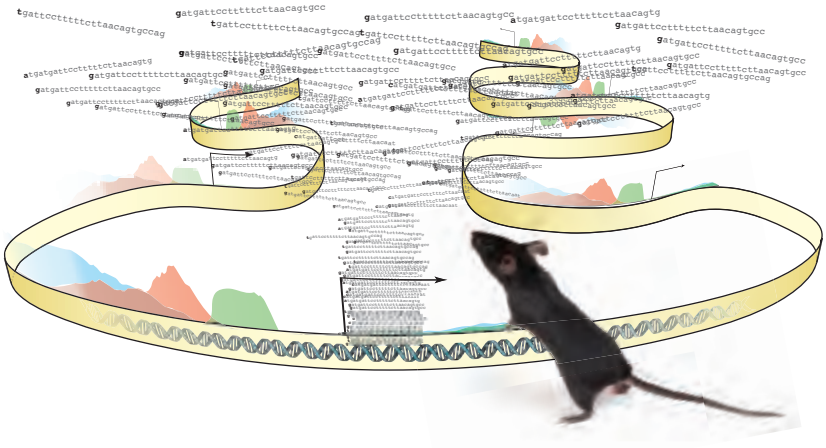

Figure 1: An artistic representation of how the nanoCAGE technique flags the gene promoters for the vast majority of mouse olfactory genes. Mouse image: Emilia Stasiak/shutterstock.com

Within the nasal cavity, millions of sensory neurons in a postage-stamp-sized patch of tissue called the olfactory epithelium control our sense of smell. Thanks to the exquisitely controlled expression of some 300 different olfactory receptor genes, each neuron can detect a small number of distinct volatile odorants. How these genes are regulated, however, has long been a mystery.

Now, an international team led by RIKEN researchers has mapped the genomic architecture of the odorant receptor repertoire in mice, revealing the start points and promoter regions involved in controlling the expression of the vast majority of these genes[1]. "Our study shows that these promoter sequences are strikingly similar between all the olfactory receptors," says Charles Plessy of the RIKEN Omics Science Center in Yokohama, who led the study.

To chart all the promoters, Plessy and colleagues first had to devise an appropriate technique. Plessy's collaborator, Piero Carninci also from the RIKEN Omics Science Center, had previously developed a method called cap-analysis gene expression (CAGE) that determines the location of transcription start sites across the whole genome[2]. But CAGE requires large quantities of RNA, which are not always obtainable from particular types of tissues, including the olfactory epithelium. The researchers therefore modified CAGE to nanoCAGE, which requires as little as 10 nanograms of RNA of biological material per sample[3].

Both CAGE and nanoCAGE work by taking all the messenger RNA transcripts in a given sample, converting them into DNA tags and then comparing the output against a reference genome to find all the transcription start sites. The investigators can then decipher the conserved DNA regulatory sequences in the immediate vicinity of the starting points that form the core promoters.

Using this approach on the minute quantities of RNA found in the olfactory epithelium of mice, Plessy's team plotted the promoters of almost 90% of the mouse olfactory receptor genes, as well as the expression of many non-coding regulatory RNAs (Fig. 1). Further bioinformatic analysis of the DNA surrounding the mapped promoters revealed a number of candidate transcription factor binding sites that help control gene expression, some of which the researchers also validated in mouse experiments.

Plessy and colleagues are now adapting the CAGE technique for even smaller biological samples: single cells. "Such a method would have wide applications in biology and medicine, and, of course, in the biology of olfactory receptors," says Plessy. "With a single-cell technology we will have the potential to make a significant contribution to the field." ■

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Development on an uneven keel

Stem cells of the fruit fly's central nervous system shed light on the mechanism that controls asymmetrical division

Animals consist of many distinct cell types, all of which originate during development from a single cell: the fertilized egg. To generate this vast cellular diversity, the egg and its descendants must divide unevenly to produce new cells with different fates. Nowhere is this process more important than in the central nervous system, where the asymmetric division of neural stem cells called neuroblasts contributes to the profusion of neurons and glial cells.

Several proteins assemble into so-called 'polarity complexes' that localize at one end of the neuroblast to help guide this unbalanced division (Fig. 1). But the mechanism that controls the orientation of these complexes has remained elusive. Now, a team of RIKEN biologists has discovered the master regulator that directs how these proteins are laid down in the neuroblasts of developing fruit fly, or *Drosophila*, embryos[1].

Fumio Matsuzaki and his colleagues at the RIKEN Center for Developmental Biology, Kobe, screened various mutant *Drosophila* embryos for defects in neuroblast polarity. They uncovered an important player in this process: a gene called '*trapped in endoderm 1*' (*Tre1*), which encodes a transmembrane receptor protein. In a series of experiments with fly strains in which they deleted the *Tre1* gene, the researchers showed that this receptor is necessary to orient the polarity of the protein complexes in a perpendicular direction relative to the neighboring epithelial cell layer.

