

GENOMICS BIOTECH VOL 6

MARCH 31, 2025

A delicate balancing act determines how many genome gateways form in cells

by [Sanford-Burnham Prebys](#)



The nuclei in our cells are miniature warehouses safeguarding the genetic blueprint for the body's biologic machinery. As warehouses go, nuclei are more like libraries than bank vaults. Too many cellular components need access to the genome to lock it down like Fort Knox. Instead, large groupings of more than 1,000 individual protein molecules called nuclear pore complexes (NPCs) pepper the dividing membrane, serving as gateways for materials and messages entering and exiting the nucleus.

While the basic need for this shuttle service is constant, scientists have shown that cells dynamically adjust their amounts of NPCs, like a retail store opening more or fewer checkout lines throughout the day. These fluctuations in genome access points have been observed in different cell types, stages of development, environmental conditions and in diseases such as neurodegeneration and cancer.

"As important as NPCs are for sustaining healthy cells, and despite the connections we and others have found to disease, we still have a lot to learn about how cells control the production of these genome gateways," said Maximiliano D'Angelo, Ph.D., associate professor in the Cancer Metabolism and Microenvironment Program at Sanford Burnham Prebys.

D'Angelo and his research team at Sanford Burnham Prebys [published findings](#) in *Cell Reports* revealing the results of screening the entire human genome to find factors influencing how many NPCs are assembled.

"Our goal was to identify the modulators of pore formation," said Stephen Sakuma, Ph.D., postdoctoral researcher at the Salk Institute, former graduate student in the D'Angelo lab and lead author of the study. "By discovering the mechanisms cells use to modulate pore formation, we may find new therapeutic approaches."

The research team found that the most influential players in the process were parts of opposing teams: the production crew making new proteins and the janitorial staff that recycle proteins and dispose of excess or misshapen proteins.

"It caught our eye that top regulators were pieces of the [protein](#) translation or degradation machinery," said D'Angelo, senior and corresponding author of the study.

"While it may seem intuitive because these processes would affect the number of nucleoporin proteins used to construct pores, this had not previously been investigated."

The scientists also uncovered the role of cellular actors involved in maintaining the messenger RNA (mRNA) that carries codes for building proteins out of the nucleus. The investigators detailed the involvement of a grouping of proteins called the CCR4-NOT complex, which is responsible for triggering the disposal of mRNA.

"We found that this complex reduces the mRNA levels, which diminishes the translation of NPC building blocks," said Sakuma. "This means it is possible to regulate the number of NPCs in different ways by altering protein translation or degradation, or by stabilizing or destabilizing mRNAs."

In addition to learning more about these top regulators, the researchers are also studying other factors identified in the genome-wide screen that may be employed to fine-tune levels of NPCs, as well as searching for small molecules that can manipulate NPCs.

With additional research, D'Angelo and his team aim to find ways to reduce NPCs in recklessly growing [cancer cells](#) to stop or delay disease progression.

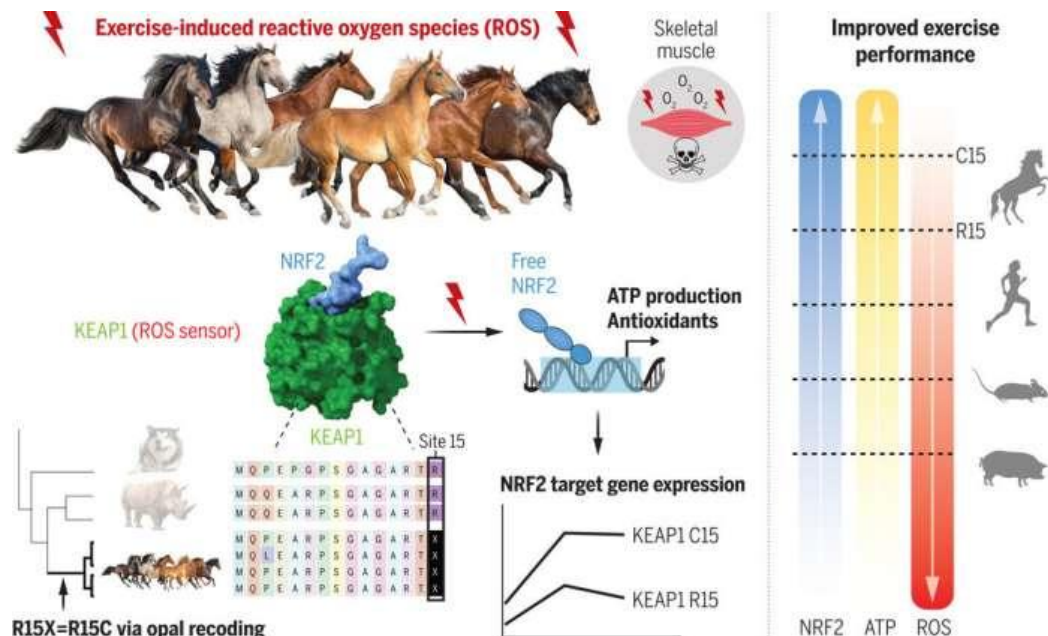
"Our previous work discovered that reducing the number of NPCs is a promising strategy for cancer treatments and we are now developing methods to do that," said D'Angelo. The group is also working to increase NPC function in brain cells afflicted with neurodegenerative diseases such as dementia.

More information: Homeostatic Regulation of Nucleoporins is a Central Driver of Nuclear Pore Biogenesis, *Cell Reports* (2025). DOI: [10.1016/j.celrep.2025.115468](https://doi.org/10.1016/j.celrep.2025.115468). [www.cell.com/cell-reports/full ... 2211-1247\(25\)00239-6](https://www.cell.com/cell-reports/full...2211-1247(25)00239-6)
Journal information: [Cell Reports](#)

MARCH 31, 2025

Horses, donkeys and zebras have adaptations that break normal genomic rules

by Justin Jackson , Phys.org



Opal recoding in horses alters protein phenotypes, enhancing exercise performance.

Credit: *Science* (2025). DOI: [10.1126/science.adr8589](https://doi.org/10.1126/science.adr8589)

A genetic mutation in horses that would typically halt protein production has become a molecular asset. Researchers at Johns Hopkins University and Vanderbilt University have identified a rare instance of genetic recoding that enhances oxygen metabolism and energy production in horses, donkeys, and zebras.

The findings, [published](#) in *Science*, provide insight into the genetic foundation of exceptional equine athletic ability, and hint at an entirely new way of dealing with stop codons.

Few mammals match horses in aerobic performance. Muscle tissue in thoroughbreds consumes oxygen at rates exceeding 360 liters per minute. Oxygen uptake per unit of body mass is more than twice that of elite human athletes. While many genes involved in muscle structure and locomotion have been studied, the genetic basis for this level of metabolic output has remained unclear.

Past research has focused largely on physical traits such as size, muscle architecture, or gait. Genomic studies have found mutations in genes affecting olfaction, keratin, and myosin, yet did not establish a direct link to aerobic metabolism.

In the current study, researchers focused on the gene KEAP1 and the KEAP1-NRF2 pathway, which regulates antioxidant responses and mitochondrial [energy production](#).

In birds, this pathway evolved to manage the oxidative stress caused by flight. In early vertebrates, it helped them adapt to environmental stressors during the transition from water to land. Researchers have proposed that a similar mechanism may have contributed to athletic equine evolution.

In preparing for their study, the researchers came across a premature stop codon in equine versions of the gene compared to other species. Located unusually early in the [protein sequence](#), the stop codon would be expected to end the transcription of the protein early, like stopping a 40-step assembly instruction after the first step. The resulting protein should be so truncated as to render it entirely nonfunctional.

Research that was meant to look into KEAP1 as a source of equine energy conversion suddenly had to confront the possibility that the gene, known to be critical to cellular redox balance and energy regulation, was not even coding. What they found instead was something truly unexpected.

In the study, "Running a genetic stop sign accelerates oxygen metabolism and energy production in horses," scientists used molecular biology and evolutionary analysis to investigate the premature stop codon in the KEAP1 gene. Genetic comparisons across all extant species of *Equus* were examined along with functional tests in horse and [human cells](#).

The team combined genetic comparisons across living horse species with cellular and molecular experiments.

They used CRISPR-Cas9 to model genetic changes in human cells, [mass spectrometry](#) to examine [protein structure](#), and metabolic assays to measure oxygen consumption and ATP production. Horse muscle and skin cells were studied alongside samples from other species to assess differences in energy output and oxidative stress responses.

What the researchers found challenged fundamental rules of genetics. The KEAP1 gene typically encodes a protein composed of more than 600 amino acids. A stop codon at

position 15 would ordinarily halt translation near the beginning, producing only 14 amino acids. That length is far too short to support any of the gene's known roles in cellular defense or energy regulation. Yet in horse cells, the protein appeared fully translated, complete and functional.

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Mass spectrometry revealed the explanation. The opal stop codon was being recoded as a cysteine, which allowed the translation process to continue. This rare form of genetic readthrough had not previously been documented in a gene like KEAP1 in any vertebrate. In horses, it enabled the cells to produce the full-length KEAP1 protein without interruption.

Analysis revealed a broad evolutionary change where KEAP1 and several components of the translation system had evolved uniquely in Equus, turning what should have been a fatal error into an evolutionary advantage.

Stop codons can sometimes be reinterpreted, allowing the cell to insert an amino acid rather than halting translation. This normally requires a specific signal in the mRNA that guides the ribosome to override the stop and insert selenocysteine. In horses, no such signal was found in the KEAP1 transcript. Yet the translation continued.

One likely explanation lies in the structure of the KEAP1 mRNA itself. The end of the transcript forms a distinctive shape that appears to attract the proteins needed for stop codon readthrough. This structure may act as an alternate signal, guiding the ribosome past the premature stop.

A second explanation comes from changes to the translation machinery itself. Two proteins involved in reading stop codons (SBP2 and eEFSec) carry mutations unique to Equus. Changes clustered in regions that help position transfer RNAs during translation.

Functional assays showed that the equine version of SBP2 alone was enough to drive recoding in a test system, even in the absence of the usual mRNA signals.

Together, the structural features in the transcript and the changes in translation factors appear to form a co-evolved solution that turns a genetic stop sign (selenocysteine) into a functional green light (cysteine).

The presence of the mutation in all modern equine species suggests it emerged early in the lineage—a change that may have allowed for increased aerobic performance, shaping the evolution of speed and endurance traits.

Roughly one in 10 human genetic disorders results from premature stop codons. A naturally occurring example of stop codon recoding that maintains balance while improving function may offer new directions for [biomedical research](#) with therapeutic approaches that aim to restore functional protein readthrough.

More information: Gianni M. Castiglione et al, Running a genetic stop sign accelerates oxygen metabolism and energy production in horses, *Science* (2025). DOI: [10.1126/science.adr8589](https://doi.org/10.1126/science.adr8589)

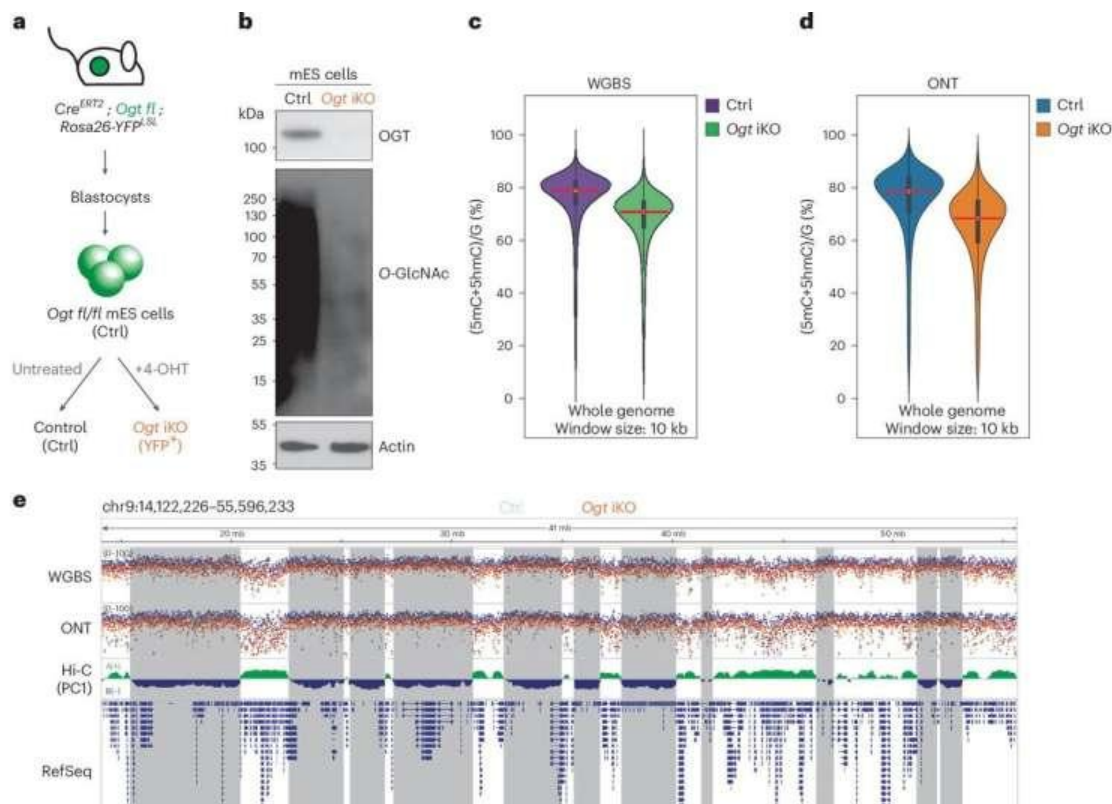
Journal information: [Science](#)

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MARCH 29, 2025

How a critical enzyme keeps potentially dangerous genes in check

by Madeline McCurry-Schmidt, [La Jolla Institute for Immunology](#)



Ogt deletion results in reduced DNA methylation genome-wide. Credit: *Nature Structural & Molecular Biology* (2025). DOI: [10.1038/s41594-025-01505-9](https://doi.org/10.1038/s41594-025-01505-9)

You may have heard of the fantastic-sounding "dark side of the genome." This poorly studied fraction of DNA, known as heterochromatin, makes up around half of your genetic material, and scientists are now starting to unravel its role in your cells.

For more than 50 years, scientists have puzzled over the genetic material contained in this "dark DNA." But there's a growing body of evidence showing that its proper functioning is

critical for maintaining cells in a healthy state. Heterochromatin contains tens of thousands of units of dangerous DNA, known as "[transposable elements](#)" (or TEs). TEs remain silently "buried" in heterochromatin in normal cells—but under many pathological conditions they can "wake up" and occasionally even "jump" into our regular genetic code.

And if that change benefits a cell? How wonderful! Transposable elements have been co-opted for new purposes through evolutionary history—for instance the RAG genes in [immune cells](#) and the genes required for driving the development of the placenta and mammalian evolution have been derived from TEs.

But TEs may also wreak havoc on our health. In just the last few years, scientists have linked heterochromatin weakening to aging, premalignancy, cancer, and autoimmune disease.

"You can think of heterochromatin as a prison for transposable elements" says La Jolla Institute for Immunology (LJI) Professor Anjana Rao, Ph.D., the lead author of a new [Nature Structural & Molecular Biology](#) study, with key collaborators Professor Geoffrey J. Faulkner, Ph.D. of the University of Queensland, Robert Crawford, Ph.D., of biomodal (formerly Cambridge EpiGenetix), and Samuel Myers, Ph.D., Assistant Professor at LJI. "When heterochromatin loses its normal suppressive function, TEs escape and in parallel, the health of cells declines."

The new study reveals a remarkable way that cells keep us safe from TEs gone wild. The researchers found that cells have taken advantage of an entire protein network to repress TE activity and keep themselves healthy.

"Reactivated transposable elements can create a lot of genomic instability," says Hugo Sepulveda, Ph.D., a Pew Latin American Postdoctoral Fellow, former Instructor at LJI, and one of the two co-first authors of the new study with LJI Instructor Xiang Li, Ph.D.

"Even just increased expression of these elements can affect the expression of nearby genes, as we show in our new paper," adds Sepulveda. "Abundant expression of transposable elements is a signature of many diseases, including cellular senescence, human aging, autoimmune disorders and many types of cancers."

How do cells keep transposable elements under control?

Meet O-GlcNAc transferase (OGT), an enzyme at the heart of many essential cellular functions. According to the new study, OGT is also a lead choreographer when it comes to suppressing TEs and keeping gene expression running smoothly.

For the new project, the researchers followed up on the fact that OGT interacts with important proteins called TET enzymes, discovered by the Rao Lab in 2009. TET proteins are part of the complex machinery that makes sure our DNA is correctly modified in our cells and that our cells activate the right transcriptional programs.

TET proteins are involved in the critical cycle of DNA modifications, where they play a role in a process that results in the removal of molecular markers that attach to DNA (an event called DNA demethylation). The most abundant DNA markers, called 5mC and 5hmC, are normally associated with transcriptional silencing and activation, respectively. Researchers have shown that 5mC is associated with genes turned "off" while 5hmC, mediated by TET proteins, is associated with [gene expression](#) turned "on."

This "on/off" epigenetic system gives our cells the flexibility to respond to environmental changes and health threats. DNA demethylation helps our immune cells spring into action if they detect a threat.

DNA demethylation is normal, but cells also need balance. You can't have TET proteins activating every gene at the same time. In normal cells, TET protein activity is restricted to the genes that need to be expressed in that particular cell type.

In the new study, the scientists harnessed Oxford Nanopore sequencing technology and other cutting-edge sequencing techniques to discover where OGT comes in. One especially important and new technique that they used is called duet evoC. This multiomics solution enabling the 6-base genome, developed by biomodal, was essential to establish that both 5mC and 5hmC were simultaneously changing at the same sites in the genome.

The researchers found that OGT protects cells by restraining TET activity. This is extremely important for controlling TE expression because it prevents the silencing modification 5mC from being converted to the activating modification 5hmC in heterochromatin.

Without OGT at the helm, TET proteins ramp up DNA demethylation in the wrong places, turning on too many genes at once, including intact TEs normally "buried" in our genetic material.

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Next steps for understanding cancers, autoimmune disease, and more

This finding shows how the non-coding regions of our genome can turn active when TET functions are altered. The new understanding of the OGT-TET partnership shows that these proteins, their mediated marks, and TE expression can affect our cells in a big way.

"We think of these elements as totally 'silent,' and therefore completely inert, but the reality is that cells have to make a huge—and constant—investment to keep TEs silent," says Sepulveda.

This new research may also prove important for future drug development. Scientists have identified numerous genes linked to cancer, but controlling their expression remains a

challenge. The new findings suggest we might stop cancer growth through interesting new avenues, such as by restraining TE activity in cancer cells.

"We want to control that activity, and we may now have an option through OGT and TETs," says Sepulveda.

Rao emphasizes that further studies are needed to investigate how OGT controls DNA modifications and TE expression—and how the dysregulation of this mechanism contributes to autoimmune disorders, cancers, and other diseases.

Additional authors of the study, "OGT prevents DNA demethylation and suppresses the expression of transposable elements in heterochromatin by restraining TET activity genome-wide," include Leo J. Arteaga-Vazquez, Isaac F. López-Moyado, Melina Brunelli, Lot Hernandez Espinosa, Xiaojing Yue, J. Carlos Angel, Caitlin Brown, Zhen Dong, Natasha Jansz, Fabio Puddu, Aurélie Modat, Jamie Scotcher, Páidí Creed, Patrick Kennedy, and Cindy Manriquez.

More information: OGT prevents DNA demethylation and suppresses the expression of transposable elements in heterochromatin by restraining TET activity genome-wide, *Nature Structural & Molecular Biology* (2025). DOI: [10.1038/s41594-025-01505-9](https://doi.org/10.1038/s41594-025-01505-9)

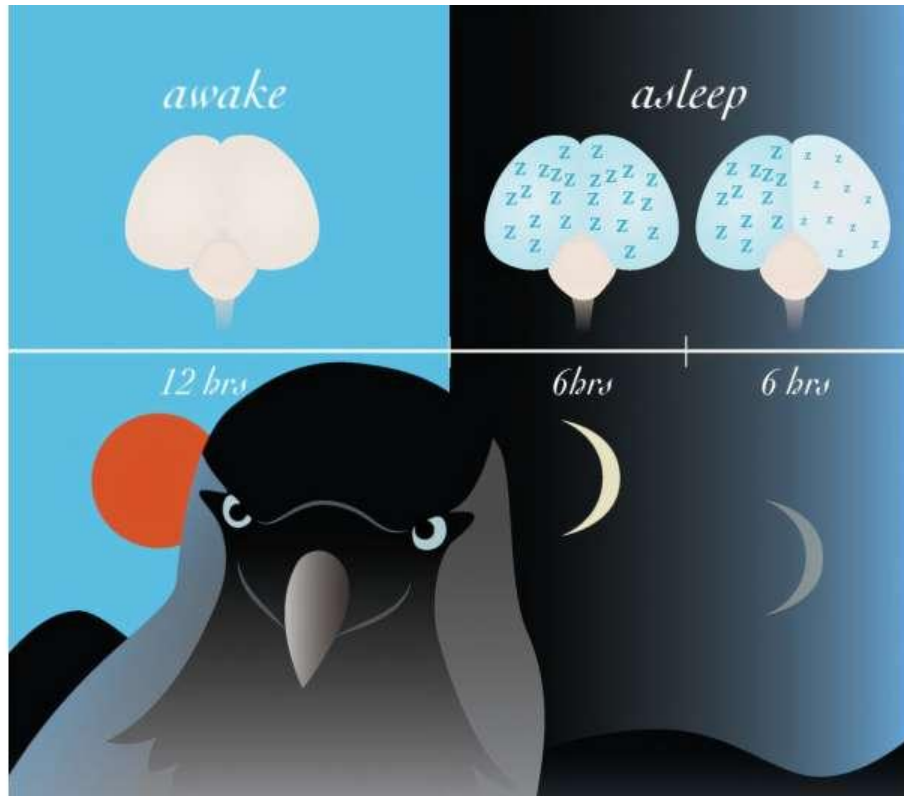
Journal information: [Nature Structural & Molecular Biology](#)

Provided by [La Jolla Institute for Immunology](#)

MARCH 31, 2025

Sleep-deprived European jackdaws trade vigilance for deep sleep

by [Max Planck Society](#)



Sleep-deprived jackdaws spent more time in deep, symmetrical sleep – especially early in the night, when the need to recover is greatest. Credit: MPI for Biological Intelligence/Julia Kuhl

As most people who have pulled an all-nighter will agree, lost sleep can leave us feeling foggy and far from our best. In some ways, birds respond similarly, often sleeping longer and more deeply after sleep loss. But unlike humans, birds can sleep with one eye open, keeping one half of the brain somewhat alert while the other sleeps deeply. This balance between vigilance and deep sleep helps them stay aware of danger while still getting some much-needed shut-eye.

However, a new study of European jackdaws shows that this strategy has its limits: when sleep-deprived, these clever, social birds were more likely to fall into [deep sleep](#) in both brain halves—even at the cost of losing vigilance. The findings offer new insight into sleep and the consequences of going without it.

Keeping an eye out

Sleep is essential across the [animal kingdom](#), but there is wide variation in how it happens. When humans sleep, our brains cycle through stages, alternating between [rapid eye movement](#) (REM) sleep and non-REM sleep roughly every 90 minutes.

Birds go through these same stages, but typically in much shorter bursts—and their sleep patterns are far more flexible than ours. One weapon in their sleep armory is the ability to sleep with one eye open during non-REM sleep, a state known as asymmetric sleep.

This is characterized by light sleep in the brain half connected to the open eye and deep sleep in the brain half connected to the closed eye. It allows birds, such as ducks, to keep one side of the brain more alert while the other enters a deeper state of sleep.

Non-REM sleep is thought to play a key role in [memory consolidation](#) and clearing waste from the brain. However, recharging one brain hemisphere with one eye open takes longer than resting both sides together in deep, symmetrical sleep. Scientists are still uncovering when, how, and why birds rely on this nap-time balancing act.

Adaptive sleep strategies

The new study of European jackdaws, led by researchers at the Max Planck Institute for Biological Intelligence and the Groningen Institute for Evolutionary Life Sciences, [published](#) in *Current Biology*, reveals a trade-off between getting sleep and staying alert.

Previous studies have shown how birds and some other animals use adaptable, vigilant sleep strategies to stay alert in challenging situations—from great frigatebirds sleeping asymmetrically mid-flight, to mallard ducks keeping one eye open when vulnerable on the outer edge of their group, to northern fur seals sleeping asymmetrically when in the water. Even humans—who do not sleep with one eye open—tend to sleep more lightly with the left half of the brain on the first night in a new environment.

This new research reveals where such strategies fall short: sleep-deprived jackdaws spent more time in deep, symmetrical sleep, while asymmetric sleep became less common—especially early in the night, when the need to recover is greatest.

"Sleep is a dangerous part of life for many animals, as it leaves them exposed to all kinds of risks," says Niels Rattenborg, group leader at the Max Planck Institute for Biological Intelligence. "Some birds can function surprisingly well on far less sleep than we can, but even that strategy appears to have its limits."

"We have found that when they're tired, jackdaws are more likely to sleep deeply—even if that means becoming more vulnerable. Observing how birds navigate the trade-off between vigilance and sleep may help us better understand sleep in general."

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Tracking tiredness

To investigate how European jackdaws recover from sleep loss—and how they switch between symmetric and asymmetric sleep—researchers studied nine [birds](#) using electroencephalograms (EEGs), which measure the activity of millions of neurons across the brain.

The researchers found that some brain areas slept more deeply than others, which may suggest that regions used more during wakefulness need deeper sleep. For example, not all parts of the jackdaws' brains responded to sleep loss in the same way. Regions involved in vision and decision-making showed stronger signals after [sleep deprivation](#), while others, like the memory-related hippocampus, were less affected.

"Our findings reveal that even the highly flexible sleep strategies used by jackdaws have limits," says Peter Meerlo, a group leader at the Groningen Institute for Evolutionary Life Sciences. "That tells us something fundamental about sleep: it's not just a passive state, but a behavior shaped by both evolution and environmental demands.

"The study offers a fresh perspective on how animals balance the need for sleep with the risk of predation or other threats—and could help us better understand how sleep loss affects brain function more broadly, including in humans."

More information: Sleep pressure causes birds to trade asymmetric sleep for symmetric sleep, *Current Biology* (2025). DOI: [10.1016/j.cub.2025.03.008](https://doi.org/10.1016/j.cub.2025.03.008). [www.cell.com/current-biology/f ... 0960-9822\(25\)00293-3](https://www.cell.com/current-biology/f...0960-9822(25)00293-3)

Journal information: [Current Biology](#)

Provided by [Max Planck Society](#)

Dual protein tagging process could lead to new treatments for immune system diseases

by Angela Yeager, [Oregon Health & Science University](#)



In a new study, researchers Jonathan Pruneda, Ph.D., right, and Michael Cohen, Ph.D., have uncovered a new way proteins can be changed inside cells, increasing understanding of how the immune system works. Credit: OHSU / Christine Torres Hicks

A study by Oregon Health & Science University researchers has uncovered a new way proteins can be changed inside cells. This discovery could be important for understanding how the immune system works.

The scientists have discovered a dual modification process they call "MARUbylation," which combines two different molecular tags, ADP-ribosylation and ubiquitylation, on the same protein. This discovery challenges the long-standing belief that each [protein modification](#) involves only one type of tag. Instead, the study, [published](#) in *The EMBO Journal*, shows that some proteins can have two tags at once, which can affect how they function in cells.

The discovery came through a collaboration between two researchers who, on the surface, studied different areas. Jonathan Pruneda, Ph.D., associate professor of molecular

microbiology and immunology in the OHSU School of Medicine, studies ubiquitylation, where a small molecule called ubiquitin attaches to a protein, marking it for various actions like being broken down or moved—like putting a tag on a protein.

Meeting leads to 'aha' moment

A meeting between the two scientists to discuss a graduate student's research led to a lightbulb moment.

"We were just chatting about post-translational modifications and realized that the two we were working on could literally fit together," Pruneda said.

The researchers were excited to find that proteins in human cells can be modified with both ADP-ribosylation and ubiquitylation. They named this process "MARUbylation."

"We realized that two completely different fields—like the ones we work in—are actually looking at the same thing," Cohen said. "No one had really connected them before. Our goal is to see if we can team up to develop new treatments, rather than coming at it from different directions."

Pruneda added, "We think it changes the message that the protein receives, which could impact how it functions in the body."

Proteins are often modified by adding small chemical tags, which change how they act in the cell. It was generally believed that each site on a protein could only be modified by one type of tag at a time. But this study shows that some proteins can have two tags at the same time, opening up new ways to understand how proteins work.

The researchers discovered that a protein called PARP10, which helps repair DNA, can be tagged with both ADP-ribose and ubiquitin. This dual modification is important when the immune system responds to signals, especially in fighting off infections.

Using special tools, the scientists confirmed that MARUbylation happens inside cells. They also found that this process can lead to further reactions inside cells, adding more complexity to how signals are managed.

"This discovery expands our understanding of how complex cellular signals are integrated," Pruneda said. "Until now, it was thought that a single modification would control protein behavior, but our work reveals that different modifications can interact and affect a protein's function in unique ways."

Discovery paves way for immune therapies

The discovery could provide new insights into diseases related to the immune system, such as [autoimmune disorders](#), cancer and [neurodegenerative diseases](#), where protein modifications play a key role. Pruneda hopes that understanding MARUbylation could lead to new treatments.

"What's interesting is that drugs targeting these processes are already in use," Pruneda said. "PARP inhibitors, for example, are being used in the clinic, and now we're starting to appreciate the biology behind these drugs."

Cohen sees the potential for their discovery to improve immune therapy, especially [cancer treatment](#).

"Cancer cells have found ways to evade the immune system, and one of the methods they use is by upregulating PARP enzymes, which helps them avoid the immune response," he said. "By inhibiting those enzymes, we can help reverse that and make cancer cells more susceptible to immune attack."

The researchers are excited to keep working together to better understand how this new modification process works and to discover new ways to target it for treatments. Pruneda and Cohen are hopeful their collaboration will lead to new therapies in the future.

"It's about using this collaboration to build tools that are more than just the sum of their parts," Cohen said. "Our different approaches and methodologies made this project a success."

In addition to Pruneda and Cohen, Daniel Bejan, Ph.D., and Rachel Lacoursiere, Ph.D., both of OHSU, co-authored this study.

More information: Daniel S Bejan et al, Ubiquitin is directly linked via an ester to protein-conjugated mono-ADP-ribose, *The EMBO Journal* (2025). DOI: [10.1038/s44318-025-00391-7](https://doi.org/10.1038/s44318-025-00391-7)

Journal information: [EMBO Journal](#)

Provided by [Oregon Health & Science University](#)

MARCH 31, 2025

Bioengineered red yeast turns wood waste into a valuable fatty acid

by Bev Betkowski, [University of Alberta](#)



Credit: University of Alberta

Forestry waste can be turned into a high-value fatty acid, thanks to a bright red yeast engineered by University of Alberta researchers.

Using wood-derived sugar as a feedstock, the strain, developed from a yeast called *Rhodospiridium toruloides*, proved capable of producing punicic acid.

