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Institute for Basic Science

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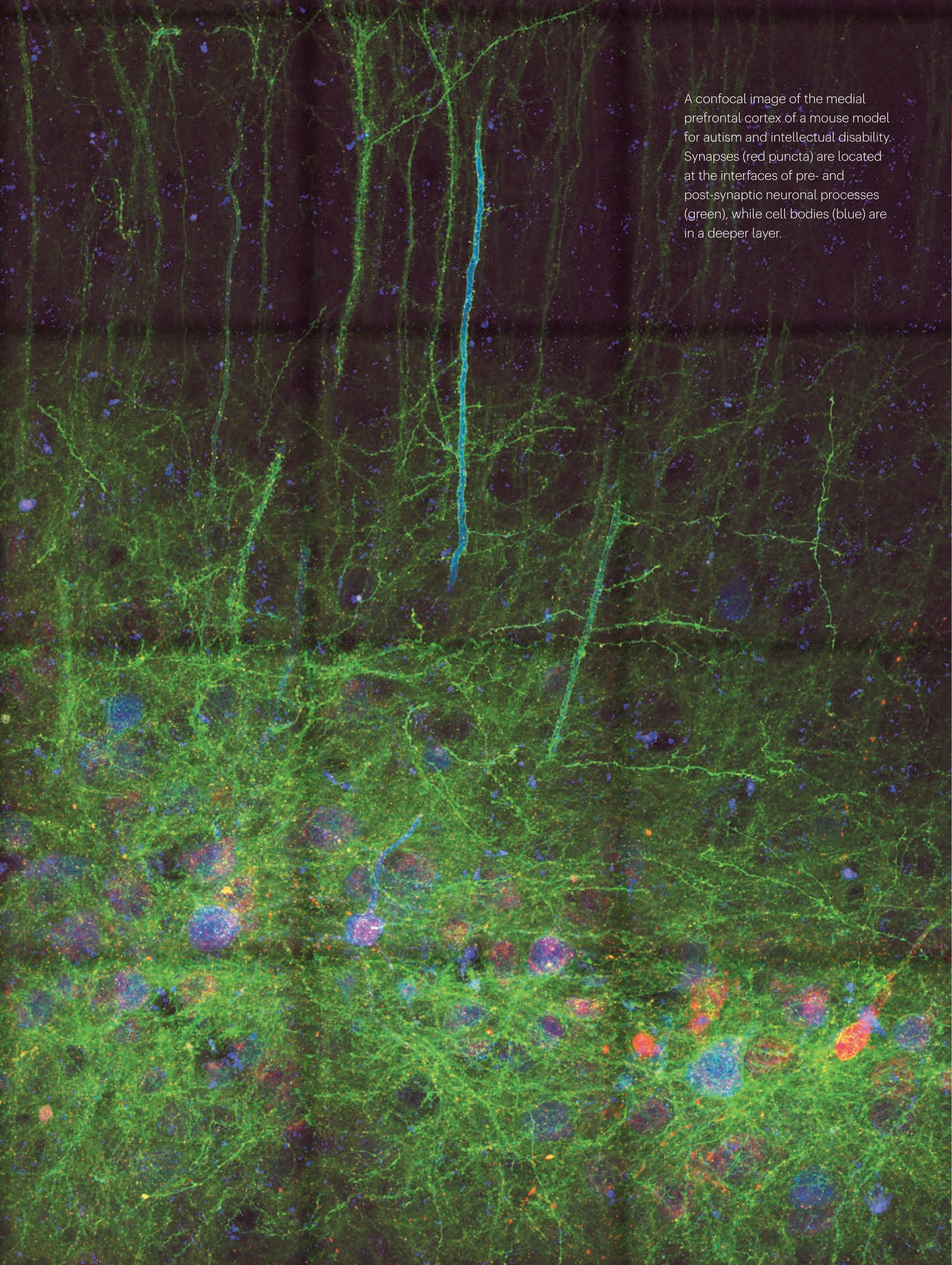

A confocal image of the medial prefrontal cortex of a mouse model for autism and intellectual disability. Synapses (red puncta) are located at the interfaces of pre- and post-synaptic neuronal processes (green), while cell bodies (blue) are in a deeper layer.

