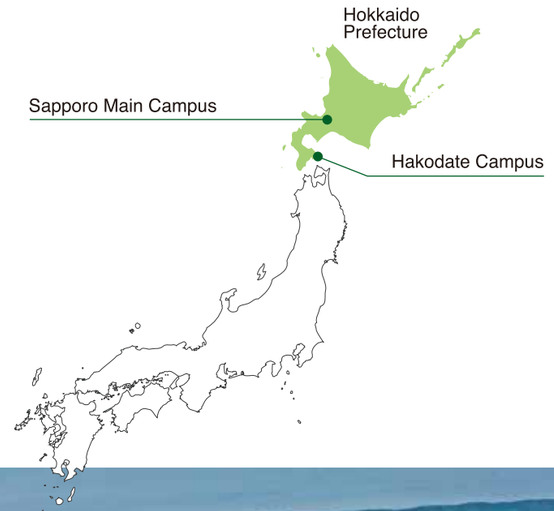
HOKKAIDO UNIVERSITY

Hokkaido University is one of the oldest, largest, and most prestigious universities in Japan. The University was originally founded as Sapporo Agricultural College in 1876 to educate students to become national leaders, and to help develop Hokkaido.

Today, our researchers in the social and natural sciences, as well as in the humanities, are advancing human knowledge through their outstanding work, which has been recognized by many institutions, including the Nobel Laureate Committee.

Boasting one of the biggest campuses in Japan, Hokkaido University houses exceptional research facilities, a university hospital and one of the world's largest research forests. This combination provides a comprehensive research environment and the highest quality education.



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Spotlight on Research

2016-2017 Hokkaido University

HOKKAIDO UNIVERSITY

Shell-swinging snails knock out predators

Some snail species were found to counterattack predators by swinging their shells, suggesting the importance of predator-prey interactions in animal evolution.

Until now, snails were thought to protectively withdraw into their shells when attacked. However, an international research team has found a pair of snail species that use their shells like a club to hit predators and knock them over.

Evolutionary scientists have been questioning how predator-prey interactions affect the evolution of the prey. However, they are yet to resolve whether this interaction induces the diversification of the prey species and its morphological features and behaviours.

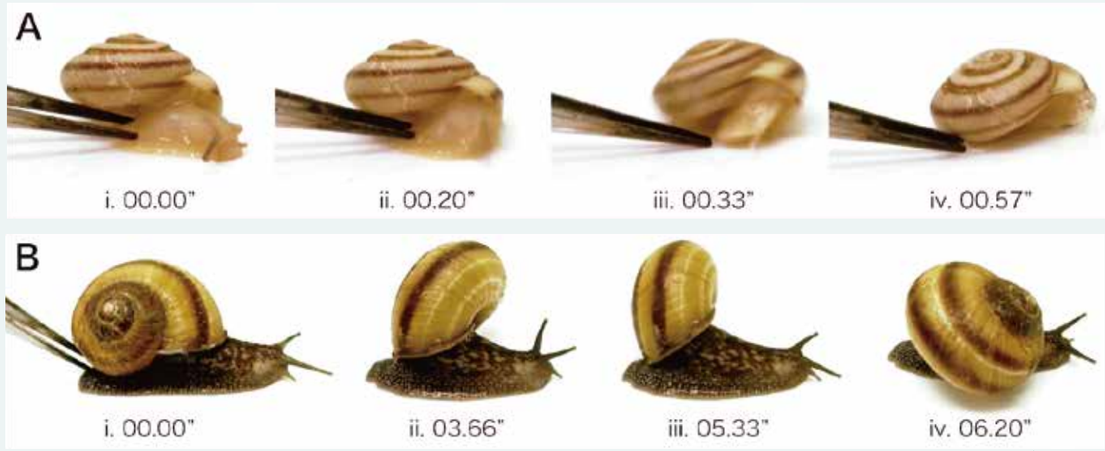
Researchers from Japan's Hokkaido University and Tohoku University collaborated with colleagues at the Russian Academy of Sciences to closely study snail species from the genus *Karaftohelix* in both countries. They observed each species' defensive behaviours against their predator, the carabid beetle, and conducted shell measurements and species comparisons. The team used DNA sequencing to analyse how closely related the species were to each other.

They found that two snail species—*Karaftohelix (Ezohelix) gainesi* in Hokkaido, Japan and *Karaftohelix selskii* in the Far East region of Russia—swing their shells to hit the carabid beetles, demonstrating a very unique, active defence strategy; while other closely related snail species withdraw their soft bodies into their shells and wait until the opponent stops attacking. "The difference in their defensive behaviours is also reflected in their shell morphology, indicating that their behaviours and shell shapes are interrelated to optimize the preferred defence strategy," says Dr. Yuta Morii, the study's lead author.

By analysing DNA sequences of each species, the team also discovered that the two active-or-passive defensive methods evolved independently in the Japanese and Russian species.

Their findings suggest that the selection of each method has led to the diversification of the behaviours, shapes and species of the snails. This study, published in the journal, *Scientific Reports,* is one of only a few to report on land snails using their shells for active defence by swinging them against a predator.

"Our study showcases the importance of predator-prey interactions along with resource competition as major selective forces affecting the evolution of morphological and behavioural traits in organisms," Dr. Morii adds.



Defense behaviors of two different snail species *Karaftohelix(Ainohelix) editha* (a) and *Karaftohelix (Ezohelix) gainesi* (b). *K. editha* withdraw their soft bodies into their shells, while *K. gainesi* swing their shells around. (Morii Y.et al.,*Scientific Reports*, November 11, 2016)

Watch the movie

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Original paper:
Morii Y., Prozorova L., Chiba S., Parallel evolution of passive and active defence in land snails. *Scientific Reports,* November 11, 2016.
DOI: 10.1038/srep35600

wavebreakmedia/Shutterstock

A new system to detect spinal deformity

A newly developed symmetry-recognition system can detect the early stages of idiopathic scoliosis, a type of spinal deformity, without the help of a specialist doctor.

Individuals with idiopathic scoliosis, many of whom are pubescent girls, suffer from serious curvature of the spine. The disease has a characteristically high affliction rate, affecting one in 50 people.

Early detection of the progressive ailment is regarded as essential for treatment, as it is effective to wear a special brace when the spine is curved by 30 degrees or more. In recent years, genetic study of the disease has progressed, boosting the development of treatments.

In accordance with stipulations in the Japanese School Health and Safety Act, elementary and junior high schools conduct physical check-ups aimed at detecting idiopathic scoliosis. However, the law leaves it up to the respective medical associations or education boards in each municipality to decide how to conduct the checks, giving rise to regional gaps in the detection rate. Another related problem is the burden placed on doctors who have to examine a large number of students within a limited time frame.

To address these issues, two scientists from different fields of research, Dr. Hideki Sudo of Hokkaido University's Graduate School of Medicine and Dr. Satoshi Kanai of the Graduate School of Information Science and Technology developed a system to evaluate the level of asymmetry on the surface of the back when measured three-dimensionally.

In a collaboration between the university and Noa Co., Ltd., the researchers developed a prototype device for detecting idiopathic scoliosis. The device is expected to go through clinical testing so that it can be used in clinics and for physical examinations at schools.

The device three-dimensionally scans multiple points on the back, enabling the evaluation of the back's symmetry from any angle in a few seconds. In this way, it is expected to enable speedy and accurate detections of idiopathic scoliosis. In the future, the researchers hope to gain government approval for the clinical use of their device.