The discovery offers potential economic wins for the forestry and [food industries](#), says study co-author Guanqun Chen, associate professor in the Faculty of Agricultural, Life & Environmental Sciences and Canada Research Chair in Plant Lipid Biotechnology. The research is [published](#) in the journal *Bioresource Technology*.

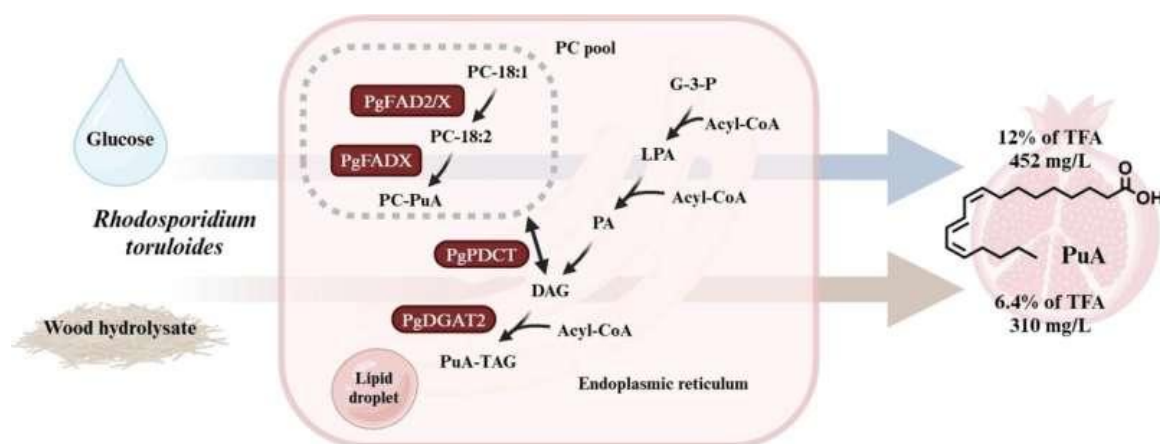
Derived mainly from the seed oil of pomegranate fruit, punicic acid offers healthy cholesterol-lowering, anti-inflammatory and anti-carcinogenic properties. However, with a very low seed-to-fruit ratio and oil yield, it's currently not financially feasible to produce for large-scale use in the food industry.

But being able to produce the fatty acid using a sugar solution derived from low-value leftovers like [wood chips](#) provides both economic and environmental benefits, Chen says,

noting that the yeast strain could also be used on agricultural byproducts such as canola and wheat straw, after pre-treatment.

"We've shown that this engineered strain can serve as an industrial platform for converting large volumes of biomass waste or byproducts into a valuable product, which may open up opportunities for creating high-value [nutritional supplements](#), functional food and animal feed ingredients.

"That creates additional revenue, improves resource efficiency and can help sustainability for these various industries."



Credit: *Bioresource Technology* (2024). DOI: 10.1016/j.biortech.2024.131422

The strain, which is now under a provisional patent application, could, for example, serve as an [alternative to using baker's yeast](#), the current approved choice for animal feed supplements, notes study co-author Juli Wang, who carried out the research as part of his Ph.D. thesis project in plant science.

"It's got high oil content and a quick growth rate that make it a better option for producing punicic acid using fermentation."

The research, conducted in collaboration with U of A professor David Bressler's Biorefining Conversions and Fermentation Lab, marks the first time *R. toruloides* was engineered to produce punicic acid.

In their experiments, the researchers genetically modified the red yeast by introducing two key enzymes from pomegranate fruit. When cultured with a sugar solution derived from the wood waste, the yeast strain produced 6.4% of its total fatty acids as punicic acid.

The discovery proves that the strain can produce a high amount of the fatty acid during fermentation, signaling the potential for producing it at the commercial level.

"We can now look at how to optimize and then scale up the fermentation process," Wang says.

The researchers plan to continue tweaking the [yeast strain](#) to boost its punicic acid content and exploring the use of other renewable feedstocks from Alberta's forestry and agricultural industries, such as sugar beet molasses.

It could also have wider-ranging uses, Chen adds. "Beyond producing punicic acid, red yeast could potentially be engineered to produce a variety of other specialty fatty acids, such as omega-3 [fatty acids](#), which have many nutraceutical applications."

More information: Juli Wang et al, Engineering *Rhodospiridium toruloides* for sustainable production of value-added punicic acid from glucose and wood residues, *Bioresource Technology* (2024). DOI: [10.1016/j.biortech.2024.131422](https://doi.org/10.1016/j.biortech.2024.131422)

Journal information: [Bioresource Technology](#)

Provided by [University of Alberta](#)

MARCH 31, 2025

Curing fashion's reliance on leather with an eco-friendly plant-based alternative

by Esther Etkin, [CSIRO](#)



Alt.

Leather's innovative green technology makes natural fibres mimic the 3D network structure of animal leathers. Credit: Alt. Leather

As the material left the curing oven, the Alt. Leather team knew it had worked—what they held in their hands looked and felt just like leather.

That moment marked a breakthrough for the Melbourne-based start-up, which has developed a revolutionary, 100% bio-based alternative to traditional leather. Made from agricultural waste and natural fibers, it offers a durable, animal-free solution with zero plastics.

Designed for industries like fashion, footwear, upholstery and automotive, the start-up is focused on using resources more efficiently. It promises a high-performance yet sustainable and circular solution that reduces the environmental impact of conventional leather production.

It was the result of Tina Funder, Alt. Leather's founder, identifying a gap in the market for alternatives to animal and synthetic leathers. Tina saw an opportunity to tap into Australia's abundance of regenerative plants and leading research facilities to transform the leather industry.

Through CSIRO's Kick-Start and RISE Accelerator programs, Alt. Leather has been able to refine their material production processes and accelerate their commercialization journey, both in Australia and internationally.

Kick-starting large-scale production

Turning an idea into a scalable product takes more than just innovation—it requires the right equipment, expertise and support. That's where we stepped in.

Lacking access to the specialized equipment needed to refine their material production processes, Alt. Leather contacted us to see if we had what they needed. Once confirmed, they applied to CSIRO Kick-Start, which promptly connected them with our Food Innovation Center team in Werribee in Melbourne's West.

The team began by testing their material on small-scale extruders, machines that shape and form material by forcing it through a mold. Once the material performed well, they moved to a larger extruder, which allowed them to test the feasibility of scaling up production.

Tina explained that these trials were crucial in determining the best processing methods.

"The structured approach of Kick-Start allowed us to test our material in a real-world setting and confirm that it could be scaled up," Tina said.

This gave Alt. Leather the confidence they were looking for. They were on the right path, paving the way for further growth and commercial viability.



Through our RISE Accelerator, Alt. Leather successfully produced handbags and footwear in India, refining their processes in a high-volume setting. Credit: Alt. Leather

On the RISE in India

Eager to expand their solution worldwide and tap into global innovation ecosystems, Alt. Leather applied to CSIRO's India Australia RISE Accelerator program to be a part of its Circular Economy cohort.

Through the program, Alt. Leather gained direct access to manufacturing systems in India, where they successfully produced handbags and footwear with manufacturers in Noida and Chennai.

Tina praised RISE for providing them with valuable firsthand experience in high-volume production environments.

"The real-world production runs in India provided valuable insights into the operational challenges of mass manufacturing. It allowed us to fine-tune our approach at an industrial scale and further improve the efficiency of our processes," Tina said.

One-on-one support from dedicated program facilitators and industry experts across India and Australia also proved to be a game-changer for the company.

"We've learned how to navigate international supply chains and manufacturing landscapes, positioning us well for global expansion," Tina said.

From prototype to global partnerships

With ongoing facilitation and support from our manufacturing team at Clayton, Alt. Leather is conducting regular formulation testing to ensure continuous improvements in their material's composition and performance. The company is also exploring partnerships with both Australian and international brands eager to incorporate their sustainable [leather](#) alternative into products.

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Tina credits the Kick-Start and RISE Accelerator teams as being instrumental in helping them to reach this stage, ensuring a smooth transition to larger-scale manufacturing.

"Our collaboration with CSIRO has been overwhelmingly positive, characterized by strong support, expert guidance, and an environment of shared innovation," Tina said.

Her team benefited from how the programs go beyond research, driving innovation through expert facilitators who connect startups and SMEs to the right expertise, equipment, and market access.

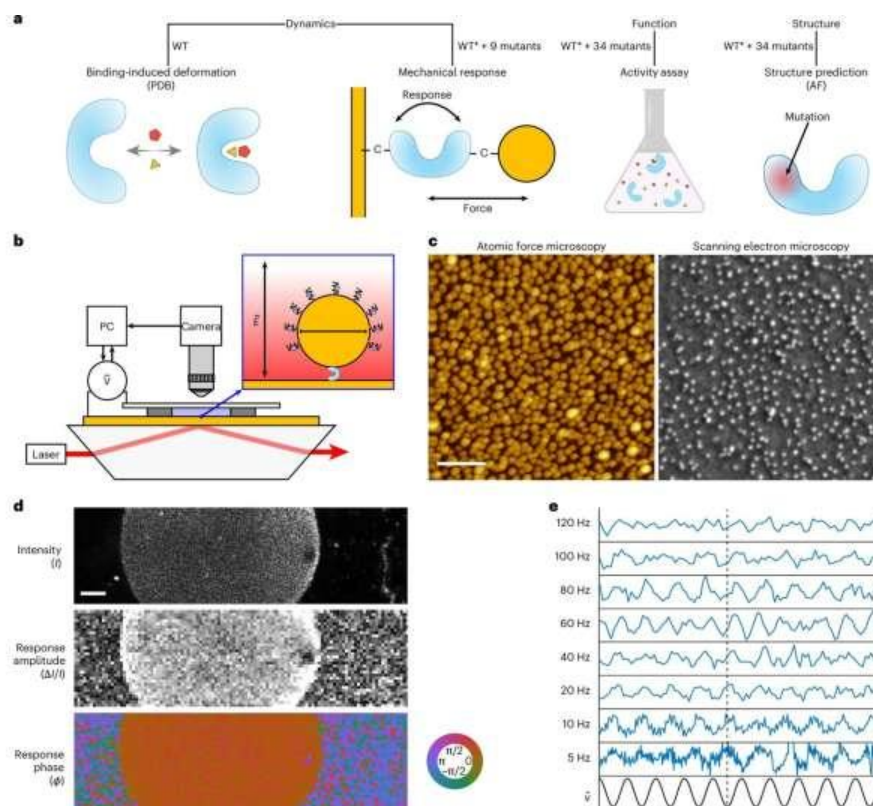
For Alt. Leather, this support has been pivotal in unlocking the commercial readiness of their sustainable, circular solution—an essential alternative as businesses face increasing pressure to reduce their environmental impact.

Provided by [CSIRO](#)

MARCH 31, 2025

Unlocking the mechanics of life: Enzymes as soft, programmable nanobots

by JooHyeon Heo, [Ulsan National Institute of Science and Technology](#)



Schematic and details of experiment. Credit: *Nature Physics* (2025). DOI: 10.1038/s41567-025-02825-9

Living cells are bustling with molecular machines that constantly process energy, matter, and information. Among these machines, proteins stand out, with enzymes being the most notable. These catalytic entities dramatically accelerate essential metabolic reactions by many orders of magnitude, facilitating the very processes that sustain life. While it has long been acknowledged that enzymes undergo movements during their catalytic cycles, measuring and predicting these internal motions and forces has proven extremely challenging.

A new study [published](#) in the journal *Nature Physics* addresses that challenge. It is the result of an international collaboration, led by Professor Tsvi Tlusty from the Department of

Physics at UNIST and Professor Elisha Moses from the Physics Department at the Weizmann Institute of Science, Israel.

The collaboration integrated [artificial intelligence](#) (AI) models with [molecular dynamics simulations](#) to predict the internal dynamics of enzymes, alongside an innovative "nano-rheology" technique to measure these dynamics with unprecedented accuracy.

The computational and experimental results culminated in the development of a new viscoelastic model of enzymes, elucidating the intertwined effects of elastic forces arising from stretching or twisting molecular bonds and friction forces (viscosity) associated with bond breaking and reforming.

"Finally, this novel physical model can explain how subtle, nanoscale motions and forces within enzymes impact their biological functions. It allows us to perceive proteins as soft robots or programmable active matter," said Professor Tlusty.

More information: Eyal Weinreb et al, Enzymes as viscoelastic catalytic machines, *Nature Physics* (2025). DOI: [10.1038/s41567-025-02825-9](https://doi.org/10.1038/s41567-025-02825-9)

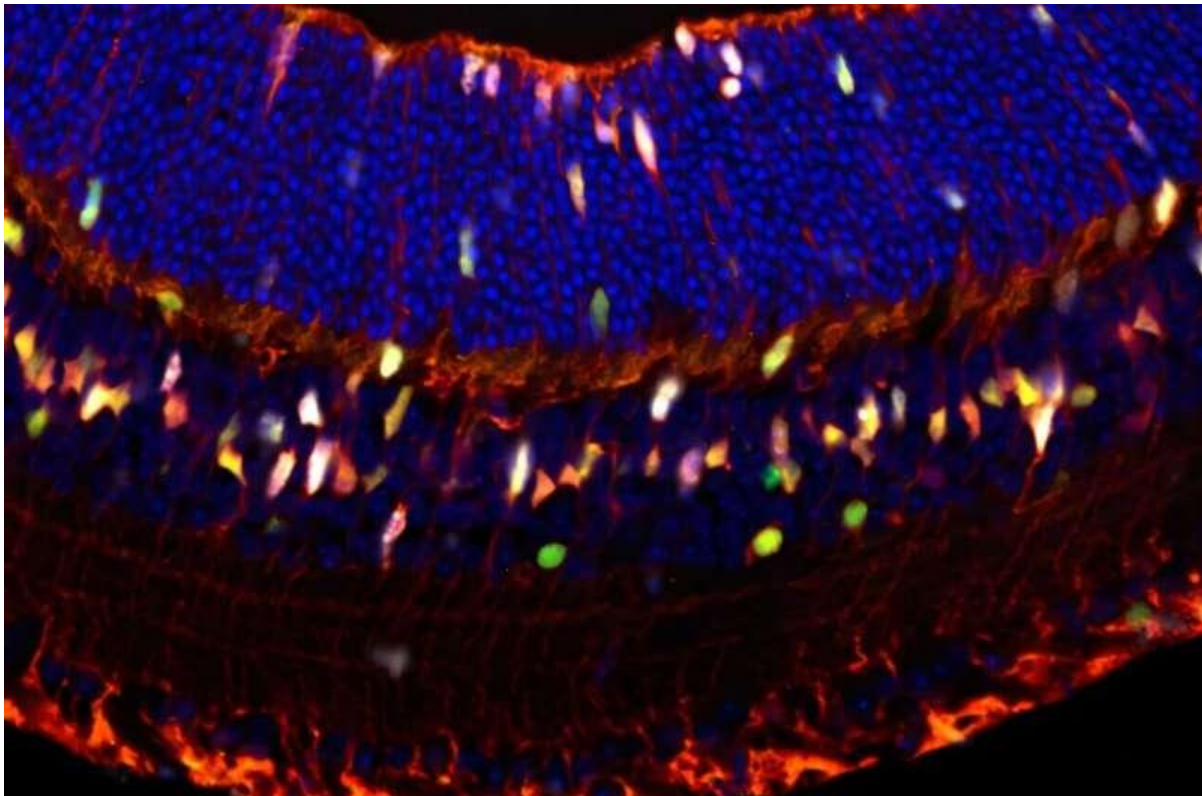
Journal information: [Nature Physics](#)

Provided by [Ulsan National Institute of Science and Technology](#)

MARCH 31, 2025

Mouse study identifies shared genes involved in hearing and vision regeneration

by [Keck School of Medicine of USC](#)



Müller glia (green) and their progeny (red) regenerate nerve cells and photoreceptors in a mouse retina. Credit: Ksenia Gnedeve/USC

The same genes could hold the key to regenerating cells in the ear and eye, according to a new mouse study from the USC Stem Cell laboratory of Ksenia Gnedeve, Ph.D., published in the [Proceedings of the National Academy of Sciences](#).

"The proliferation of [progenitor cells](#) in response to injury is a crucial step in the regeneration of sensory receptors, but this process is blocked in the mammalian inner ear and retina. By understanding the genes that enforce this block, we can advance efforts to

restore hearing and vision in patients," said Gnedeva, an assistant professor in the USC Tina and Rick Caruso Department of Otolaryngology—Head and Neck Surgery, and the Department of Stem Cell Biology and Regenerative Medicine at the Keck School of Medicine of USC.

In the study, first authors Eva Jahanshir and Juan Llamas from the Gnedeva lab focused on a group of interacting genes called the Hippo pathway, which serve as a "stop growing" signal that the lab has shown to inhibit [cell proliferation](#) in the ear during embryonic development. In their experiments, the scientists demonstrated that the Hippo pathway also suppresses the regeneration of damaged sensory receptors in the ear and eye of adult mice.

The scientists used an experimental compound that the lab earlier developed to inhibit a key protein in the Hippo pathway: LATS1/2. When exposed to this drug-like compound in a Petri dish, the progenitor cells, known as supporting cells, responded by proliferating in the utricle, which is a sensory organ in the inner ear that helps with balance. However, the same cells did not respond in the organ of Corti, which is the hearing [sensory organ](#).

The scientists next identified what was blocking this important step towards sensory cell regeneration in the organ of Corti—a gene encoding a protein called p27^{Kip1}—and showed that this inhibitory protein was also high in the retina.

They created a transgenic mouse in which the level of p27^{Kip1} could be reduced in the inner ear and the retina to see how that would impact the proliferation of progenitor cells in response in both organs.

In these mice, inhibiting the Hippo pathway effectively caused supporting cells proliferation in the organ of Corti, an important step towards the regeneration of the ear's sensory cells.

In the retina, inhibiting the Hippo pathway induced the proliferation of progenitor cells known as Müller glia. Surprisingly, the researchers discovered that some of the Müller glia progeny, without further manipulation, converted to sensory photoreceptors and other neuronal cell types in the retina.

"There have been reports that p27^{Kip1} levels drop following injury, so that might offer a brief window of opportunity for using a drug-like compound to inhibit the Hippo pathway and encourage regeneration in the ear and the eye," said Gnedeva.

"Alternatively, it could be possible to develop another drug-like compound to reduce p27^{Kip1} levels. So, our discoveries have identified potential new targets for stimulating the [regeneration](#) of both hearing and vision."

Additional co-authors are Yeeun Kim, Kevin Biju, and Sanyukta Oak from the Gnedeva Lab.

More information: Gnedeva, Ksenia, The Hippo pathway and p27Kip1 cooperate to suppress mitotic regeneration in the organ of Corti and the retina, *Proceedings of the*

National Academy of Sciences (2025). DOI:

[10.1073/pnas.2411313122](https://doi.org/10.1073/pnas.2411313122). doi.org/10.1073/pnas.2411313122

Journal information: *Proceedings of the National Academy of Sciences*

Provided by [Keck School of Medicine of USC](#)

APRIL 1, 2025

Protective gene found to preserve mitochondria during kidney disease progression

by Justin Jackson , Medical Xpress



Credit: Pixabay/CC0 Public Domain

Research led by Children's Hospital of Fudan University in China has found that a gene called pancreatic progenitor cell differentiation and proliferation factor (PPDPF) helps protect kidney cells by supporting enzymes involved in maintaining cellular energy levels during chronic kidney disease.

Chronic kidney disease affects approximately 15% of the global population and is currently the ninth leading cause of death worldwide. Treatments that can slow the progression of this condition remain limited.

Genome-wide association studies have identified nearly 800 genetic loci associated with kidney function, yet more than 90% of these variants are located in noncoding regions.

Specific genes and [molecular mechanisms](#) involved in early-stage [chronic kidney disease](#) remain incompletely understood.

PPDPF was selected for investigation after showing strong genomic associations with kidney function in large-scale population studies.

Variants linked to decreased kidney performance were also associated with changes in PPDPF expression across multiple types of expression quantitative trait locus (eQTL) analysis, including bulk tissue, cell-type specific, and meta-analyses. Although the gene has been studied in other physiological and pathological contexts, its role in kidney disease had not been experimentally tested.

In the study, "PPDPF preserves integrity of proximal tubule by modulating NMNAT activity in chronic kidney diseases," [published](#) in *Science Advances*, researchers integrated [genome-wide association studies](#) on [kidney function](#) and multi-omic analysis with the goal of understanding kidney fibrogenesis from the earliest cellular events.

Kidney samples were collected from both mouse models and previously published human datasets to examine gene activity during early-stage injury.

In the mouse experiments, researchers analyzed three control kidneys, three collected one day after obstruction-induced injury, and two collected five days after injury. Human data included samples from individuals with [acute kidney injury](#) and preimplantation kidney donors, drawn from single-cell and bulk RNA sequencing datasets.

Bulk and single-cell RNA sequencing were performed on mouse kidneys following induced injury to track [gene expression](#) over time. Genetically modified mice lacking PPDPF were developed using CRISPR-Cas9, and additional models were created through chemical exposure, surgical obstruction, and aging.

Human kidney data were analyzed from existing single-cell sequencing datasets and gene expression databases. Researchers used gene knockdown and overexpression in kidney cells, along with biochemical assays to measure mitochondrial activity, NAD⁺ levels, and protein interactions related to PPDPF function.

PPDPF was found to be strongly expressed in healthy proximal tubule cells and increased during the early stages of kidney injury in both mouse models and human samples.

Experimental loss of PPDPF impaired mitochondrial structure and function, leading to reduced NAD⁺ levels. Mice lacking PPDPF (knockout) developed more severe kidney damage in multiple models of chronic kidney disease, including those caused by aging, chemical injury, and urinary obstruction.

Supplementation with NAD⁺, but not with its metabolic precursor NMN, reduced signs of kidney injury in these mice. Overexpression of PPDPF improved mitochondrial activity,

increased NAD⁺ levels, enhanced NMNAT activity, and reduced markers of fibrosis and injury in renal tissue.

According to the authors, the findings suggest that "PPDPF is a regulator of NAD⁺ homeostasis involved in modulating CKD progression," which strongly supports targeting PPDPF as a potential therapy for kidney fibrosis with possibilities for future chronic kidney disease interventions.

More information: Xiaoliang Fang et al, PPDPF preserves integrity of proximal tubule by modulating NMNAT activity in chronic kidney diseases, *Science Advances* (2025). DOI: [10.1126/sciadv.adr8648](https://doi.org/10.1126/sciadv.adr8648)

Shin-ichiro Imai, PPDPF: Preventing kidney disease through NAD⁺ regulation, *Science Advances* (2025). DOI: [10.1126/sciadv.adw6815](https://doi.org/10.1126/sciadv.adw6815)

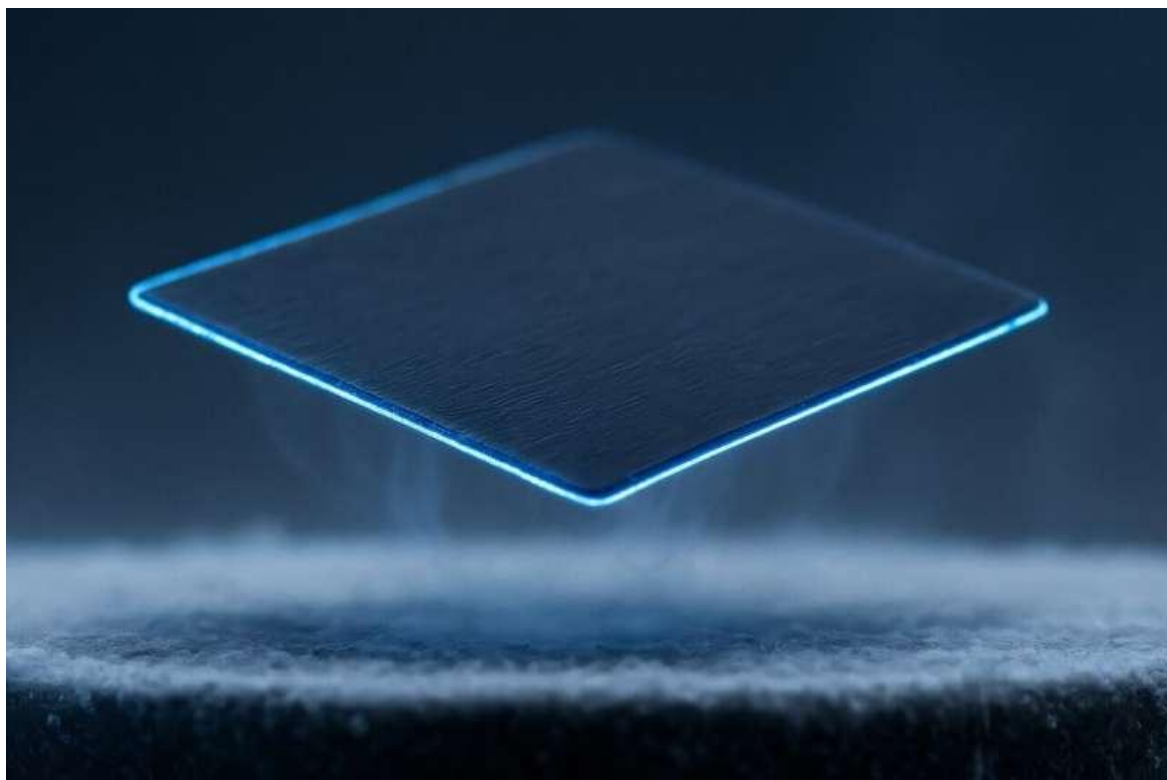
Journal information: [Science Advances](#)

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APRIL 1, 2025

Magnesium becomes a possible superconductor near the 2D limit

by Alessio Zaccone



Ultra-thin superconductor sheet. Credit: ChatGPT

Magnesium is a common chemical element, an alkaline earth metal, which is highly chemically reactive and is very light (even lighter than aluminum). Magnesium is abundant in plants and minerals and plays a role in human physiology and metabolism. In the cosmos, it is produced by large aging stars.

Among its physical properties, while it is a good conductor of electricity, magnesium is not known to be a superconductor. Superconductors are particularly promising materials with the potential to revolutionize [energy transmission](#), [medical imaging](#), and quantum computing, and are defined by their ability to conduct electricity without resistance below a certain critical temperature.

Recently, with my colleague Giovanni Ummarino from Turin Polytechnic, I have started challenging the textbook paradigm that states only certain elements in the periodic table can be superconductors. In particular, my colleague and I have shown that the phenomenon of [quantum confinement](#) can turn non-superconducting elements into superconductors. Our research is [published](#) in *Condensed Matter*.

Here by quantum confinement I mean the phenomenon in which the energy of a quantum particle, such as an electron, can greatly increase when it's spatially confined, an effect that is ultimately due to the Heisenberg uncertainty principle—the more you constrain the spatial position of a quantum particle, the larger its energy fluctuations become.

In our previous work, my colleague and I have shown that this applies to noble metals such as gold, copper, and silver, which we predicted to become superconductors when processed into very thin sheets of about half a nanometer in thickness.

Now, our calculations predict that even magnesium can become a superconductor when processed into ultra-thin films of thickness lower than 1 nanometer (one-billionth of a meter). The calculations have no adjustable parameters and use ab-initio computations of the electronic and lattice structure of material. The key quantity which is predicted is the critical temperature at which the material turns from being a normal metal to being a superconductor, and is evaluated as a function of the film thickness.

Surprisingly, in this case, the critical temperature that can be reached by miniaturizing magnesium nano-sheets of about half nanometer thickness is as high as 10 Kelvin. This is an important consideration because it means that [liquid helium](#) can be used to cool the material down to achieve superconductivity instead of using much more expensive cooling technologies.

Indeed, the liquid helium cooling technology can be used down to 4.5 Kelvin, hence enabling the cooling of magnesium ultra-thin sheets to observe the predicted effect. This prediction, if confirmed experimentally, can radically transform the current technologies used for quantum electronics and [quantum information](#) and reduce their environmental impact.

This is evident if you consider that the most common material currently employed to make qubits (the fundamental unit of information, similar to a bit in classical computing, but can exist in a superposition of states, meaning it can represent 0, 1, or both simultaneously) is aluminum, which has a [critical temperature](#) of 1.6 Kelvin, hence below the liquid helium temperature.

If our prediction is confirmed, using magnesium instead of aluminum could lead to much more environmentally sustainable technologies for [quantum computing](#).

This story is part of [Science X Dialog](#), where researchers can report findings from their published research articles. [Visit this page](#) for information about Science X Dialog and how to participate.

More information: Giovanni Alberto Umbarino et al, Possible Superconductivity in Very Thin Magnesium Films, *Condensed Matter* (2025). DOI: [10.3390/condmat10010017](#)

Bio:

Alessio Zaccone received his Ph.D. from the Department of Chemistry of ETH Zurich in 2010. From 2010 till 2014 he was an Oppenheimer Research Fellow at the Cavendish Laboratory, University of Cambridge.

After being on the faculty of Technical University Munich (2014–2015) and of University of Cambridge (2015–2018), he has been a full professor and chair of theoretical physics in the Department of Physics at the University of Milano since 2022. Awards include the ETH Silver Medal, the 2020 Gauss Professorship of the Göttingen Academy of Sciences, the Fellowship of Queens' College Cambridge, and an ERC Consolidator grant ("Multimech").

Research contributions include the analytical solution to the jamming transition problem (Zaccone & Scossa-Romano PRB 2011), the analytical solution to the random close packing problem in 2d and 3d (Zaccone PRL 2022), the theory of thermally-activated reaction rate processes in shear flows (Zaccone et al PRE 2009), the theory of crystal nucleation under shear flow (Mura & Zaccone PRE 2016), the theoretical prediction of boson-like peaks in the vibrational spectra of crystals (Milkus & Zaccone PRB 2016; Baggioli & Zaccone PRL 2019), the theory of the glass transition in polymers (Zaccone & Terentjev PRL 2013), the theoretical and computational discovery of topological defects in glasses (Baggioli, Kriuchevskiy, Sirk, Zaccone PRL 2021), and the theoretical prediction of superconductivity enhancement effects due to phonon damping (Setty, Baggioli, Zaccone PRB 2020).

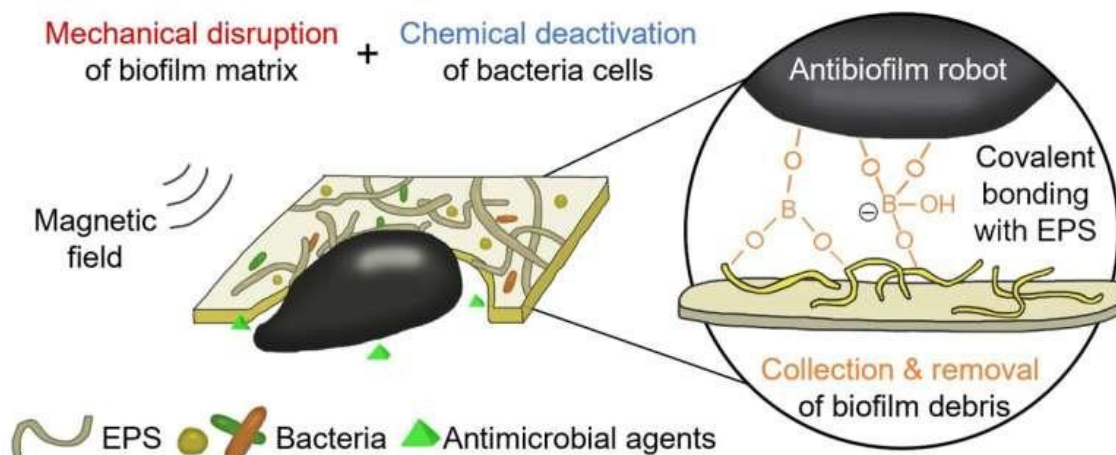
Research interests range from the statistical physics of disordered systems (random packings, jamming, glasses and the glass transition, colloids, nonequilibrium thermodynamics) to solid-state physics and superconductivity.