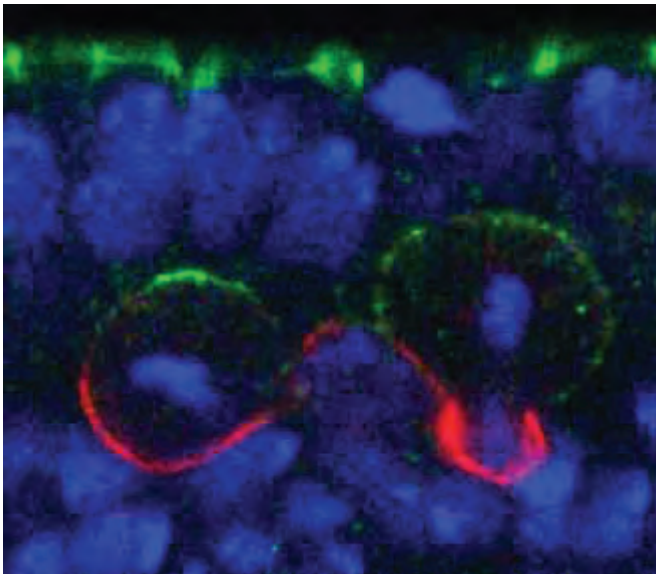

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Figure 1: Neuroblasts localize polarity complexes (green) on the epithelial side (top) and divide perpendicular to the epithelium in a normal *Drosophila* embryo.

Further dissections of protein–protein interactions revealed that *Tre1* recruits and orthogonally orients a critical polarity complex, known as Par, through a cascade of apically localized protein intermediaries. First, *Tre1* activates a subunit of an important signal transducing molecule to recruit the protein Pins, which regulates spindle orientation. Another protein, called Inscuteable, then acts as a molecular link between Pins and Par to ensure that every component is in the proper location.

"The Par-complex is known to regulate the formation of cell polarity in various cell types including stem cells and neurons," explains team member and co-author Shigeki Yoshiura. "So this process might be involved in the orientation of the polarity of various cell types during development."

With *Tre1* emerging at the top of the hierarchy controlling the orientation of polarity complexes in the neuroblast, Matsuzaki and colleagues are turning their attention to finding its regulator. "We still do not know which molecule or molecules act as the extrinsic signal from epithelial cells," Yoshiura says. The RIKEN team is also investigating whether this mechanism is conserved through evolution and is applicable to mammalian neural stem cells. ■

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Clones off to a bad start

Time-lapse imaging of embryos reveals complications that undermine cloning efficiency and potentially contribute to human fertility issues

In 1996, the technique known as somatic cell nuclear transfer (SCNT) transformed the idea of cloning from science fiction into reality. SCNT entails removing the nucleus from an adult somatic cell of the animal being cloned (Fig. 1), and then transplanting it into an oocyte from which the nucleus has been extracted. However, the success rate remains low, and the inability to directly link SCNT-associated abnormalities with embryonic viability has made it difficult to understand why. Now, an imaging technique devised by Kazuo Yamagata of the RIKEN Center for Developmental Biology in Kobe and colleagues has revealed a key checkpoint in this process[1].

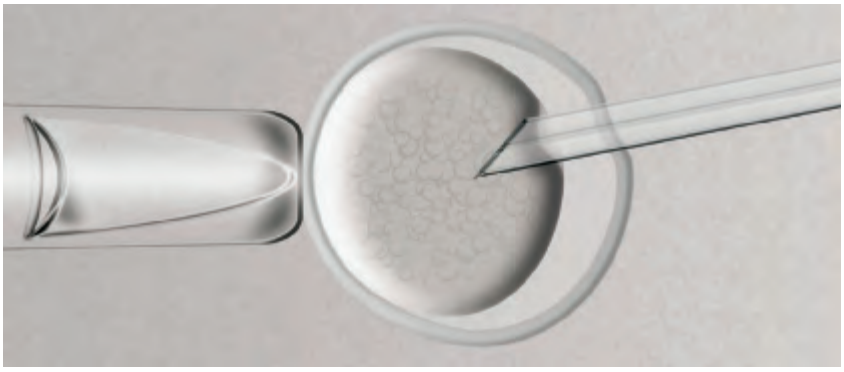

Figure 1: The removal of a nucleus from an oocyte as a prelude to SCNT.

Like any good spy, biologists snooping into the inner workings of embryonic development avoid interfering with the target of their surveillance. Unfortunately, standard imaging techniques are traumatic: cells are forced to overexpress fluorescent proteins before being bombarded with powerful lasers to illuminate the proteins. "This can cause what is known as 'photo-toxicity', which reduces the viability of the cell," explains Yamagata.

His team therefore adapted a technique that they first developed in 2009[2]. They injected mouse oocytes with fixed amounts of RNA molecules encoding a nuclear protein and a cytoplasmic protein, each carrying a different fluorescent label. Using a specially designed microscope, the researchers collected time-lapse imaging data as the embryos developed over the next four days. Importantly, once the injected RNA was expended, the embryos continued to develop normally, revealing which changes proved most damaging to overall viability.

This imaging approach revealed that the SCNT embryos were highly prone to disruptions in how their genetic material was partitioned during cell division, a characteristic termed 'abnormal chromosomal segregation' (ACS). Some embryos exhibiting ACS developed normally and yielded apparently healthy mouse pups. However, when ACS emerged during the first three cell divisions, subsequent development was irreparably sabotaged, suggesting the existence of a critical window in which normal cell division is essential. "I think our [work] is the first to [show] a direct link between chromosome segregation errors and SCNT failure," says Yamagata.