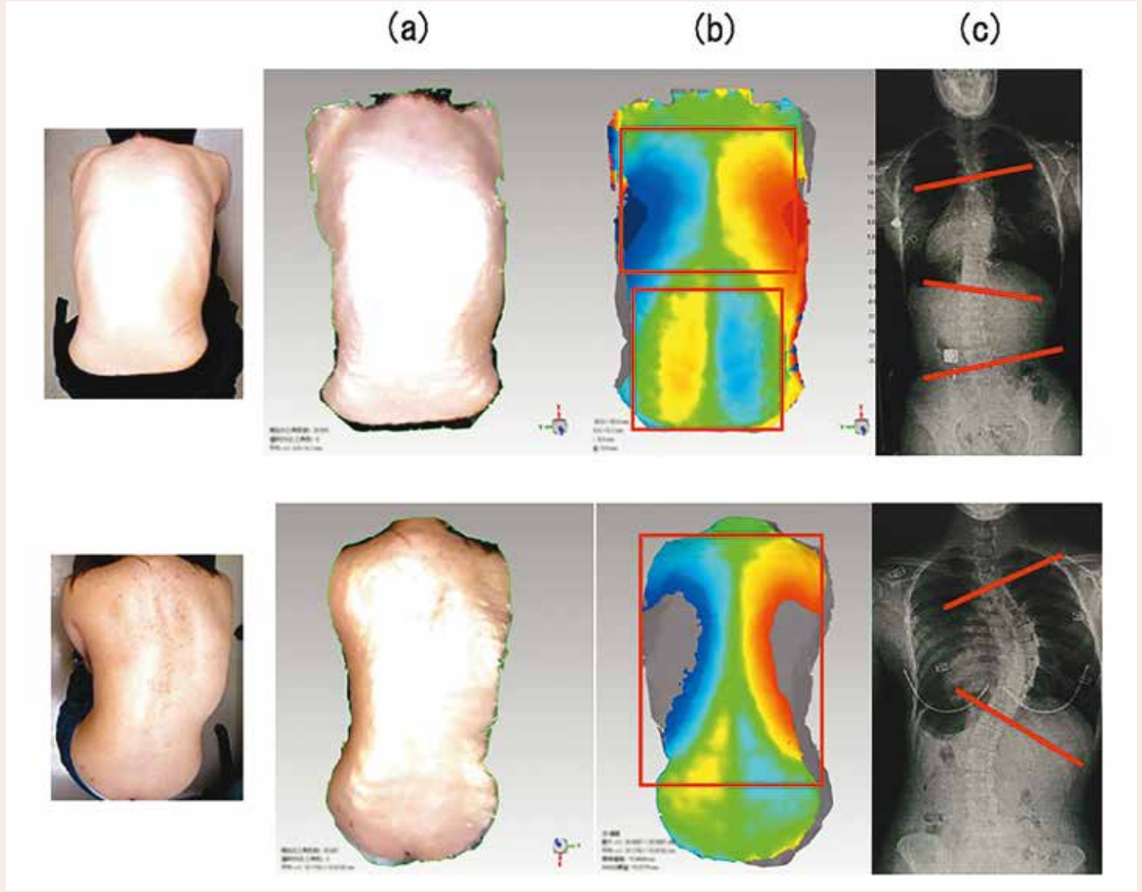

Image analyses of idiopathic scoliosis sufferers using a three-dimensional, back-surface-symmetry-recognition system
Top: images of a case in which a patient is to be treated with a brace. The thoracic vertebra curves by 34 degrees.
Bottom: images of a case in which a patient requires surgery. The thoracic vertebra curves by 60 degrees.
(a): a three-dimensional image of the back's surface
(b): the system evaluates the degree to which a patient's back deviates from the ideal symmetry for a human back within a few seconds. The larger the deviation, the deeper the color.
(c): comparison to X-ray photos. Deviations in the image correspond with curvatures.
Images: Hokkaido University/Noa Co., Ltd.

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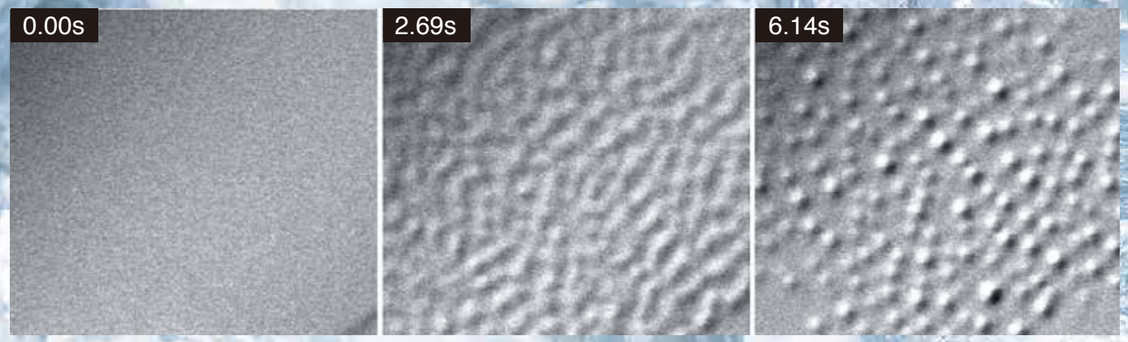
Why is the surface of ice wet?

A 150-year-old mystery surrounding the surface melting of ice crystals is now answered by using an advanced optical microscope.



Figures illustrating the process in which a QLL, a thin layer of water on ice, transforms to a state of partial wetting. At the start (0.00 seconds), the surface of the ice is completely covered by the QLL. After six seconds, the layer has turned into droplets (Scale bar: 10 μm). (Murata K. et al., *PNAS*, October 17, 2016)

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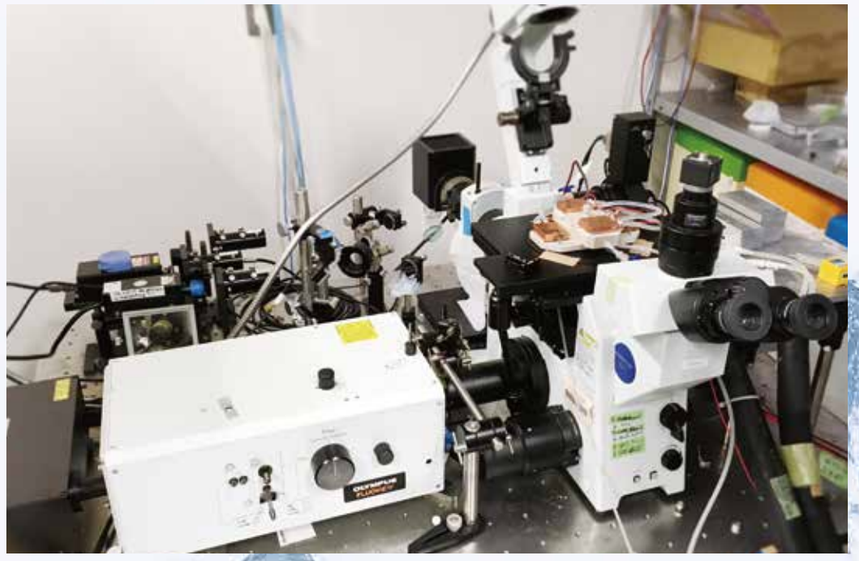


The advanced optical microscope developed by the research group is able to detect the difference in a surface's height at angstrom resolution.

"Ice is wet on its surface": Since this phenomenon, called surface melting, was mentioned by British scientist Michael Faraday more than 150 years ago, the question of why water on the surface of ice does not freeze in a subzero environment remained unanswered.

In the search for the underlying mechanism behind surface melting, Dr. Ken-ichiro Murata of Hokkaido University and his collaborators used a special optical microscope jointly developed with Olympus Corporation. The microscope enabled them to observe how thin water layers, or quasi-liquid layers (QLLs), are born and disappear at various temperatures and vapor pressure levels.

According to the researchers' findings, thin water layers do not homogeneously and completely wet the surface of ice—a discovery that runs contrary to conventional wisdom. QLLs, therefore, are not able to stably exist at equilibrium, and thus vaporize.

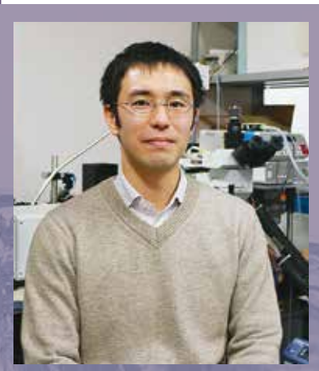
Furthermore, the team discovered that QLLs form only when the surface of ice is growing or sublimating, under supersaturated or unsaturated vapor conditions. This finding strongly suggests that QLLs are a metastable transient state formed through vapor growth and sublimation of ice, but are absent at equilibrium.