Journal information: [Condensed Matter](#)

APRIL 1, 2025

Liquid-bodied robot enables precise eradication of implant-related biofilm infections

by [The Chinese University of Hong Kong](#)



The research team has pioneered a triple synergistic antibiofilm system, including physical biofilm disruption, chemical bacteria deactivation, and biofilm debris removal to prevent

recurrent infections. Credit: Adapted from *Science Advances* (2025). DOI: 10.1126/sciadv.adt8213

An international research team led by the Chinese University of Hong Kong (CUHK) has achieved a breakthrough in the field of medical microrobots by developing the world's first antibiofilm liquid-bodied magnetic-controlled robot.

They have also introduced new features, including unique viscoelastic properties that allow the robot to adapt to diverse operational environments and a triple synergistic antibiofilm mechanism, paving the way for innovative solutions to combat [biofilm](#) infections. The research is [published](#) in *Science Advances*.

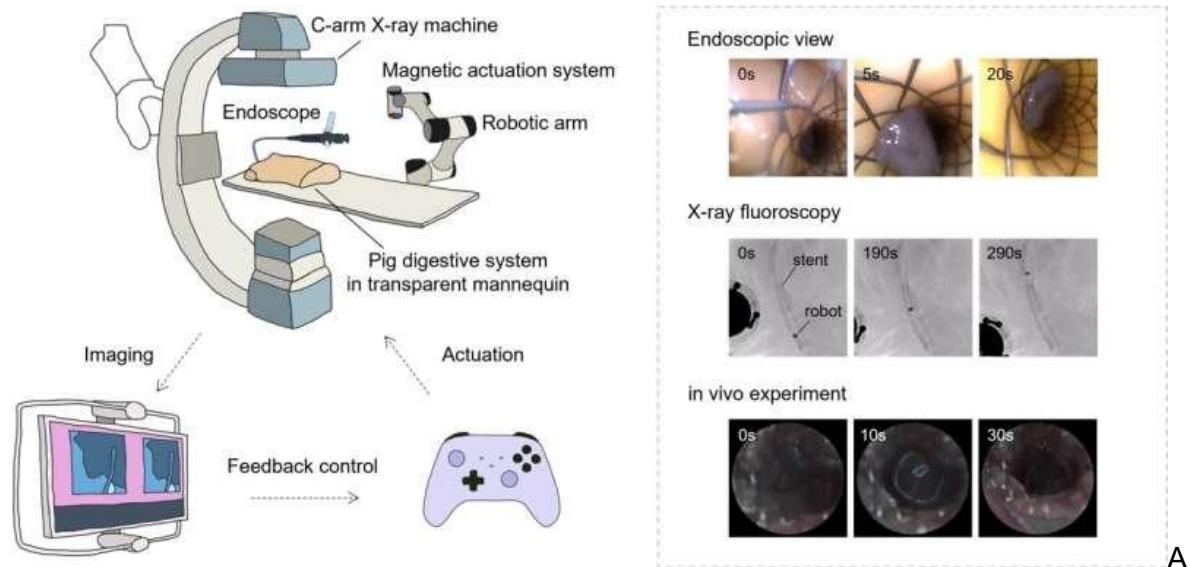
The team was led by Professor Zhang Li from the Department of Mechanical and Automation Engineering in CUHK's Faculty of Engineering—in partnership with Nanyang Technological University (Singapore) and the Max Planck Institute for Intelligent Systems (Germany).

The challenge of biofilm infections

The World Health Organization (WHO) declared [antimicrobial resistance](#) (AMR) as one of the top 10 global public health threats facing humanity in 2019, causing nearly 5 million deaths per year globally. AMR is not only related to the emergence of resistant bacterial strains but also significantly due to the formation of biofilm barriers, where bacteria adhere to surfaces and secrete substances.

Medical implants inside the human body that lack immune protection are highly susceptible to biofilm infections. Traditional antibiotic therapy struggles to penetrate biofilm barriers, while surgical removal of infected implants carries risks of secondary trauma.

The team previously developed magnetic microrobots to combat biofilm infections on implants. However, research revealed that while magnetically controlled hydrogel robots could navigate simple tubular structures, they struggled to adapt to complex surfaces such as medical stents and meshes, leaving residual biofilm. In light of these challenges, the team developed the world's first antibiofilm magnetic-controlled liquid-bodied robot.



micro-robotic surgical platform is utilized to control and navigate the liquid-bodied robot. Credit: Adapted from *Science Advances* (2025). DOI: 10.1126/sciadv.adt8213

Two new features for combating biofilm infections

The newly developed liquid-bodied robot uses a dynamic cross-linked magnetic hydrogel with unique viscoelasticity that aids in eliminating biofilms within the human body. Professor Zhang explained, "By precisely modulating external magnetic fields, the robot can switch between viscoelastic behavioral modes. In elastic mode, it rotates, rolls and overcomes obstacles within the body. In liquid mode, it deforms into a fluid robot to infiltrate crevices and eradicate any biofilm within them."

The robot also features a triple synergistic antibiofilm mechanism, including physical biofilm disruption, chemical bacteria deactivation and biofilm debris removal. First, magnetic forces transmitted through the robot's motion mechanically disrupt biofilm structures and weaken their protective effects; then, the antimicrobial agents released by the robot target planktonic bacteria cells; and finally, the robot forms bonds with biofilm fragments, which prevents infections from recurring.

The liquid-bodied robot performed exceptionally in tests on infected medical implants. Biofilm on a 3D-structured hernia mesh was reduced by 84% after treatment, while 87% of bacteria on a metal biliary stent were killed.

Professor Zhang added, "Our team pioneered dual-modality navigation using endoscopy and X-ray imaging, enabling precise control of the robot through metal stents in pig bile ducts. In a [mouse model](#) with infected stents, complete weight recovery was observed within 12 days, with a 40% reduction in inflammation indicators compared to the control group. Traditional miniature robots often compromise between accessibility and driving force. This technology achieves both."

The team is collaborating with Nanyang Technological University's Lee Kong Chian School of Medicine to develop upgraded antibiofilm robots, with plans to advance to large animal trials and prepare for human clinical studies.

Professor Joseph Sung from Lee Kong Chian School of Medicine, a co-author of the study, commented, "Biliary biofilm infections have long been a focus of my research. When solidified biofilm completely blocks a patient's bile duct, conventional therapies often fail. This liquid robot offers a novel solution. We aim to integrate next-generation antimicrobial agents and validate its efficacy in clinical settings."

More information: Bonan Sun et al, Liquid-bodied antibiofilm robot with switchable viscoelastic response for biofilm eradication on complex surface topographies, *Science Advances* (2025). DOI: [10.1126/sciadv.adt8213](https://doi.org/10.1126/sciadv.adt8213)

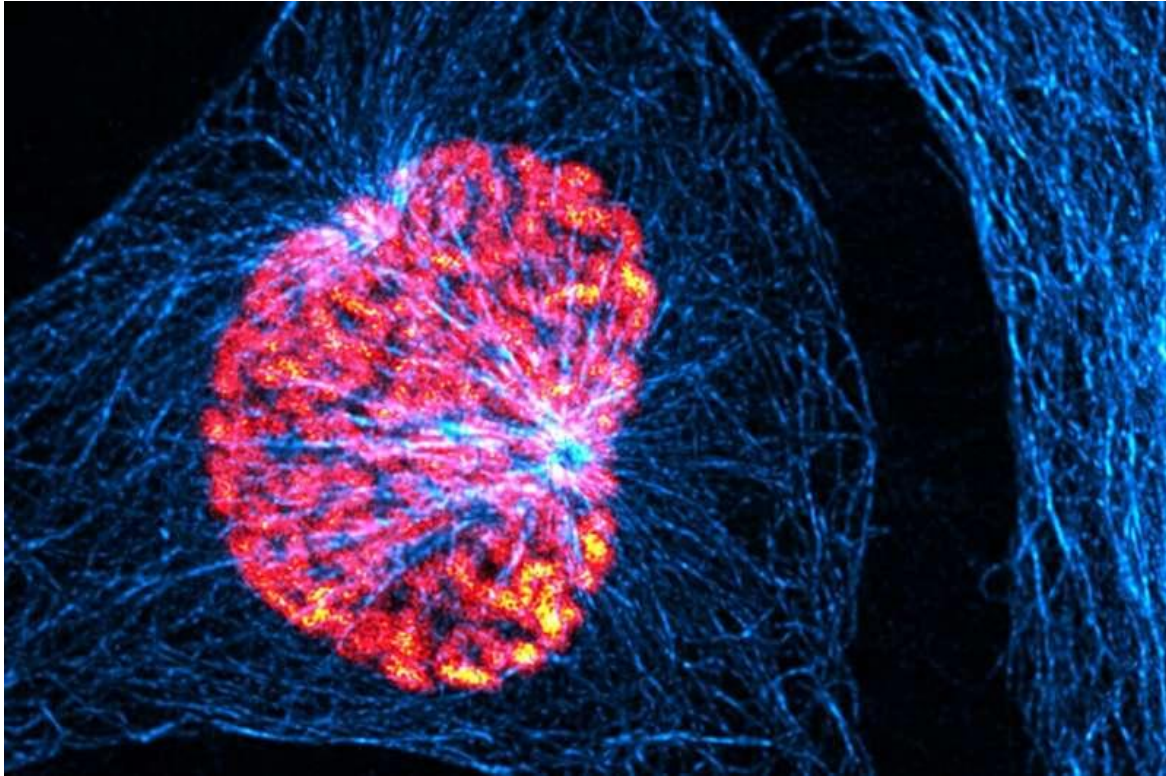
Journal information: [Science Advances](#)

Provided by [The Chinese University of Hong Kong](#)

APRIL 1, 2025

A starting signal for cell division: Molecular switch ensures that cells divide at the right time

by Carmen Rotte, [Max Planck Society](#)



A cultured human cell (HeLa cell) in prophase. Chromosomes are shown in shades of red, microtubules are marked in blue. 3D image taken with a confocal microscope. Credit: Monica Gobran, Max Planck Institute for Multidisciplinary Sciences

About 100 cells divide every second in our body. A key protein in cell division is a protein kinase termed Plk1, because it activates other proteins involved in this process. Plk1 is also overexpressed in many types of cancer. This makes it a promising target for cancer therapies. However, drugs that inhibit Plk1 have often proven ineffective.

New findings by researchers led by Peter Lenart and Monica Gobran [published](#) in *The EMBO Journal* may help to improve therapeutic approaches. They discovered a previously unknown function of Plk1: It regulates the timely onset of [cell division](#). When the protein is inhibited, cells start dividing many hours later.

Cell division allows a single fertilized egg to develop into a living being, our skin to renew itself, and wounds to heal. Before each cell division, termed mitosis, the genetic information must first be duplicated. This ensures that each chromosome in the cell that is ready to divide receives two copies of genetic information.

Once started, cell division normally proceeds through all the stages until two genetically identical daughter cells are formed. During this process, the chromosomes are connected to the poles of the cell with the help of molecular "pulling ropes"—called the spindle apparatus—aligned next to each other, and finally pulled to the opposite cell poles.

The cell is then divided between the spatially separated sets of chromosomes. Erroneous or uncontrolled cell division can have serious consequences, leading to diseases such as cancer.

Plk1 plays a key role in this regulatory process. It activates other proteins involved in cell division by adding a molecular tag, a phosphate group. However, its exact function in the early phase of cell division has been controversial in research.

"Previous studies suggested that Plk1 is essential for cells to start dividing at all," says Lenart, who heads the research group Cytoskeletal Dynamics in Oocytes at the Max Planck Institute (MPI) for Multidisciplinary Sciences in Göttingen (Germany).

Right timing of cell division

His group has now discovered that Plk1 is not essential for the start of cell division. "Rather, it acts as a molecular switch to ensure that cells start dividing at the right time. Plk1 is crucial for the correct timing," the cell biologist reports.

When the researchers inhibited Plk1 in living cells, the cells remained in the prophase of mitosis for up to 10 hours—this normally only takes about 15 minutes. In this phase, the cell prepares for cell division by compacting, or "condensing," the chromosomes.

"A key moment in the laboratory was when, after many hours, we suddenly observed the chromosomes condensing and the cell continuing its division cycle," says Gobran, first author of the study.

A new microscopy assay developed by Gobran made this discovery possible. The Ph.D. student succeeded in imaging hundreds of individual live cells condensing their chromosomes over a period of more than 24 hours during the cell division cycle.

Cells divide differently

The experiments also revealed another finding: Cells divide very individually, even if they belong to the same cell type. "Some cells lag behind in the cell cycle, while others do not even begin to divide." Individual cells also responded very differently to the inhibited protein, as Lenart adds, "It has been overlooked so far that cell division starts even without Plk1, just later than normal."

With the help of their colleague Antonio Politi, the researchers were able to reproduce the variable behavior of the cells using mathematical modeling and thus explain how Plk1 acts as a catalyst for the start of cell division.

Prophase can be studied in detail for the first time

In collaboration with the institute's experts in [mass spectrometry](#) as well as [data analysis](#) and biostatistics, Henning Urlaub and Juliane Liepe, the team also succeeded in identifying which proteins in the early prophase are labeled with a phosphate group.

"With this methodological approach, we now have a technique that allows us to stop cells in prophase before cell division begins. This phase is normally very short and has been difficult to study at the cellular and biochemical level," Lenart notes.

New approaches for cancer therapy

The researchers' findings could provide a new approach for future cancer therapies. "In combination with other compounds that prevent mitosis, Plk1 inhibitors could have a greater therapeutic benefit," says the research group leader.

A next goal of the research group is to understand the role of Plk1 in the specialized division of egg cells, called meiosis. Human egg cells, for example, spend decades in the prophase state.

More information: Monica Gobran et al, PLK1 inhibition delays mitotic entry revealing changes to the phosphoproteome of mammalian cells early in division, *The EMBO Journal* (2025). DOI: [10.1038/s44318-025-00400-9](https://doi.org/10.1038/s44318-025-00400-9)

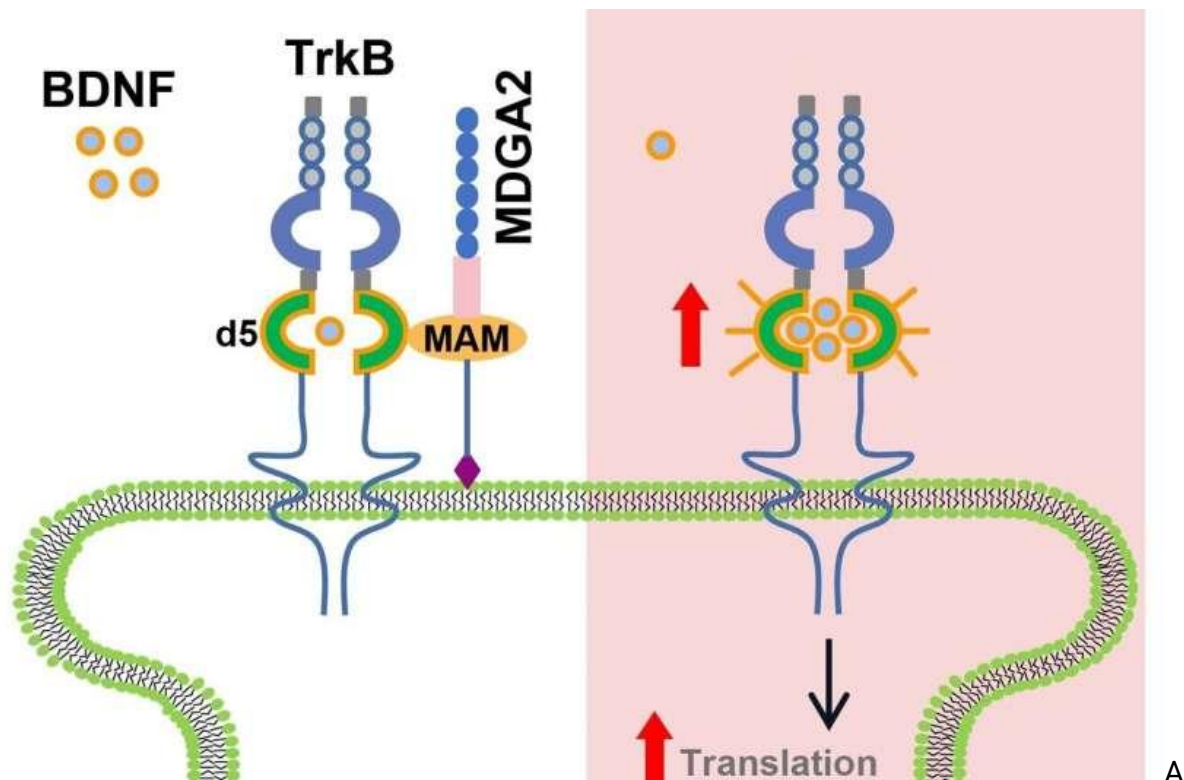
Journal information: [EMBO Journal](#)

Provided by [Max Planck Society](#)

APRIL 1, 2025

Balance between two competing nerve proteins deters symptoms of autism in mice, study finds

by [Public Library of Science](#)



scheme showing the mechanism underlying MDGA2-mediated BDNF/TrkB signaling pathway. Credit: Zhao D et al., 2025, *PLoS Biology*, CC-BY 4.0

(creativecommons.org/licenses/by/4.0/)

In mice, autism symptoms arise when a certain pair of competing nerve proteins falls out of equilibrium, according to a study published in the open-access journal *PLoS Biology* by Dongdong Zhao of Wenzhou Medical University, China, Yun-wu Zhang of Xiamen University, China, and colleagues.

Approximately 1% of the world's population is considered to have Autism Spectrum Disorder (ASD), exhibiting a series of social and cognitive symptoms. Previous research has linked certain [genetic factors](#) to ASD, including many associated with neuron activity, but it remains unclear exactly how these factors are related.

In this study, Zhao, Zhang and colleagues used [mice](#) to examine the activity of two neuronal proteins suspected to be linked to ASD.

MDGA2 is a protein involved in the transmission of nerve signals, and certain mutations in the MDGA2 gene have been identified in ASD patients. Experimental trials revealed that mice with reduced levels of MDGA2 exhibited ASD-like symptoms, including repetitive grooming and altered [social behavior](#).

These mice also exhibited increased activity in certain nerve synapses and increased levels of BDNF, another neuronal protein that has been linked to ASD and functions through binding and activating the TrkB protein. When these mice were treated with an artificial peptide that mimicked MDGA2 and inhibited BDNF/TrkB activity, the symptoms lessened.

Based on these results combined with previous research, the authors suggest that MDGA2 and BDNF maintain a natural balance by competing with each other for TrkB protein binding sites, and disruption to this system can lead to regulatory changes in [neuron activity](#) related to ASD.

This protein system might be a promising target for future therapeutic treatments, but further investigation will be required into the exact functions of this system and its relationship to ASD symptoms.

Yun-wu Zhang adds, "Mutations in the MDGA2 gene causes autism spectrum disorders (ASD) but the underlying mechanism is elusive. Our study reveals a novel role of MDGA2 in keeping the BDNF/TrkB signaling at bay for normal excitatory neuronal activity, and demonstrates that MDGA2 deficiency results in aberrant BDNF/TrkB activation and elevated excitatory neuronal activity, leading to ASD-like phenotypes in mice."

More information: Zhao D, et al. Mdga2 deficiency leads to an aberrant activation of BDNF/TrkB signaling that underlies autism-relevant synaptic and behavioral changes in mice. *PLOS Biology* (2025). DOI: [10.1371/journal.pbio.3003047](https://doi.org/10.1371/journal.pbio.3003047)

Journal information: [PLOS Biology](#)

Provided by [Public Library of Science](#)

APRIL 3, 2025

Stem cell barcoding reveals how the brain and inner ear are formed

by [Karolinska Institutet](#)

Researchers at Karolinska Institutet have developed a method that shows how the nervous system and sensory organs are formed in an embryo. By labeling stem cells with a genetic "barcode," they have been able to follow the cells' developmental journey and discover how the inner ear is formed in mice.

The discovery, [published](#) in *Science*, could provide important insights for future treatment of hearing loss.

"Our study shows how different cell types arise from stem cells in the embryo and how they are organized to create important structures in the brain," explains Emma Andersson, docent at the Department of Cell and Molecular Biology, Karolinska Institutet, Sweden. "You could say that we have created a family tree for the cells of the nervous system and the inner ear."

Replacing damaged cells

The researchers used a technique where they injected a virus into mouse stem cells at an early stage of development. The virus contained a genetic 'barcode' that was integrated into the DNA of the stem cells and then inherited as the cells divided. By following this code, the researchers could track how the cells developed into different types of neurons and cells in the inner ear.

The results showed that cells in the inner ear, which are crucial for hearing, develop from two main types of [stem cells](#). This knowledge could lead to new treatments for hearing loss.

"Tracing the origin and development of cells gives us a unique opportunity to understand the basic mechanisms behind [hearing](#) loss," says Andersson. "It can help us find new ways to repair or replace damaged cells in the inner ear."

Exploring the nervous system

The team now plans to use the method to study other parts of the nervous system, but also how the rest of the body develops. They hope their work will lead to new insights and treatments for various genetic and developmental diseases.

"We are only at the beginning of understanding the complex processes behind nervous system development," says Andersson.

"Our method opens up many exciting opportunities to explore how the nervous system and the rest of the body are formed during embryonic [development](#). In addition, the technique can reduce the number of mice used in research."

She led the study with Jingyan He, a postdoctoral fellow, and Sandra de Haan, a former Ph.D. student in Andersson's research group.

More information: Sandra De Haan et al, Ectoderm barcoding reveals neural and cochlear compartmentalization, *Science* (2025). DOI:

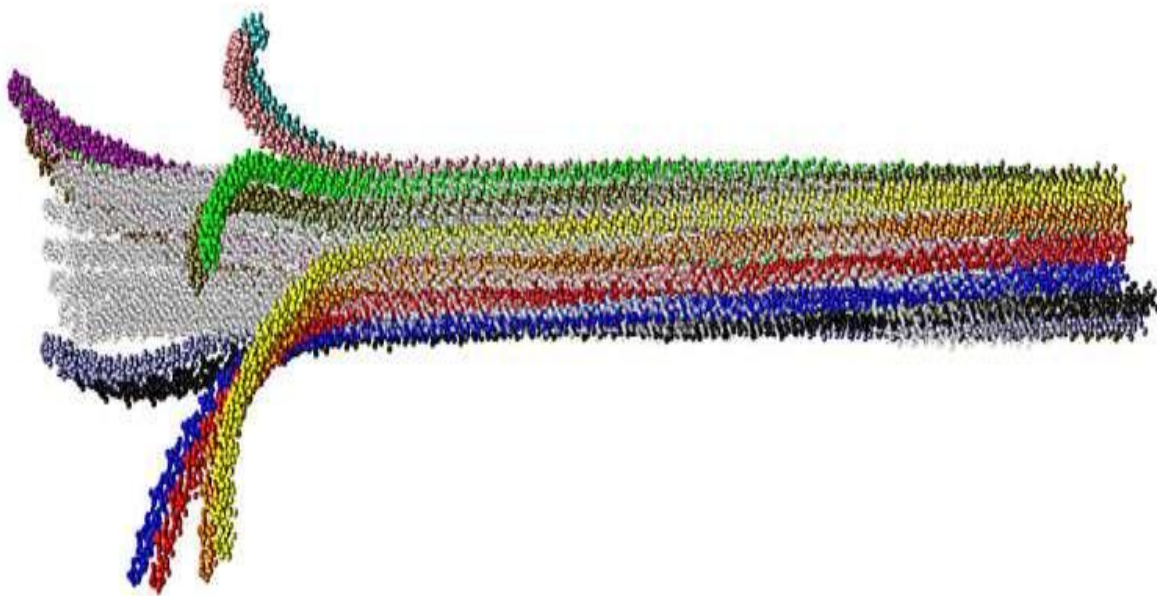
[10.1126/science.adq9248](https://doi.org/10.1126/science.adq9248). www.science.org/doi/10.1126/science.adq9248

Journal information: [Science](#)

Provided by [Karolinska Institutet](#)

Supercomputer models microtubule dynamics, offering new insights into neurodegenerative diseases

by Jorge Salazar, [University of Texas at Austin](#)



An image of a large segment of a microtubule with a peeling tip. The colors highlight the different protofilaments that make up the tubule. The protofilaments are long biopolymers consisting of the tubulin protein that binds GTP and chemically hydrolyzes it to GDP. Shown in a microtubule tip region consisting of about 1200 tubulin proteins. The simulations by the team discovered that the protofilaments of the peeling tips tend to cluster differently whether

the tubulin is in the GTP or GDP state, an important feature of their behavior in cells, e.g., to regulate force generation by the microtubules on key regions of the cell such as its nucleus.

Credit: Gregory Voth, University of Chicago

Each day, a human adult loses on average 50 to 70 billion cells, which die from natural causes alone. New cells replace lost ones by the complex process of cell division, which relies on what scientists call molecular machines to transport chemical cargo to where it is needed for reactions that keep us alive.

Long polymers called microtubules (MT) play a key role in [cell division](#) and chemical transport, paving the way for [molecular machines](#) and pushing the nucleus apart to split it. Microtubules are dynamic structural polymers composed of protein building blocks called tubulin that add and lose fragments at their ends.

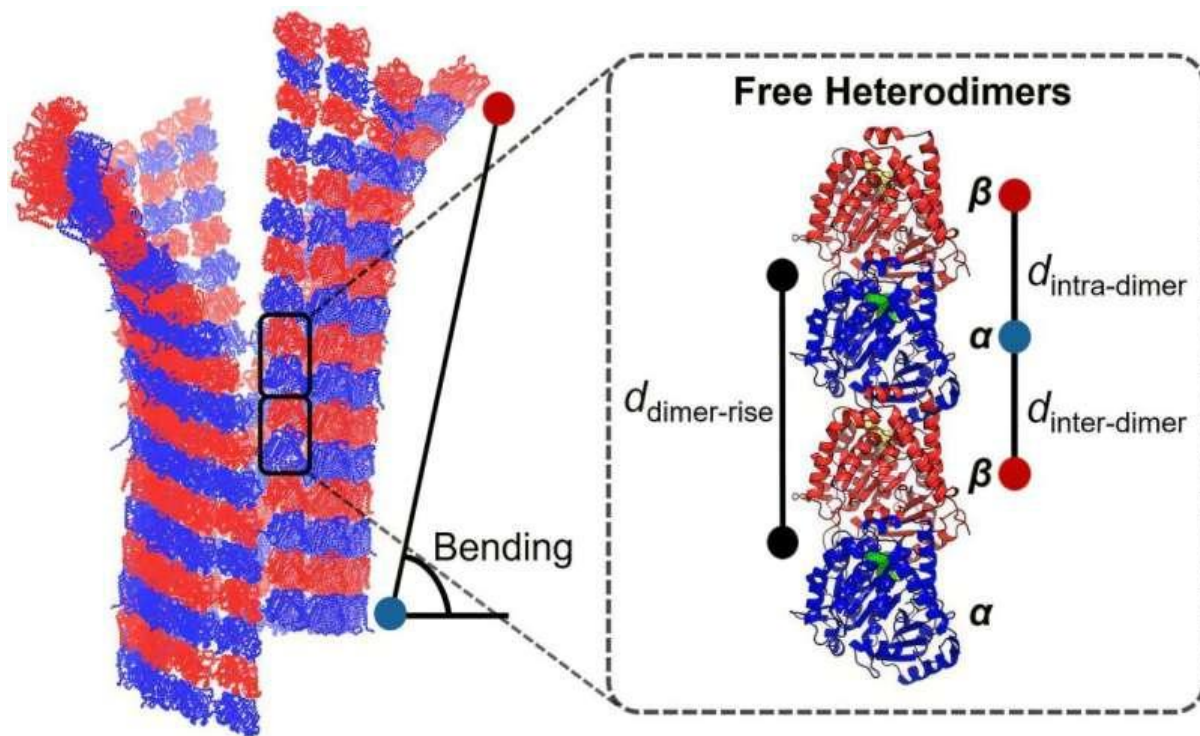
Supercomputer simulations by University of Chicago and University of Utah scientists have revealed new behavior happening at [microtubule](#) tips, the location where they grow or shrink. This basic research in microtubule stability could help lead to a better understanding of neurodegenerative diseases such as Alzheimer's and Parkinson's as well as aid in design of cancer drugs.

"One of the huge mysteries of the microtubule is what goes on at their tips," said Gregory Voth, the Haig P. Papazian Distinguished Service Professor of Chemistry at the University of Chicago.

Voth co-authored [research](#) published in the *Biophysical Journal* (January 2025) that investigated the chemical conversion through hydrolysis of the nucleoside Guanosine-5'-triphosphate (GTP) into Guanosine diphosphate (GDP) happening at microtubule tips. This conversion of GTP to GDP at microtubule tips speeds up both their polymerization and depolymerization, collectively known as MT "dynamic instability," which facilitates its growth or breakdown.

"It used to be thought that the tips would splay out, like a ram's horn, only after the microtubule chemically changed GTP into GDP," Voth explained. "But that's not true now. This really changes the picture. The tips are always more or less splayed out. The challenging question is whether there was a difference in splaying with GTP or GDP at the MT tip, and the [supercomputer simulations](#) were able to help reveal that."

What's more, Voth and colleagues were able to achieve a two-fold computational speedup in their simulations. This feat generated all-atom molecular dynamics data and fed that to a machine learning method that could carry the simulation all the way through to the relaxed state of the MT tip, 5.875 microseconds of evolution on a system of 21 to 38 million atoms. Their results revealed key but subtle differences in the structures of MT tips depending on whether they are bound with GTP or GDP.



Supercomputer simulations revealed new behavior happening at the tips of microtubules, dynamic structural polymers composed of building blocks called tubulin, that assemble into polymer 'protofilaments', that in turn assemble into the microtubule. Slightly splayed MT tip structure simulated illustrating (a) A 14 protofilaments (PFs) $\times$ 8 heterodimers MT tip, with α -tubulin and β -tubulin backbone traces colored in blue and red, respectively. Dashed box shows GDP (green) and GTP (yellow) nucleotides bound to α - and β -tubulin monomers. Credit: DOI: 10.1016/j.ijhcs.2025.103460

Voth reported using 56 million Frontera central processing unit (CPU) core hours to generate four microseconds of all-atom molecular dynamics (AA MD) simulations, an unprecedented length of trajectory for such a large system.

The team's "equation-free" multi-scale simulation method incorporated machine learning to extend the simulation to 5.875 microseconds, saving 15 million CPU hours over AA MD alone and accessing dynamical behavior that cannot at present be readily seen in the AA MD alone.

"Without Frontera, we could not have done it," Voth said. "The big data from Frontera feeds the machine learning algorithm that extends its range beyond what the AA MD can do. They work synergistically together to achieve scales."