Scientists have hypothesized that epigenetic abnormalities—disruptions in chemical modifications associated with chromosomal DNA—undermine SCNT success, and Yamagata's team has found preliminary evidence potentially connecting these abnormalities. "Our data clearly suggest that some linkage between epigenetic status and genetic stability may exist," he says. Understanding this connection and other contributors to early-stage ACS should benefit humans as well as mice. "It is well documented that infertility and early pregnancy loss are caused by chromosome instability," explains Yamagata. ■

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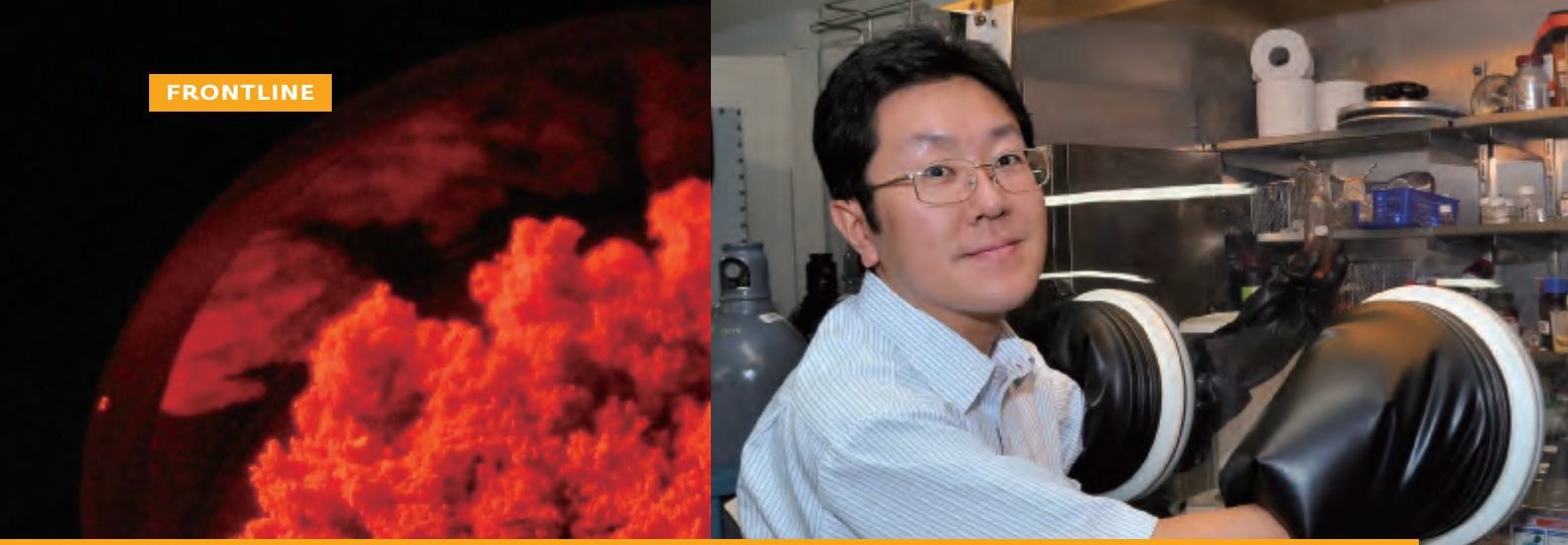

TSUKASA MATSUO

Deputy Unit Leader
Functional Element-Organic Chemistry Unit
RIKEN Advanced Science Institute

Combining elements to create highly functional materials

In a world-first, Dr. Tsukasa Matsuo, Deputy Unit Leader of the Functional Element-Organic Chemistry Unit, and coworkers successfully synthesized a compound with four silicon atoms connected in the form of a rhombus. This achievement attracted great attention because an atom of an element connected in a nonconventional form has the potential to exhibit excellent functions. This success is expected to lead to innovations not only in basic chemistry but also electronics and energy conservation technology. The team is now working on synthesizing new iron compounds, aiming to create a powerful magnet which does not contain rare metals.

Substances created by the wisdom of humankind

"Strangely, there is no organosilicon compound in nature that consists of a combination of carbon and silicon atoms," notes Matsuo. When he joined the research laboratory of Professor Hideki Sakurai, he was impressed by the professor's words: 'Every organosilicon compound is a manufactured substance created by the wisdom of humankind'.

Carbon is a core element in the organic substances that constitute the human body, whereas silicon, which is a major component of the rocks that constitute the earth, is a key element of inorganic substances, and is also used in glass and semiconductors.

In the periodic table of the elements, silicon is located just below the position of carbon (Fig. 2). Many elements in the same group in the periodic table have similar chemical characteristics. "Carbon and silicon, however, have completely different functions in nature," Matsuo explains. "We are combining carbon and silicon atoms in nonconventional ways, aiming to create new materials with excellent functions."

The functions of π-electrons

"The main players are π-electrons because they serve the functions of organic materials," says Matsuo.

A single bond is a covalent bond in which a pair of electrons is shared by two atoms, a double bond comprises two pairs of electrons, and a triple bond three pairs of electrons. A double bond or a triple bond consists of two types of bond—π-bond and σ-bond, whereas a single bond consists of only a σ-bond, which has a strong bonding force and can form the skeleton of a molecule. On the other hand, the π-bond has a weaker bonding force than the σ-bond. "It is the π-electron that forms the π-bond. These π-electrons can move quite freely around a compound depending on how the two atoms are connected (Fig. 3)."

Dr. Hideki Shirakawa, a professor emeritus at the University of Tsukuba, won the Nobel Prize in Chemistry in 2000 for his success in creating a plastic that can conduct electricity, in which the π-electron plays a key role.

Some metals such as iron and copper have "free electrons," which can move freely away from their atoms. When a voltage is applied to such a metal, the free electrons move in one direction and form an electric current. On the other hand, plastic is usually an insulator that does not conduct electricity because it is an organic substance and does not have free electrons.