"Our results contradict the conventional understanding that supports QLL formation at equilibrium," says Dr. Ken-ichiro Murata.

"However, comparing the energy states between wet surfaces and dry surfaces, it is a corollary consequence that QLLs cannot be maintained at equilibrium. Our findings may contribute towards the understanding of various phenomena that involve surface melting, such as the lubrication on ice, formation of an ozone hole, and generation of electricity in thunderclouds."

Their research is likely to provide a universal framework for understanding surface melting on other crystalline surfaces too.

Researcher Details



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Murata K. et al., Thermodynamic origin of surface melting on ice crystals.
Proceedings of the National Academy of Sciences of the United States of America,
October 17, 2016.
DOI: 10.1073/pnas.1608888113

The gene of autumn colors

Researchers have found Mendel's *Stay-Green* gene encodes an enzyme that extracts magnesium from chlorophyll, adding clarity to understanding how the pigment degrades.

In plants, the pigment chlorophyll plays a central role in photosynthesis: the process of converting sunlight to energy. This process involves creating a flow of electrons by removing one from a molecule and transferring it to another. The first step happens when an electron is transferred from chlorophyll to a compound called pheophytin a.

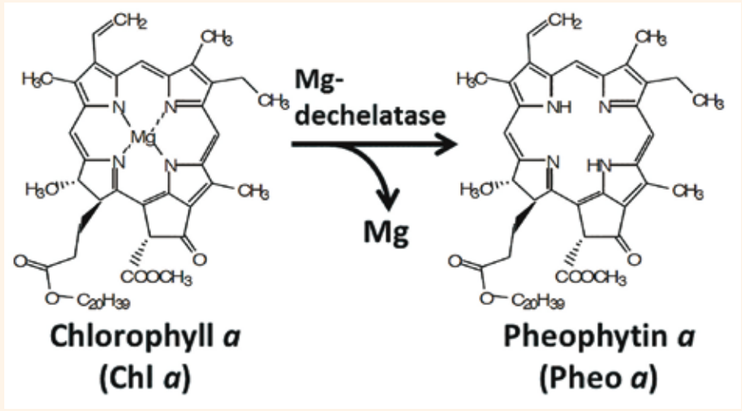
Autumn leaf colors occur when chlorophyll degrades as a normal part of leaf aging or "senescence", playing an important role in nitrogen recycling. The process of chlorophyll degradation is triggered when an enzyme extracts magnesium (Mg) from chlorophyll. Researchers have named the enzyme Mg-dechelatase, but have never been able to detect its actual presence in experiments.

Dr. Yousuke Shimoda, Dr. Hisashi Ito, and Dr. Ayumi Tanaka at Hokkaido University have demonstrated that a gene with known involvement in chlorophyll degradation, called Stay-Green (SGR), codes for Mg-dechelatase.

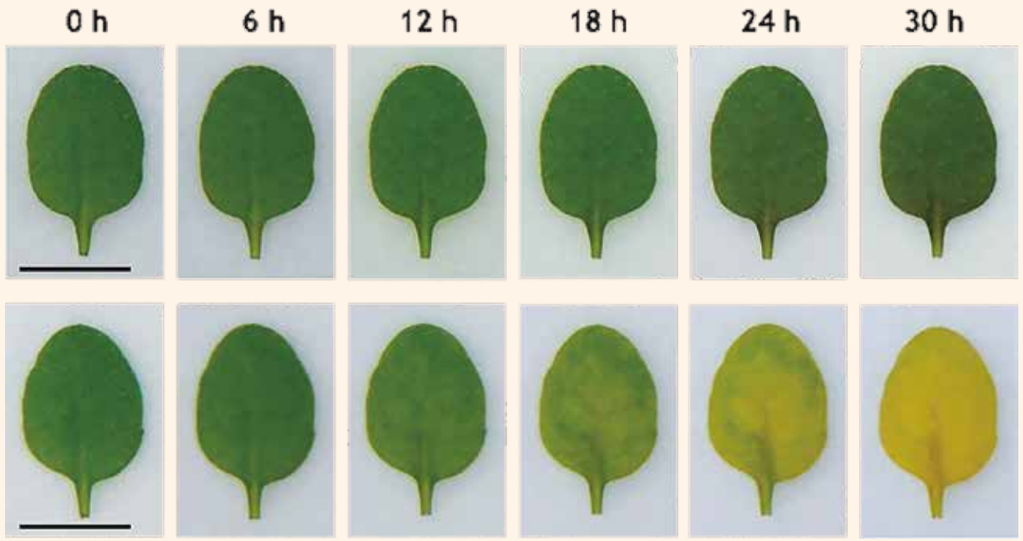
Stay-Green mutants allow leaves to retain greenness during senescence. This gene was among several that led Gregor Mendel to establish the basic laws of genetics in the 19th century while studying the characteristics of peas over several generations. However, it has long been unknown what the gene actually encodes.

The team transiently induced SGR in fully green leaves of a small flowering plant called thale cress. They found this resulted in a reduction of chlorophyll levels. They also incubated chlorophyll in a test tube with SGR, which resulted in its conversion to pheophytin a. Chlorophyll can only be converted to pheophytin a by extracting Mg from it. The experiments strongly suggest that Mg-dechelatase is involved in chlorophyll degradation via SGR.

The team's results also suggest that SGR can also extract Mg from chlorophyll embedded in the light-harvesting complex, therefore leading to its degradation. "It remains unclear whether SGR plays a role via Mg-dechelatase activity in supplying pheophytin a for the process of photosynthesis" says Dr. Hisashi Ito. "Little is known about the mechanism by which an enzyme extracts a metal ion from an organic compound. Our study may lead to the discovery of novel reaction mechanisms."



Degradation of chlorophyll starts when Mg is extracted from the molecule by Mg-dechelatase. The resulting pheophytin a also plays a role in photosynthesis. (Shimoda Y et al., *The Plant Cell,* September 7, 2016)



Stay-Green (SGR) gene induces color changes in leaves. SGR was experimentally induced (bottom) in *Arabidopsis* and compared with the normal leaves (top). Excised leaves were observed for up to 30 hours. (Shimoda Y. et al., *Plant Cell,* September 7, 2016)

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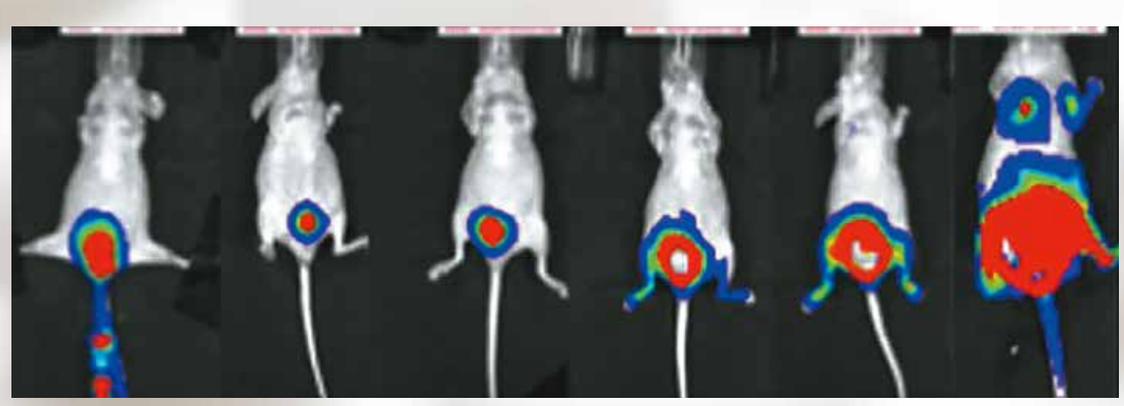
Original paper:
Shimoda Y., Ito H., Tanaka A., Arabidopsis STAY-GREEN, Mendel's green cotyledon gene, encodes magnesium-dechelatase. *The Plant Cell,* September 7, 2016.
DOI: 10.1105/tpc.16.00428

Cold medicine could stop cancer spread

A nonsteroidal anti-inflammatory drug used for treating colds suppresses the spread of bladder cancers and reduces their chemoresistance in mice, raising hopes of a future treatment for advanced bladder cancers.