Voth contrasts these MT tips methods with [prior work](#) completed on Frontera on HIV-1 capsid modeling that employed coarse-grain model methods to show how the deadly virus enters the cell nucleus. Coarse-grain models simplify the resolution scale, and if done well they retain all the key physics of intractable computer simulations.

Like the coarse-grain work done with HIV-1, Voth's team used state-of-the-art images of microtubules from cryo-electron tomography as snapshots that elucidated critical structural differences and [conformational changes](#) between GDP- and GTP-bound microtubules.

"Supercomputers provide the necessary and accurate data for utilizing machine learning to discover new behavior of critically important collections of proteins in your cells," Voth said. "It's a beautiful story. Starting from the fundamental 'big iron' Frontera simulation and then going up in scale. And in the end, we discovered new behavior pertinent to living cells."

The study authors are Jiangbo Wu, Siva Dasetty, Daniel Beckett, Yihang Wang, Weizhi Xue, Andrew L. Ferguson, and Gregory A. Voth of the University of Chicago; and Tomasz Skora, Tamara C. Bidone of the University of Utah.

More information: Jiangbo Wu et al, Data-driven equation-free dynamics applied to many-protein complexes: The microtubule tip relaxation, *Biophysical Journal* (2025). DOI: [10.1016/j.bpj.2025.01.009](https://doi.org/10.1016/j.bpj.2025.01.009)

Journal information: [Biophysical Journal](#)
Provided by [University of Texas at Austin](#)

APRIL 3, 2025

Scientists develop a way to scale up spatial genomics and lower costs

by Alessandra DiCorato, [Broad Institute of MIT and Harvard](#)



Spatial map of cell types in a mouse embryo. Each colored dot represents a different cell type. Credit: Chenlei Hu, Chen lab

Spatial transcriptomics technologies opened the door for new kinds of biological measurements, allowing scientists to generate detailed maps of where genes are expressed in tissue. But most methods rely on expensive and time-intensive imaging that requires specialized equipment.

A new method developed by researchers at the Broad Institute promises to make spatial transcriptomics easier for scientists to use. The approach eliminates the need for imaging and instead uses [computational methods](#) to reconstruct the spatial locations of gene expression.

The team showed that by using their method, they could map larger sections of tissue more quickly and cheaply than with previous methods. They add that, more importantly, the new approach requires no specialized equipment and can be used by more researchers around the world. The [work](#) appears in *Nature Biotechnology*.

"Our work converts imaging into [molecular biology](#)—just a reaction in a [test tube](#)," said Fei Chen, who is a senior author on the study, a core institute member at the Broad, and an

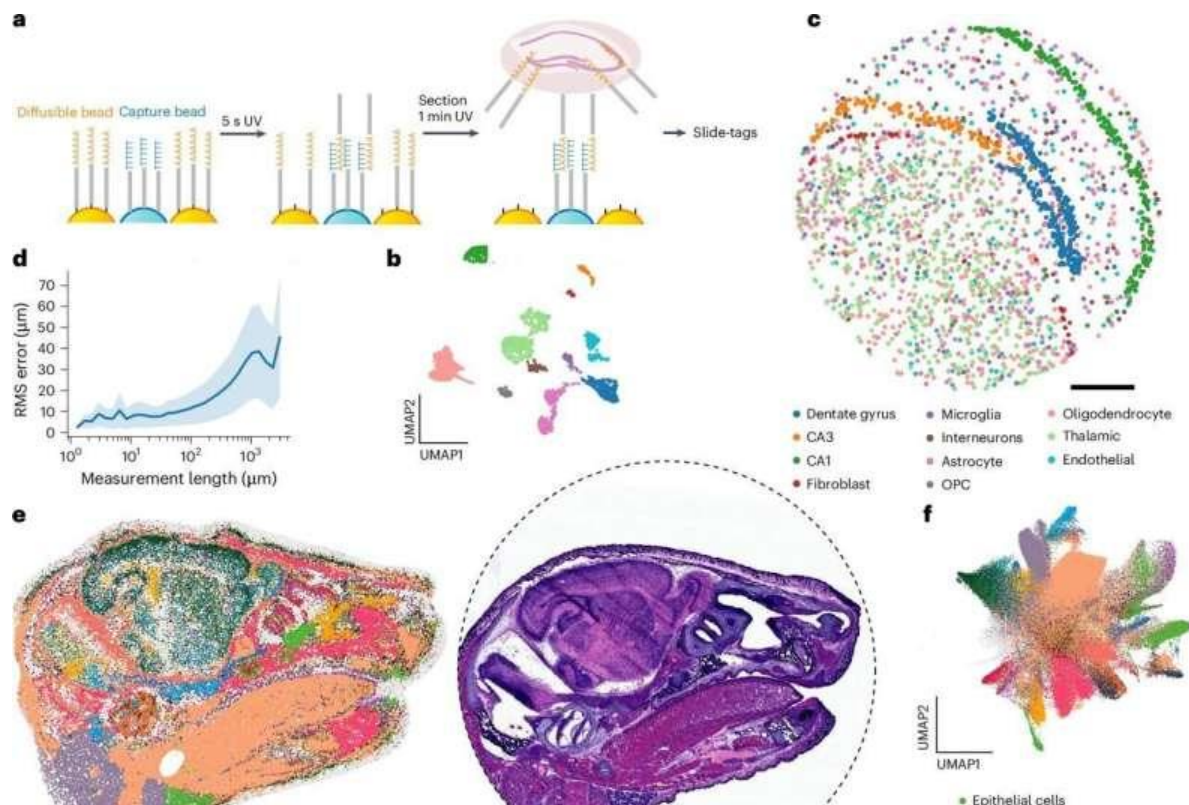
assistant professor in the Department of Stem Cell and Regenerative Biology at Harvard University. "That means anybody can use this approach if they have the algorithm and some common materials."

"When biologists think about spatial locations, they might think they need to look at samples with [light microscopy](#) or [electron microscopy](#)," added Chenlei Hu. Hu is the first author on the work and a Harvard graduate student in Chen's lab. "But we've found that we can computationally infer physical locations instead."

UMAP epochs during reconstruction of P1 Mouse Embryo. Credit: *Nature Biotechnology* (2025). DOI: 10.1038/s41587-025-02612-0

Mapping with beads

The new findings build on a technique called Slide-seq, which was developed by Chen, Broad core institute member Evan Macosko, and colleagues in 2019. The method generates high-resolution maps of gene expression across tissue. Researchers first collect images of an array of DNA-barcoded [beads](#) on a slide, creating a reference that tells the location of each bead. Next, they place a tissue section on the beads and dissolve it, leaving messenger RNA from the tissue bound to the barcoded beads. They then load the beads into a sequencer and use specialized software to create a map of gene expression across the tissue. In the past, Chen's lab made the arrays and imaged them for other scientists. Their microscope was under near-constant use. But lingering in their minds was the possibility that they could infer the location of each bead with sequencing alone, eliminating the need for imaging.



Reconstruction enables diverse spatial transcriptomics measurements at scale.

Credit: *Nature Biotechnology* (2025). DOI: 10.1038/s41587-025-02612-0

They thought that if you knew the distance between every pair of beads on the array, you could reconstruct their spatial positions—in the same way you can locate a cell phone by knowing its distance from satellites.

When she joined Chen's lab, Hu thought it might be possible to pinpoint the location of the beads by measuring how much molecules diffuse between them. She and her colleagues built a new kind of bead array containing both "transmitter" and "receiver" beads, each with DNA barcodes.

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When exposed to UV light, the barcodes cleave from the transmitter beads, diffuse away, and are captured by the receiver beads. Receiver beads that are closer to transmitters will capture more DNA barcodes as they diffuse from the transmitters.

Slide-seq's sequencing step can measure the level of these captured barcodes, providing information not only about gene expression, but also the location of the beads. Hu then used an algorithm commonly used in single-cell analysis called Uniform Manifold Approximation and Projection (UMAP) to reconstruct the beads' original locations on the slide.

When the researchers used their method and the image-based Slide-seq to analyze the same sample, they found very little difference. Without the time-intensive imaging step, Chen's team was able to map gene expression across larger sections of tissue than before: areas up to 1.2 centimeters wide of mouse embryo [tissue](#) (previous maps covered only about 3 millimeters). The Chen group is now working with the Macosko lab to map areas as large as 7 centimeters, close to the size of entire organs in people.

"We're no longer limited by how long it takes us to image something," Chen said.

"Eventually we'd like to analyze the whole human brain. That just wasn't possible with other technologies."

More information: Hu, C. et al, Scalable spatial transcriptomics through computational array reconstruction, *Nature Biotechnology* (2025). DOI: [10.1038/s41587-025-02612-0](https://doi.org/10.1038/s41587-025-02612-0). www.nature.com/articles/s41587-025-02612-0

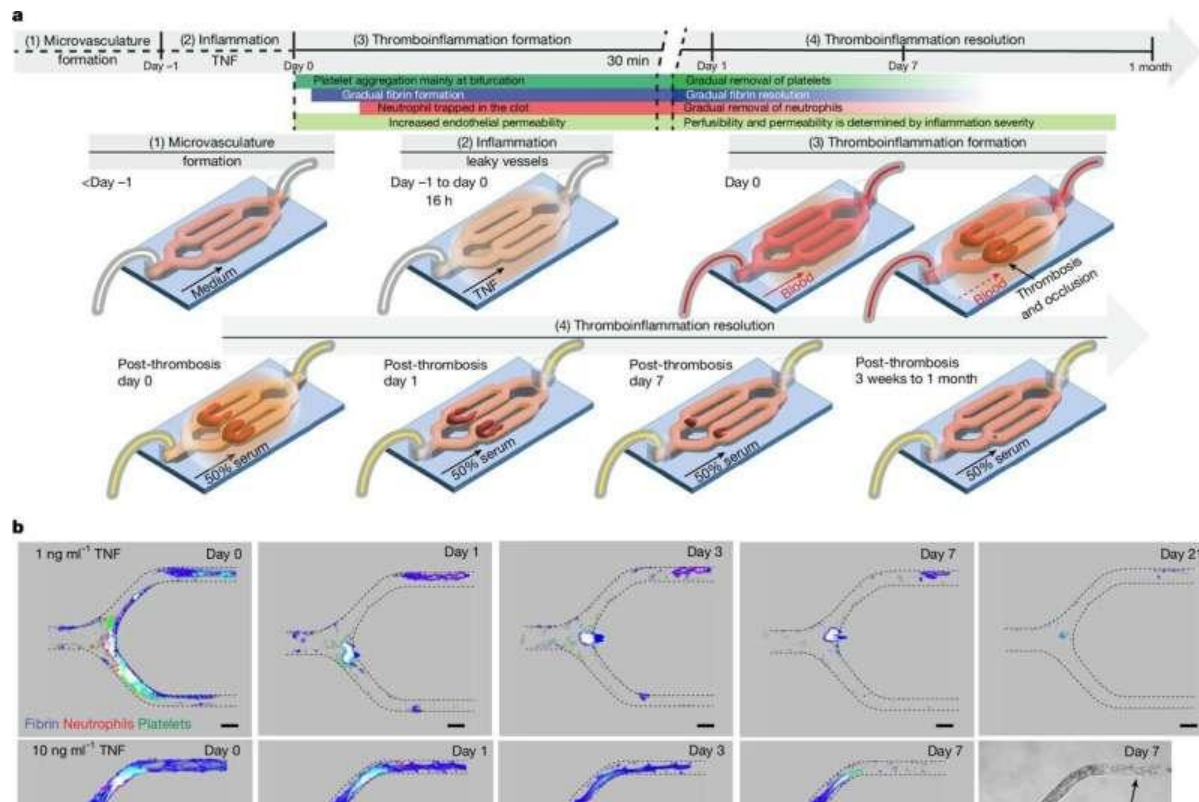
Journal information: [Nature Biotechnology](#)

Provided by [Broad Institute of MIT and Harvard](#)

APRIL 3, 2025

Blood clots on a chip: New model could improve thromboinflammation treatment

by [Emory University](#)



The hydrogel-based thromboinflammation-on-a-chip model enables monitoring of thromboinflammation formation and its resolution over long timescales.

Credit: *Nature* (2025). DOI: 10.1038/s41586-025-08804-7

Blood clots are associated with life-threatening conditions such as sepsis, sickle cell disease, heart attack, and stroke.

However, new research from Emory University may revolutionize how clinicians understand and treat these harmful blood clots, or thrombi, a byproduct of a condition called thromboinflammation. In a study [published](#) in *Nature*, researchers have discovered the potential to provide life-saving medications to patients with blood clots at the right time, with the right dose, in novel combinations, based on a new model.

To gain these insights, researchers developed a thromboinflammation-on-a-chip model that can sustain the clots for several months in a more accurate, human-like manner, leveraging 3D microvessels on a chip. This novel model allows the thrombi to exist in human blood and veins for months and resolve as they would naturally in a real patient.

Researchers are then able to track the blood clot and measure the effectiveness of various treatment options. This model differs from existing models, which can only sustain blood clots for short periods. Additionally, this new model includes the real cells necessary for clot resolution, whereas other lab models do not.

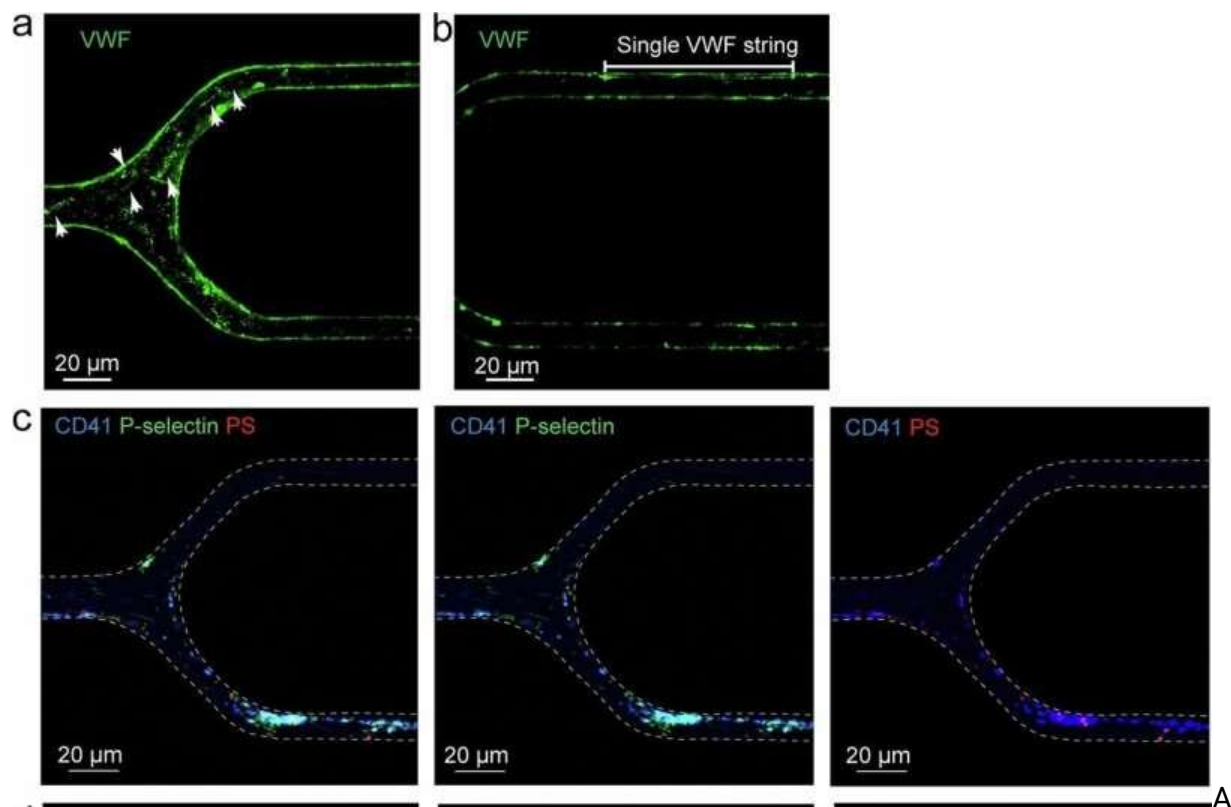
Wilbur Lam, corresponding author of the study, professor at Emory University and clinician at Children's Healthcare of Atlanta, explains that little is known about how blood clots are resolved in real life after one survives a stroke or [heart attack](#), but replicating the process on a chip can reveal critical information in the application or development of new treatments.

Thromboinflammation forms in the thromboinflammation-on-a-chip model-A. A representative video showing all imaging channels (bright field; green, platelets; red, neutrophils; blue, fibrin), capturing a 30 min perfusion of healthy whole blood into the microvasculature pre-exposed to 10 ng ml⁻¹ TNF for 16 h. Credit: *Nature* (2025). DOI: 10.1038/s41586-025-08804-7

"Because we created this system where we observe a blood clot on a chip over long periods of time, such as days to weeks, we can map out its entire resolution process, and that has never been done before," says Lam, MD, Ph.D. "This is significant because animal models are challenging. While extremely difficult to closely observe a clot in a specific part of a mouse for weeks, we can now do it on a chip and are able to monitor it closely."

Yongzhi Qiu, a corresponding author of the study, also emphasized the importance of the model's life-like accuracy. "Our practical measure is so unique because it is hard to study thrombi in clinical settings due to the low spatial resolution of existing tools, so it's harder to clearly see how these clots resolve," says Qiu, Ph.D. and assistant professor in the Department of Pediatrics at Emory University School of Medicine.

For this study, Qiu also developed the hydrogel for this model using human blood in a human vein, making it the only model to integrate 3D microvessels that can be stressed and monitored under physiologically relevant conditions.



16-hour exposure to TNF induces vWF release by the endothelium, facilitating platelet aggregation in the thromboinflammation-on-a-chip model. Credit: *Nature* (2025). DOI: 10.1038/s41586-025-08804-7

Charting the future of blood clotting treatment

In addition to stroke or [cardiac arrest](#), it's noteworthy that hypertension, diabetes, severe trauma, burns, and other infections are also factors in developing thromboinflammation, leaving much of the nation at risk.

Since this [model](#) opens the door to understanding how [blood clots](#) naturally resolve, researchers can now further study the timing, dosage, and impact of existing medical interventions, as well as possible new combinations. One such discovery from this study is the vital role of neutrophils, which both resolve thrombi and create inflammation—a double-edged sword, according to Lam.

Additionally, this study reveals that the treatment used after a stroke, tPA, or Tissue Plasminogen Activator, also directly repairs any vasculature which was previously unknown.

The study also suggests that combining existing mediations may protect the endothelial function, or the opening and closing of arteries, in patients with [sickle cell disease](#). Finally, this study notes that those experiencing bone marrow transplantation may benefit from certain drug combinations to protect against veno-occlusive disease, a condition resulting from high doses of chemotherapy that can cause liver damage by blocking small veins in the liver.

"One of the biggest things about being able to create thrombi under inflammatory conditions is that we are now able to map it out over time and develop hypotheses about which drugs would be most helpful, in which context, and importantly, when," says Lam, making the study the cornerstone of future research and clinical trials in the quest to save lives.

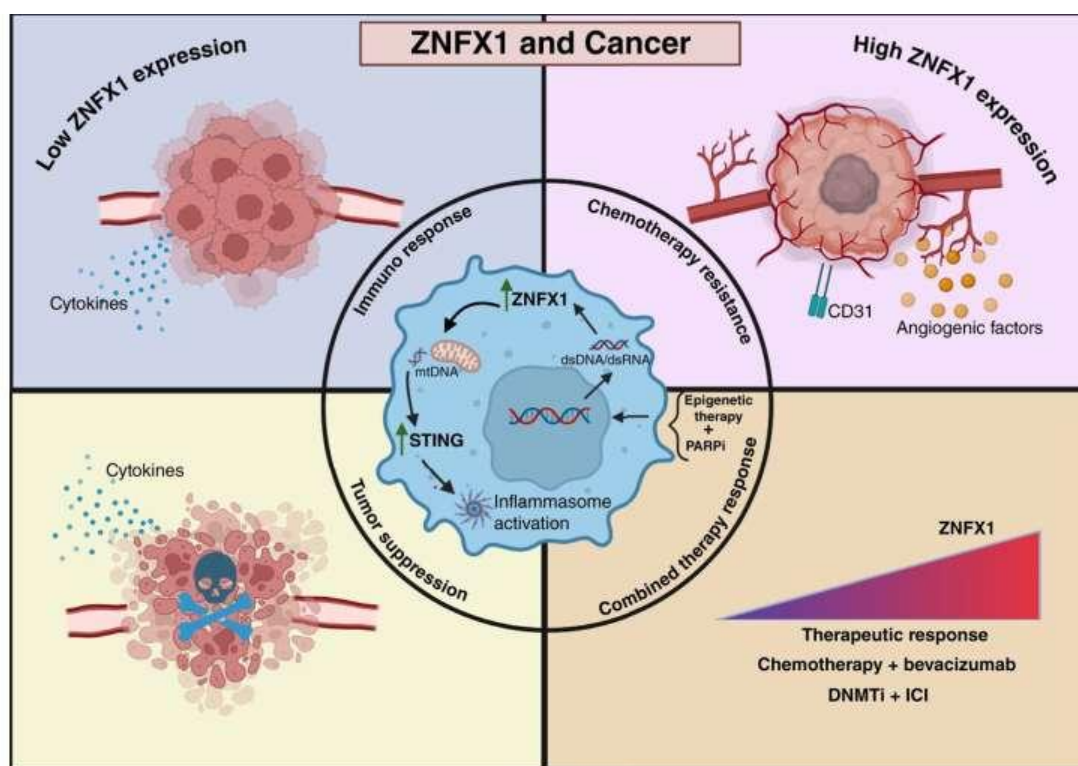
More information: Wilbur Lam, Clinically relevant clot resolution via a thromboinflammation-on-a-chip, *Nature* (2025). DOI: [10.1038/s41586-025-08804-7](https://doi.org/10.1038/s41586-025-08804-7). www.nature.com/articles/s41586-025-08804-7

Journal information: *Nature*
Provided by [Emory University](#)

APRIL 3, 2025

'Master regulator' gene could lead to more effective treatment for patients with ovarian cancer

by [University of Maryland School of Medicine](#)



Created in BioRender. Stojanovic, L. (2025) <https://BioRender.com/t85w514>

Graphical Abstract. Credit: *Cancer Research* (2025). DOI: [10.1158/0008-5472.CAN-24-1286](https://doi.org/10.1158/0008-5472.CAN-24-1286)
In a study co-led by the University of Maryland School of Medicine (UMSOM), researchers have identified a "master regulator" gene, ZNFX1, that may act as a biomarker to help guide

treatment in future clinical trials involving patients with therapy-resistant ovarian cancer, according to a study recently [published](#) in *Cancer Research*.

A group of researchers from several institutions, including the University of Maryland School of Medicine (UMSOM), Indiana University School of Medicine-Bloomington, and the Johns Hopkins University School of Medicine, looked at patient ovarian cancer databases and found that high levels of ZNFX1 correlate with how patients with advanced stage disease will respond to certain therapies, making it a potential predictor of therapy responses.

ZNFX1 also correlated with an increase in overall survival in a previously conducted phase three clinical trial where patients received the cancer drug bevacizumab in combination with chemotherapy. In addition, the study showed that two cancer drugs, DNA methyltransferase inhibitors (DNMTi) and PARP inhibitors, increase the expression of ZNFX1 and serve as a gateway to tumor suppressing inflammatory responses in [cancer cells](#).

"ZNFX1 may serve as a biomarker to facilitate more personalized therapy in ovarian cancer patients," said senior author, Feyruz V. Rassool, Ph.D., professor of radiation oncology at UMSOM and co-director of the experimental therapeutics program at the University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center (UMGCCC).

"Our findings build upon our previous research into DNMTi and PARP inhibitors to find potential uses for these drugs in treating different forms of cancer."

Taofeek K. Owonikoko, MD, Ph.D., UMGCCC's Executive Director and the Marlene and Stewart Greenebaum Distinguished Professor of Oncology at UMSOM, said, "The identification of ZNFX1 as a potential biomarker in ovarian cancer treatment offers a path forward for further research in a clinical setting. UMGCCC is committed to advancing new therapies and bringing forward [scientific discoveries](#) that have the potential to improve outcomes for patients."

More information: Lora Stojanovic et al, ZNFX1 Functions as a Master Regulator of Epigenetically Induced Pathogen Mimicry and Inflammasome Signaling in Cancer, *Cancer Research* (2025). DOI: [10.1158/0008-5472.CAN-24-1286](https://doi.org/10.1158/0008-5472.CAN-24-1286)

Journal information: [Cancer Research](#)

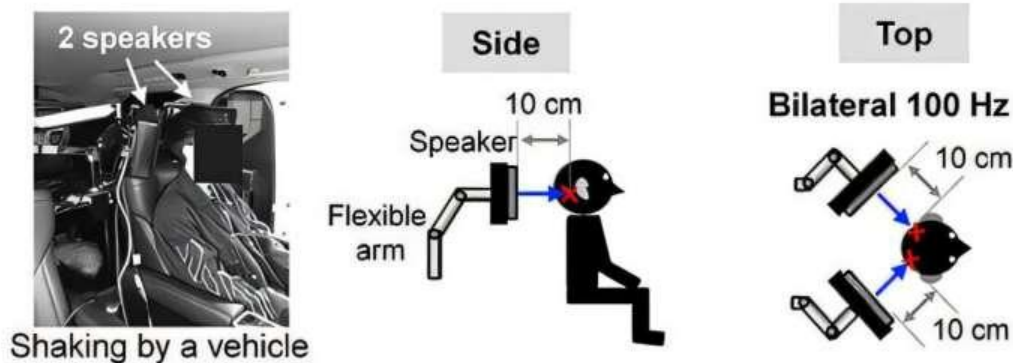
Provided by [University of Maryland School of Medicine](#)

APRIL 4, 2025

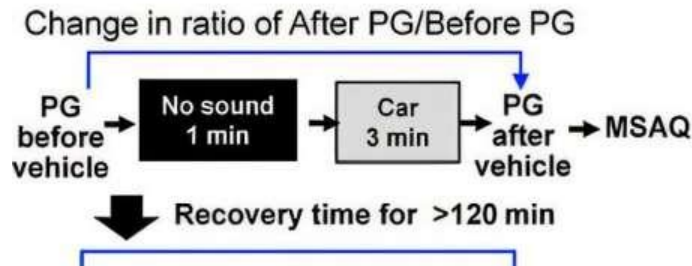
Sound therapy effectively reduces motion sickness by stimulating inner ear

by [Nagoya University](#)

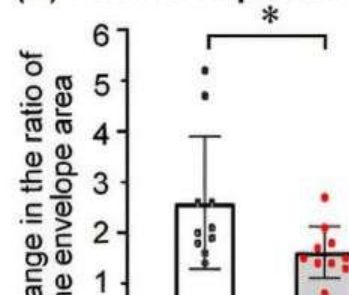
(A) Setting of pure tone exposure in a vehicle



(B) Protocol of posturography (PG)



(C) Results of posturography



Effects of exposure to a pure tone on hearing levels in humans. Credit: *Environmental Health and Preventive Medicine* (2025). DOI: 10.1265/ehpm.24-00247

A research group led by Takumi Kagawa and Masashi Kato at Nagoya University Graduate School of Medicine has discovered that using "a unique sound stimulation technology"—a device that stimulates the inner ear with a specific wavelength of sound—reduces motion sickness. Even a single minute of stimulation reduced the staggering and discomfort felt by people that read in a moving vehicle.

ADVERTISING

The results, [published](#) in *Environmental Health and Preventive Medicine*, suggest a simple and effective way to treat this common disorder.

"Our study demonstrated that short-term [stimulation](#) using a unique sound called 'sound spice' alleviates symptoms of motion sickness, such as nausea and dizziness," Kagawa

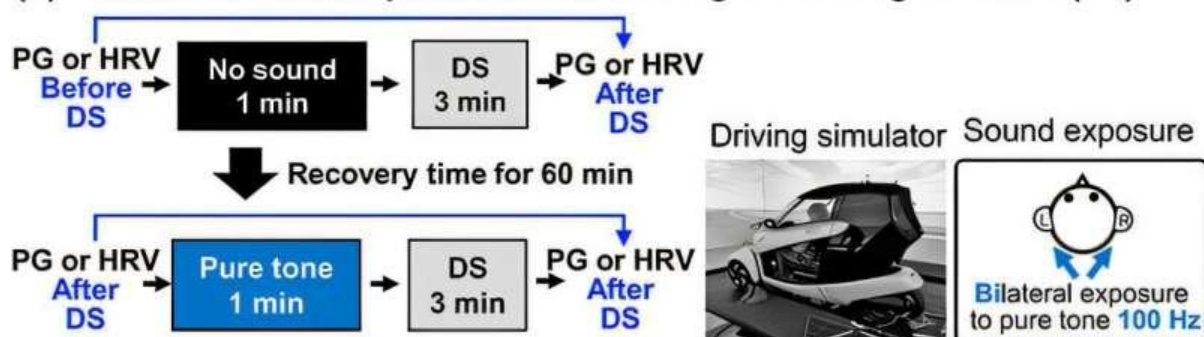
said. "The effective sound level falls within the range of everyday environmental noise exposure, suggesting that the sound technology is both effective and safe."

The discovery is an important expansion of recent findings about sound and its effect on the inner ear. Increasing evidence has suggested that stimulating the part of the inner ear associated with balance using a unique sound can potentially improve balance. Using a [mouse model](#) and humans, the researchers identified a unique sound at 100 Hz as being the optimal frequency.

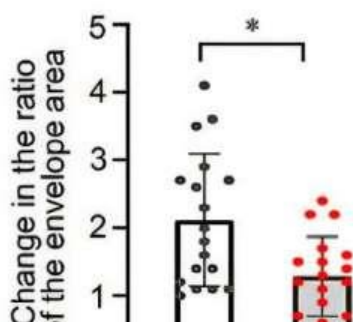
"Vibrations at the unique sound stimulate the otolithic organs in the inner ear, which detect linear acceleration and gravity," Kato explained. "This suggests that a unique sound stimulation can broadly activate the vestibular system, which is responsible for maintaining balance and spatial orientation."

To test the effectiveness of the devices, they recruited voluntary participants who were exposed to the unique sound. Following the stimulation, motion sickness was induced by a swing, a driving simulator, or riding in a car. The researchers used [postural control](#), ECG readings, and Motion Sickness Assessment Questionnaire results to assess the effectiveness of the stimulation.

(A) Protocol of sound exposure for the shaking of a driving simulator (DS)



(B) Effect on balance assessed by posturography (PG)



Imbalance caused by a vehicle in human subjects without pure tone exposure.

Credit: *Environmental Health and Preventive Medicine* (2025). DOI: 10.1265/ehpm.24-00247

Exposure to the unique sound before being exposed to the driving simulator enhanced sympathetic nerve activation. The researchers found symptoms such as "lightheadedness" and "nausea," which are often seen with motion sickness, were alleviated.

"These results suggest that activation of sympathetic nerves, which are often dysregulated in motion sickness, was objectively improved by the unique sound exposure," Kato said.

"The health risk of short-term exposure to our unique sound is minimal," Kagawa said. "Given that the stimulus level is well below workplace noise safety standards, this stimulation is expected to be safe when used properly."

Their results suggest a safe and effective way to improve [motion sickness](#), potentially offering help to millions of sufferers. The researchers plan to further develop the technology with the aim of practical application for a variety of travel situations, including air and sea travel.