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Foreword

Human society has advanced through discovering novel natural phenomena and creating new knowledge. The Institute for Basic Science (IBS) is pursuing these vital activities in Korea. Founded in November 2011, the institute is celebrating its tenth anniversary this year. Guided by its vision of 'Making discoveries for humanity and society', IBS aspires to join the ranks of the world's leading institutions in basic science. Through making groundbreaking discoveries, we seek to disseminate knowledge that benefits society and humanity.

The four guiding principles of IBS are excellence, autonomy, creativity and openness. We select researchers and evaluate their outcomes based solely on their scientific excellence and creativity. Scientists are assured maximum autonomy in carrying out their research. IBS is always open to scientists with aspirations in basic research.

The core of IBS is its research centres, which are key units of research in each area of basic science. The first nine centres opened in 2012. Now, a decade later, 30 centres are operating the fields of mathematics, physics, chemistry, life science, Earth science and various interdisciplinary areas, and they have around 1,800 research personnel (including students). Just this year, IBS established the Korea Virus Research Institute to respond to COVID-19 and to prepare for future pandemics. In line with IBS's policy of integrating basic science capabilities and resources in Korea, the research centres are located throughout South Korea: nine centres are at IBS Headquarters in Daejeon, 13 campus centres are affiliated with the research-oriented universities KAIST, GIST, UNIST and POSTECH, while nine extramural centres are located in premier universities in Korea, including Seoul National University.

As it enters its second decade, IBS will continue to contribute to humanity by answering the big questions about nature and the Universe.

Do Young Noh
President
Institute for Basic Science

10th ANNIVERSARY A Decade of New Discoveries
ibs Institute for Basic Science

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A decade of new discoveries

South Korea's Institute for Basic Science (IBS) has revolutionized the country's approach to the type of fundamental research that underpins breakthroughs with the potential to change society. With IBS in its tenth year, researchers reflect on what makes IBS so valuable and what the next decades will bring.

Starting with some ambitious goals and a handful of research centres in 2012, the Institute for Basic Science (IBS) — South Korea's flagship research organization for pure research — has developed into a web of more than 30 research centres that cover fields as diverse as underground physics, genome engineering, climate physics, biology, biomedical science and quantum nanoscience. Fostering an environment of scientific creativity and limitless imagination is challenging, but this is what IBS set out to achieve, providing research centres with a substantial endowment of funding and the freedom to set their own agendas. For researchers, this is a dream come true, and the IBS research system has inspired a new level of creativity, adaptability and nimbleness.

Pivoting to deal with an emergent threat

The director of the IBS Center for RNA Research in Seoul, one of IBS's first clutch of centres, Narry Kim has nurtured her group into a rich research ecosystem of eight teams undertaking fundamental research across molecular cell biology, biochemistry, proteomics, genomics, regenerative medicine and viral immunology.

"This approach to research was really a new concept in South Korea when we started in 2012," Kim recalls. "Setting up an institute from scratch was an adventure, an exciting experiment where we felt free to explore audacious new ideas and recruit the researchers we wanted. We also had the freedom to change direction when needed and reallocate funding and resources."

For many experimentalists, the COVID-19 pandemic jeopardized their research, but for Kim and her team, it was an opportunity to repay society. "When the COVID-19 pandemic first hit in January 2020, we knew we had to shift direction to address this emerging crisis using all the expertise at our disposal. In our case, it was the experience and expertise in viral RNA metab-

IBS headquarter building in Daejeon, South Korea.

olism we had accumulated since the MERS threat six years earlier."

Like SARS-CoV-2, the virus responsible for Middle-East Respiratory Syndrome (MERS) is a coronavirus, which, like all other coronaviruses, depends on RNA metabolism for survival. Simply put, a coronavirus particle is a strand of RNA wrapped in a protein envelope. When it latches onto one of our own cells using its enigmatic spike protein, it invades the cell and hijacks the cellular machinery to reproduce more of the viral RNA. It is thus vital to understand and describe the RNA genome sequence in order to develop countermeasures against the virus.