Tumor growth in the xenograft bladder cancer model was monitored using a bioluminescence imaging system. Forty-five days after inoculation, metastatic tumors were detected in the lungs, liver and bone. (Matsumoto R. et al., *Scientific Reports,* October 4, 2016)

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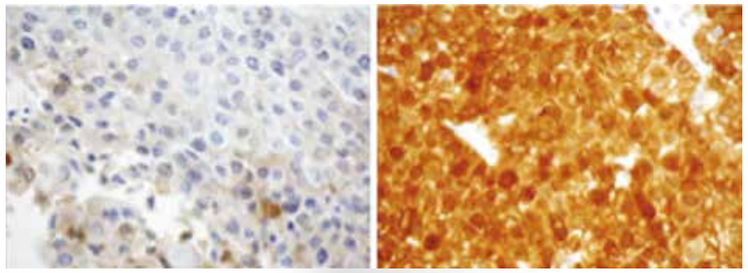

Expression of AKR1C1 in a primary bladder tumor (left) and a metastatic lung tumor (right) in humans. (Matsumoto R. et al., *Scientific Reports,* October 4, 2016)

Bladder cancer is the seventh most common cancer in males worldwide. Every year, about 20,000 people in Japan are diagnosed with bladder cancer, of whom around 8,000—mostly men—succumb to the disease. Bladder cancers can be grouped into two types: non-muscle-invasive cancers, which have a five-year survival rate of 90 percent, and muscle-invasive cancers, which have poor prognoses. The latter are normally treated with anticancer drugs such as cisplatin, but tend to become chemoresistant. This thus allows it to spread to organs, such as the lungs and liver, and to bone.

In recent research, human bladder cancer cells labeled with luciferase were inoculated into mice, creating a xenograft bladder cancer model. The primary bladder xenograft gradually grew and, after 45 days, metastatic tumors were detected in the lungs, liver and bone. By using a microarray analysis including more than 20,000 genes for the metastatic tumors, the team discovered a three- to 25-fold increase of the metabolic enzyme aldo-keto reductase 1C1 (AKR1C1). They also found high levels of AKR1C1 in metastatic tumors removed from 25 cancer patients, proving that the phenomena discovered in the mice also occur in the human body. Along with anticancer drugs, an inflammatory substance produced around the tumor, such as interleukin-1β, increased the enzyme levels.

The researchers also identified for the first time that AKR1C1 enhances tumor-promoting activities and proved that the enzyme blocks the effectiveness of cisplatin and other anticancer drugs.

The researchers finally discovered that inoculating flufenamic acid, an inhibitory factor for AKR1C1, into cancerous bladder cells suppressed the cells' invasive activities and restored the effectiveness of anticancer drugs. Flufenamic acid is also known as a nonsteroidal anti-inflammatory drug used for treating common colds.

The team's discovery is expected to spur clinical tests aimed at improving prognoses for bladder cancer patients. In the latest cancer treatments, expensive molecular-targeted drugs are used, putting a large strain on both the medical economy and the state coffers. "This latest research could pave the way for medical institutions to use flufenamic acid—a much cheaper cold drug—which has unexpectedly been proven to be effective at fighting cancers," says Dr. Shinya Tanaka of the research group.

This research was conducted in collaboration with Dr. Nobuo Shinohara of the Department of Renal and Genitourinary Surgery at Hokkaido University; the article's lead author is Ryuji Matsumoto, a postgraduate student at Hokkaido University.

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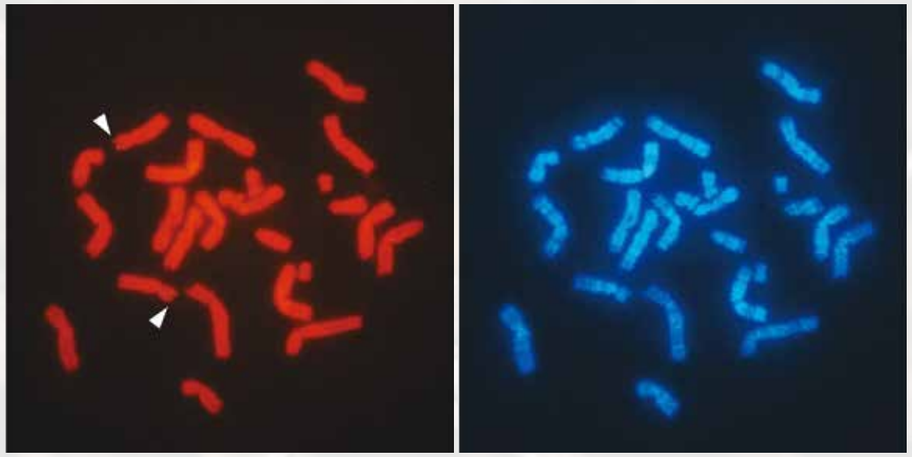
Original paper:
Matsumoto R. et al., Aldo-keto reductase 1C1 induced by interleukin-1β mediates the invasive potential and drug resistance of metastatic bladder cancer cells. *Scientific Reports,* October 4, 2016. DOI: 10.1038/srep34625

How to be a male without the Y chromosome

Key sex-determining genes continue to operate in a mammalian species that lacks the Y chromosome, a new finding toward better understanding sex differentiation.



Chromosomal location of the sex-related gene AMH (arrowheads) in male *T. osimensis.* Chromosomes are double-stained with different fluorescent substances (red and blue) for a precise gene mapping.
(Otake T. and Kuroiwa A., *Scientific Reports,* September 9, 2016)

In most placental mammals, the Y chromosome induces male differentiation during development, whereas embryos without it become female. The sex-determining gene SRY is present on the Y chromosome and induces other regulatory genes that suppress female differentiation. The Amami spiny rat (*Tokudaia osimensis*) is exceptional as it lacks a Y chromosome and thus the SRY gene, raising the question of why male differentiation can still occur.

Dr. Tomofumi Otake and Dr. Asato Kuroiwa of Hokkaido University in Japan performed gene mapping to determine the chromosomal locations of sex-related genes in the *T. osimensis* genome. They then compared its nucleotide and amino acid sequences with those of the mouse and rat. Furthermore, using cultured cells, they examined how the sex-related genes were regulated.

SRY has been well-investigated in previous research and is known to turn on a range of regulatory genes such as Sox9 and AMH that play an important role in male differentiation. The team's results suggest that, even though there is no SRY gene in *T. osimensis,* the regulatory genes that normally turn on are present and operate as they do in other placental mammals.

"We speculate that there is an unknown gene that acts as a substitute for SRY in *T. osimensis,*" says Dr. Kuroiwa. "The mammalian Y chromosome has been shrinking through an evolutionary process by reducing the number of its genes, and some scientists think that it will completely disappear at some point. I hope our research will help in the understanding of the sex determination mechanism that is independent of the Y chromosome and its evolutionary aspect."

The Amami spiny rat (*Tokudaia osimensis*) lacks a Y chromosome.