More information: Yishuo Gu et al, Just 1-min exposure to a pure tone at 100 Hz with daily exposable sound pressure levels may improve motion sickness, *Environmental Health and Preventive Medicine* (2025). DOI: [10.1265/ehpm.24-00247](https://doi.org/10.1265/ehpm.24-00247)
Provided by [Nagoya University](#)

APRIL 4, 2025

A smart wearable for ear-based high-precision health sensing By [Karlsruhe Institute of Technology](#)



With the open-source platform "OpenEarable 2.0," scientists transform simple earphones into health meters. Credit: TECO, KIT

Wearables such as smartwatches, fitness trackers, or data glasses have become an integral part of our everyday lives. They record health data, monitor your sleep, or calculate your calorie consumption.

ADVERTISING

Researchers from Karlsruhe Institute of Technology (KIT) have developed the open-source platform "OpenEarable." It integrates a multitude of sensors into wireless earphones with the aim to enhance health measurements and safety applications in medicine, industry, and everyday life. The scientists are currently presenting their platform at [Hannover Messe](#) from March 31 to April 4.

Wearable technologies have made significant progress in recent years, but many of the existing systems are either proprietary, i.e., not customizable by others, or their measurement capabilities are limited.

With OpenEarable 2.0, a research team headed by Dr. Tobias Röddiger from KIT's TECO research group moves one step further: The open-source platform for ear-based sensor applications enables developers to create customized software. With a unique combination of sensors, more than 30 physiological parameters can be measured directly at the ear—from heart rate and breathing patterns to fatigue and body temperature.

"Our aim was to create an open and high-precision solution for health monitoring that goes far beyond what is possible with today's commercial wearables," says Röddiger.

"OpenEarable 2.0 provides a platform for researchers and developers that is easily customizable and scalable. This allows them to program the earphones individually for specific requirements." Thanks to its open accessibility, the platform promotes collaboration and the development of further innovations.

Versatile sensor technology for comprehensive applications

The earphones are equipped with a wide range of sensors: For example, multiple microphones detect vibrations in the skull to register eating activities. They are also used for speech recognition in noisy environments; motion sensors can detect falls and biosensors measure health indicators such as oxygen saturation and body temperature.

"Positioning the sensors at the ear is perfect for [precise measurements](#)," explains Röddiger. "The ear allows us to capture many important signals that are hard to access elsewhere on the body."

The wireless earphones communicate via Bluetooth LE Audio, an energy-saving version of wireless data transmission. The collected data is processed and analyzed in real time via a mobile app and a web dashboard.

From research to practice

The potential of OpenEearable 2.0 goes far beyond mere laboratory applications. The scientists conducted several studies to validate their platform. "It was found that the platform captures physiological data very accurately and reliably and that its measurements yield more precise results than the established standard measurements," says Röddiger.

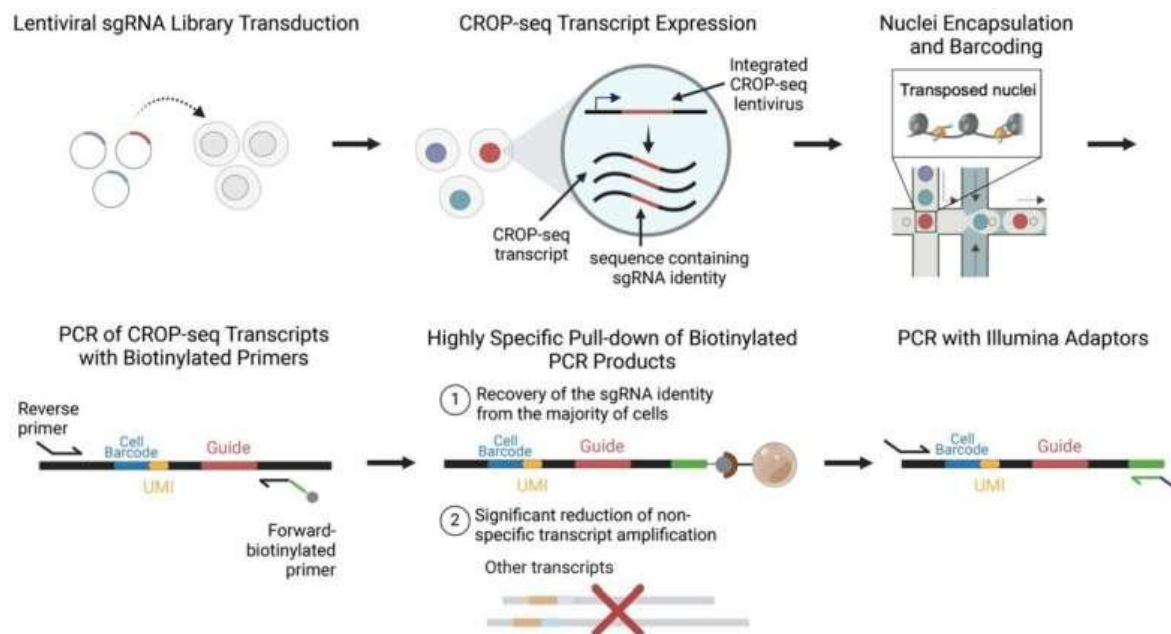
It can thus contribute to the early detection of diseases in medical diagnostics, increase safety in industry, or support athletes by providing a detailed performance analysis.

"With OpenEearable 2.0, we can not only improve the current state of wearable technology, but also open up completely new fields of application such as the development of wearables with real added value for medicine," says Röddiger. "Our next step is to further optimize the platform and to test it in various real-life scenarios."

Provided by [Karlsruhe Institute of Technology](#)

APRIL 4, 2025

Novel genomic screening tool enables precision reverse-engineering of genetic programming in cells by [Dana-Farber Cancer Institute](#)



Schematic of Perturb-multiome's biotinylation enrichment procedure to retrieve the identity of the sgRNA. Created in BioRender. Credit: *Science* (2025). DOI: 10.1126/science.ads7951 Collaborative research led by investigators at Dana-Farber/Boston Children's Cancer and Blood Disorders Center defines a novel approach to understanding how certain proteins called transcription factors determine which genetic programs will drive cell growth and maturation. The study is [published](#) in the journal *Science*.

The method, called "Perturb-multiome," uses CRISPR to knock out the function of individual transcription factors across many blood cells at once. The researchers then perform single-cell analyses on each cell to measure the effects of the editing, including identifying which genes have been turned on or off and which genes are accessible (based on epigenetic markers). The team applied this tool to immature blood cells to identify the important [transcription factors](#)—and DNA regions that code for them—that strongly affect how [blood cells](#) develop.

They discovered that many of the DNA regions they identified as important for driving blood cell production are also regions known to harbor mutations linked to blood disorders. The DNA regions they identified as important occupy less than 0.3% of the genome, but they explain a disproportionately large share of the genetic influence on blood cell features and specialization.

In earlier work, investigators from this team and other collaborators used [genome-wide association studies](#) to identify the transcription factor responsible for switching off fetal hemoglobin after birth, laying the groundwork for the development of gene therapy for sickle cell disease and beta thalassemia.

This new Perturb-multiome approach enables researchers to systematically reveal how thousands of transcription factor variants influence blood cell production and influence disease risk, creating opportunities for finding many more novel targeted therapies for blood disorders.

More information: Jorge Diego Martin-Rufino et al, Transcription factor networks disproportionately enrich for heritability of blood cell phenotypes, *Science* (2025). DOI: [10.1126/science.ads7951](#)

Journal information: [Science](#)

Provided by [Dana-Farber Cancer Institute](#)

Scientists just discovered a single molecule that may treat rare, devastating mitochondrial diseases

May 1, 2025

Scientists found a compound that appears to counter common mutations behind POLG-related diseases, rare conditions that harm mitochondrial DNA.



POLG-related diseases are a diverse family of conditions all caused by mutations in a gene for a key mitochondrial protein. A newfound molecule could be a promising treatment. (Image credit: KATERYNA KON/SCIENCE PHOTO LIBRARY via Getty Images)

Mitochondria — the powerhouses of cells — carry unique DNA that is mutated in specific diseases, causing cells to be starved of energy. Now, scientists have uncovered a first-of-its-kind molecule that can reverse the effects of common mutations behind these genetic disorders.

"They [the mutations] can cause very different diseases for which no cure is available," said [Carlo Viscomi](#), an associate professor in the University of Padova's Department of Biomedical Science and Padua Neuroscience Center in Italy.

"I think the paper really makes a breakthrough," said Viscomi, who was not involved in the research but previously collaborated with some of the authors. "It may open amazing possibilities for these conditions."

One limitation of the work is that it did not demonstrate how well the molecule works in a living animal or person, Viscomi said. But off the back of the research, scientists went on to develop a similar molecule that's [now being tested in a trial with humans](#). That trial is

being run by Pretzel Therapeutics, which several authors of the paper are affiliated with as founders, consultants, employees or shareholders. The trial will [test the safety](#) of the drug in healthy individuals, and next year, the company plans to run a trial with people with mitochondrial diseases.

The team's background research was "an important step" toward launching the ongoing trial, study co-author [Claes Gustafsson](#), a professor in the Department of Medical Biochemistry and Cell Biology at the University of Gothenburg in Sweden, told Live Science.

Related: [Malfunctioning mitochondria may drive Crohn's disease, early study hints](#)

"Extremely variable" diseases

The study, published in April in the journal [Nature](#), focused on polymerase gamma-related diseases, called [POLG-related diseases](#) for short. These rare, inherited conditions affect an estimated 1 in 10,000 people worldwide and are caused by mutations in the POLG gene, which codes for a key protein in mitochondria.

The researchers theorized that if they could find a drug that enhanced the activity of healthy POLG, the same drug might work on mutant versions, too. They began by screening a diverse collection of 270,000 compounds to see how they impacted the activity of healthy POLG. This revealed one promising molecule that the team then chemically tweaked, to increase its potency, and tested on common mutants. They dubbed the optimized version of the molecule PZL-A.

In the study, the researchers focused on just four POLG mutants, rather than studying all 300. However, about 70% of people with POLG diseases carry at least one of these four mutations, they noted.

The team used a technique called cryogenic electron microscopy to reveal in fine detail how the molecule interacted with each mutant and with healthy POLG. The protein is composed of three parts that fit together: one "A" component and two "B" components. The analysis revealed that the PZL-A compound sits in a pocket between A and B. That pocket happens to be "unaffected by the most common disease-causing [POLG] mutations," the authors noted in their paper.

By binding there, the molecule enhances the overall stability of the protein; this, in turn, boosts its ability to replicate and repair DNA, regardless of whether a mutation is present. "They didn't test all the existing mutations, but the mutations they tested, they seem all to be 'rescued,' in a sense, by using this compound," Viscomi said.

The researchers backed up these initial findings by running lab-dish experiments with cells from patients with the four common mutations they explored. First, the researchers depleted the mitochondrial DNA in the cells, to see how quickly the cells could recover that lost DNA. Cells treated with the compound recovered their DNA far faster than untreated cells did, and even kept up with the healthy version of the protein in some experiments.

"I wasn't prepared for this outcome — that we would actually find one stone that will kill all these birds," Gustafsson said. "But we did."

Copeland agreed, saying, "I'm surprised that such a small molecule can stabilize the mutant forms of POLG," as well as stabilize and alter the activity of healthy versions of the protein.

The team has begun testing the compound on additional POLG mutants. So far, they've found that "we see effects in many of these other mutations," Gustafsson said. That recent work has yet to be published. Meanwhile, the clinical trial has just begun to test a molecule that is "structurally very much related" to PZL-A, he added.

The clinical trials will be needed to see if the newfound compound causes any unacceptable side effects and whether it has the expected effects in humans, Copeland said. If it does prove safe and effective, "I'm assuming the patient would have to be on continuous treatment for the duration of their life," he added.

Such a treatment would fulfill an unmet need for people with these diseases, as current treatments are not aimed at curing the conditions but at [managing patients' symptoms](#). In addition, Viscomi and Gustafsson both noted that the depletion of mitochondrial DNA is tied to diseases of aging, including neurodegenerative conditions. So it may be that, beyond POLG diseases, scientists could explore additional applications for the compound.

SCIENTISTS WARN OF DNA HACKING: NEW STUDY REVEALS TERRIFYING EMERGING THREATS IN GENOMIC SEQUENCING

APRIL 30, 2025

In a striking new warning from cybersecurity and biotechnology experts, researchers have revealed that DNA hacking may soon become the next frontier in cyber warfare.

A new study published in [IEEE Access](#) has identified critical security gaps in next-generation sequencing (NGS) technologies that could expose highly personal genetic information to cyberattacks, espionage, and even biological sabotage.

According to the researchers, the surge in genomic data collection has outpaced the development of security frameworks to protect it. The result? Our most personal data—[our DNA](#)—is increasingly at risk of cyber exploitation.

“Genomic data is one of the most personal forms of data we have. If compromised, the consequences go far beyond a typical data breach,” co-author and microbiologist at the Shaheed Benazir Bhutto Women’s University, Dr Mahreen-Ul-Hassan, said in a [statement](#). “If compromised, the consequences go far beyond a typical data breach.”

NGS has revolutionized healthcare and biomedical research by enabling the rapid, cost-effective sequencing of DNA and RNA. Millions of people worldwide have used it for ancestry testing, disease diagnosis, cancer screening, and personalized medicine.

However, as the technology has accelerated scientific discovery and offered life-changing health insights, it has also opened Pandora’s box of [cyber-biosecurity](#) risks.

This newly published study is one of the first to present a step-by-step threat analysis of the entire sequencing pipeline—from raw data generation and sample preparation to cloud-based analysis and data interpretation—exposing a range of novel vulnerabilities unique to the NGS process.

Study authors, including researchers from the UK, Saudi Arabia, and Pakistan, describe a landscape in which genomic data, unlike any other digital record, is both permanent and deeply personal. A stolen credit card can be replaced, they note. However, if your information is compromised by DNA hacking, there’s no taking it back. Once it’s out, it’s out forever.

One of the study’s most alarming revelations is the possibility of DNA hacking, where DNA itself is used as a vehicle to carry malicious code. In an earlier [proof-of-concept experiment](#), scientists demonstrated that it is theoretically possible to encode malware into synthetic DNA.

When sequenced, the biological sample could produce digital output that exploits vulnerabilities in bioinformatics software, ultimately allowing an attacker to gain unauthorized access to the sequencing computer.

This type of DNA [hacking](#) is not just conceptual. A research team at the University of Washington successfully demonstrated it, making it

the first instance of DNA being used to breach a computer system. The implications are profound: a malicious DNA strand could disrupt a lab's sequencing run or compromise a hospital's genomic database.

Another vulnerability lies in the re-identification of supposedly anonymous genomic data. Even when names are removed, researchers have shown that DNA samples—especially those containing short tandem repeats, or STRs—can be cross-referenced with public genetic genealogy databases to infer surnames and other identifying information.

When combined with publicly available demographic data like age and zip code, this can lead to successful re-identification of individuals. In [one case](#), between 84% and 97% of participants in the Personal Genome Project were re-identified using this method. This kind of breach doesn't just violate privacy—it has real-world consequences, including risks of blackmail, discrimination, and medical fraud.

The study also explores how emerging technologies, especially artificial intelligence, may inadvertently accelerate these risks. With AI capable of bridging complex gaps in knowledge, adversarial actors could use AI tools to generate attack strategies that exploit specific vulnerabilities in bioinformatics pipelines.

The authors express concern that AI could be used to generate malicious code, manipulate DNA synthesis orders, or design custom malware that targets the computational tools responsible for analyzing genomic data.

“Despite its importance, cyber-biosecurity remains one of the most neglected and poorly understood research disciplines and is leaving a critical gap in global biosecurity,” lead author from the University of Portsmouth's School of Computing, Dr Nasreen Anjum, said. “To make sure our DNA information stays safe and is used only for good, we're urging more research and collaboration to find ways to keep this powerful technology secure.”

The research references real-world case studies that underscore the urgency of these risks. Recent cyberattacks on healthcare and

pharmaceutical companies have demonstrated the potential for devastating breaches.

For instance, in 2024, Octapharma Plasma in the U.S. [suffered a ransomware](#) attack that compromised sensitive personal information. Similarly, Japanese pharmaceutical firm [Eisai](#) faced massive logistical and production delays after a cyberattack disrupted their systems.

Although these attacks did not directly involve sequencing data or DNA hacking, they highlight how vulnerable biotech and healthcare infrastructures remain to digital exploitation. As sequencing becomes more integrated with clinical practice and public health infrastructure, it is only a matter of time before NGS platforms become a direct target.

One of the study's most significant contributions is the introduction of a new cyber-biosecurity taxonomy designed explicitly for next-generation sequencing.

Unlike conventional cybersecurity models, which focus on network vulnerabilities and software flaws, this new framework extends into the biological domain. It identifies specific threat vectors at every stage of the NGS workflow.

These include synthetic DNA-based malware attacks, sample multiplexing exploitation, adversarial manipulation of sequencing workflows, and inference attacks that exploit genomic linkage disequilibrium to predict health conditions from partial DNA sequences.

The authors explain that each phase of the NGS workflow presents its own unique set of vulnerabilities. In the initial stages, where DNA is extracted from samples such as blood or tissue, threats like re-identification attacks and physical theft of biological material can occur.

Even manual handling procedures are not immune. If an insider tampers with or substitutes a sample during extraction, it could corrupt the entire sequencing process and lead to dangerous or misleading conclusions in clinical or forensic contexts.

The study outlines several cyber risks during the library preparation stage, where DNA fragments are processed and tagged for sequencing. Automated liquid handling robots and barcode tracking systems used in high-throughput labs often rely on connected software platforms.

If these are compromised—whether through malware, ransomware, or a supply chain attack—the integrity of genetic data can be irreparably damaged. The study also describes multiplexed DNA injection attacks, where a malicious DNA sample introduced into a pooled batch can manipulate sequencing outcomes or cause misattribution of genetic material across different samples.

The vulnerabilities extend into the core computational steps as well. Base calling software, responsible for translating fluorescent signals into DNA sequences, can be hijacked to insert artificial mutations or produce inaccurate reads.

DNA Hackers could exploit sequencing devices' weak encryption or outdated firmware to manipulate results. Such tampering could lead to false diagnoses or incorrect treatment plans in a clinical setting. During quality control and data preprocessing, threats include malicious code injection into files and ransomware attacks on cloud-based data storage hubs like [Illumina's](#) BaseSpace Sequence Hub.

The bioinformatics analysis phase is particularly vulnerable due to its reliance on complex software pipelines and large-scale computational resources. A cyberattack here could silently alter genetic variant calls, obscure critical mutations, or even erase valuable clinical insights. The authors note that once these data are interpreted and integrated into medical records or research databases, the consequences of such manipulation may go unnoticed until it's too late.

The researchers offer a series of recommendations to mitigate the escalating risks of DNA hacking. They call for developing secure sequencing protocols, robust access controls, and mandatory encryption at every step of the genomic workflow.

Laboratories should adopt multi-factor authentication for all data access points and regularly audit the software and firmware systems used in sequencing equipment.

Open-access genetic databases must be hardened with strong password policies, two-factor authentication, and tighter user verification protocols. Many of these platforms still allow data queries without login credentials, creating a massive vulnerability in the global genomic infrastructure.

The authors also advocate for integrating anomaly detection systems powered by [artificial intelligence](#) to monitor for unusual patterns in sequencing workflows that could signal potential DNA hacking.

More importantly, they emphasize the need for interdisciplinary collaboration. Too often, cybersecurity professionals and biotechnologists operate in silos. Bridging that divide, the study argues, is essential for building resilient genomic ecosystems capable of withstanding evolving cyber threats.

Underlying all these technical considerations is a broader ethical concern. As genomic data becomes central to personalized medicine, the potential for misuse or abuse grows.

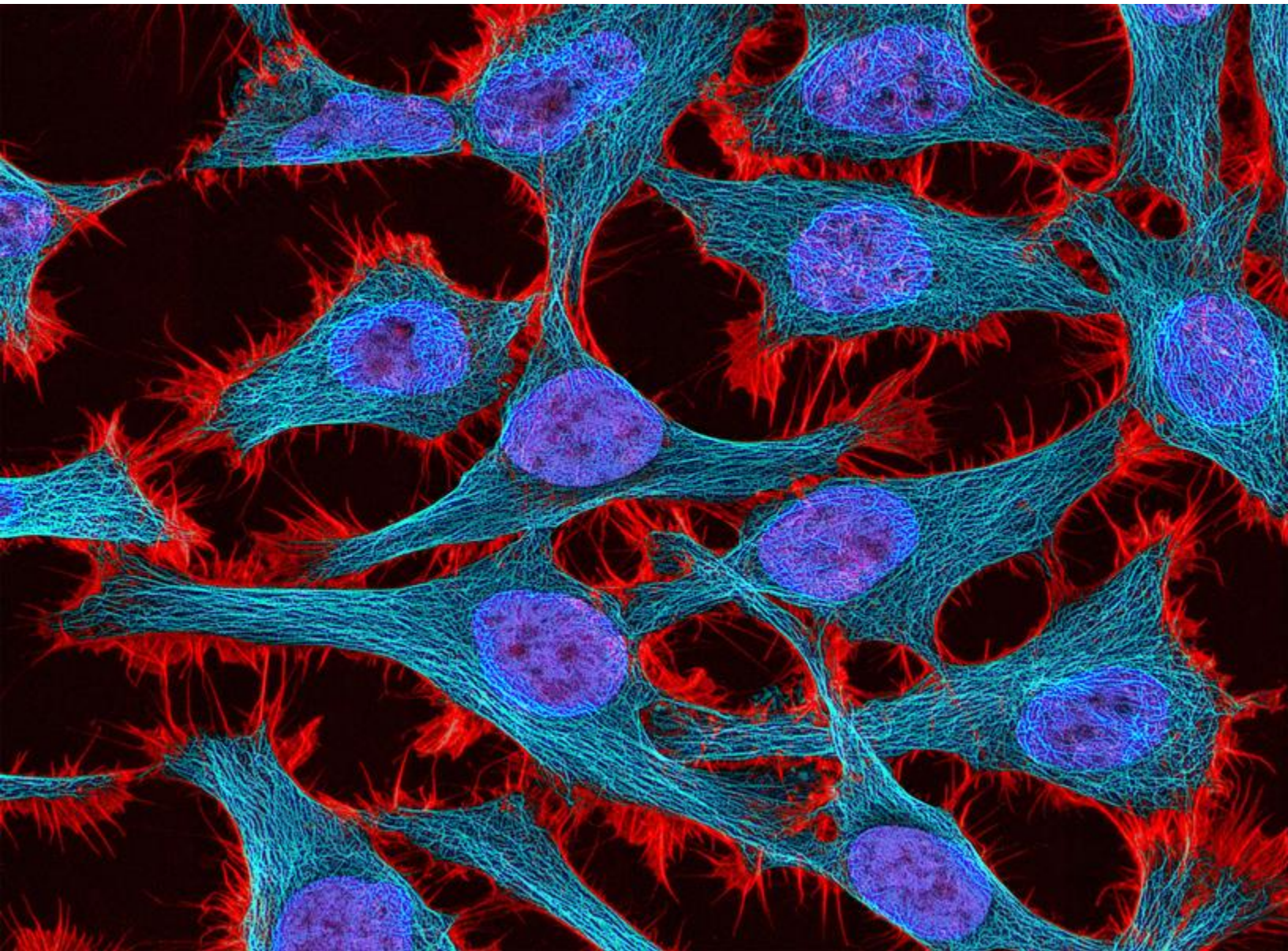
Genetic discrimination, coercion, and data exploitation are no longer just hypothetical risks. Without strong protections, public trust in genomic research could erode, setting back scientific progress for years.

Ultimately, the study serves as a call to action. As sequencing costs continue to drop and access to genomic technologies expands, the risk landscape will grow more complex. What's at stake is data privacy, research integrity, public health, and national security.

“Our work is a wake-up call. Protecting genomic data isn't just about encryption – it's about anticipating attacks that don't yet exist,” Dr. Anjum said. “We need a paradigm shift in how we secure the future of precision medicine.”

Gene circuits enable more precise control of gene therapy

The circuits could help researchers develop new treatments for fragile X syndrome and other diseases caused by mutations of a single gene. MIT April 28, 2025



In human cells, MIT engineers showed that they could use a new method to deliver genes that could help treat diseases including fragile X syndrome, a disorder that leads to intellectual disability and other developmental problems.

Credits:

Credit: National Institutes of Health

Many diseases are caused by a missing or defective copy of a single gene. For decades, scientists have been working on gene therapy treatments that could cure such diseases by delivering a new copy of the missing genes to the affected cells.

Despite those efforts, very few gene therapy treatments have been approved by the FDA. One of the challenges to developing these treatments has been achieving control over how much the new gene is expressed in cells — too little and it won't succeed, too much and it could cause serious side effects.

To help achieve more precise control of gene therapy, MIT engineers have tuned and applied a control circuit that can keep expression levels within a target range. In human cells, they showed that they could use this method to deliver genes that could help treat diseases including fragile X syndrome, a disorder that leads to intellectual disability and other developmental problems.

“In theory, gene supplementation can solve monogenic disorders that are very diverse but have a relatively straightforward gene therapy fix if you could control the therapy well enough,” says Katie Galloway, the W. M. Keck Career Development Professor in Biomedical Engineering and Chemical Engineering and the senior author of the new study.

MIT graduate student Kasey Love is the lead author of the paper, which [appears today in *Cell Systems*](#). Other authors of the paper include MIT graduate students Christopher Johnstone, Emma Peterman, and Stephanie

Gaglione, and Michael Birnbaum, an associate professor of biological engineering at MIT.

Delivering genes

While gene therapy holds promise for treating a variety of diseases, including hemophilia and sickle cell anemia, only a handful of treatments have been approved so far, for an inherited retinal disease and certain blood cancers.

Most gene therapy approaches use a virus to deliver a new copy of a gene, which is then integrated into the DNA of host cells. Some cells may take up many copies of the gene, while others don't receive any.

“Simple overexpression of that payload can result in a really wide range of expression levels in the target genes as they take up different numbers of copies of those genes or just have different expression levels,” Love says. “If it's not expressing enough, that defeats the purpose of the therapy. But on the other hand, expressing at too high levels is also a problem, as that payload can be toxic.”

To try to overcome this, scientists have experimented with different types of control circuits that constrain expression of the therapeutic gene. In this study, the MIT team decided to use a type of circuit called an incoherent feedforward loop (IFFL).

In an IFFL circuit, activation of the target gene simultaneously activates production of a molecule that suppresses gene expression. One type of molecule that can be used to achieve that suppression is microRNA — a short RNA sequence that binds to messenger RNA, preventing it from being translated into protein.

In this study, the MIT team designed an IFFL circuit, called “ComMAND” (Compact microRNA-mediated attenuator of noise and dosage), so that a microRNA strand that represses mRNA translation is encoded within the therapeutic gene. The microRNA is located within a short segment called an intron, which gets spliced out of the gene when it is transcribed into mRNA. This means that whenever the gene is turned on, both the mRNA and the microRNA that represses it are produced in roughly equal amounts.

This approach allows the researchers to control the entire ComMAND circuit with just one promoter — the DNA site where gene transcription is turned on. By swapping in promoters of different strengths, the researchers can tailor how much of the therapeutic gene will be produced.

In addition to offering tighter control, the circuit’s compact design allows it to be carried on a single delivery vehicle, such as a lentivirus or adeno-associated virus, which could improve the manufacturability of these therapies. Both of those viruses are frequently used to deliver therapeutic cargoes.

“Other people have developed microRNA based incoherent feed forward loops, but what Kasey has done is put it all on a single transcript, and she showed that this gives the best possible control when you have variable delivery to cells,” Galloway says.

Precise control

To demonstrate this system, the researchers designed ComMAND circuits that could deliver the gene FXN, which is mutated in Friedreich’s ataxia — a disorder that affects the heart and nervous system. They also delivered the gene Fmr1, whose dysfunction causes fragile X syndrome. In tests in human

cells, they showed that they could tune gene expression levels to about eight times the levels normally seen in healthy cells.

Without ComMAND, gene expression was more than 50 times the normal level, which could pose safety risks. Further tests in animal models would be needed to determine the optimal levels, the researchers say.

The researchers also performed tests in rat neurons, mouse fibroblasts, and human T-cells. For those cells, they delivered a gene that encodes a fluorescent protein, so they could easily measure the gene expression levels. In those cells, too, the researchers found that they could control gene expression levels more precisely than without the circuit.

The researchers now plan to study whether they could use this approach to deliver genes at a level that would restore normal function and reverse signs of disease, either in cultured cells or animal models.

“There's probably some tuning that would need to be done to the expression levels, but we understand some of those design principles, so if we needed to tune the levels up or down, I think we'd know potentially how to go about that,” Love says.

Other diseases that this approach could be applied to include Rett syndrome, muscular dystrophy and spinal muscular atrophy, the researchers say.

“The challenge with a lot of those is they're also rare diseases, so you don't have large patient populations,” Galloway says. “We're trying to build out these tools that are robust so people can figure out how to do the tuning, because the patient populations are so small and there isn't a lot of funding for solving some of these disorders.”

The research was funded by the National Institute of General Medical Sciences, the National Science Foundation, the Institute for Collaborative Biotechnologies, and the Air Force Research Laboratory.

Researchers Use Big Data to Find a Longevity Target

High levels of this protein may shave nearly a year off lifespan.

Apr 16, 2025

Researchers publishing in *Aging Cell* have used large databases to discover **a causal relationship between multiple genes and overall mortality risk**, finding a new potential target in the process.

Putting -omics databases to work

These researchers introduce their study by discussing genetic databases, which have previously been used to determine associations of specific genes with longevity [1], particularly in cases of extreme longevity [2]. Using molecular quantitative trait loci (QTLs) cements this understanding, translating the genes into their expressed proteins and pathways in a way that gives researchers some understanding as to how and why certain genes lead to longer or shorter lifespans [3]. These databases have been used to identify druggable targets for specific conditions, such as stroke [4].

These researchers aimed to build on that work by combining multiple -omics sources into a cohesive whole, using advanced statistical techniques and a close look at protein interactions in order to discover potential druggable targets for longevity. They found several proteins that appear to extend lifespan, but they also found the reverse.

This study used three metrics: parental lifespan, being in the top 1% of longevity, and being in the top 10% of longevity. The latter two groups had tens of thousands of data points, and the first had over a million. As expected, the researchers found strong genetic correlations between overall lifespan and extreme longevity.

Multiple needles in a large haystack

Because of the sheer number of genes and related proteins that were tested, the standard p value of 0.05 was insufficient. Instead, the researchers began looking at over 500 proteins with that low of a p value, but after filtration, co-localization, and comparison between different databases, they found 14 proteins with extremely small p values, meaning that they are nearly certain to have longevity-related effects.

The researchers looked at plasma expression and found that many of the related genetic pathways have been documented to severely amplify the likelihood of common causes of death. For example, *HYKK* is related to lung cancer, *NRG1* is related to stroke, *NTN5*, *ADD1*, and *BECN1* are all related to metabolic issues, and *SRFBP1* is related to blood pressure. Other genes showed their effects when their proteins were expressed in specific tissues. These included *LPA* in the liver and *DNAJA4* in the thyroid and skin.