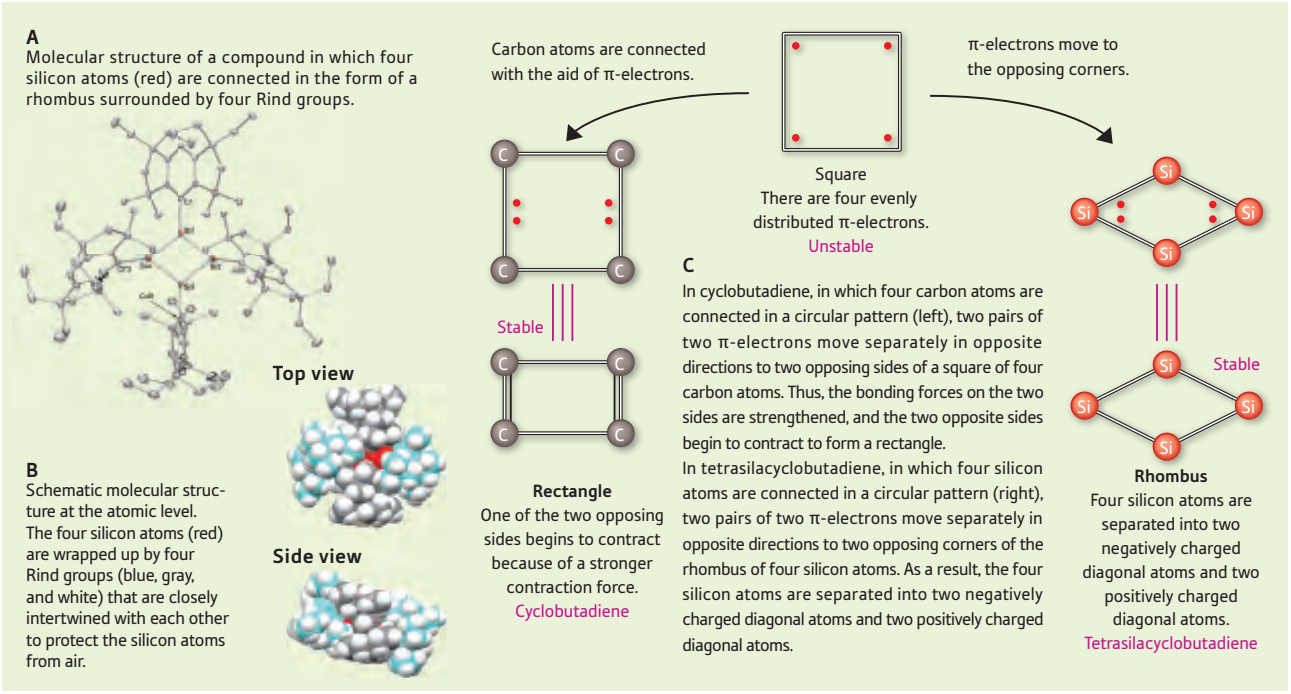

Figure 1: The world's first synthesized tetrasilacyclobutadiene molecule in which four silicon atoms are connected in a circular pattern

This molecule is a compound with four silicon atoms connected in a circular pattern and has four π-electrons. Close examination of the compound is expected to clarify the properties of π-electrons and how silicon atoms are connected, as well as pave the way for creating highly functional materials.

"The electroconductive plastic that Dr. Shirakawa created is an organic compound called polyacetylene, which is a long chain of carbon atoms with alternating single bonds and double bonds, with each carbon connected to a single hydrogen atom (Fig. 4). Dr. Shirakawa added bromine and iodine atoms to make the π-electrons in the material easier to move, thus creating an electroconductive plastic material."

Electroconductive plastics, which are lighter than metals, are now widely used in mobile phones and various other electronic devices.

Rind groups make the impossible possible

"By controlling the movement of π-electrons, we can not only create materials that can conduct electricity, but also those that have different colors or light-emitting properties." Today, research to create organic substances with excellent functions is conducted around the world. But what is unique about the work of Matsuo and his team is that they are attempting to use the π-electrons of elements in and after the third row, or Period 3 in the periodic table, typically silicon-based π-electrons. To do this, it is necessary to stabilize double or triple bonds between silicon atoms. "Until the 1970s, this stabilization was thought to be impossible, because double or triple bonds between the atoms in and after Period 3 have a weak bonding force and tend to disintegrate easily as soon as they react with oxygen or water in the air."

In 1981, a compound with double bonds between silicon atoms was created for the first time in the world. This compound was synthesized by utilizing "steric protection groups" that wrap the compound to protect it from reacting with the air. Since then, researchers have created various compounds with double bonds or triple bonds between silicon atoms; however, most of these compounds disintegrate within several minutes when exposed to the air, because conventional steric protection groups cannot protect the compounds for long. As a result, the compounds have not been used for materials.

This situation continued until 2010, when Matsuo and his team succeeded in creating the world's first compound that has double bonds between silicon atoms and is stable in the air for over one year, namely naphthyl-substituted disilene (Fig. 5). "It has carbon atoms and Rind groups connected to its double bonds between silicon atoms and can emit light at room temperature. This light-emission is due to the interaction between silicon-based and carbon-based π-electrons."