"We understood the urgency and set out to analyse the genome of SARS-CoV-2 as quickly as possible, leveraging our in-house facilities and multidisciplinary expertise in sequencing and bioinformatics," says Kim. "IBS funding allowed us to set up our own complete sequencing facility. Our high-resolution SARS-CoV-2 genome map has since been widely used by many researchers."

As part of a longer term, fundamental research programme, Kim's team is now comparing the genomes of various coronaviruses. They are also studying RNA-mediated immunity, including how cellular immune systems deal with foreign RNA. "SARS-CoV-2 is unlikely to be the last virus to affect humanity, and so we need to prepare for the next pandemic," warns Kim. "IBS allows us to think long term, combine different disciplines, and develop young researchers through the Young Scientist Fellowship to incubate teams that will continue this research into the future."

"WE NEED TO PREPARE FOR THE NEXT PANDEMIC"

Understanding the critical role of the vascular system in major diseases

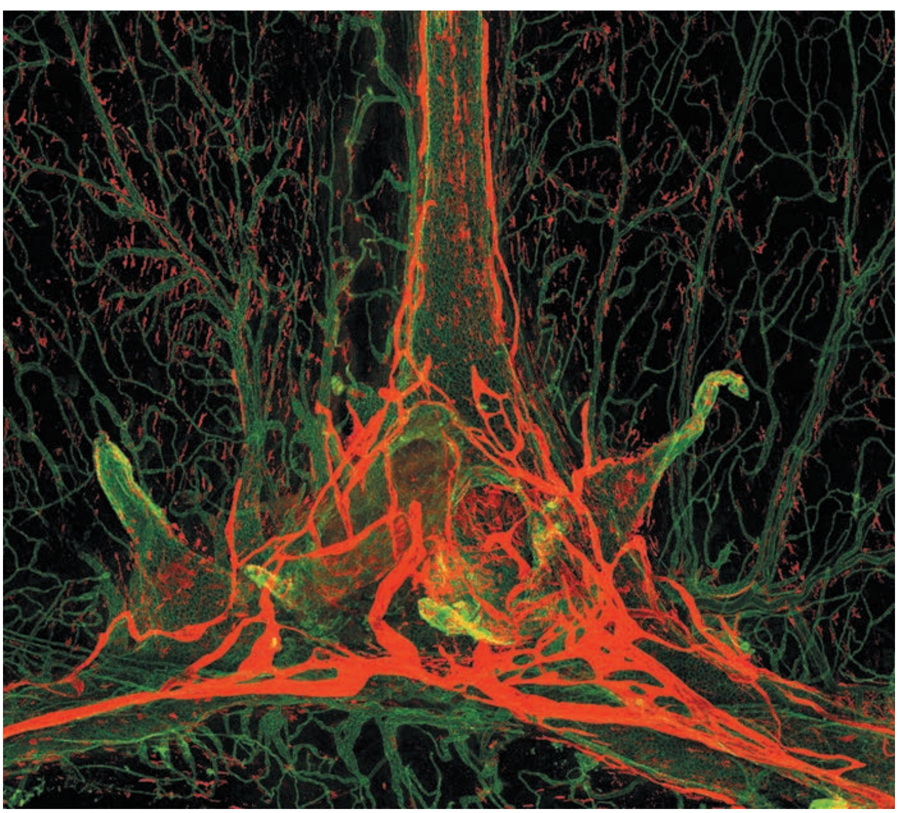
Gou Young Koh has long been studying the vascular system in humans. He first proposed the idea that each human organ has its own unique system and physiology of blood and lymphatic vessels. His concept was novel 15 years ago, but his elucidation of a system of discrete vasculatures is now commonly accepted and has opened up many new areas of anatomical and physiological research. With the establishment of the IBS Center for Vascular Research in 2015, Koh was finally given the resources and time to explore some of the fundamental questions that this discovery presents.

"It really was a dream come true to have the opportunity to lead fundamental research in this new area that I helped to create," says Koh. "We began our research looking at the lymphatic system — how it works, how it drains waste fluids from the brain, and how cancer cells can move through lymphatic vessels and survive and thrive in the draining lymph node, which is full of T cells and other immune cells that should make it a very hostile environment."