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Original paper:
Otake T. and Kuroiwa A., Molecular mechanism of male differentiation is conserved in the SRY-absent mammal, *Tokudaia osimensis. Scientific Reports,* September 9, 2016.
DOI: 10.1038/srep32874

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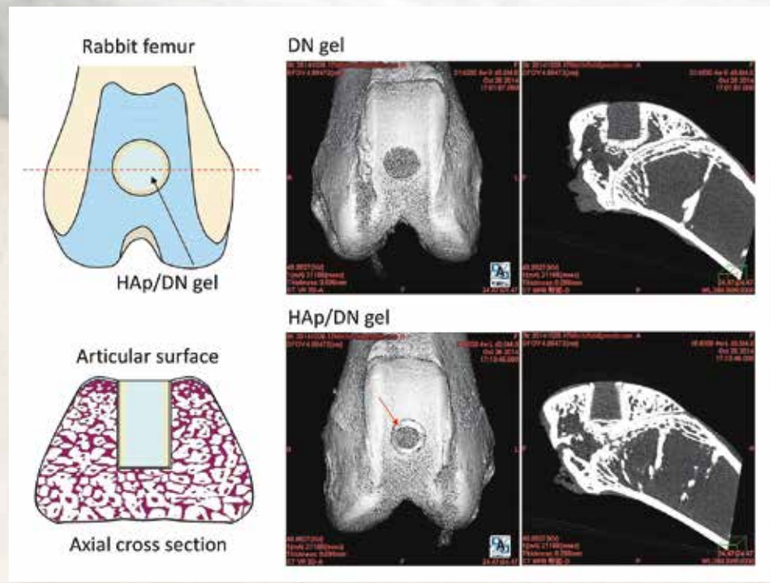
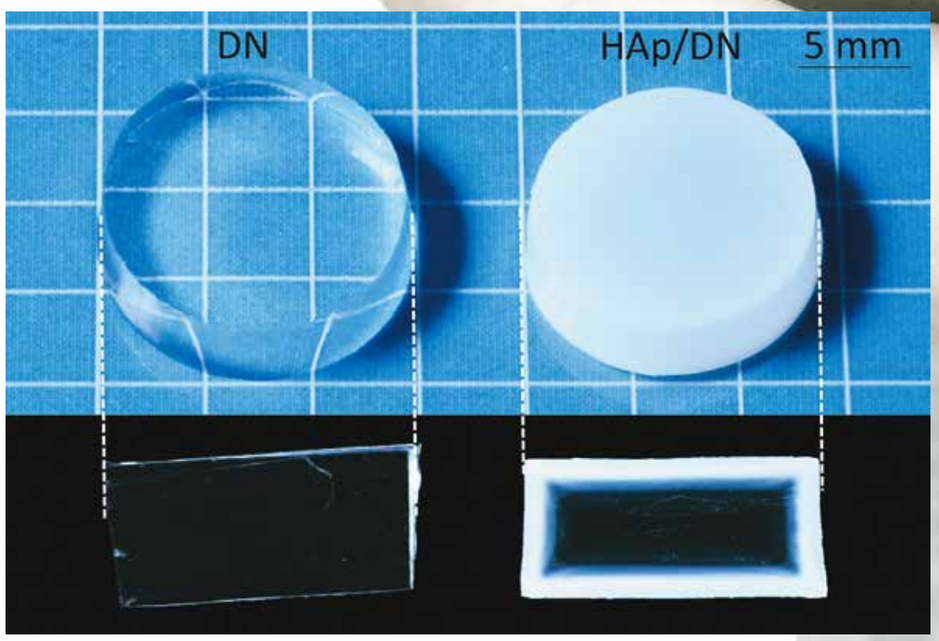
Bonding to bones strongly

Scientists have developed a new kind of hydrogel that bonds spontaneously and strongly to defected bones, suggesting potential use in the treatment of joint injuries.



The DN gel and HAp/DN gel implanted in rabbit femurs. The Micro-CT image shows HAp/DN gel has the same contrast as the bone HAp (indicated with the red arrow); the cross-section shows that the boundaries of the bone and the HAp layer are fused. (Nonoyama T. et al., *Advanced Materials,* May 17, 2016)



The DN gel (left) and the newly developed HAp/DN gel (right) and their cross sectional views. (Nonoyama T. et al., *Advanced Materials,* May 17, 2016)

When soft supporting human tissues—including cartilage and ligaments, which are joined firmly to bones—are damaged, they cannot spontaneously repair inside the body. The use of artificial supporting tissues has the potential to significantly ameliorate damage to soft tissues. Progress has hitherto been hampered by the lack of materials that are strong, yet soft and pliant, for adhering to bone.

The research group at Hokkaido University had previously developed a tough, high-strength network gel, called double-network gel (DN gel), that exhibited excellent performance such as low wear and inductive function for cartilage regeneration. However, as the gel's main component is water, it was difficult for it to bond with other surfaces—a major stumbling block in its practical application.

The new gel, however, overcomes this problem. The team successfully added hydroxyapatite (HAp), the major inorganic component of bone, to the surface of DN gel by dipping it in calcium solution and phosphate solution. The HAp-coated DN gel (HAp/DN gel) was then transplanted into a defected bone in a rabbit. Four weeks later, the team observed that the gel had bonded to the bone very strongly, while the non-coated gel had not bonded at all. Electron-microscopic analysis revealed that the newly formed bone component in the defected area had penetrated into the gel surface, and fused to it seamlessly.

Tough, nontoxic hydrogel that adheres strongly to bone is a major advance in the treatment of joint and soft tissue injuries. The research results are also promising for the potential application of tough hydrogel materials as cartilages. "The bonding between HAp/DN gel and bone mimics physiological bonding seen with cartilage, ligament and tendon, causing less stress to the body. We expect that the gel could be used to firmly attach artificial ligaments or tendons to bone," said Dr. Jian Ping Gong, one of the lead authors of the paper.

This research was supported by Hokkaido University's Global Institution for Collaborative Research and Education (GI-CoRE).

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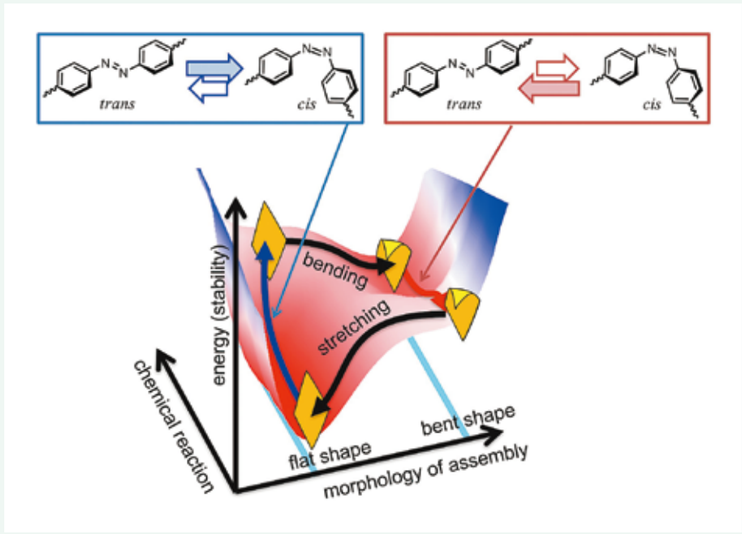
Nonoyama T. et al., Double-Network Hydrogels Strongly Bondable to Bones by Spontaneous Osteogenesis Penetration. *Advanced Materials,* May 17, 2016.
DOI: 10.1002/adma.201601030

On the path toward molecular robots

Newly developed light-powered molecular motors repetitively bend and unbend, bringing us closer to molecular robots.

Watch the movie

A crystalline assembly of azobenzene derivative and oleate showed oscillatory bending-unbending motion under continuous 435-nm light irradiation. The frequency of oscillation increased with increasing light intensity. (Ikegami T. et al., *Angewandte Chemie International Edition,* May 19, 2016)



Schematic illustration of each step of the self-oscillatory motion.

Researchers are working on mimicking cellular systems to develop molecular motors that can move or even deliver drugs to target tissues. Engineering such motors may ultimately lead to molecular robots that can execute more complex tasks. To this end, researchers must find ways to convert motion at the molecular level to motion at the macroscopic level. They also must find ways to cause chemical reactions to repeat autonomously and continuously.

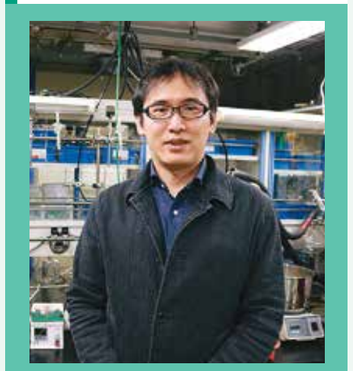
Dr. Yoshiyuki Kageyama, Dr. Sadamu Takeda and colleagues at Hokkaido University's Department of Chemistry have successfully created a chemical compound, or a crystalline assembly, which autonomously repeated flipping under blue light.

The team made crystals composed of an organic compound, called azobenzene, commonly used in dye manufacturing, and oleic acid, commonly found in cooking oil. Azobenzene molecules take two structurally different forms: *cis* and *trans*. They repetitively convert from one form to the other under blue light. The scientists tested if this would influence the structure of the azobenzene-oleic acid crystal, which contained unequal amounts of *cis*- and *trans*-azobenzene.