A protein worthy of suppression

One gene in particular, however, stood out as being particularly dangerous: *PDAP1*. In every statistical model that the researchers used, having high expression of *PDAP1* was correlated with a higher likelihood of mortality according to UK Biobank data. People over the age of 60 in that database with high levels of the PDAP1 protein were statistically likely to live nearly a year shorter than people with low levels.

Epigenetic clocks, including PhenoAge and the mortality predictor GrimAge, confirmed this finding: people with more *PDAP1* expression get older faster. The protein PDAP1 has been previously linked to cancer, but these researchers connected it to a host of other issues, including waist circumference, high blood pressure, hormone imbalances, and heart failure.

The researchers then decided to directly examine PDAP1 in the cellular context, and they found that it has bidirectional causality with senescence. First, they caused lung fibroblasts to enter senescence through multiple replications; PDAP1 expression increased in these cells as they entered a pre-senescent state. Inducing senescence through radiation or chemicals yielded similar results.

Similarly, introducing PDAP1 into these fibroblasts drove them senescent in a dose-dependent manner, as measured by well-known biomarkers, including p16, p21, and SA- β -gal. By silencing PDAP1 through RNA from the 60th passage onward in these cells, the researchers were able to decrease the rate at which these cells became senescent, allowing them to survive for more passages before eventually being unable to replicate further: knocking down PDAP1 extended their Hayflick limit.

This study was based on broad genetic databases and cells, and there were no animals involved. However, even with those limitations, it is clear that PDAP1 is a protein worth further exploring as a druggable target. If this protein can be safely downregulated in living people, it may decrease the rate of senescence, aid in metabolism, and allow people to live longer. Preclinical models and clinical trials can determine if this is the case.

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APRIL 7, 2025

Gene discovery reveals potential for growing new heart arteries

by Sara Zaske, [Stanford University](#)



An illustrated model of the human heart showing the right-dominant pattern of a posterior descending artery (in red above) that supplies oxygenated blood to the back of the heart. For most people, this artery extends from the right main coronary artery, but for some it comes from the left. For others, both sides have one, and these arteries are roughly equal in size. Credit: Ella Maru Studio

Most people have right-dominant hearts—which to a doctor or a researcher means they have an artery that extends from the right side of their hearts to supply oxygenated blood to the back side. For some people, this artery, called the posterior descending artery, comes from the left side or from both directions. A study has found that the gene CXCL12 is connected to this artery's formation and that its directional pattern is set very early in human development.

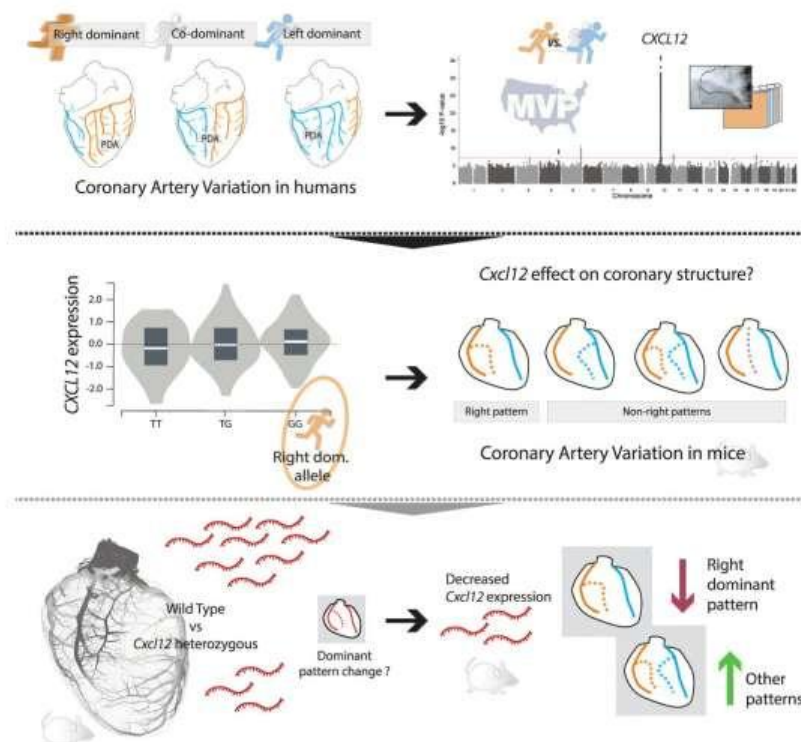
The [findings](#), reported in the journal *Cell*, represent a step toward developing "medical revascularization," a long-term goal of Stanford researchers to create a treatment for blocked or limited-flow arteries by growing new ones to compensate.

"For the first time, we have evidence of a gene that regulates the development of one of the most important types of arteries in the human body," said Kristy Red-Horse, co-senior author of the study and biology professor in the Stanford School of Humanities and Sciences. "And if we know the development pathways of these important arteries, then we can perhaps regrow them by reintroducing these pathways in a diseased heart."

Several coronary arteries deliver blood and oxygen to the **human heart**: The two main arteries are on the front of the heart, on the right and left sides. To supply oxygenated blood to the back of the heart, the posterior descending artery branches off from one of those main arteries.

For an estimated 80% of humans, that artery comes from the right main coronary artery, but for about 10%, it comes from the left. In another 10%, there are two of these arteries of roughly equal size that branch off the right and left main arteries and extend to the back of the heart.

To better understand what determines this arterial patterning, Red-Horse collaborated with co-senior author Tim Assimes, associate professor of cardiovascular medicine in the Stanford School of Medicine.



Graphical abstract. Credit: *Cell* (2025). DOI: 10.1016/j.cell.2025.02.005

Assimes, who also treats patients at the Palo Alto VA Medical Center, saw an opportunity in the large medical data set from the Department of Veterans Affairs' Million Veteran Program. It contains information on more than 60,000 veterans who have undergone angiograms, a medical imaging procedure to detect possible artery blockages. This data

includes whether their hearts had right-, left- or co-dominant arteries on the back as well as genetic samples.

The researchers conducted [genetic analysis](#) and found ten locations within the human DNA code tied to the development of the artery on the back of the heart—the strongest of which was CXCL12. Previous work from Red-Horse's group had already shown that mice who received a dose of the protein associated with the gene CXCL12 grew new arterial branches in their damaged heart tissue, so the latest finding in humans indicates that the gene and its protein play a critical role in human artery formation as well.

"We now have evidence that this patterning of our two major coronary arteries is controlled by differences in our DNA code we inherit from our parents, and the top signal is near a gene that is also responsible for the growth and development of coronary arteries," Assimes said.

After finding this connection, the researchers imaged fetal hearts and found that CXCL12 was expressed at the time the directional dominance of the posterior descending artery was established. Further experiments with mice also showed that reducing the protein produced by CXCL12 caused those mice to develop left- or co-dominant patterns.

Whether having the more common right-dominant artery pattern ultimately confers more or fewer protections against heart disease is not yet known.

Yet, the discovery of the gene that potentially controls this branching opens up the possibility of discovering ways to make new collateral arterial branches, meaning purposefully growing additional arteries that could still deliver oxygen to the heart when another artery is blocked. Currently, treatments to relieve limited or blocked arteries are invasive and mechanical, such as open-heart bypass surgery and the placement of artificial stents.

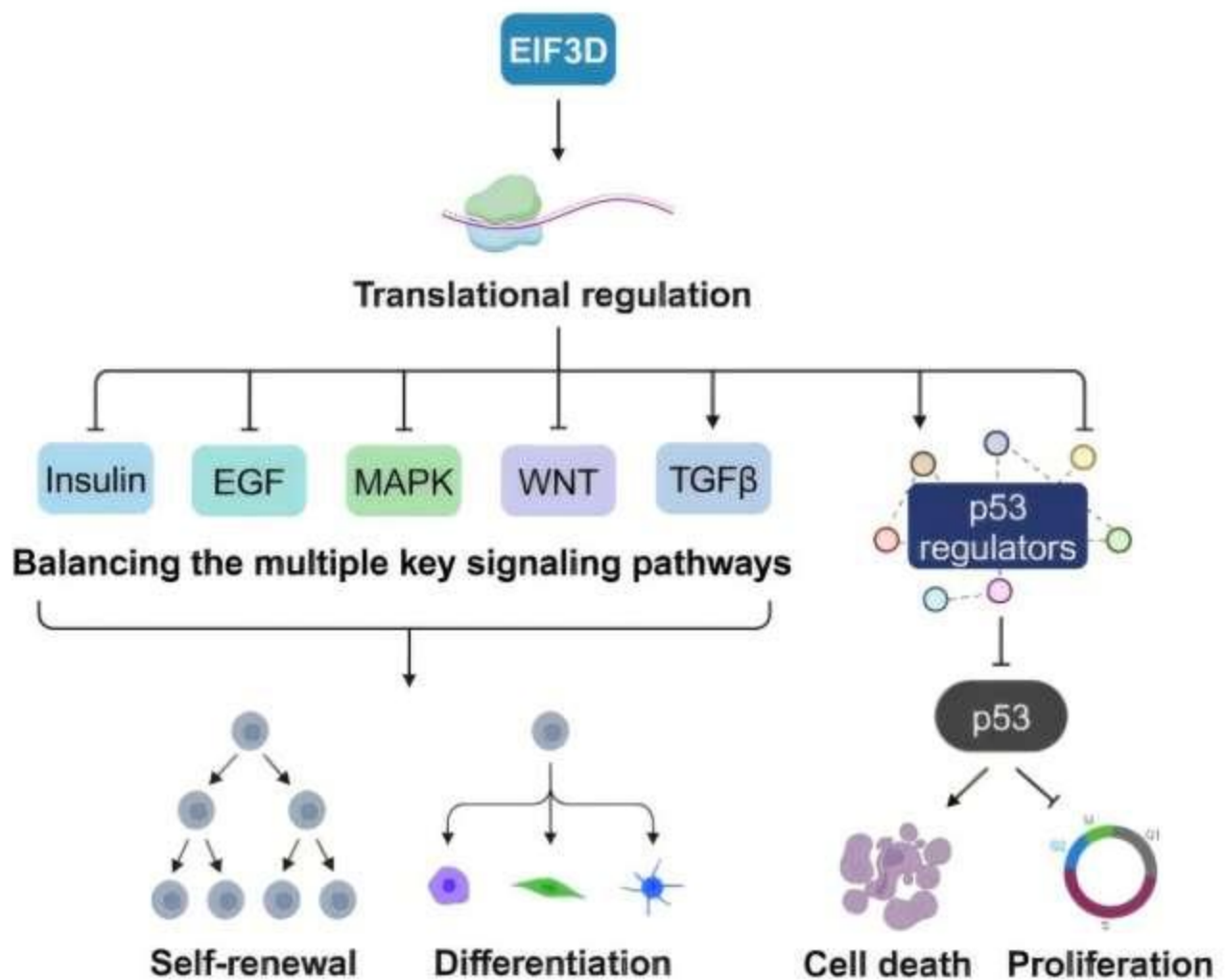
Next, the researchers plan to investigate the DNA variants that cause differences in expression of CXCL12 and work on designing ways to target the gene activation toward the creation of a therapeutic treatment.

More information: Pamela E. Rios Coronado et al, CXCL12 drives natural variation in coronary artery anatomy across diverse populations, *Cell* (2025). DOI: [10.1016/j.cell.2025.02.005](https://doi.org/10.1016/j.cell.2025.02.005)

Journal information: [Cell](#)
Provided by [Stanford University](#)

CRISPR screen identifies EIF3D as critical regulator of stem cell pluripotency maintenance

by [Kyoto University](#)



Schematic representation of the model describing how EIF3D-mediated translational regulation balances homeostasis of critical signaling pathways in primed pluripotency.

Credit: *Science Advances* (2025). DOI: 10.1126/sciadv.adq5484

A team of CiRA researchers has uncovered the crucial role of EIF3D—a protein translational regulator—in primed pluripotency. The research is [published](#) in the journal *Science Advances*.

According to the central dogma of molecular biology, information flows from DNA to RNA to protein. While much is known about [pluripotency](#)—the ability to differentiate into any other cell type in the body and to divide indefinitely—in terms of transcriptional and epigenetic regulation, as well as [signal transduction](#), how protein translation ties these control mechanisms together remains largely underexplored.

To identify genes important for maintaining primed pluripotency—a state poised for differentiating into various cell types in the body, the research team, led by Associate Professor Kazutoshi Takahashi and Assistant Professor Chikako Okubo, began with a genome-wide genetic screen based on CRISPR interference (CRISPRi) that systemically reduces the expression of every single gene in the genome of a pluripotent stem cell (PSC) line.

By monitoring a standard marker of undifferentiated cells at different time points after shutting down [gene expression](#), the researchers can determine whether a specific gene positively or negatively regulates pluripotency.

Notably, they discovered genes associated with protein translation to influence pluripotency substantially. In particular, they focused on EIF3D, which dramatically reduced cells with primed pluripotency and belongs to the EIF3 family that interacts with EIF4G2, a translational regulator known to maintain primed pluripotency.

Using an induced pluripotent stem (iPS) cell line with suppressed EIF3D expression, the researchers also observed morphological changes and growth defects. Further analysis showed that these cells had reduced gene expression of transcription factors promoting pluripotency.

Conversely, the transcriptional targets of p53—a cell cycle regulator often mutated in cancers—such as CDKN1A and MDM2—were upregulated in these cells. In addition, markers of cellular stress and senescence were induced.

Remarkably, the [protein expression](#) of p53 was significantly increased in cells with suppressed EIF3D expression despite unchanged expression at the RNA level, suggesting that reduced EIF3D leads to the translational dysregulation of p53.

To further investigate the role of EIF3D in maintaining pluripotency, the research team examined the gene expression profile of cells with suppressed EIF3D expression, cells with suppressed core pluripotency transcription factors, and cells differentiated into the three major cell germ layers.

Cells with reduced EIF3D lacked strong marker expression related to primed PSC or germ line cells, thus assuming a state different from other cells in the comparison.

When the research team specifically examined messenger RNAs (mRNAs) being translated in cells with suppressed EIF3D expression, they determined that EIF3D is involved in directing the binding of protein translation machinery to certain mRNAs in primed PSCs.

Furthermore, many genes associated with pluripotency were downregulated in its absence, thus affecting multiple signaling cascades, including the p53 pathway, that regulate primed pluripotency.

Through this work, the research team revealed the critical role of EIF3D in safeguarding primed pluripotency. Moreover, it further highlights the impact of translational regulation on pluripotency.

By improving our understanding of factors controlling pluripotency, this discovery helps to propel the basic study of stem cells and their practical application for next-generation medicine purposes.

More information: Chikako Okubo et al, EIF3D safeguards the homeostasis of key signaling pathways in human primed pluripotency, *Science Advances* (2025). DOI: [10.1126/sciadv.adq5484](https://doi.org/10.1126/sciadv.adq5484)

Journal information: [Science Advances](#)
Provided by [Kyoto University](#)

APRIL 21, 2025

Study reveals new genetic mechanism behind autism development

by [The Hospital for Sick Children](#)

Credit: Unsplash/CC0 Public Domain

Scientists from The Hospital for Sick Children (SickKids) and the University of Las Vegas, Nevada (UNLV) have uncovered a genetic link between autism spectrum disorder (ASD) and a rare genetic condition called myotonic dystrophy type 1 (DM1).

The study, [published](#) in *Nature Neuroscience*, suggests that while ASD has previously been characterized by a loss of gene function, another mechanism may be leading to the social behaviors often observed in individuals with ASD.

DM1 is an inherited condition which causes progressive muscle loss and weakness. While ASD is present in around 1% of the general population, it is 14 times more likely to develop in people with DM1.

The study revealed that the [genetic variation](#) that causes DM1—tandem repeat expansions (TREs) in the DMPK gene—also impacts [brain development](#). The research team found that the effects of TREs interfere with a critical process called gene splicing, which is essential for gene function.

The disruption causes a protein imbalance that can result in mis-splicing of multiple genes involved in brain function, and may explain why some of the social and behavioral outcomes of ASD develop in people with DM1.

"Our findings represent a new way to characterize the genetic development of autism," explains Dr. Ryan Yuen, Senior Scientist in the Genetics & Genome Biology program at SickKids.

"By identifying the molecular pathway behind this connection, we can begin to investigate new approaches to ASD diagnosis and the development of precision therapies that release these proteins back into the [genome](#)."

What are TREs?

TREs occur when sections of a DNA strand are repeated two or more times, and the likelihood of those repeats causing errors in gene function increases each time.

In 2020, Yuen discovered that [TREs are genetic contributors to autism](#), identifying more than 2,588 different places in the genome where TREs were much more prevalent in people with ASD. Similarly, people with DM1 have a TRE in the DMPK gene.

"A variation really stood out to me that we see in rare neuromuscular diseases," says Dr. Łukasz Sznajder, a research lead and Assistant Professor at UNLV. "This is how we started connecting the dots. We found a molecular link, or overlap, which we believe is the core of causing autistic symptoms in children with myotonic dystrophy."

Gene splicing a key contributor to the development of ASD

As the tandem repeat expands in the DMPK gene, the research team, including collaborators at the University of Florida and Adam Mickiewicz University (Poland), found its altered RNA binds to a protein that is involved in gene splicing regulation during brain development.

This so-called "toxic RNA" depletes the protein and prevents it from binding to other RNA molecules in important areas of the genome, causing a protein imbalance which results in mis-splicing other genes.

"TREs are like a sponge that absorbs all these important proteins from the genome. Without this [protein](#), other areas of the genome don't function properly," explains Yuen.

The Yuen Lab and Sznajder Lab are already exploring whether this mis-splicing is happening in other genes associated with ASD, as well as how their findings could inform precision therapies that release these proteins back into the genome.

Some of this work is already underway. In 2020, Dr. Christopher Pearson, Senior Scientist in the Genetics & Genome Biology program at SickKids, identified a [molecule that can contract TREs in Huntington's disease](#).

While more research is needed to identify how this could be applied to other conditions, the team remains optimistic their findings could inform future research and care for DM1, ASD and other conditions.

More information: Łukasz J. Sznajder et al, Autism-related traits in myotonic dystrophy type 1 model mice are due to MBNL sequestration and RNA mis-splicing of autism-risk genes, *Nature Neuroscience* (2025). DOI: [10.1038/s41593-025-01943-0](https://doi.org/10.1038/s41593-025-01943-0)

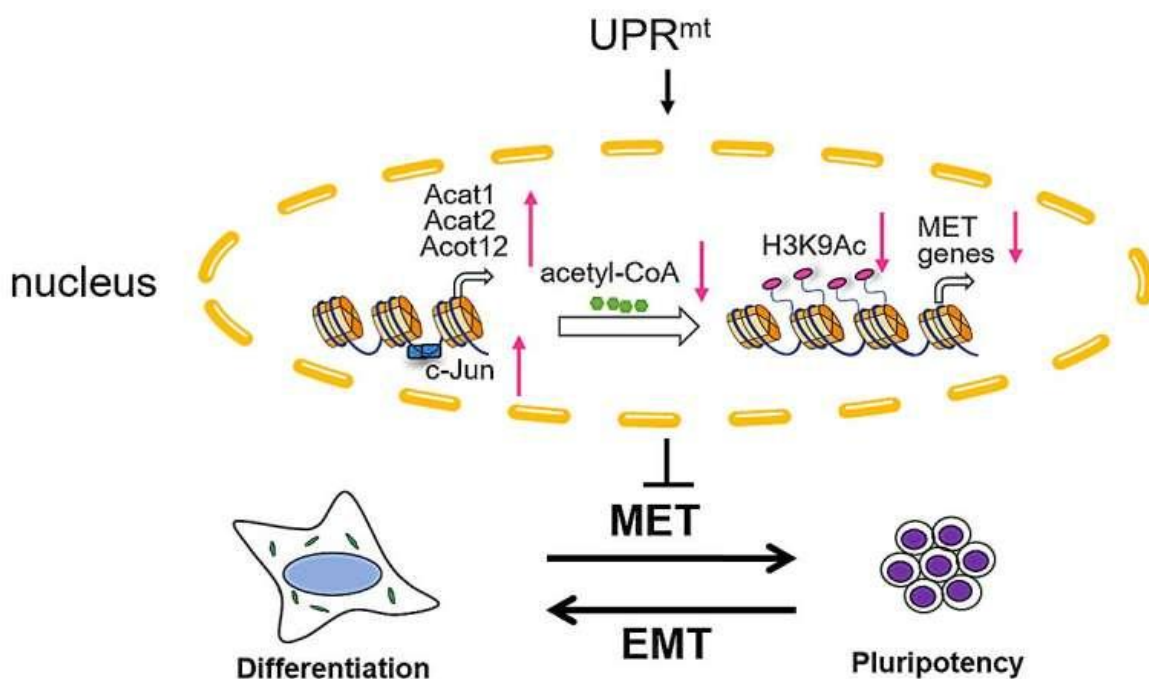
Journal information: [Nature Neuroscience](#)

Provided by [The Hospital for Sick Children](#)

APRIL 16, 2025

Researchers discover new mode of mitochondrial regulation in stem cell fate

by Li Yali, [Chinese Academy of Sciences](#)



Scheme showing the role of activated UPR^{mt} during the early phase of reprogramming.

Credit: Prof. Liu's team

Mitochondria play a crucial role in acquiring pluripotency and determining cell fate. The mitochondrial unfolded protein response (UPR^{mt}) serves as an important retrograde regulatory pathway that communicates from mitochondria to the nucleus. Various factors, including imbalances in mitochondrial protein homeostasis, elevated reactive oxygen species (ROS), discrepancies in mitochondrial and nuclear gene expression, and mitochondrial dysfunction, can all activate UPR^{mt} . The activation of this pathway regulates gene expression, thereby influencing cellular physiological or pathological processes.

In nematodes, UPR^{mt} has been shown to delay aging, and its regulatory and activation mechanisms are relatively well understood. However, in mammalian cells, the regulatory mechanisms of UPR^{mt} are more complex, and its role in cell fate determination and development has not been extensively reported.

To address this challenge, a research team led by Prof. Liu Xingguo from the Guangzhou Institutes of Biomedicine and Health of the Chinese Academy of Sciences has [published](#) a study in *Nature Metabolism*. They discovered that UPR^{mt} is transiently activated during the early stages of acquiring pluripotency and gradually diminishes thereafter.

They also identified c-Myc as a key factor in the activation of UPR^{mt}—overexpression of c-Myc significantly increased the expression of Hsp60, a marker of UPR^{mt}, while other transcription factors (such as Sox2, Klf4, and Oct4) did not exhibit similar effects.

Further research revealed that the activation of UPR^{mt} during pluripotency acquisition inhibits the mesenchymal-to-epithelial transition (MET). Notably, UPR^{mt} also plays a regulatory role in MET during early mammalian differentiation and in tumors. The activation of UPR^{mt} can enhance the migration and invasion capabilities of cancer cells.

In exploring the underlying mechanisms, the team identified c-Jun, a novel key factor in the UPR^{mt} retrograde signaling pathway. c-Jun, a proto-oncogene, inhibits the acquisition of pluripotency, and the activation of UPR^{mt} promotes c-Jun expression.

Through [transcriptional regulation](#), c-Jun upregulates the expression of acetyl-CoA metabolic enzymes, thereby reducing acetyl-CoA levels. Since acetyl-CoA is closely associated with histone acetylation, the researchers discovered that UPR^{mt} activation decreases histone acetylation, particularly the level of H3K9 acetylation (H3K9Ac).

The study also found that activated UPR^{mt} reduces the binding of H3K9Ac to the promoter regions of epithelial-related genes (such as E-cadherin and Epcam). This reduction in H3K9Ac levels leads to decreased expression of these epithelial-related genes, ultimately suppressing MET. By supplementing precursors of acetyl-CoA (such as acetate, citrate, and pyruvate), the researchers were able to restore H3K9Ac levels, along with the expression of MET-related genes.

In summary, this study is the first to reveal the molecular mechanism by which UPR^{mt}, through c-Jun, reduces acetyl-CoA levels and decreases [histone acetylation](#), inhibiting MET and hindering the acquisition of pluripotency. It highlights how mitochondrial pathways regulate MET and suggests that this regulatory mode exists in early differentiation and tumor contexts, indicating a broad biological mechanism.

This discovery offers new insights into how mitochondria retroactively regulate the nucleus and influence cell fate determination, potentially paving the way for advancements in [regenerative medicine](#) and new targets for cancer therapy.

This study was conducted in collaboration with several research groups, including Guangzhou Medical University, the Innovation Center for Regenerative Medicine and Health at the Hong Kong Institute of Innovation under the Chinese Academy of Sciences, and The Chinese University of Hong Kong.

More information: Zhongfu Ying et al, The mitochondrial unfolded protein response inhibits pluripotency acquisition and mesenchymal-to-epithelial transition in somatic cell reprogramming, *Nature Metabolism* (2025). DOI: [10.1038/s42255-025-01261-6](https://doi.org/10.1038/s42255-025-01261-6)

Journal information: [Nature Metabolism](#)

APRIL 16, 2025

How local regulations helped create certainty and safety principles that enabled biotech's massive growth

by Peter Dizikes, [Massachusetts Institute of Technology](#)



MIT historian of science Robin Scheffler looks at the public discussions over safety and regulations that, once established, helped the biotechnology industry thrive in the Boston area. Credit: Emily Dahl; MIT News

It's considered a scientific landmark: A 1975 meeting at the Asilomar Conference Center in Pacific Grove, California, shaped a new safety regime for recombinant DNA, ensuring that researchers would apply caution to gene splicing. Those ideas have been so useful that in the decades since, when new topics in scientific safety arise, there are still calls for Asilomar-type conferences to craft good ground rules.

There's something missing from this narrative, though: It took more than the Asilomar conference to set today's standards. The Asilomar concepts were created with academic research in mind—but the biotechnology industry also makes products, and standards for that were formulated after Asilomar.

"The Asilomar meeting and Asilomar principles did not settle the question of the safety of genetic engineering," says MIT scholar Robin Scheffler, author of a newly published research paper on the subject.

Instead, as Scheffler documents in the paper, Asilomar helped generate further debate, but those industry principles were set down later in the 1970s—first in Cambridge, Massachusetts, where politicians and concerned citizens wanted local biotech firms to be good neighbors. In response, the city passed safety laws for the emerging industry. And rather than heading off to places with zero regulations, local firms—including a fledgling Biogen—stayed put. Over the decades, the Boston area became the world leader in biotech.

Why stay? In essence, regulations gave biotech firms the certainty they needed to grow—and build. Lenders and real-estate developers needed signals that long-term investment in labs and facilities made sense. Generally, as Scheffler notes, even though "the idea that regulations can be anchoring for business does not have a lot of pull" in economic theory, in this case, regulations did matter.

"The trajectory of the industry in Cambridge, including biotechnology companies deciding to accommodate regulation, is remarkable," says Scheffler. "It's hard to imagine the American [biotechnology industry](#) without this dense cluster in Boston and Cambridge. These things that happened on a very local scale had huge echoes."

Scheffler's article, "Asilomar Goes Underground: The Long Legacy of Recombinant DNA Hazard Debates for the Greater Boston Area Biotechnology Industry," is [published](#) in the latest issue of the *Journal of the History of Biology*. Scheffler is an associate professor in MIT's Program in Science, Technology, and Society.

Business: Banking on certainty

To be clear, the Asilomar conference of 1975 did produce real results. Asilomar led to a system that helped evaluate projects' potential risk and determine appropriate safety measures. The U.S. federal government subsequently adopted Asilomar-like principles for research it funded.

But in 1976, debate over the subject arose again in Cambridge, especially following a cover story in a local newspaper, the Boston Phoenix. Residents became concerned that recombinant DNA projects would lead to, hypothetically, new microorganisms that could damage [public health](#).

"Scientists had not considered urban public health," Scheffler says. "The Cambridge recombinant DNA debate in the 1970s made it a matter of what your neighbors think."

After several months of hearings, research, and public debate (sometimes involving MIT faculty) stretching into early 1977, Cambridge adopted a somewhat stricter framework than the federal government had proposed for the handling of materials used in recombinant DNA work.

"Asilomar took on a new life in local regulations," says Scheffler, whose research includes government archives, news accounts, industry records, and more.

But a funny thing happened after Cambridge passed its recombinant DNA rules: The nascent biotech industry took root, and other area towns passed their own versions of the Cambridge rules.

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"Not only did cities create more safety regulations," Scheffler observes, "but the people asking for them switched from being left-wing activists or populist mayors to the Massachusetts Biotechnology Council and real estate development concerns."

Indeed, he adds, "What's interesting is how quickly safety concerns about recombinant DNA evaporated. Many people against recombinant DNA came to change their thinking." And while some local residents continued to express concerns about the environmental impact of labs, "those are questions people ask when they no longer worry about the safety of the core work itself."

Unlike federal regulations, these local laws applied to not only lab research but also products, and as such they let firms know they could work in a stable business environment with regulatory certainty. That mattered financially, and in a specific way: It helped companies build the buildings they needed to produce the products they had invented.

"The [venture capital](#) cycle for biotechnology companies was very focused on the research and exciting intellectual ideas, but then you have the bricks and mortar," Scheffler says, referring to biotech production facilities. "The bricks and mortar is actually the harder problem for a lot of startup [biotechnology companies](#)."

After all, he notes, "Venture capital will throw money after big discoveries, but a banker issuing a construction loan has very different priorities and is much more sensitive to things like factory permits and access to sewers 10 years from now. That's why all these towns around Massachusetts passed regulations, as a way of assuring that."

To grow globally, act locally

Of course, one additional reason biotech firms decided to land in the Boston area was the [intellectual capital](#): With so many local universities, there was a lot of industry talent in the region. Local faculty co-founded some of the high-flying firms.

"The defining trait of the Cambridge-Boston biotechnology cluster is its density, right around the universities," Scheffler says. "That's a unique feature local regulations encouraged."

It's also the case, Scheffler notes, that some biotech firms did engage in venue-shopping to avoid regulations at first, although that was more the case in California, another state where

the industry emerged. Still, the Boston-area regulations seemed to assuage both industry and public worries about the subject.

The foundations of biotechnology regulation in Massachusetts contain some additional historical quirks, including the time in the late 1970s when the city of Cambridge mistakenly omitted the recombinant DNA safety rules from its annually published bylaws, meaning the regulations were inactive. Officials at Biogen sent them a reminder to restore the laws to the books.

Half a century on from Asilomar, its broad downstream effects are not just a set of research principles—but also, refracted through the Cambridge episode, key ideas about public discussion and input; reducing uncertainty for business, the particular financing needs of industries; the impact of local and regional regulation; and the openness of startups to recognizing what might help them thrive.