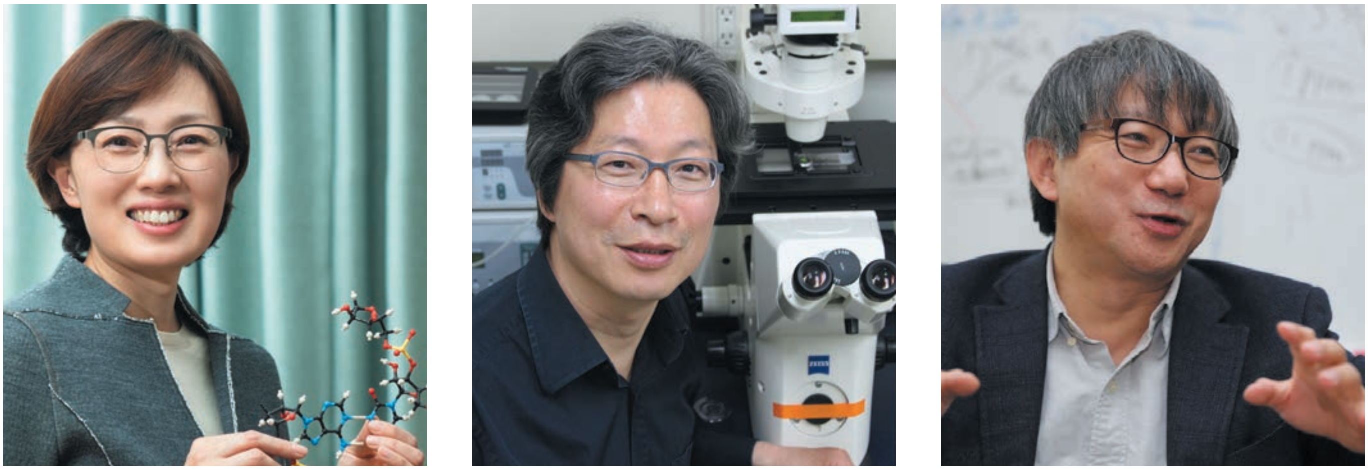
Their knowledge of blood and lymphatic vasculatures proved invaluable in rising to the challenge of COVID-19. Koh didn't hesitate to redirect his team to study the pathogenesis of COVID-19. They used screening assays to systematically explore how COVID-19 is contracted, how the virus initially infects the respiratory tract, and how it is then able to colonize other parts of the body. This allowed them to discover a new vascular system of the nose, which appears to play a critical role in SARS-CoV-2 infection.

"When we dissected the pathogenesis step-by-step, we found new and unique vessels in the nasal cavity, and we are currently studying whether they are closely related with a systemic spread of SARS-CoV-2 infection," says Koh. "This hints at the possibility of increasing immunity via the nasal cavity, and of nasal delivery of preventatives or treatments, as well as the potential role of nasal epithelial cells in disease progression."

Koh credits the unique research environment at IBS as a key factor in his team's success. "Having the facilities and all the expertise across different disciplines here in the one centre, and



A fluorescence micrograph of meninges — thin layers of tissue covering a mouse brain. The meningeal lymphatic vessels (red) constantly sprout and regress, while perivascular macrophages (red) keep surveying the brain's surface to prevent pathogens from entering.



Photographs of (left to right) Narry Kim, Gou Young Koh, and Yeongduk Kim.

being able to coordinate all that research toward a single goal are what makes IBS special," he says.

Seeking new depths to unlock the mysteries of the Universe

In an active iron mine under a mountain just over 100 kilometres east of Seoul, one of the world's most advanced physics experiments is about to begin. A kilometre below ground, Yemilab is Korea's new flagship underground physics research facility, adding to the world-class research already being conducted at the shallower Yangyang Underground Laboratory to the north.

"Our main purpose is to discover new knowledge about dark matter in the Universe," says Yeongduk Kim, director of the IBS Center for Underground Physics. "Since establishing our research centre more than eight years ago, we have advanced our understanding of the properties of neutrinos — subatomic particles that have a tiny mass but are energetic enough to be detected if generated by nuclear reactors. They are one of the prime candidates for the dark matter thought to make up most of the mass in the Universe."