By applying blue light to the crystals in solution, the team observed, under a microscope, an oscillatory bending-unbending motion of the thin crystals, suggesting the existence of two stable structures, bent or unbent, depending on the *cis*/*trans* ratio. The frequency of the motion increased when the light intensity was increased. Some crystal complexes even exhibited 'swimming-like' motions in the water. Previously reported light-responsive materials have been limited in their ability to deform. The properties of the compounds in the Hokkaido University-developed crystals, however, allowed for a two-step switching mechanism, resulting in regular repetitive oscillations.

"The ability to self-organize rhythmic motions, such as the repetitive flipping motion we observed, is one of the fundamental characteristics of living organisms," says Dr. Kageyama. "This mechanism can be used in the future to develop bio-inspired molecular motors and robots that will find applications in wide areas, including medicine."

Researcher Details



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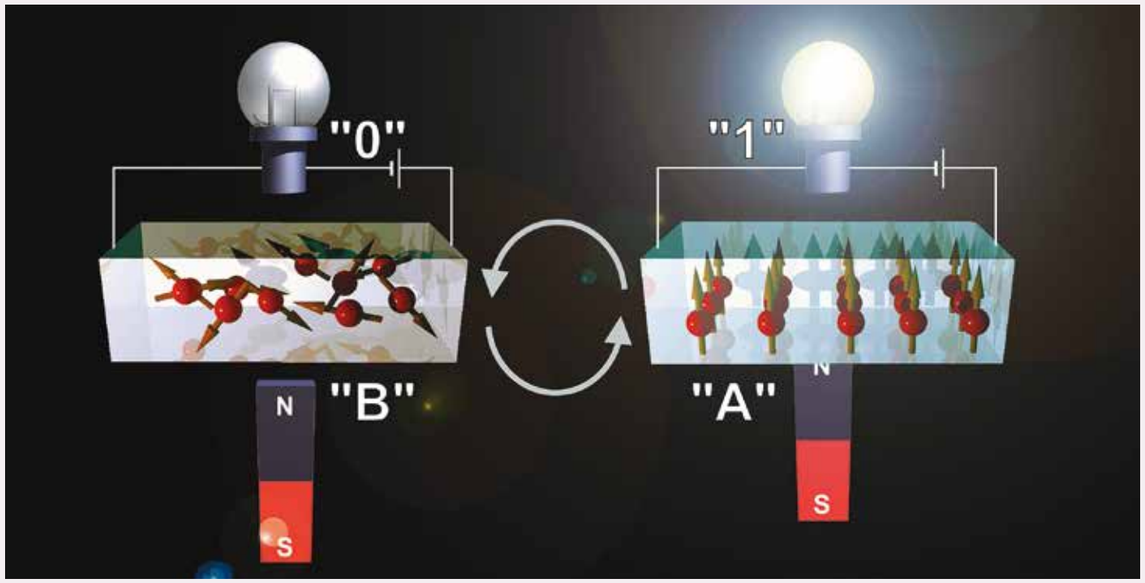
Original paper:
Ikegami T. et al., Dissipative and Autonomous Square-Wave Self-Oscillation of a Macroscopic Hybrid Self-Assembly under Continuous Light Irradiation. *Angewandte Chemie International Edition,* May 19, 2016. DOI: 10.1002/anie.201600218

This work was funded by Japan Science and Technology Agency (JST)'s PRESTO program and was supported by Hokkaido University's CRIS OPEN FACILITY.

The switch that could double USB memory

jakkrit pimpru/Shutterstock

Scientists have developed a device that employs both magnetic and electronic signals, which could provide twice the storage capacity of conventional memory devices.



Using two forms of strontium cobalt oxide with different oxygen content, the device can be switched from an insulating/non-magnet state to a metallic/magnet state simultaneously by electrochemical oxidation/reduction reaction at room temperature in air.

Conventional USB flash drives are electronic data storage devices. They store information by using millions of small gates that process information into"words"consisting of various combinations of the numbers 0 and 1.

A team of scientists at Hokkaido University's Research Institute for Electronic Science investigated the possibility of using a magnetic signal along with the electronic signal to allow double the storage capacity in these "multiplex writing/reading" devices. In addition to the binary 0/1 method of storing information, this would add an A/B store for the information as well. To do this would require finding a material that can switch back and forth from a magnet to a non-magnet state.

The team investigated two forms of strontium cobalt oxide (SrCoOx): one is an insulating non-magnet while the other is a metal magnet. By changing the oxygen content in this compound, the team could cause it to switch between the two forms.

However, the two methods currently available to do this have big drawbacks. One method requires using a high temperature heat treatment. This would make it impossible to be used in devices that work at room temperature, such as your mobile phone. The other method involves using a dangerous alkaline solution. This would require a device that is sealed so that the solution does not leak. This method is difficult to miniaturize and is thus not suitable for information storage devices.

The team developed a new method to use strontium cobalt oxide safely at room temperature. They applied a thin film of sodium tantalate, which can be used at room temperature without leaking alkaline solution, over layers of strontium cobalt oxide. When a three-volt current was applied (or about one-seventh of the voltage required in currently available USB flash drives), the insulating form of $SrCoO_{2.5}$ reversibly switched to its metal magnet form, $SrCoO_3$, in three seconds. By comparison, current devices can store information in 0.01 seconds. Making the device smaller would shorten the time needed for the compound to switch between an insulator and a magnet, the researchers say. This would allow the storage of an even larger number of photos and videos in mobile phones, for example.

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Original paper:
Katase T. et al., Reversibly switchable electromagnetic device with leakage-free electrolyte. *Advanced Electronic Materials,* Mar 29, 2016.
DOI: 10.1002/aelm.201600044.

Extraordinary cancer resistance

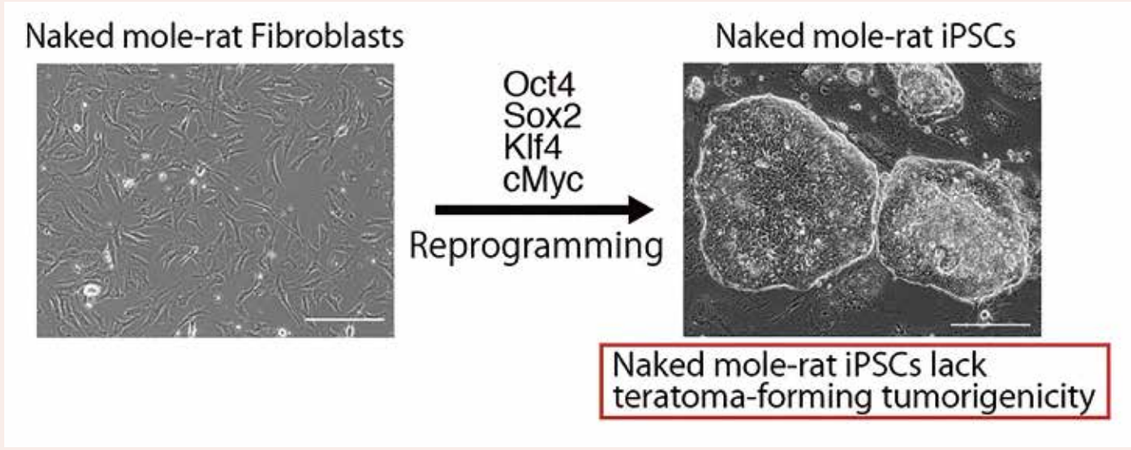
belizar/Shutterstock

Scientists are getting closer to understanding the anti-cancer mechanism of an African subterranean animal by making induced pluripotent stem cells.

The naked mole-rat (*Heterocephalus glaber*) is the longest-living rodent (longevity; 30 years) and exhibits an extraordinary resistance to cancer.

Naked mole-rats (NMR) are the longest-living rodent species and exhibit "extraordinary" resistance to cancer. Mole-rats live up to 30 years, 10 times longer than mice, and captured colonies almost never show any type of cancer. According to a collaborative research team from Hokkaido University and Keio University in Japan, understanding these animals' anti-cancer mechanisms may help advance treatment for humans in the future.