Key to the successful synthesis of the compound is a new type of steric protection group called Rind groups, which were developed by Dr. Kohei Tamao, Director of the RIKEN Advanced Science Institute and Unit Leader of the Functional Elemento-Organic Chemistry Unit. In 1981, a prototype chemical reaction for synthesizing Rind groups was reported, but was hardly ever used by researchers. Tamao, however, came up with ways to use the reaction for synthesizing Rind groups during his time at Kyoto University.

A Rind group is a giant molecule consisting of many carbon and hydrogen atoms. It can be easily synthesized, and in contrast with conventional steric protection groups, the number of atoms can be changed to adjust the size or bulkiness. Thus, the target compound can be tightly wrapped by Rind groups by adjusting their sizes, protecting the compound from the air for a long time.

"In fact, I temporarily moved away from organosilicon chemistry for a while to study the reactions of nitrogen or carbon monoxide using metal complexes. However, I developed a new catalytic reaction that can convert carbon dioxide into methane using a silicon hydride compound called silane. Just as I was wondering about my future, Dr. Tamao called me over to RIKEN. In 2007, I joined RIKEN because I thought I could take

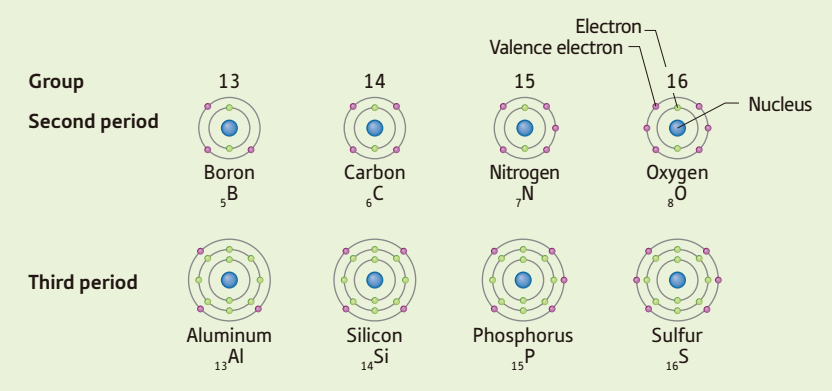

Figure 2: Elements around carbon and silicon in the periodic table

Each element has a different number of electrons orbiting its atomic nucleus. The electrons orbiting the outermost shell of an atom (valence electrons) play a key role in chemical reactions such as covalent bonding. Elements that belong to the same group have the same number of valence electrons and often have the same chemical characteristics.

advantage of my accumulated knowledge and experience and I had a strong interest in Rind groups, which seemed capable of doing things that are conventionally considered impossible."

Matsuo and his team have created about 20 Rind groups of various sizes resulting in a succession of new compounds. "We are using unique steric protection groups called Rind groups to create compounds in which the atoms of an element are combined in a non-conventional form such as double bonds of silicon atoms, as well as new materials that exhibit excellent functions by utilizing the functions of silicon-based π-electrons."

"During the process of creating a new compound, we assemble a molecular model and try rolling the model on the floor to see whether or not it is stable," explains Matsuo.

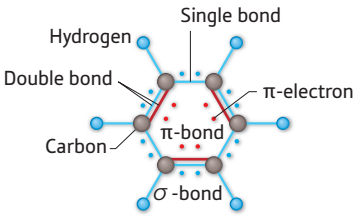

Figure 3: Benzene and π-electron

Benzene (C_6H_6) consists of a regular hexagon of six carbon atoms with alternating single bonds and double bonds. One of the double bonds is a π-bond and the other is a σ-bond that makes up the skeleton. The π-electrons responsible for the π-bond can move freely. In a benzene molecule, six π-electrons are moving around the regular hexagon, thus stabilizing the molecule.

A rhombus formed by four silicon atoms

Matsuo and his team were amazed when they saw a structural model of a compound built up by Dr. Katsunori Suzuki, Research Scientist at the RIKEN Advanced Science Institute because the four silicon atoms of the model were arranged in the form of a rhombus (Fig. 1, A). The synthesis of tetrasilacyclobutadiene, in which four silicon atoms are connected in a circular pattern, had never been achieved at that time. In March 2011, Matsuo and his coworkers published their findings in the US journal *Science*, and their research won widespread acclaim because it allows us to better understand the essence of chemical bonding.

Benzene, consisting of a regular hexagon of six carbon atoms, is very stable (Fig. 3). "Benzene has six π-electrons: They move around the regular hexagon, averaging the bonding force between carbon atoms. This makes the structure stable because of the balanced bonding force," explains Matsuo.

"Strangely, however, cyclobutadiene, which has four carbon atoms in a circular pattern, is quite unstable and is not easy to synthesize. It is very mysterious because its properties remain unknown, so it is dubbed the 'Mona Lisa' of organic chemistry."

In cyclobutadiene, which has four π-electrons, two pairs of two π-electrons move separately in opposite directions to two opposing sides of a square consisting of four carbon atoms. Thus, the bonding forces on the two sides are strengthened, and the square is deformed into a stabilized rectangle (left in C, Fig. 1). "Cyclobutadiene molecules, however, cannot remain stable for a long time. They tend to disintegrate immediately unless they are tightly wrapped with some molecules for protection because they readily combine with each other," says Matsuo.

The situation is different with tetrasilacyclobutadiene molecules, in which four silicon atoms are formed in a circular pattern. "We predicted that the four silicon atoms would form a rectangle, but actually they formed a rhombus instead," explains Matsuo. "We wondered if we had produced a compound different from tetrasilacyclobutadiene."