Hunting for neutrinos, however, is a monumental undertaking. Their properties have been theoretically studied in terms of double-beta decay, in which two neutrons in an atomic nucleus are simultaneously transformed into two protons without emitting any neutrinos. The best hope for detecting this decay is to prepare dense, high-purity crystals containing isotopes with the highest decay potential, and monitor them at low temperature, deep underground away from sources of interference. This requires a huge team of experts in particle, nuclear and experimental physics, crystal growth, sensor technology and cryogenics at temperatures a fraction of a degree above absolute zero.

"Breakthroughs in this area of physics take decades and contributions from many different fields working together cohesively," explains Kim. "Through the Center for Underground Physics, we have now completed the first phase of the Yemilab as our first major goal, and we will soon establish ourselves as one of the leading experiments in this field in the world."

Kim knows that this project is only viable with IBS's vision for basic research. "It is only thanks to IBS that such long-term fundamental research such as this is possible here in South Korea," he says.

The 782-metre-long access tunnel to the underground physics research facility Yemilab.

Illuminating the formation of glass

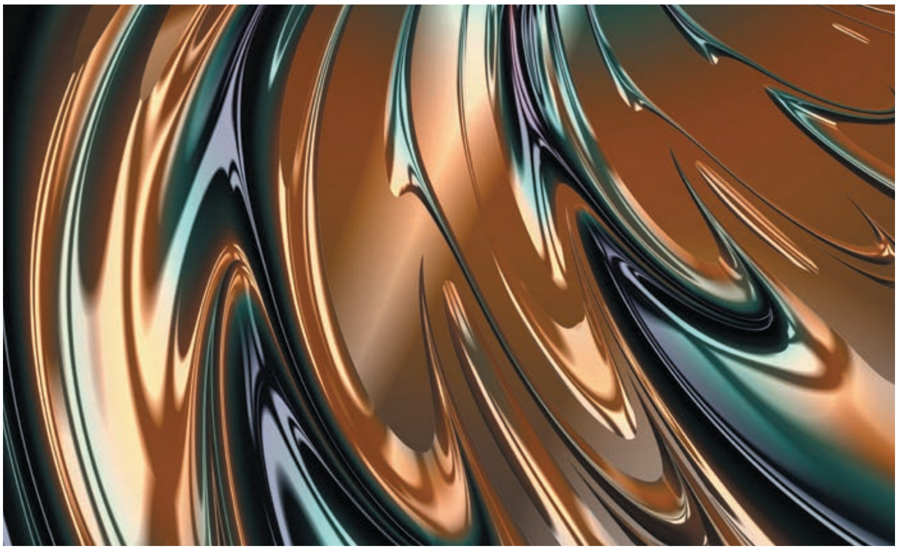
Glass-forming liquids becoming increasingly cage-y as they cool to a solid-like state

The point at which glass-forming substances transition from a liquid to a solid-like state as they cool has been probed by using laser beams to perturb suspended particles.

As conventional liquids cool and start to solidify, their atoms or particles begin to lock into position with their neighbours. But glasses lack the ordered structure of conventional solids. Instead, they have a rigid, amorphous structure, but the details of how this structure forms remained unclear.

Now, researchers at the Institute for Basic Science in South Korea have probed this transition by using a laser-based approach.

They identified the formation of local domains, or cages, in which particles begin to lock with their neighbours and move in a coordinated manner. As the material cooled further, the cages became more rigid and began to merge with each other, driving the onset of solid-like behaviour.



Reference

1. *Nature* **587,** 225–229 (2020).
doi: 10.1038/s41586-020-2869-5

The tale of mixed tails

Enzymes put different nucleotides onto messenger RNA tails to protect the molecules from degradation

By adding atypical building blocks to the protective tails of messenger RNA molecules, two newly discovered enzymes delay the degradation of those gene transcripts, giving the cell more time to make encoded proteins.

Researchers from the Institute for Basic Science identified the two enzymes that intermittently decorate RNA tails with nucleotides other than adenosine, the usual one found in pure stretches at the end of most gene transcripts.