The research team took skin fibroblast tissue from adult mole-rats and reprogrammed the cells to revert to pluripotent stem cells. These are called induced pluripotent stem cells (iPSCs) and, like embryonic stem cells, are capable of becoming any type of tissue in the body. However, these stem cells can also form tumors called teratomas when transplanted back into the animals.



iPSCs derived from the naked mole-rat lack teratoma-forming tumorigenicity due to a species-specific ERAS mutation and an ARF-dependent tumor suppression mechanism.

When the mole-rats' iPSCs were inserted into the testes of mice with extremely weak immune systems, the team discovered that they didn't form tumors in contrast to human iPSCs and mouse iPSCs. Upon further investigation, they found that a tumour-suppressor gene called alternative reading frame (ARF), which is normally suppressed in mouse and human iPSCs, remained active in the mole-rat iPSCs.

The team also found that ERAS, a tumorigenic gene expressed in mouse embryonic stem cells and iPSCs, was mutated and dysfunctional in the mole-rat iPSCs. When the researchers disabled the ARF gene, forced the expression of the mouse ERAS gene in the mole-rat iPSCs, and then inserted them into the mice, the mice grew large tumors.

When researchers suppressed the ARF gene in mole-rat cells during the reprogramming process to iPSCs, the cells stopped proliferation with sign of cellular senescence, while the opposite happens with mouse cells. Researchers theorize that this further helps protect the naked mole-rat by reducing the chance for tumor formation. They call this ARF suppression-induced senescence (ASIS) and it appears to be unique to the naked mole-rat.

These findings could help researchers figure out how human iPSCs can be used for treating patients without forming tumors, which is one of the major challenges associated with undifferentiated iPSCs.

"Further research into the detailed mechanisms underlying ASIS in naked mole-rats may shed new light on cancer resistance in the mole-rats" said Dr. Kyoko Miura, an associate professor at Hokkaido University. "The results may contribute to the generation of non-tumorigenic human-iPSCs, enabling safer cell-based therapeutics in the future."

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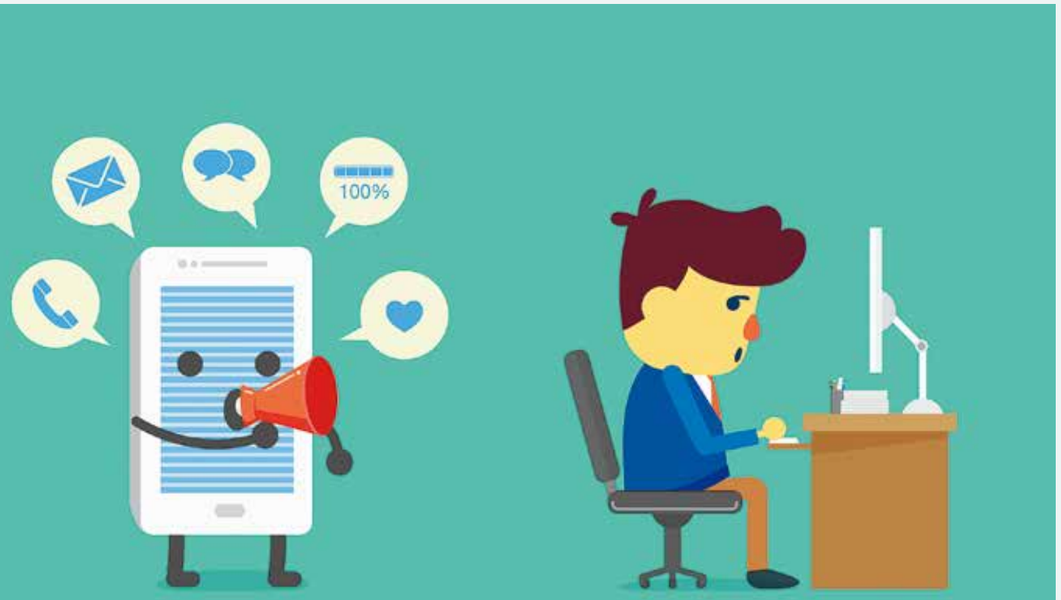
Original paper:
Miyawaki S. et al., Tumour resistance in induced pluripotent stem cells derived from naked mole-rats. *Nature Communications*, May 10, 2016.
DOI: 10.1038/ncomms11471

Who gets most distracted by cell phones?



solar22/Shutterstock

Two researchers from Hokkaido University have empirically verified that the mere presence of a cell phone or smartphone can adversely affect our cognitive performance. The phenomenon was particularly marked among individuals who infrequently use such devices.

While it was well known that the use of cell phones or smartphones (hereafter, mobile phones) could cause oversights and delays in judgment, how the presence of such devices affects cognitive functioning was not well studied.

As a part of their research, Dr. Jun-ichiro Kawahara of Hokkaido University's Graduate School of Letters and Motohiro Ito of Chukyo University (a special research student at Hokkaido University's Graduate School of Letters) measured the effect of mobile phones on the ability to pay attention of 40 undergraduate students.

mrmohock/Shutterstock

The participants were split into two groups: a "mobile-phone conditions" group and a "control conditions" group. For the former, the researchers placed a mobile phone (that did not belong to the participant being tested) next to a computer monitor, asked the participant to search for a target character amongst other characters that appeared on the monitor screen, and then measured the time it took to search for the target character. For the latter group, a memo pad of the same size as the phone was placed by the monitor, and the same experiment was conducted. Thereafter, participants were asked about how frequently they use and how attached they are to the internet.

According to the experiment's results, "mobile-phone conditions" participants took longer to find the target character than the control group, indicating that participants were automatically distracted by the presence of the phone, impairing cognitive performance. This effect was more pronounced in people who infrequently use the internet. On the other hand, it was found that heavy users were not distracted by the phone and rather more efficient to notice the target when it appeared on the side of the monitor where the mobile phone was placed. These results suggest that the influence of a mobile phone on the examinee's cognitive performance differed depending on the degree of their internet usage.

The researchers hypothesize that people are automatically drawn to the presence of a mobile phone, and there are individual differences in how one attempts to ignore it. In conclusion, Dr.Kawahara notes "The mere presence of a mobile phone was a distraction among infrequent internet users. However, among frequent internet users, the device might have served as a spatial cue from which their visual system starts searching the target."

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Original paper:
Kawahara J. and Ito M., Effect of the Presence of a Mobile Phone during a Spatial Visual Search. *Japanese Psychological Research,* Vol. 59, No. 2, 2017.
DOI: 10.1111/jpr.12143

HOKKAIDO UNIVERSITY

65,000 hectares of campus resources...

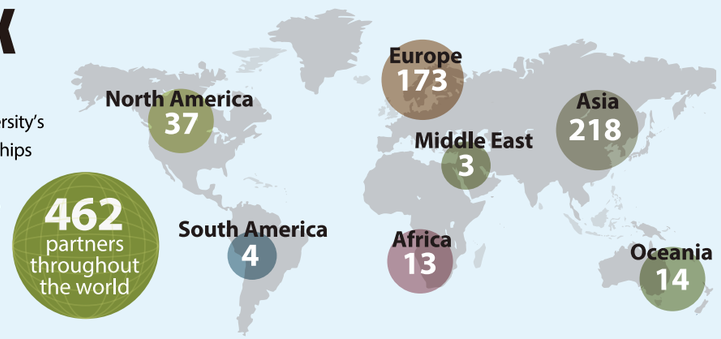
UNIVERSITY A GLANCE

- Established 1876
- Sapporo Campus Size 180ha
- Total Research Staff 2,093
- Total Research Budget 2016 20.2 Billion Yen
- Total Student Numbers 18,074

FACILITIES

WORLD WIDE NETWORK

Hokkaido University has forged 462 International Partnerships throughout the world, and these linkages reflect Hokkaido University's global outlook and a history of productive international relationships for research, teaching and learning and engagement.
The number of bilateral international agreements contains those signed at both a university-wide level (172 agreements) and departmental-wide level (290 agreements).