Later, theoretical calculations by Prof. Kazuyoshi Tanaka, a co-researcher at Kyoto University, clarified that in tetrasilacyclobutadiene, two pairs of two π-electrons move separately in opposite directions to two diagonal corners, causing the opposing silicon atoms to be negatively charged and the silicon atoms in the remaining diagonal corners to be positively charged. Thus, the four silicon atoms in a circular pattern are deformed into a stabilized rhombus (right in C, Fig. 1). "Prof. Tanaka's theory convinced us that we had succeeded in creating tetrasilacyclobutadiene."

This research clarified that the π-electrons in cyclobutadiene exhibit different properties from those in tetrasilacyclobutadiene. Molecular structures with silicon-based π-electrons are generally difficult to stabilize, and most properties of the π-electrons have not been clarified. Thus, π-electrons are expected to have excellent functions. The research being conducted by Matsuo and his team is highly evaluated because it greatly contributes to the analysis.

Furthermore, the laboratory is using Rind groups to create a compound with six silicon atoms connected in a circular pattern. "Many chemists around the world are trying to synthesize such compounds, but no one has succeeded yet. We are closest to achieving synthesis," says Matsuo. The Functional

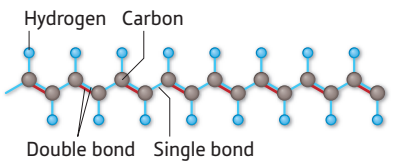

Figure 4: Polyacetylene

Dr. Hideki Shirakawa made the π-electrons in the carbon atoms of polyacetylene easy to move, thereby creating an electroconductive plastic material.

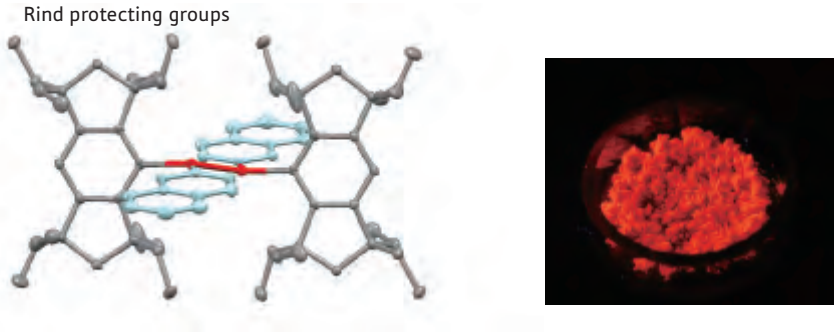

Figure 5: Naphthyl-substituted disilene

Left: Carbon atoms (blue) and Rind groups (gray) are connected to the double bonds between silicon atoms (red). Right photograph: This compound emits light at room temperature.

Elemento-Organic Chemistry Unit is scheduled to end in March 2012. "We are now working to achieve such a compound, and we believe we can do it."

Matsuo hopes to further his research in the future. "I would like to create a new compound by substituting silicon atoms for the carbon atoms in the electroconductive polyacetylene created by Dr. Shirakawa. If the silicon-based π-electrons are made easier to move, the new compound may form a material having superior functions to electroconductive polyacetylene."

Creating a powerful magnet containing no rare metals

"We have already created various compounds using Rind groups, and now we want to research various applications, focusing on creating compounds with excellent functions," outlines Matsuo.

There are two promising compounds: one is a compound with silicon-based π-electrons like silicon-based polyacetylene, and the other is a compound that can exhibit excellent functions when silicon-based π-electrons interact with carbon-based π-electrons, like light-emitting naphthyl-substituted disilene. "There are still various challenges remaining for the practical use of organic EL devices made of naphthyl-substituted disilene. For example, they lose half their brightness in just over an hour. However, if this research makes further progress, I believe we can create energy-saving light-emitting materials that consume less energy."

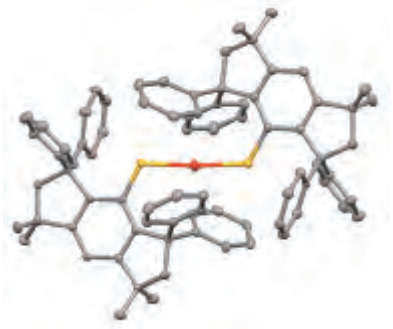

Figure 6: Linear two-coordination ion complex

Sulfur atoms (yellow) and Rind groups (gray) are connected to both sides of a single iron atom (red) in a linear fashion. The compound exhibits a powerful internal magnetic field.

The compounds that Matsuo and his team have created by using Rind groups are not limited to those containing silicon atoms. "In fact, more than half of the compounds contain no silicon atoms. We have focused on the inherent characteristics of various elements and created various compounds that contain representative elements such as boron, phosphorus, sulfur and germanium, and transition metals such as iron, copper and gold."

In general, iron compounds are not stable unless a single iron atom is connected to 4 to 6 atoms. However, Matsuo and his team succeeded in synthesizing a "linear two-coordination iron complex," in which sulfur atoms and Rind groups are linearly connected to both sides of a single iron atom (Fig. 6).

"We are conducting joint research on iron compounds with Dr. Isao Watanabe and Dr. Yoshio Kobayashi, Senior Research Scientist at the RIKEN Nishina Center for Accelerator-Based Science. Physicists seek out interesting substances and have special skills for measuring their properties. On the other hand, chemists use synthetic skills to create such substances and supply them to physicists. We measured a synthesized linear two-coordination iron complex and found that the complex exhibits a powerful internal magnetic field. We think that this achievement resulted from earlier research supported by the RIKEN Coordination Promotion Fund," explains Matsuo.