THE ENZYMES THUS OFFER A HITHERTO UNAPPRECIATED LAYER OF PROTECTION FOR RNA

When digestive proteins then come along to eliminate the RNA, they encounter the non-adenosine residues in the impure tails, which causes them to slow down their destructive trimming of the molecule. The enzymes thus offer a hitherto unappreciated layer of protection for RNA that helps regulate gene activity in healthy and diseased states.

The findings could help drug companies develop more stable and long-lasting RNA-based therapies.

Reference

1. *Science* **361,** 701–704 (2018).
doi: 10.1126/science.aam5794

Spin of single atomic nuclei measured for first time

Scientists succeed in measuring the spin of single atomic nuclei

Researchers have detected the nuclear magnetism, or nuclear spins, of individual atoms on a surface for the first time. This method is promising as a powerful probe of the chemical environment of individual atoms.

Electrons have a quantum property known as spin, which gives rise to the magnetic properties of a material. Some atomic nuclei also have a net spin; it is this property that is used in magnetic resonance imaging (MRI). But while MRI can detect the spin of a large number of nuclei, until now no one had succeeded in detecting the nuclear spin of a single atom.

Now, by combining a scanning tunnelling microscope with measurements of electron spin, researchers at the Institute for Basic Science in South Korea have detected the spins of individual iron and titanium atoms on a magnesium oxide surface.

In the future, nuclear spin could be used to store quantum information.

Reference

1. *Science* **362**, 336–339 (2018).
doi: 10.1126/science.aat7047

Using electric fields to control magnetic swirls

Tunable magnetic swirls bring next-generation magnetic memory devices a step closer

Researchers have realized highly tunable tiny magnetic swirls, which are promising for forming the basis of super-efficient memory devices.

Since their discovery a decade ago, nanoscale magnetic whirlpools known as skyrmions have been generating much interest because they could lead to faster data storage devices that are more energy efficient. But for skyrmions to be used in practical applications they need to be easier to control.

FOR SKYRMIONS TO BE USED IN PRACTICAL APPLICATIONS THEY NEED TO BE EASIER TO CONTROL.

Now, a team that included researchers at the Institute for Basic Science in South Korea has generated skyrmions in an ultrathin ferromagnetic layer overlaid with a ferroelectric layer. They showed that the skyrmion properties can be controlled by manipulating the ferroelectric layer, which is much easier than controlling the skyrmions directly.

This should allow the high tunability of ferroelectric devices to be combined with the advantages that skyrmions bring for data storage.

Reference

1. *Nature Materials* **17,** 1087–1094 (2018).
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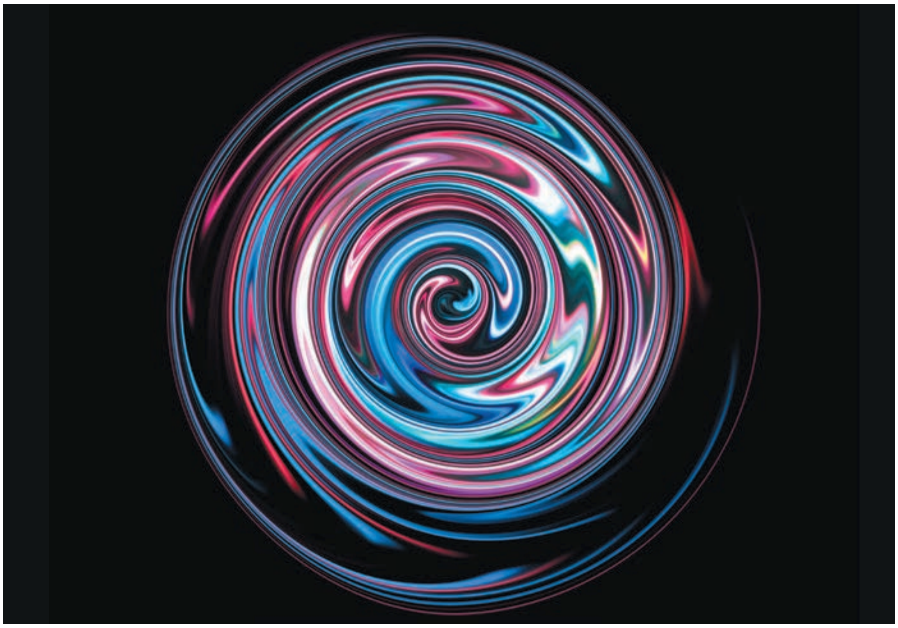