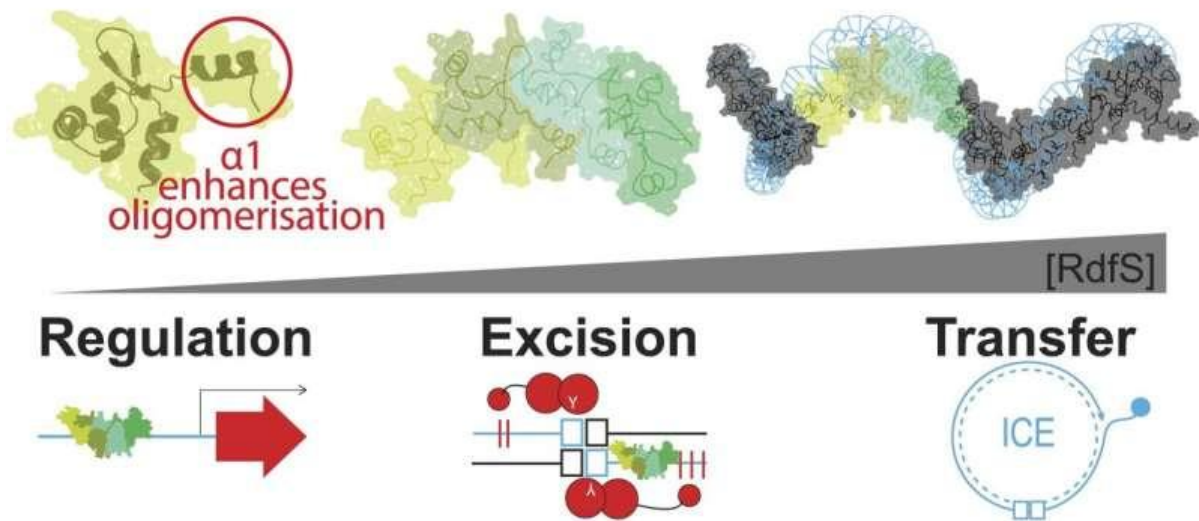
"It's a different way to think about the legacy of Asilomar," Scheffler says. "And it's a real contrast with what some people might expect from following scientists alone."

More information: Robin Wolfe Scheffler, Asilomar Goes Underground: The Long Legacy of Recombinant DNA Hazard Debates for the Greater Boston Area Biotechnology Industry, *Journal of the History of Biology* (2025). DOI: [10.1007/s10739-025-09806-x](https://doi.org/10.1007/s10739-025-09806-x)
Provided by [Massachusetts Institute of Technology](https://www.mit.edu/)

APRIL 16, 2025

New insights into protein-DNA interactions reveal cellular machinery secrets

by [University of Western Australia](#)



Credit: *Nucleic Acids Research* (2025). DOI: 10.1093/nar/gkaf249

New research pioneered by The University of Western Australia is shedding light on the intricate dance between proteins, DNA and RNA—the fundamental building blocks that carry out cellular processes and underpin all life, including plants, humans and bacteria.

Led by Professor Charlie Bond from UWA's School of Molecular Sciences, a team of scientists has contributed to three studies published in *Nucleic Acids Research*, showcasing unprecedented three-dimensional models of how [protein](#) molecular machines assemble on DNA or RNA.

"We've essentially been watching life's machinery in action at the molecular level," Professor Bond said.

"By visualizing how these complex structures assemble and function, we're opening doors to entirely new approaches in diagnostics and therapeutic interventions."

The [first study](#), helmed by postdoctoral research fellow at the University of Wollongong Nicholas Marzano and UWA researcher Brady Johnston, found that a family of tiny coiled molecules from plants, known as PPR proteins, function like microscopic springs, compressing when they bind to RNA molecules.

"This mechanism allows remarkable precision in molecular targeting within cells and points toward innovative RNA-based diagnostic tools, and potential interventions for genetic disorders or to introduce new traits into plants," Dr. Marzano said.

The [second study](#), under Ph.D. candidate Heidar Koning and ARC DECRA research fellow Andrew Marshall from UWA's School of Molecular Sciences, in partnership with researchers at Monash University and the University of Melbourne, showed how human proteins NONO and SFPQ form sophisticated complexes that orchestrate gene activity in the cell nucleus.

"These findings provide crucial insights for developing targeted approaches to regulate [gene expression](#) in both health and disease states," Koning said.

The [last study](#), undertaken by Curtin University Research Fellow Dr. Callum Verdonk, in collaboration with Professor Bond and Assistant Professor Josh Ramsay from Curtin University, revealed how a DNA-binding protein called RdfS forms helical structures or twisting forms that control the process of DNA transfer between agricultural bacteria.

"DNA is literally cut out of one bacterium's genome and transferred over to another with the help of RdfS protein," Dr. Verdonk said. "The bacteria can form a symbiosis with plants and are used as an environmentally friendly alternative to chemical fertilizer."

More information: Nicholas Marzano et al, Single-molecule visualization of sequence-specific RNA binding by a designer PPR protein, *Nucleic Acids Research* (2024). DOI: [10.1093/nar/gkae984](https://doi.org/10.1093/nar/gkae984)

Heidar J Koning et al, Structural plasticity of the coiled–coil interactions in human SFPQ, *Nucleic Acids Research* (2024). DOI: [10.1093/nar/gkae1198](https://doi.org/10.1093/nar/gkae1198)

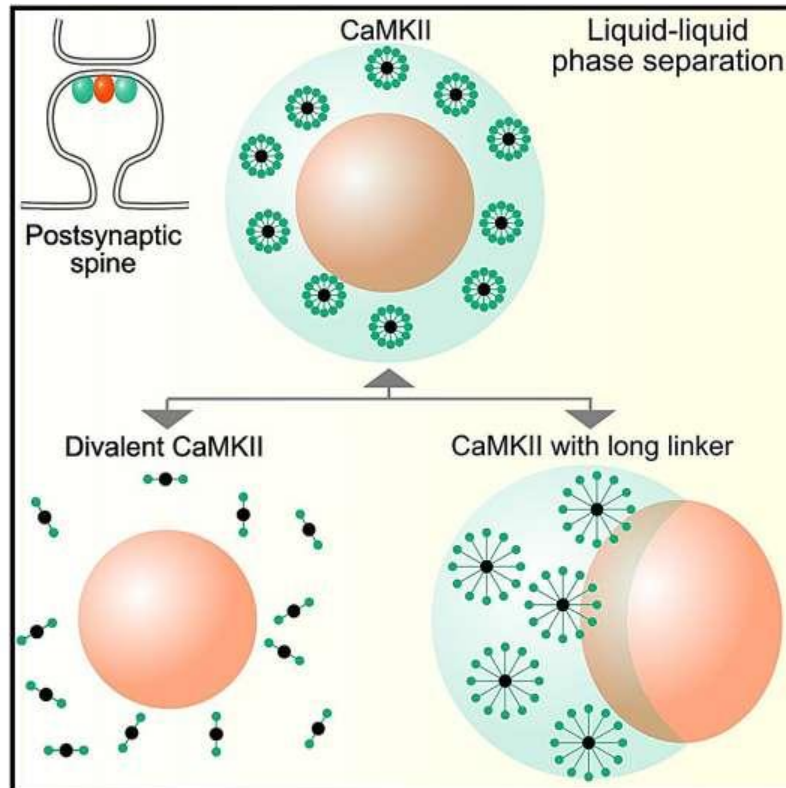
Callum J Verdonk et al, Structural basis for control of integrative and conjugative element excision and transfer by the oligomeric winged helix–turn–helix protein RdfS, *Nucleic Acids Research* (2025). DOI: [10.1093/nar/gkaf249](https://doi.org/10.1093/nar/gkaf249)

Journal information: [Nucleic Acids Research](#)
Provided by [University of Western Australia](#)

APRIL 16, 2025

Simulating protein structures involved in memory formation

by Fujita Health University



Computational models show that even subtle modifications in the synaptic protein CaMKII completely alter the resulting protein structures. Given how the formation and stability of these structures appear to be essential for memory, these findings could shed light on the nature of various neurological disorders. Credit: Dr. Vikas Pandey from Fujita Health University, Japan Image source link: <https://doi.org/10.1016/j.celrep.2025.115504>

Complex protein interactions at synapses are essential for memory formation in our brains, but the mechanisms behind these processes remain poorly understood. Now, researchers from Japan have developed a computational model revealing new insights into the unique droplet-inside-droplet structures that memory-related proteins form at synapses. They discovered that the shape characteristics of a memory-related protein are crucial for the formation of these structures, which could shed light on the nature of various neurological disorders.

Our brain's remarkable ability to form and store memories has long fascinated scientists, yet most of the microscopic mechanisms behind memory and learning processes remain a mystery. Recent research points to the importance of biochemical reactions occurring at

postsynaptic densities—specialized areas where neurons connect and communicate. These tiny junctions between [brain cells](#) are now thought to be crucial sites where proteins need to organize in specific ways to facilitate learning and memory formation.

More specifically, a [2021 study](#) revealed that memory-related proteins can bind together to form droplet-like structures at postsynaptic densities. What makes these structures particularly intriguing is their unique "droplet-inside-droplet" organization, which scientists believe may be fundamental to how our brains create lasting memories. However, understanding exactly how and why such complex protein arrangements form has remained a significant challenge in neuroscience.

Against this backdrop, a research team led by Researcher Vikas Pandey from the International Center for Brain Science (ICBS), Fujita Health University, Japan, has developed an innovative computational model that reproduces these intricate protein structures.

Their paper, published online in [Cell Reports](#) on April 7, 2025, explores the mechanisms behind the formation of multilayered protein condensates. The study was co-authored by Dr. Tomohisa Hosokawa and Dr. Yasunori Hayashi from the Department of Pharmacology, Kyoto University Graduate School of Medicine, and Dr. Hidetoshi Urakubo from ICBS, Fujita Health University.

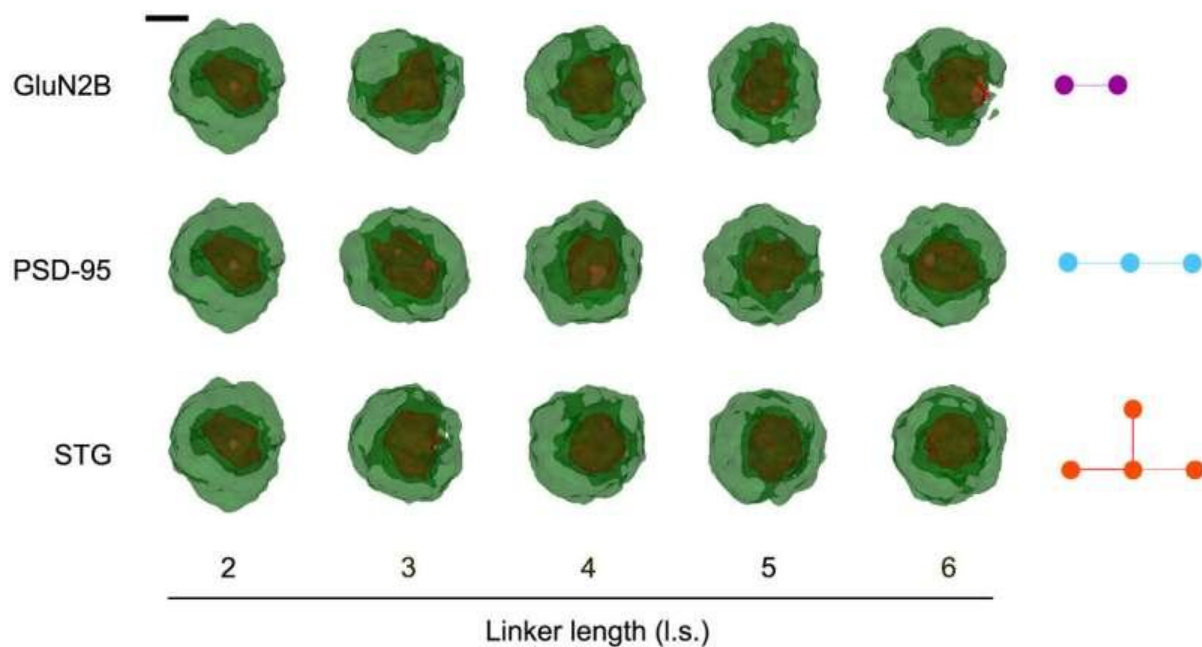
Activation of CaMKII results in PIP formation, related to Figure S1G. Credit: *Cell Reports* (2025). DOI: 10.1016/j.celrep.2025.115504

The researchers focused on four proteins found at synapses, with special attention to Ca²⁺/calmodulin-dependent protein kinase II (CaMKII)—a protein particularly abundant in postsynaptic densities. Using computational modeling techniques, they simulated how these proteins interact and organize themselves under various conditions. Their model successfully reproduced the formation of the above-mentioned "droplet-inside-droplet" structures observed in earlier experiments.

Through simulations and detailed analyses of the physical forces and chemical interactions involved, the research team shed light on a process called liquid-liquid phase separation (LLPS); it involves proteins spontaneously organizing into condensates without membranes that sometimes resemble the organelles found inside cells.

Crucially, the researchers found that the distinctive "droplet-inside-droplet" structure appears as a result of competitive binding between the proteins and is significantly influenced by the shape of CaMKII, specifically its high valency (number of binding sites) and short linker length.

These shape-related properties of CaMKII result in low surface tension and slow diffusion, allowing the protein condensates to remain stable for extended periods. This stability enables the sustained activation of downstream signaling pathways necessary for synaptic plasticity, which is the cellular basis for learning and memory.



PIP formation is independent of the linker length of GluN2B, PSD-95, and STG. Rendered shapes of CaMKII and STG phases were plotted if the linker length of GluN2B, PSD-95, or STG was changed between 2 and 6 l.s. Scale bar, 10 l.s. Credit: *Cell Reports* (2025). DOI: 10.1016/j.celrep.2025.115504

"Our results revealed new structure–function relationships for CaMKII as a synaptic memory unit. This is the first systematic and mechanistic study investigating the divergent structure of protein-regulated multiphase condensates," says Dr. Pandey.

These findings could pave the way toward a better understanding of the possible mechanisms of [memory formation](#) in humans. However, the long-term implications of this research extend well beyond basic neuroscience.

Defects in synapse formation have been associated with numerous neurological and mental health conditions, including schizophrenia, autism spectrum disorders, Down syndrome, and Rett syndrome.

"Overall, the [computational model](#) developed in this study could serve as an important platform for investigating these conditions, potentially leading to new diagnostic tools and therapeutic approaches," explains Dr. Pandey.

More information: Vikas Pandey et al, Multiphasic protein condensation governed by shape and valency, *Cell Reports* (2025). DOI: [10.1016/j.celrep.2025.115504](https://doi.org/10.1016/j.celrep.2025.115504)

Journal information: [Cell Reports](#)
 Provided by [Fujita Health University](#)

APRIL 16, 2025

How glycolysis drives early embryonic cell decisions

by [Max Planck Society](#)

The illustration portrays an early gastruloid resembling Pac-Man, navigating through a maze that spells out "GLYCOLYSIS," eventually facing a road bifurcation with paths leading to success or failure. On its way, the gastruloid-PacMan needs to avoid the ghosts in the form of the complexes I-IV of the electron transport chain. To be successful, the gastruloid-Pac-Man needs to avoid the ghosts while consuming all the sugar (dots), thus illustrating the path gastruloids need to follow to reach an embryo-like state. Credit: Alba Villaronga-Luque, Ryan G Savill et. al / MPI-CBG

Glycolysis is an ancient metabolic activity. It consists of a set of reactions that convert glucose into energy. This central process allows cells to grow, divide, and stay alive. It has accompanied life since its origin, from single cells to complex organisms like mammals.

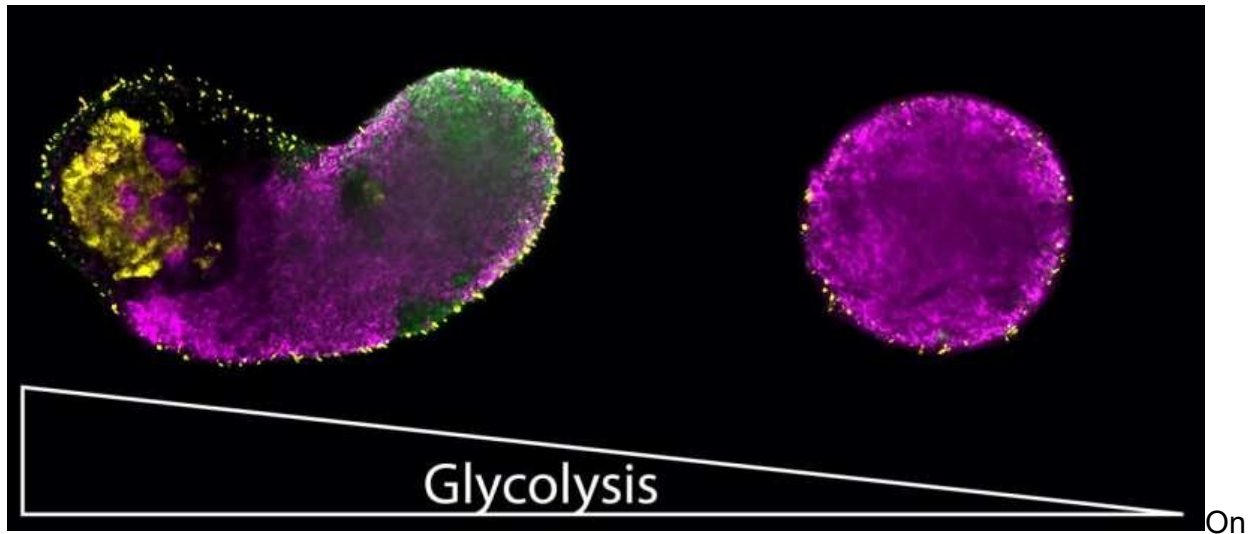
Scientists have extensively studied the role of metabolism in individual cells to understand how it influences their energetic state, but little has been studied about the effect of glycolysis on the decisions that cells or groups of cells make.

Now, researchers at EMBL Barcelona, Spain, and at the Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG) in Dresden, Germany, have uncovered the instructive potential of glycolysis. They show that rather than exclusively providing energy to the cell, glycolysis is able to control, at different stages of early embryonic development, cell fate decisions and the end-state appearance of stem cell-based embryo models.

In two back-to-back publications in the journal *Cell Stem Cell*, researchers from the groups of Vikas Trivedi at EMBL Barcelona and Jesse Veenvliet at the MPI-CBG have used gastruloids and trunk-like structures, in vitro stem cell-based embryo models composed of mouse [embryonic stem cells](#), to study the early steps in the formation of the body plan—a process that lays the foundation for future organ development.

Kristina Stapornwongkul, postdoc in the Trivedi group and incoming group leader at the Institute of Molecular Biotechnology (IMBA) in Vienna, Austria, [studied](#) the role of glycolysis by changing the glucose concentration in the media where cells live and feed.

Alba Villaronga-Luque and Ryan Savill, both doctoral students in the Veenvliet group, [studied](#) why some trunk-like structures look more like the natural embryo than others by using machine learning to integrate imaging data with profiles of active genes and metabolites over time and found a critical role for glycolysis.



On the left: Glycolysis allows stem cell-based embryo-like models to develop the three germ layers that give rise to many different cell types: ectoderm (magenta), mesoderm (green) and endoderm (yellow). On the right: If glycolysis is inhibited, only ectodermal cells can develop. Credit: Kristina Stapornwongkul

Stapornwongkul realized that blocking glycolysis disrupted the formation of two important tissue types: mesoderm—which later develops into muscles, bones, or blood—and endoderm—which gives rise to organs like the liver or the lungs.

Instead, more cells decided to turn into ectoderm tissue, the type that eventually gives rise to our nervous system.

This study shows that glycolysis helps activate key signaling pathways (Wnt, Nodal, and Fgf) that guide cells towards mesoderm and endoderm fates. When glycolysis was blocked, the signals weakened and cells developed into ectoderm cells. However, when these signals were artificially boosted, normal cell fate decisions were restored, even without glycolysis taking place.

This highlights the crucial role of metabolism as an upstream regulator/activator of specific signaling pathways that influence cellular decisions. Being able to control cell fate through altering media composition means that one could also direct cell differentiation towards the tissue type one is interested in.

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"What was most surprising to me was this clear dual role of glycolysis: its bioenergetic function is important for growth and its signaling function crucial for cell fate decisions. When we inhibited glycolysis, we clearly saw the loss of the endoderm and mesoderm, but we were able to rescue these cell types by activating the signaling pathways, even in the absence of glycolysis, meaning without restoring growth," Stapornwongkul said.

"This shows that we can decouple glycolysis's bioenergetic role from its role as an upstream signaling regulator, underlining the existence of two distinct functions during early development."

"The exciting thing about Kristina's work is the hierarchical relationship between metabolism and signaling, at least in the earliest stages of organismal development. This result contributes to an emerging perspective on the relationship between metabolism and patterning, a subject of interest to other labs within EMBL and beyond," Trivedi said.

"From an evolutionary perspective, this is exciting because metabolism predates signaling: even single-cell organisms rely on metabolism, while signaling emerged later in evolution. This has sparked my curiosity about the role of metabolism in the origin of multicellularity. This study marks the beginning of an exciting new direction for my group."

Villaronga-Luque and Savill found that early changes in metabolism cause differences in the end-state appearance of trunk-like structures, a stem-cell-based model of embryonic trunk development that forms the tissues giving rise to the spine (mesoderm) and the spinal cord (ectoderm).

These structures make it possible to study mammalian embryo development, which is otherwise hidden in the uterus of the mothers, in large numbers of samples without the need for animal experiments. Although many characteristics of these stem cell-based embryo models are similar to those of an embryo, they are unable to develop into fully functional organisms.

A major hurdle for their widespread use is that they are much more variable than the embryo: even when grown under identical conditions, some stem cell clumps develop into structures very similar to the embryo, whereas others don't. Such variability makes it harder to use them for research purposes that require a highly reproducible baseline, such as disease modeling or toxicity studies.

Villaronga-Luque and Savill observed that, specifically, the balance between two different processes that produce energy—glycolysis and oxidative phosphorylation—affects the variability of the stem cell-based embryo models. With glycolysis, cells make energy by breaking down glucose.

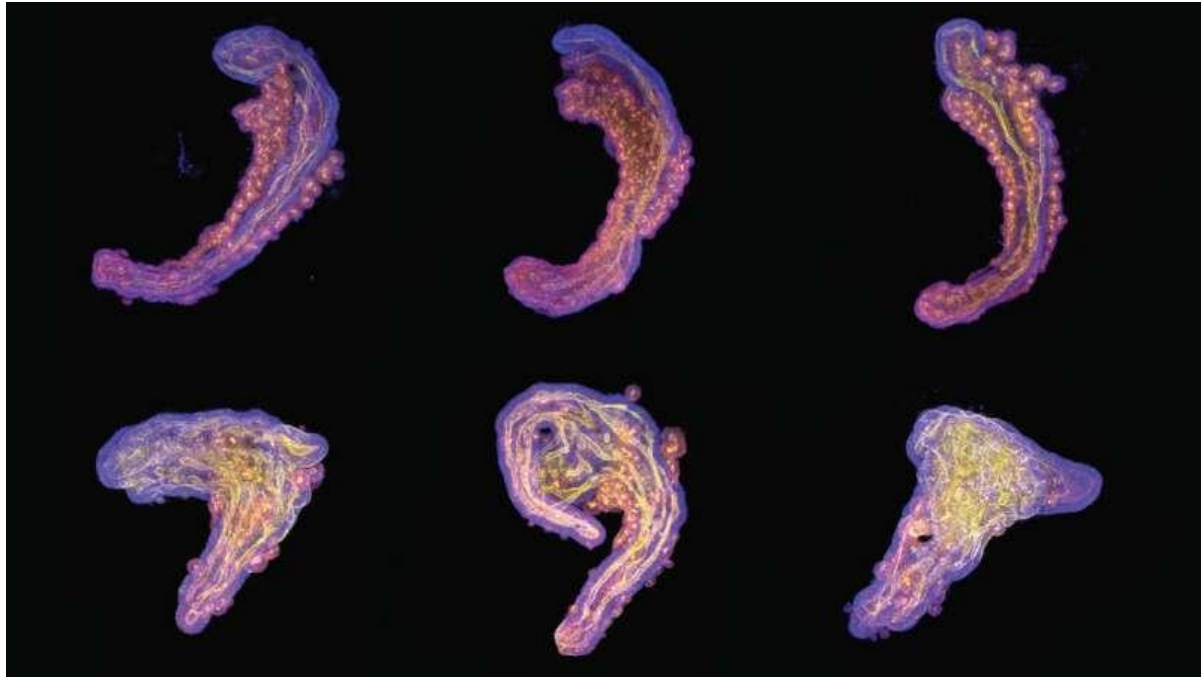
The trunk-like structures with a sort of "sweet tooth," depending more on glycolysis to obtain their energy by breaking down sugar, develop the most similarly to an embryo, whereas the ones that lacked the "sweet tooth" mostly formed ectoderm.

Like Stapornwongkul, they found that glycolysis activates signaling pathways like Wnt that influence cellular decisions and, eventually, how much the structures resemble the embryo. Finally, they showed that boosting glycolysis with drugs improved the appearance of the trunk-like structures.

"To uncover the reason for this variability in stem cell-based embryo models, you need to have measures early in the development to see what goes wrong. However, such measurements typically destroy the sample, such that we don't know if it will develop into a

successful structure or not. This is the challenge we were able to tackle," Villaronga-Luque said.

"By combining quantitative imaging analysis with machine learning, we found key characteristics of the structures that can predict how their development will turn out. With this predictive power in hand, we could then investigate the expression profiles of structures for which the end state would otherwise be unknown," said Savill.



Collage of stem-cell-based embryo models of the embryonic trunk. Those in the upper row have a 'sweet tooth', depending more on glycolysis to obtain their energy and resulting in a more embryo-like appearance. In contrast, those in the bottom row have less of a 'sweet tooth', which results in them producing too much neural tissue, and looking less like an embryonic trunk. Credit: Alba Villaronga-Luque, Ryan G Savill et. al / MPI-CBG

"By being able to predict the future appearance of a stem cell-based embryo model, our team could show that the early metabolic state controls how much the model looks like the embryo, which can be regulated by altering the metabolic activity with drugs," Veenvliet said.

"Such predictive power for stem cell-based embryo models and also other types of organoids has the potential not only to help to make new fundamental biological discoveries but also to improve stem cell-based embryo models for applications that require high reproducibility, including disease modeling, genetic screens, and toxicity studies."

These studies mark the beginning of a new paradigm for developmental and tissue biology. It brings metabolism to the spotlight for studying the early stages of development, giving the research community a new tool to study early cell decisions and embryo development.

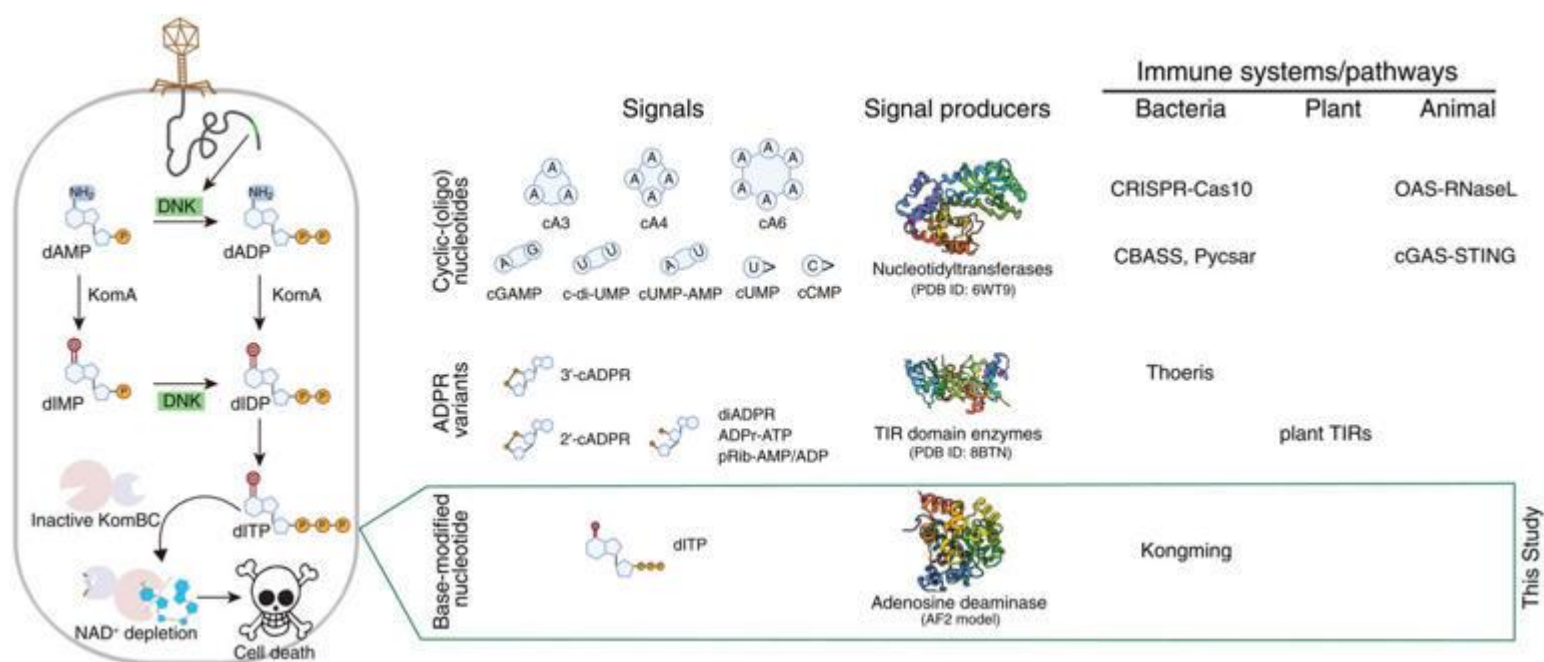
Excitingly, the two studies show that at different stages of embryogenesis, [glycolysis](#) acts through a similar mechanism to ensure proper development of the body plan.

More information: Kristina S. Stapornwongkul, et al, Glycolytic activity instructs germ layer proportions through regulation of Nodal and Wnt signalling, *Cell Stem Cell* (2025). DOI: [10.1016/j.stem.2025.03.011](https://doi.org/10.1016/j.stem.2025.03.011). [www.cell.com/cell-stem-cell/fulltext/S1364-5909\(25\)00101-8](https://www.cell.com/cell-stem-cell/fulltext/S1364-5909(25)00101-8)

Alba Villaronga-Luque, et al. Integrated molecular-phenotypic profiling reveals metabolic control of morphological variation in a stem-cell-based embryo model, *Cell Stem Cell* (2025). DOI: [10.1016/j.stem.2025.03.012](https://doi.org/10.1016/j.stem.2025.03.012). [www.cell.com/cell-stem-cell/fulltext/S1364-5909\(25\)00102-X](https://www.cell.com/cell-stem-cell/fulltext/S1364-5909(25)00102-X)

Journal information: *Cell Stem Cell*
 Provided by [Max Planck Society](https://www.mpsociety.org)

Bacteria use ancient war trick to outsmart viruses—and it could help us fight superbugs



Mechanism of a nucleobase-modified nucleotide immune signaling in bacteria.

Scientists have discovered a new type of immune defense in *E. coli* bacteria that turns viral infection machinery against the virus itself. Named after the Chinese military strategist Kongming—who famously used enemy weapons to defeat them—the system reveals a novel immune signaling pathway. This discovery could inform the development of future biotech tools and phage therapy as an alternative to antibiotics.

More than 1,800 years ago in China, legendary military strategist Zhuge Liang, known as Kongming, faced a superior force. But instead of making his own weapons, he had the enemy deliver them to him. Using empty boats covered in straw, he tricked the enemy into firing thousands of arrows at the boats. After the battle, his army collected the arrows and used them themselves.

Now, new research co-led by the University of Copenhagen, Denmark, and Huazhong Agricultural University in China, shows that bacteria have developed a similar defense strategy in their fight against viral attacks.