Powerful magnets are indispensable for high-tech products and energy-saving technology. For example, using powerful magnets enables the creation of small, and light-weight motors that consume less power. Today, neodymium magnets are widely used for powerful magnets, but neodymium metal is unevenly distributed around the world. Many other highly functional materials used today are also unevenly distributed, or they contain rare metals with few resources. Thus, chemistry today requires the creation of highly functional materials containing ordinary, abundant elements such as iron, sulfur, and silicon.

"I would like to create a powerful magnet from a compound that combines ordinary elements such as iron complex," outlines Matsuo. "This is not easy, but it is one of our major objectives." From October 2011, Matsuo is conducting his own research on iron compounds as a part of the Sakigake Project (New Materials Science and Element Strategy) supported by the Japan Science and Technology Agency (JST). This research project will be headed by Prof. Hideo Hosono of the Tokyo Institute of Technology, who discovered an iron-based superconductor.

Matsuo and his team are working to create highly functional materials by bringing together the wisdom of researchers. These materials are expected to contribute significantly to solving problems related to energy-saving and resources.

ABOUT THE RESEARCHER

Tsukasa Matsuo was born in Hokkaido, Japan, in 1970. He graduated from Tohoku University with both Bachelor of Science (1994) and Master of Science (1996) degrees under the direction of Professor Hideki Sakurai and Professor Mitsuo Kira. He received his PhD (1999) from the University of Tsukuba, supervised by Professor Akira Sekiguchi. He became Assistant Professor at the Tsukuba Advanced Research Alliance in 1999, and moved to the Institute for Molecular Science as Assistant Professor in 2001 to study with Associate Professor Hiroyuki Kawaguchi. In 2007, he was appointed Deputy Unit Leader of the Functional Element-Organic Chemistry Unit at RIKEN. In April 2012, he was appointed Associate Professor at the Department of Applied Chemistry, Faculty of Science and Engineering, Kinki University. His main research interests are organoelement and organometallic chemistry.

The RIKEN translation team

Transcending the language barrier

Who are you and what do you do at RIKEN?

We are a small group in the Strategies and Communications Section of the Global Relations Office at RIKEN Headquarters on the Wako campus in Saitama, northwest of Tokyo. The team was formed just over six years ago and currently consists of five people: three Americans and one Japanese for translating between Japanese and English, and one Chinese for translating between Japanese and Chinese. We help to facilitate communication not only within RIKEN, but also between RIKEN and the outside world, by translating the large volume of documents generated daily by the various administrative divisions and offices at RIKEN.

How has your work changed since the team was formed?

The volume of our work has increased steadily over the years as RIKEN evolves into an ever-more internationally oriented organization. In an indirect way we help to generate information on RIKEN's diverse scientific activities and infrastructure for an increasingly globalized audience. The development of RIKEN's capacity to communicate in foreign languages is still a work in progress, but there is certainly more information available in English within RIKEN today than there was a few years ago.

What are the biggest challenges you face in your work?

Translation is an imperfect way of conveying information between different languages because it provides only an approximate meaning of the original. At worst, translation can even lead to confusing or misleading information. Many of the Japanese documents produced by RIKEN are complex and use bureaucratic language, which can be challenging to render accurately in other languages. Language barriers are also inherently associated with cultural barriers, which are much more difficult to transcend. This is especially important within RIKEN, where so many different nationalities and cultures are represented.

How do you address the cultural differences in your work at RIKEN?

The documents we translate range from routine notices to important policy statements, but each receives the same high level of professional commitment and attention to detail. When translating, we often have long discussions as to what is actually meant by the Japanese text and how to convey that meaning in English. Sometimes we have to contact the original writer of the document for background information. We also discuss the contents with RIKEN's administrative staff, who are always receptive to our suggestions and work closely with us to draft accurate and easy-to-read documents.

What is the best thing about your job at RIKEN?

The translation team promotes cross-cultural communication by highlighting not only the different communication styles between Japanese, English and Chinese, but also the different cultural values that underlie those styles. During the translation process we discover new cultural perspectives that help us to render the core message—not just the words—of the original text. This cultural exchange is a real joy and improves communication skills for both the Japanese and non-Japanese staff at RIKEN. We are proud to be contributing to the ongoing internationalization of RIKEN.

CONTACT INFORMATION

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A day of discovery at RIKEN

The RIKEN Open Day is a once-a-year opportunity for budding scientists and the interested public to get to know more about the cutting-edge research being conducted by the organization's researchers. The Open Days are held at each of RIKEN's five main institutes in Wako, Tsukuba, Yokohama, Kobe and Harima, as well as the Sendai and Nagoya facilities, and typically attract over 20,000 visitors.

The first Open Day in 2012 was held on 20–21 April at the Tsukuba Institute, where visitors had the chance to see the work being done at the BioResource Center (BRC).

Visitors had the chance to participate in various activities at the RIKEN Open Day

The Wako Institute, RIKEN's administrative headquarters and home to several of its major research centers, accepted visitors on 21 April and provided an array of hands-on experiments and events. Visitors to the campus were introduced to nanoscience, superconductivity, lasers and biotechnology, as well as brain science, supercomputing, molecular simulations and magnetism. There was also the opportunity for visitors to take a closer look at RIKEN's facilities for heavy ion beams and nuclear physics.