DNA editor's mistakes mapped

Adenine base editors make few errors, but greater precision is still needed ahead of their use in the clinic

Genome-editing tools known as adenine base editors (ABEs) have a much lower error rate than the much-touted CRISPR–Cas9 gene-editing method, and are thus considered safer for therapeutic applications. But ABEs still cause some unwanted changes to DNA, highlighting the need for technological improvements.

MORE PRECISION AND SPECIFICITY IS NEEDED BEFORE ABES CAN BE SAFELY USED TO FIX DISEASE-CAUSING MUTATIONS IN PEOPLE.

ABEs make a particular conversion between two of the four DNA letters — swapping an adenine for a guanine. Sometimes, however, they alter the genome in undesired ways.

To characterize the off-target activity of ABEs, researchers from the Institute for Basic Science in South Korea adapted a sequencing assay they had previously developed for calculating the accuracy of CRISPR–Cas9. They showed that ABEs make few mistakes — but when they do, the errors are different from those caused by other types of gene-editing tools.

The team concluded that more precision and specificity is needed before ABEs can be safely used to fix disease-causing mutations in people.

Reference

1. *Nature Biotechnology* **37,** 430–435 (2019). doi: 10.1038/s41587-019-0050-1

Mapping nanoparticles atom by atom

Nanoparticles made under identical conditions can differ considerably from each other

Precise maps of the atoms in nanoparticles reveal that even nanoparticles from the same batch differ significantly from each other.

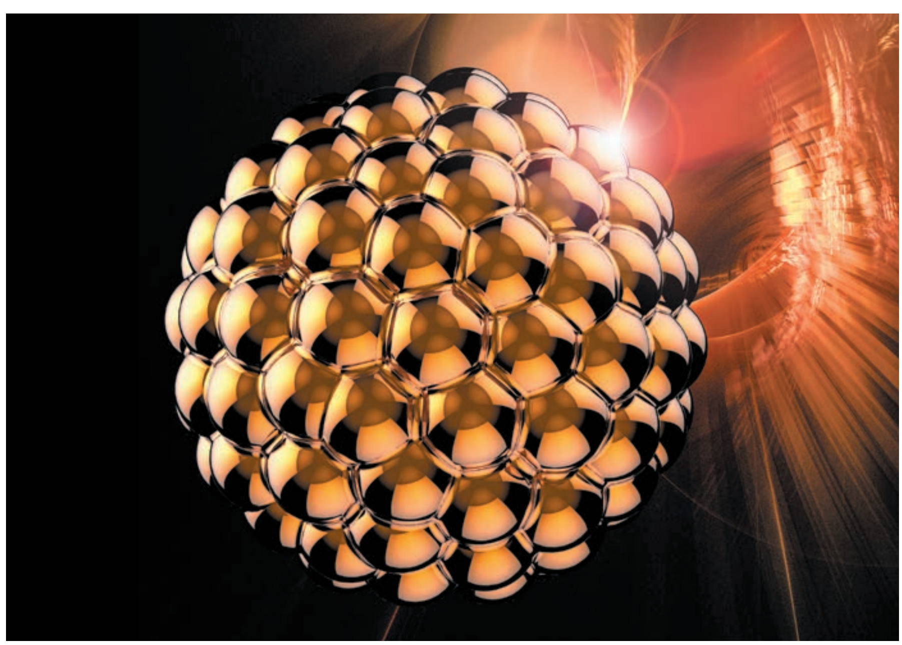
Nanoparticles have found uses in applications as diverse as cosmetics, medicine, catalysis and batteries. Scientists desire to understand exactly how the properties of nanoparticles depend on their size and structure, but it has been difficult to image nanoparticles in solution at sufficiently high resolution.