Museum

Hokkaido University has spent more than 130 years collecting, preserving, studying and storing around 4 million specimens and materials. Among these items are more than 10,000 precious specimens that serve as benchmarks for their respective species. The museum also plays an important role in the training and education of both students and local citizens.

Botanic Gardens

Hokkaido University Botanic Gardens are the oldest of their kind in Japan, opening in 1886. Today, the site is 400 m², and consists mainly of old growth trees including alpine varieties. The resource rich gardens hold around 4,000 kinds of plants and a museum, known as the Natural History Museum, which exhibits Ainu artifacts, and local archaeological and biological specimens.

Experimental Forests

Hokkaido University's network of University Forests consist of six experimental forests, a tree breeding station, a tree nursery, and two experimental stands and cover around 700 km². The University Forests range from cool-temperate forests to warm temperate forests including one that has the largest field training station amongst any Japanese university. All research is focused around forest dynamics, forest environment and function, conservation biology, as well as regional resource management.

Marine Stations

Covering both fresh and salt-water, Hokkaido University owns six marine stations which conduct research on farming techniques, genetic engineering, oceanography, and marine ecology, conservation and diversity. These outposts offer regular field work to students of both science and fisheries science.

Livestock Farm

Research and education on livestock production and sustainable landuse is carried out at Shizunai Livestock Farm. Particular research carried out on the farm include but is not limited to: studies on keeping native Hokkaido horses; high roughage feeding systems for growing and fattening cattle; management systems for grazing cattle in uneven pastures; behavioral studies for grazing animals in sloped mountainous lands; physico-chemical properties of meadow soils and runoff of sloped grasslands.

Marine Research Vessels

The Oshoro Maru (left) as well as the smaller Ushio Maru are training ships which belong to Hokkaido University's School of Fisheries Sciences. They are used as facilities for students to conduct experiments and receive hands-on training as well as for research. The vessels play an important role in investigating marine-related physics, chemistry, biology, and biological production sciences as well as data collection.

Contributing Towards the R e solution of Global Issues

Age and Prestige

Hokkaido University is one of the oldest, largest, and most prestigious universities in Japan. The university has the largest number of faculties out of Japan's national universities, covering almost all areas of the humanities and sciences. Furthermore, we are one of the leading institutions for research activities in Japan and around the world.

The breadth and depth of pioneering research conducted at Hokkaido University has seen the cultivation of many great thinkers. Our alumni include a Nobel laureate, business leaders, research pioneers, artists and prolific writers. Hokkaido University is determined in its aim to develop curious minds that can embrace challenges and reveal new global perspectives to find solutions which change society for the better.

Internationally renowned research

With one Nobel Prize, two recipients of the prestigious 'Order of Culture' and twenty-one recipients of the Japan Academy Prize, Hokkaido University has produced a wealth of talent - and with this, ground breaking research. Emeritus Professor Akira Suzuki, who worked tirelessly for decades at Hokkaido University, won a Nobel Prize in Chemistry in 2010. The prize was awarded for his research on "palladium-catalyzed cross couplings in organic synthesis." His breakthrough was that he produced a more stable, nontoxic reaction compared to other reactions in inorganic synthetic chemistry, and in doing so changed the face of manufacturing, including the production of pharmaceuticals. Other notable alumni include two Stockholm Water Prize Laureates - Dr. Takeshi Kubo who is renowned for his long and distinguished career in organizing Tokyo's massive sewage system (awarded in 1994), and Dr. Takashi Asano for his outstanding contributions on the efficient use of water in the domain of wastewater reclamation, recycling and reuse.

Global Research Center for Food and Medical Innovation (FMI)

Established in 2015, the Center promotes research and development toward the creation of an ageless society in which people of all ages lead healthy, active lives. In such a society, the focus of health promotion is shifted from hospitals to homes, that of health maintenance from medical treatment to prevention, and that of health-related information management from a distributed approach led by medical institutions to a unified concept led by individuals. The Center also provides opportunities for casual interaction among researchers and locals through the publicly open spaces on its first and second floors. The facility is expected to serve as a place for locals and people from industry and academia to share a variety of novel ideas toward true innovation.

https://www.fmi.hokudai.ac.jp/en/about_fmi/index/

Arctic Research Center (ARC-HU)

The ARC-HU conducts cutting-edge interdisciplinary research through projects such as the Belmont Forum on the sustainable use of marine resources in the Arctic and carbon management in Eastern Siberia. The ARC-HU is the center of excellence of Arctic research in Japan, and is a part of the Japan Arctic Research Network Center (J-ARC Net) in collaboration with the Arctic Environment Research Center, the National Institute of Polar Research, and the Institute of Arctic Climate and Environment Research run by the Japan Agency for Marine-Earth Science and Technology. J-ARC Net promotes collaborative research actions by industrial, governmental and academic institutions on Arctic issues especially those conducted using interdisciplinary approaches. J-ARC Net also introduces newcomers to Arctic research by providing introductory seminars and courses on Arctic issues so as to nurture personnel who can contribute to solving problems in the Arctic region.

http://www.arc.hokudai.ac.jp/en/

Global Institution for Collaborative Research and Education (GI-CoRE)

GI-CoRE is a faculty organization under the direct control of the university's president to bring together world-class researchers from around the world to conduct collaborative research with those at the university. The purpose of GI-CoRE is to promote and support international collaborative research and education that leverages the university's strengths and distinctive features. At the present, GI-CoRE consists of six global stations: the Global Station for Quantum Medical Science and Engineer-ing (GSQ), Zoonosis Control (GSZ), Food, Land and Water Resources (GSF), Soft Matter (GSS), Big Data and Cybersecurity (GSB) and Arctic Research (GSA).

https://gi-core.oia.hokudai.ac.jp/main

Global Facility Center (GFC)

The mission of the GFC is to support on campus researchers and students as well as off-campus and international research and educational activities through the creation of the most advantageous system for advance equipment sharing. The Center is operating and maintaining the research infrastructure on campus, and providing the contracting services such as for the instrumental analysis and for the development of the prototype machine. The Center is an Asian front runner in the field. The Center welcomes researchers from external research and business organizations. More than 150 different types of scientific equipment, instruments, and associated devices are available for use, including the only Isotope Imaging Microscope in the world, the 1.6-m diameter optical infrared telescope named "Pirka", the Next-Generation Sequencing system, and other cutting edge facilities (TEM, MS, NMR, etc.).

For more details, please email

contact@gfc.hokudai.ac.jp.

COLLABORATING WITH HOKKAIDO UNIVERSITY

Institute of Low Temperature Science
http://www.lowtem.hokudai.ac.jp/en/index.html

Research Institute for Electronic Science
http://www.es.hokudai.ac.jp/english/

Institute for Genetic Medicine
http://www.igm.hokudai.ac.jp/en/index.php

Institute for Catalysis
http://www.cat.hokudai.ac.jp/index-e.html

Slavic-Eurasian Research Center
http://src-h.slav.hokudai.ac.jp/index-e.html

Information Initiative Center
http://www.iic.hokudai.ac.jp/En/index.html

Research Center for Zoonosis Control
http://www.czc.hokudai.ac.jp/en/index.html

Central Institute for Isotope Science
http://www.hokudai.ac.jp/radiois/index_eng.html

Research Center for Integrated Quantum Electronics
http://www.rciqe.hokudai.ac.jp/en/

Field Science Center for Northern Biosphere
https://www.fsc.hokudai.ac.jp/home_en/

Center for Advanced Tourism Studies
http://www.cats.hokudai.ac.jp/en/

Center for Ainu and Indigenous Studies
http://www.cais.hokudai.ac.jp/english/

Center for Experimental Research in Social Sciences
http://lynx.let.hokudai.ac.jp/cerss/en/

Center for Environmental and Health Sciences
http://www.cehs.hokudai.ac.jp/en/

Arctic Research Center
http://www.arc.hokudai.ac.jp/en/

Research Development Section

The aim of the Research Development Section is to promote research activities at Hokkaido University. This includes analyses of our institute's research outputs, providing support for large scale inter-departmental and cross disciplinary projects, and planning and organizing various research development schemes. The RDS can also act as a point of contact for international researchers wanting to learn more about collaborating with the university.

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