A number of lectures were held throughout the day, covering fields such as cell fate, genetic recombination and photosynthesis. Visitors had the chance to use a scanning electron microscope and even a femtoscope, and to investigate protein structures and learn about the mechanism of memory.

The third of this year's Open Days was held at the Harima Institute, home of the SPring-8 radiation synchrotron and SACLA X-ray Free Electron Laser (XFEL) facilities, on 29 April.

The RIBA (Robot for Interactive Body Assistance) II on display at the RIKEN Open Day

The Yokohama Institute and the Nagoya and Sendai facilities will hold open days for the public later this summer. The Yokohama Institute will welcome guests on 29 September with the facilities at Nagoya and Sendai both opening on 4 August. The additional dates will give visitor who missed the events at Wako another chance to experience RIKEN at first hand. ■

Tenth CDB Symposium on Quantitative Developmental Biology

On 25–27 March 2012, the RIKEN Center for Developmental Biology (CDB) held its tenth annual symposium, this year on the topic of Quantitative Developmental Biology. The symposium was attended by around 160 participants from 14 countries, providing an opportunity to review and experience experimental, computational, and theoretical approaches to the study of developmental principles. The 31 talks of the symposium were augmented by the presentation of over 70 posters, giving researchers in quantitative developmental biology the chance to discuss their work with peers from around the world.

This year's event was co-organized by Shigeo Hayashi and Tatsuo Shibata from the CDB, as well as Suzanne Eaton of the Max Planck Institute of Molecular Cell Biology and Genetics in Germany, Shigeru Kondo of Osaka University, and Shuichi Onami of the RIKEN Quantitative Biology Center, with support of 11 participating organizations. ■

Participants came from around the world to attend the CDB Symposium 2012

RIKEN delegation visits leading Indian research institutes

As part of RIKEN's ongoing program of extending its network of research links with top-level international institutions across the globe, a management delegation from RIKEN visited India between 26 February and 2 March on a five-day tour of top Indian institutes located in Delhi, Hyderabad and Bangalore. The RIKEN personnel were accompanied by representatives from the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the Japanese Embassy in India. During the visit, which built on previous missions to the subcontinent such as that led by RIKEN President Ryoji Noyori in 2006, the combined delegation met senior academic staff and high-ranking officials from such leading national institutions as the Indian Institute of Science, the Indian Institute of Technology Delhi, the University of Hyderabad, the National Centre for Biological Sciences (NCBS) and the Jawaharlal Nehru Centre for Advanced Scientific Research, and participated in guided tours of their respective research facilities. In addition, the group from Japan held talks with senior officials from the Department of Biotechnology and the Department of Science and Technology of the Ministry of Science, where they discussed the possibility of reactivating a 2006 Memorandum of Understanding between RIKEN and the Indian government as a basis for future research collaborations, and as a prelude to 60th anniversary celebrations to be held this year which mark the establishment of formal diplomatic relations between Japan and independent India. In total, the delegation visited ten universities, institutes and government organizations as well as the India office of the University of Tokyo located in Bangalore. The Japanese delegation was warmly and enthusiastically welcomed by their Indian counterparts and held fruitful discussions about a range of potential opportunities for further strengthening academic ties, including the possibility of holding joint seminars, creating collaborative research programs with RIKEN and setting up a joint research center between the NCBS and the RIKEN Center for Developmental Biology. ■

RIKEN personnel engaged in talks with officials from the University of Hyderabad

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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.

For further information on the research presented in this publication or to arrange an interview with a researcher, please contact
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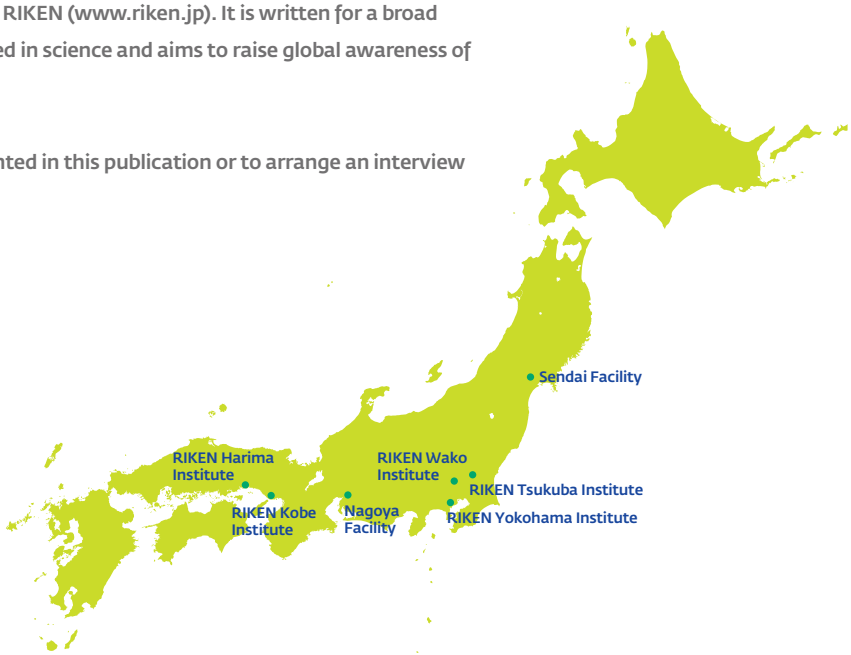

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