Now, a team that included researchers from the Institute for Basic Science in South Korea has used an electron microscopy technique to construct three-dimensional images of the 600 or so atoms in individual platinum nanoparticles in solution.

They found that even nanoparticles made in the same batch have substantially different structures. Such structural differences could cause significant variations in properties and so need to be factored in when making and analysing nanoparticles.

Reference

1. *Science* **368,** 60–67 (2020). doi: 10.1126/science.aax3233



Tropics feel the heat from afar

The equator could bear the brunt of global warming thanks to fossil fuel emissions at higher latitudes

Future enhanced equatorial warming will be exacerbated by high-latitude climate processes.

Climate models regularly predict that future warming will be more severe at the equator, but scientists are unsure why.

When a team led by researchers from the Institute for Basic Science modelled global-warming patterns after a sudden quadrupling of atmospheric carbon dioxide, they found that the Earth's surface heated up faster at the equator.

When they limited the fourfold increase in carbon dioxide to within the tropics, equatorial temperatures rose by 0.74 degrees Celsius, whereas when it was applied to an equivalent area outside the tropics, the equator warmed by 1.02 degrees Celsius.

The enhanced warming was largely caused by a weakening of an atmospheric system that usually carries heat up and away from the equator, as well as changes in cloud cover and slowing ocean currents.

If fossil fuel emissions continue to rise, high-latitude ocean warming, especially in the North Pacific, will alter the impacts of complex tropical climate systems such as El Nino.

Reference

1. *Nature Climate Change* **10,** 124–129 (2020).
doi: 10.1038/s41558-019-0667-6

How repetitive eye movements can suppress trauma

The neural pathway by which repetitive eye movements can suppress the fear of past traumatic events has been discovered

Neuroscientists have uncovered the neural basis behind a treatment for post-traumatic stress disorder.

One way to treat post-traumatic stress disorder is to present visual stimuli to a patient that stimulate repetitive eye movements while getting them to recall a trauma. This treatment can result in long-lasting healing in some cases, but no-one knew how it worked.

Now, by using optogenetics to investigate the effect of the therapy in the brains of traumatized rats, a team led by researchers at the Institute for Basic Science in South Korea has discovered the neural pathway behind the treatment.

Rats that received the treatment exhibited enhanced activity between two brain regions: the superior colliculus (a brain region associated with eye movement and attention) and the mediodorsal thalamus (a brain area connected to the superior colliculus). The mediodorsal thalamus in turn communicates with the basolateral amygdala, a brain area that controls fear expression and stores fear memory.

Reference

1. *Nature* **566,** 339–343 (2019).
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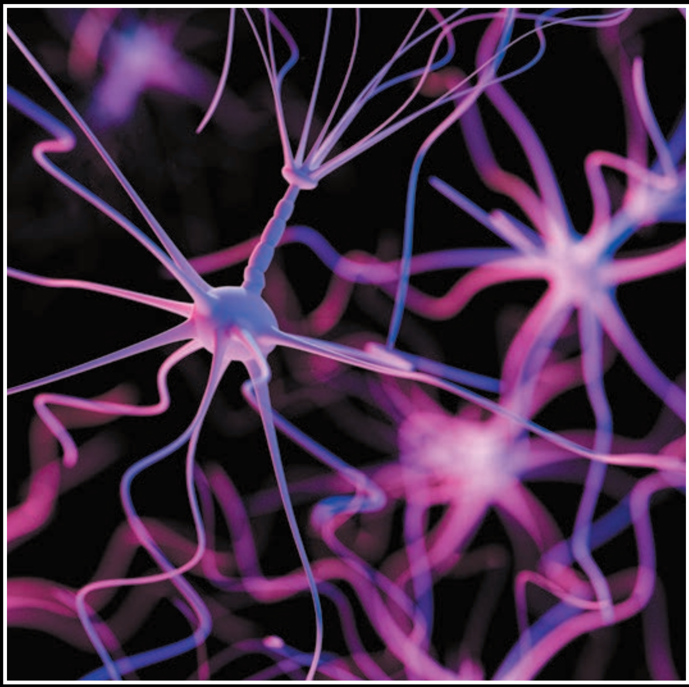

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