The newly discovered immune system, which the researchers have dubbed Kongming, allows an attacking virus to bring about its own defeat. When a virus infects the bacteria, Kongming uses one of the virus' own enzymes to activate a deadly defense that stops the infection.

"We've discovered a new antiviral signaling pathway in bacteria that, ironically, relies on a viral enzyme to produce the alarm signal that triggers defense—just like the historical Kongming, who used the production of enemy's own arrows against them, explains Assistant Professor Rafael Pinilla-Redondo from the Department of Biology at the University of Copenhagen, who is one of the researchers leading the study.

The researchers discovered the Kongming defense system in *E. coli*, a bacterium which is commonly found in our intestines. However, they identified variants of the Kongming system across diverse bacteria in the environment, indicating that this antiviral strategy is widespread. The research was just [published](#) in the journal *Science*.

Stops viruses from spreading

When a virus attacks bacteria, it needs to copy its own genetic material in order to spread quickly. To do this, some viruses use specialized enzymes called nucleotide kinases, which help to rapidly produce the building blocks required for the genetic information to be replicated.

Kongming defense hijacks the enzyme to make something completely different—an immune signal molecule that instead triggers a defense against the virus. This signal causes the bacterium to commit suicide, which stops the virus.

"The bacterium sacrifices itself to stop the virus—which may sound dramatic, but it's an incredibly effective strategy. By dying, it takes the virus down with it, preventing the infection from spreading to other bacteria in the population. It's a bit like blowing up a bridge to stop an advancing enemy," explains Rafael Pinilla-Redondo.

But are viruses defenseless against this strategy? Not at all—some have evolved countermeasures in the ongoing arms race with Kongming.

"Some viruses have figured out how to get around Kongming," says Ruiliang Zhao, one of the co-first authors of this work and a Ph.D. student at Copenhagen university. "They carry special enzymes that break down the molecules needed to trigger the system. It's their way of cutting off the cables of the alarm before it goes off."

More than just a fascinating biological mechanism

Bacterial infections have challenged humanity since the dawn of time, and antibiotics have long been our main line of defense. But in recent decades, the rise of antibiotic-resistant bacteria, mainly due to antibiotic overuse, has become a major global health concern.

One promising alternative is phage therapy—the use of viruses that specifically infect and kill unwanted bacteria. But bacteria aren't defenseless; they've evolved a wide arsenal of antiviral strategies, including systems like Kongming, that can block phage infection.

"To develop effective phage therapies, we need to understand the natural immune systems bacteria use to resist viral attacks," says Rafael Pinilla-Redondo. "By characterizing defenses like Kongming—and the tricks phages used to bypass them—we can better design phage therapy strategies and improve their clinical success."

Furthermore, the molecular machinery driving Kongming may also be harnessed for future biotechnological applications. The signaling molecule that specifically activates the system—dITP—has also been linked to human diseases, including

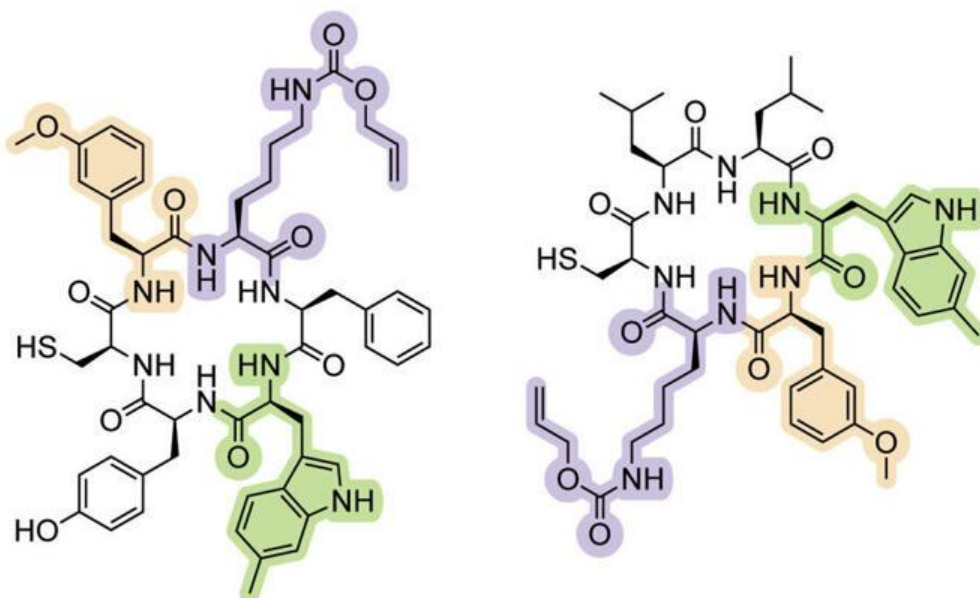
cancer. Because Kongming's immune effector complex is highly specific to this molecule, it may inspire new tools in synthetic biology and diagnostics.

"Since the Kongming immune effector complex specifically responds to dITP, it could be used to detect this non-canonical nucleotide—opening the door to interesting biotechnological applications," concludes Zhao.

More information: Zhifeng Zeng et al, Base-modified nucleotides mediate immune signaling in bacteria, *Science* (2025). DOI: [10.1126/science.ads6055](https://doi.org/10.1126/science.ads6055)

Provided by University of Copenhagen

Scientists expand the genetic alphabet to create new proteins



Examples of the >100 macrocycles generated in this study. Colored components represent new-to-nature amino acids that were incorporated into either peptide. Credit: Scripps Research

It's a dogma taught in every introductory biology class: Proteins are composed of combinations of 20 different amino acids, arranged into diverse sequences like words. But researchers trying to engineer biologic molecules with new functions have long felt limited by those 20 basic building blocks and strived to develop

ways of putting new building blocks—called non-canonical amino acids—into their proteins.

Now, scientists at Scripps Research have designed a new paradigm for easily adding non-canonical amino acids to proteins. Their approach, described in [Nature Biotechnology](#) on September 11, 2024, revolves around using four RNA nucleotides—rather than the typical three—to encode each new amino acid.

"Our goal is to develop proteins with tailored functions for applications in fields spanning bioengineering to drug discovery," says senior author Ahmed Badran, Ph.D., an assistant professor of chemistry at Scripps Research. "Being able to incorporate non-canonical amino acids into proteins with this new method gets us closer to that goal."

For a cell to produce any given protein, it must translate a strand of RNA into a string of amino acids. Every three nucleotides of RNA, called a codon, correspond to one amino acid. But many amino acids have more than one possible codon; for instance, RNA reading the sequences UAU and UAC both correspond to the amino acid tyrosine. It's the job of small molecules called transfer RNAs (tRNAs) to link each amino acid to its corresponding codons.

Recently, researchers aiming to add completely new amino acids to a protein have created strategies to reassign a codon. For instance, the UAU codon could be linked to a new amino acid by changing the tRNA for UAU; this would result in UAU being read by the cell as corresponding to a building block other than tyrosine. But at the same time, every instance of UAU in the cell's genome would need to become UAC, in order to prevent the new amino acid from being integrated into thousands of other proteins where it doesn't belong.

"Creating free codons by whole genome recoding can be a powerful strategy, but it can also be a challenging undertaking since it requires considerable resources to build new genomes," says Badran. "For the organism itself, it can be difficult to predict how such codon changes influence genome stability and host protein production."

Badran and his colleagues wanted to create an efficient plug-and-play strategy that would only incorporate the chosen non-canonical amino acid(s) into specific sites in a target protein, without disrupting the cell's normal biology or requiring

the entire genome to be edited. That meant using tRNA that wasn't already assigned to an amino acid. Their solution: a four-nucleotide codon.

The team knew that in a few situations—such as bacteria quickly adapting to resist drugs—four-nucleotide codons had naturally evolved. So, in their new work, the researchers studied what caused cells to use a codon with four nucleotides rather than three. They discovered that the identities of the sequences nearby to the four-base codon were critical—frequently used codons enhanced how the cell could read a four-nucleotide codon to incorporate a non-canonical amino acid.

Badran's group then tested whether they could alter the sequence of a single gene so that it had a new four-nucleotide codon that would be correctly used by the cell.

The method worked: When the researchers surrounded a target site with three-letter, frequently used codons and maintained sufficient levels of the four-nucleotide tRNA, the cell incorporated any new amino acid that was attached to the corresponding four-letter tRNA. The research team repeated the experiment with 12 different four-nucleotide codons and then used the technique to design more than 100 new cyclic peptides—called macrocycles—with up to three non-canonical amino acids in each.

"These cyclic peptides are reminiscent of bioactive small molecules that one might find in nature," says Badran. "By capitalizing on the programmability of protein synthesis and the diversity of building blocks accessible by this approach, we can create new-to-nature small molecules that will have exciting applications in drug discovery."

He adds that, compared with previous approaches to non-canonical amino acid incorporation, this new method is easy to use since it involves altering only one gene rather than a cell's entire genome. Additionally, more non-canonical amino acids could be used in a single protein since there are more possible four-nucleotide codons than three-nucleotide ones.

"Our results suggest that one can now easily and effectively incorporate non-canonical amino acids at diverse sites in a wide array of proteins," says Badran. "We're excited about these possibilities for our ongoing work and to provide this capability to the broader community."

He notes that the technique could be used to re-engineer existing proteins—or create entirely new ones—that have utility in a range of sectors, including medicine, manufacturing and chemical sensing.

In addition to Badran, authors of the study, "Efficient Genetic Code Expansion Without Host Genome Modifications," are Alan Costello, Alexander Peterson, David Lanster and Zhiyi Li of Scripps; and Gavriela Carver of Princeton University.

More information: Alan Costello et al, Efficient genetic code expansion without host genome modifications, *Nature Biotechnology* (2024). DOI: [10.1038/s41587-024-02385-y](https://doi.org/10.1038/s41587-024-02385-y)

Provided by The Scripps Research Institute

APRIL 24, 2025

Can technology transform health science? The promise of exposomics

by Tim Paul , [Columbia University's Mailman School of Public Health](#)



Credit: Pixabay/CC0 Public Domain

Every breath we take, every meal we eat, and every environment we encounter leaves a molecular fingerprint in our bodies—a hidden record of our lifelong exposures. In this [week's edition](#) of the journal *Science*, leading researchers in the field of exposomics explain how cutting-edge technologies are unlocking this biological archive, ushering in a new era of disease prevention and personalized medicine. The scientists lay out a roadmap to overcome technical and logistical challenges and realize the field's full potential.

Exposomics explores how the complex interplay of environmental factors—from pollutants in our water and food to social and psychological stressors—shapes our biology. By studying these combined exposures, researchers can uncover how they collectively influence health, from metabolism and heart function to brain health and disease risk.

The Perspectives article is led by the Banbury Exposomics Consortium—an interdisciplinary group of scientists who gathered at Cold Spring Harbor's Banbury Center in 2023 to define

the core principles of this rapidly evolving field. Gary Miller, Ph.D., a foremost expert in exposomics and faculty member at Columbia University Mailman School of Public Health, was the lead organizer of the Consortium.

Exposomics in action

The young field is already proving its transformative potential. Researchers analyzing molecular evidence identified a specific industrial solvent as the culprit behind kidney disease clusters among factory workers. In another study, scientists merged satellite pollution mapping with residential location information to reveal how airborne particulates prematurely age the brain. Scientists analyzing thousands of circulating molecules pinpointed TMAO, a gut microbiome metabolite produced when eating red meat and dairy, as a previously overlooked major contributor to heart attack risk.

These discoveries are made possible by cutting-edge technologies and tools such as wearable sensors that track chemical exposures in real-time, [satellite imagery](#) that maps pollution down to city blocks, and ultra-sensitive mass spectrometers that detect compounds present at just one part per trillion.

A wider lens on our health

While genetics provides our biological blueprint, it explains only a fraction of chronic disease risk. The exposome captures everything that happens to us, from industrial chemicals to social stressors. Unlike traditional studies examining single exposures in isolation, exposomics integrates advanced tools to understand how environmental, social, and psychological factors collectively interact with our biology.

This approach synergizes powerfully with other "omics" sciences. When combined with genomics, proteomics, and metabolomics, exposomics creates the first complete picture of health determinants. The authors envision a future where all major disease studies incorporate exposome analysis as standard practice.

Systematically analyzing these complex interactions can improve [drug development](#), uncover hidden drivers of disease, and address health disparities. The approach bridges precision medicine and population health.

The way forward

Miller and colleagues outline critical priorities for advancing exposomics. These include the development of more sensitive technologies, such as wearable or minimally invasive tools that measure an individual's exposome; the creation of a human exposome reference to enable analysis and contextualization at the population scale; and the implementation of standardized protocols to enable AI-driven analysis of complex datasets. The field must also address ethical considerations around data privacy and the need for greater focus on the social determinants of health, the authors write.

Newly launched U.S. and European exposomics hubs now provide the infrastructure for worldwide collaboration, standardizing methods, harmonizing data, and training researchers in the cross-disciplinary skills needed to advance this field. These centers form the critical backbone for the future progress of exposomics.

"We're now building the first systematic framework to measure how all exposures—from chemical to social—interact with biology across the lifespan. Our goal is to create actionable strategies for healthier lives," says Miller.

More information: Gary W. Miller et al, Integrating exposomics into biomedicine, *Science* (2025). DOI: [10.1126/science.adr0544](https://doi.org/10.1126/science.adr0544)

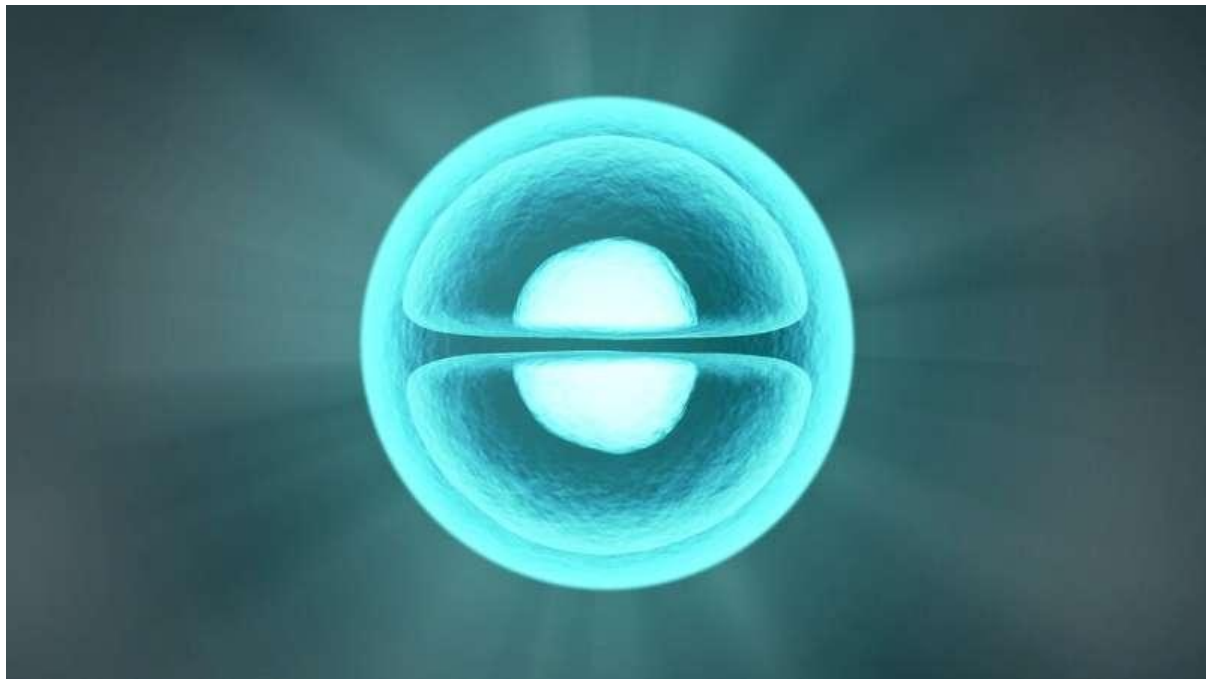
Journal information: [Science](#)

Provided by [Columbia University's Mailman School of Public Health](#)

APRIL 25, 2025

Super stem cells become better versions of themselves by changing their diet

by [University of Copenhagen](#)



Credit: Pixabay/CC0 Public Domain

In a new study, researchers from the University of Copenhagen have successfully created stem cells that are better at developing into other cell types, like a younger, fitter version of themselves—by changing their diet. These stem cells are better than normal stem cells at creating specialized cells like liver, skin or nerve cells, which is a core trait of stem cells.

The study, "[Altering metabolism programs cell identity via NAD⁺-dependent deacetylation](#)" has been published in *The EMBO Journal*.

"We show that by changing their diet, the stem cells can rejuvenate and turn into 'super stem cells.' It forces them to metabolize their energy in a different way than they normally would, and that process essentially reprograms the stem cells," says first author Robert Bone, Assistant Professor at the Novo Nordisk Foundation Center for Stem Cell Medicine, also known as reNEW.

"The net result is that they behave like they are from an earlier stage of development, which enhances their ability to develop, or differentiate, into other types of cells."

Specifically, the researchers changed what type of sugar the stem cells have available in the medium they grow in. The cells use the sugar to generate energy.

"What is really striking is that they're not just better at differentiating, but they stay fit and keep healthy much better over time compared to stem cells in standard culture conditions. And it is done with a relatively simple method," says corresponding author Joshua Brickman, Professor at reNEW.

Could improve fertility treatment

"There are many potential future usages of 'super stem cells,'" Joshua Brickman points out.

"Given that we now have a simple means to rejuvenate cells, we want to investigate how this trick could work on a variety of cell types. For example, can we use this diet to revitalize liver or heart cells and use them to treat patients with [congestive heart failure](#) or liver cirrhosis? Perhaps we could use this trick to regenerate aging cells and treat diseases such as Parkinson's disease, osteoporosis or diabetes."

One area the researchers are interested in is fertility treatment, specifically IVF. It turns out that the "super stem cells" are good at producing a certain type of tissue that forms during early embryonic development and which is important for successful IVF treatment.

"One of the things that the 'super stem cells' seem to be better at making is a cell lineage that becomes something called the yolk sac. Previous research has found that the formation of a yolk sac in embryos cultured in a dish is very important for their ability to implant and become successful pregnancies," says Robert Bone.

"We hope to improve IVF technology by developing a culture for IVF that uses the same metabolic process. Hopefully, it can be used as part of the embryo culture regime that they use in the clinic to improve success rates of implantation," Joshua Brickman adds.

Stem cells

Stem cells are fundamental and unique cells in our bodies that can replicate themselves and evolve into other, specialized cell types like liver, skin or nerve cells in a process known

as differentiation. Embryonic stem cells (ESCs) are grown from an embryo and maintained in a dish. These cells can be developed into specialized cell types in a dish.

In the future, researchers believe that stem cells can be used to develop new treatments that replace or repair damaged tissues and organs or to restore functions that have been lost due to diseases or damages. This is known as regenerative medicine.

The method

In this study, researchers have created a new culture medium for [embryonic stem cells](#) (ESCs) from mice. Simply put, they replaced a type of sugar in the culture known as glucose with a different sugar, galactose. This change of "diet" blocks normal glucose metabolism and restricts the cells' source of energy to a metabolic process known as oxidative phosphorylation.

By changing their nutrient source, the ESCs are reprogrammed into an earlier stage of development which enhances their ability to differentiate into other types of cells.

The researchers found that a specific signaling protein known to regulate aging in cells was activated by the change in sugar metabolism. This in turn made other key proteins bind to DNA better.

The net result of the new metabolic process is that the DNA is more densely "packed" in areas with redundant genetic information and not in areas with important, relevant instructions. This both turns down the volume of irrelevant information and amplifies the directly relevant information.

This improved "signal-to-[noise ratio](#)" causes the stem cells to have a better understanding of what they should do and behave like they are from an earlier developmental stage, performing better as stem cells.

A deterioration of the "signal-to-noise ratio" is also behind certain features of aging, the researchers found: It is almost like taking your grandparents to a crowded restaurant, and they can't hear for two reasons: you aren't speaking loudly enough, and they can't filter out the [background noise](#). Aging [stem cells](#) may have the same problem listening to their own genomes.

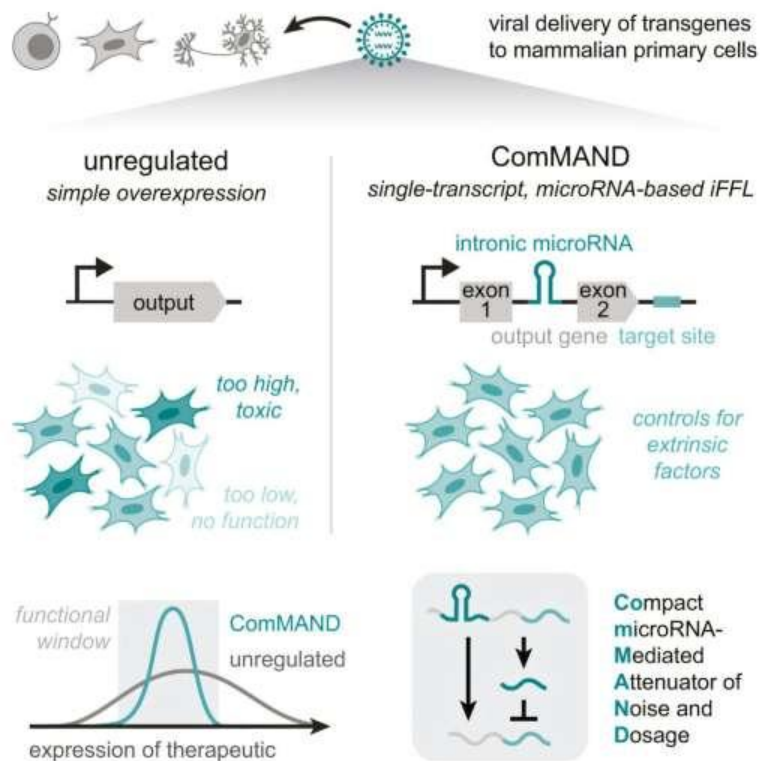
More information: Altering metabolism programs cell identity via NAD⁺-dependent deacetylation, *The EMBO Journal* (2025). DOI: [10.1038/s44318-025-00417-0](https://doi.org/10.1038/s44318-025-00417-0)

Journal information: [EMBO Journal](#)
Provided by [University of Copenhagen](#)

APRIL 28, 2025

Compact gene circuit uses microRNA to fine-tune therapy for rare diseases

by Anne Trafton, [Massachusetts Institute of Technology](#)



Credit: *Cell Systems* (2025). DOI: 10.1016/j.cels.2025.101269

Many diseases are caused by a missing or defective copy of a single gene. For decades, scientists have been working on gene therapy treatments that could cure such diseases by delivering a new copy of the missing genes to the affected cells.

Despite those efforts, very few [gene therapy treatments](#) have been approved by the FDA. One of the challenges to developing these treatments has been achieving control over how much the new gene is expressed in cells—too little and it won't succeed, too much and it could cause serious side effects.

To help achieve more precise control of gene therapy, MIT engineers have tuned and applied a control circuit that can keep [expression levels](#) within a target range. In [human cells](#), they showed that they could use this method to deliver genes that could help treat diseases including Fragile X syndrome, a disorder that leads to intellectual disability and other developmental problems.

"In theory, gene supplementation can solve monogenic disorders that are very diverse but have a relatively straightforward gene therapy fix if you could control the therapy well enough," says Katie Galloway, the W. M. Keck Career Development Professor in Biomedical Engineering and Chemical Engineering and the senior author of the new study.

MIT graduate student Kasey Love is the lead author of the paper, which is [published](#) in *Cell Systems*. Other authors of the paper include MIT graduate students Christopher Johnstone, Emma Peterman, and Stephanie Gaglione, and Michael Birnbaum, an associate professor of biological engineering at MIT.

Delivering genes

While gene therapy holds promise for treating a variety of diseases, including hemophilia and [sickle cell anemia](#), only a handful of treatments have been approved so far, for an inherited retinal disease and certain blood cancers.

Most gene therapy approaches use a virus to deliver a new copy of a gene, which is then integrated into the DNA of host cells. Some cells may take up many copies of the gene, while others don't receive any.

"Simple overexpression of that payload can result in a really wide range of expression levels in the target genes as they take up different numbers of copies of those genes or just have different expression levels," Love says. "If it's not expressing enough, that defeats the purpose of the therapy. But on the other hand, expressing at too high levels is also a problem, as that payload can be toxic."

To try to overcome this, scientists have experimented with different types of control circuits that constrain expression of the therapeutic gene. In this study, the MIT team decided to use a type of circuit called an incoherent feedforward loop (IFFL).

In an IFFL circuit, activation of the target gene simultaneously activates production of a molecule that suppresses gene expression. One type of molecule that can be used to achieve that suppression is microRNA—a short RNA sequence that binds to messenger RNA, preventing it from being translated into protein.

In this study, the MIT team designed an IFFL circuit, called "ComMAND" (Compact microRNA-mediated attenuator of noise and dosage), so that a microRNA strand that represses mRNA translation is encoded within the therapeutic gene. The microRNA is located within a short segment called an intron, which gets spliced out of the gene when it is transcribed into mRNA. This means that whenever the gene is turned on, both the mRNA and the microRNA that represses it are produced in roughly equal amounts.

This approach allows the researchers to control the entire ComMAND circuit with just one promoter—the DNA site where gene transcription is turned on. By swapping in promoters of different strengths, the researchers can tailor how much of the therapeutic gene will be produced.

In addition to offering tighter control, the circuit's compact design allows it to be carried on a single delivery vehicle, such as a lentivirus or adeno-associated virus, which could improve the manufacturability of these therapies. Both of those viruses are frequently used to deliver therapeutic cargoes.

"Other people have developed microRNA based incoherent feed forward loops, but what Kasey has done is put it all on a single transcript, and she showed that this gives the best possible control when you have variable delivery to cells," Galloway says.

Precise control

To demonstrate this system, the researchers designed ComMAND circuits that could deliver the gene FXN, which is mutated in Friedreich's ataxia—a disorder that affects the heart and nervous system. They also delivered the gene Fmr1, whose dysfunction causes Fragile X syndrome. In tests in human cells, they showed that they could tune gene expression levels to about eight times the levels normally seen in healthy cells.

Without ComMAND, gene expression was more than 50 times the normal level, which could pose safety risks. Further tests in animal models would be needed to determine the optimal levels, the researchers say.

The researchers also performed tests in rat neurons, mouse fibroblasts, and human T-cells. For those cells, they delivered a gene that encodes a fluorescent protein, so they could easily measure the gene expression levels. In those cells, too, the researchers found that they could control gene expression levels more precisely than without the circuit.

The researchers now plan to study whether they could use this approach to deliver genes at a level that would restore normal function and reverse signs of disease, either in cultured cells or animal models.

"There's probably some tuning that would need to be done to the expression levels, but we understand some of those [design principles](#), so if we needed to tune the levels up or down, I think we'd know potentially how to go about that," Love says.

Other diseases that this approach could be applied to include Rett syndrome, [muscular dystrophy](#) and spinal muscular atrophy, the researchers say.

"The challenge with a lot of those is they're also rare diseases, so you don't have large patient populations," Galloway says. "We're trying to build out these tools that are robust so people can figure out how to do the tuning, because the patient populations are so small and there isn't a lot of funding for solving some of these disorders."

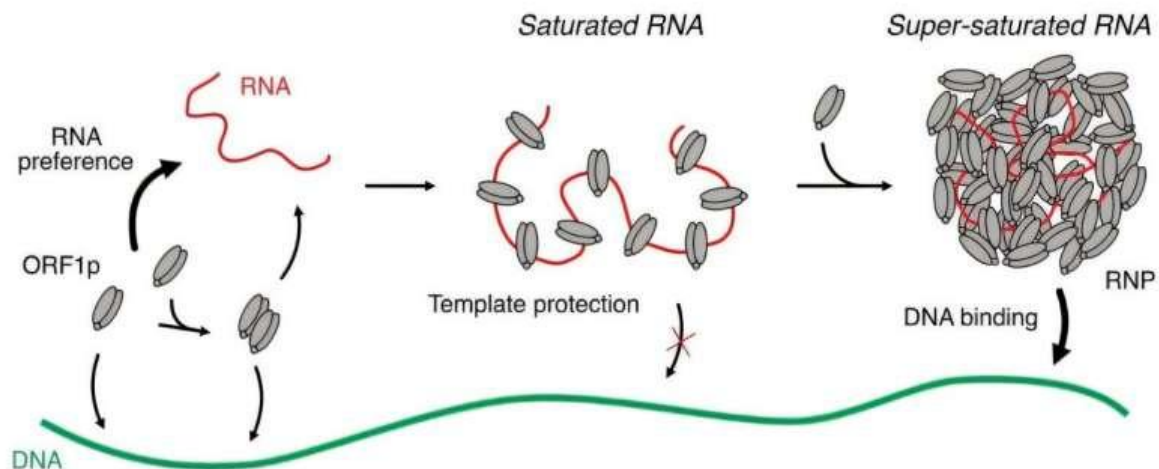
More information: Kasey S. Love et al, Model-guided design of microRNA-based gene circuits supports precise dosage of transgenic cargoes into diverse primary cells, *Cell Systems* (2025). DOI: [10.1016/j.cels.2025.101269](https://doi.org/10.1016/j.cels.2025.101269)

Journal information: [Cell Systems](#)

MAY 2, 2025

How 'jumping genes' infiltrate DNA during cell division

by [NYU Langone Health](#)



Model for ORF1p-RNP formation and DNA recognition. ORF1p forms homo trimers and higher-order oligomers that can bind to DNA but have a clear preference for RNA. Credit: Sarah Zernia et al

Viruses are known to use the genetic machinery of the human cells they invade to make copies of themselves. As part of the process, viruses leave behind remnants throughout the genetic material (genomes) of humans. The virus-like insertions, called "transposable elements," are snippets of genetic material even simpler than viruses that also use host cell machinery to replicate.

Nearly all these inserted elements have been silenced by our cells' defense mechanisms over time, but a few, nicknamed "jumping genes," can still move around the human genome like viruses. Just one, called long interspersed nuclear element 1 (LINE-1), can still move by itself.

As an element type that behaves like the retrovirus HIV, the LINE-1 "retrotransposon" is first copied into a molecule of RNA, the genetic material that partners with DNA, and then the RNA LINE-1 copy is converted back into DNA in a new place in the genome.

In this way, retrotransposons add code to the human genome every time they move, which explains why 500,000 LINE-1 repeats now represent a "staggering" 20% of the [human genome](#). These repeats drive genome evolution, but can also cause [neurological diseases](#), cancer, and aging when LINE-1 randomly jumps into essential genes, or triggers an immune response like a virus to cause inflammation.

To copy itself, however, LINE-1 must enter each cell's nucleus, the inner barrier that houses DNA.

Now a new study, [published](#) online in the journal *Science Advances*, reveals that LINE-1 binds to cellular DNA during the brief periods when nuclei break open as cells continually divide in two, creating replacements to keep tissues viable as we age.

The research team found that LINE-1 RNA takes advantage of these moments, assembling into clusters with one of the two proteins it encodes, ORF1p, to hold tightly to DNA until the nucleus reforms after cell division.

Led by researchers at NYU Langone Health and the Munich Gene Center at Ludwig-Maximilians-Universität (LMU) München in Germany, the work revealed specifically that LINE-1 can only bind to DNA when ORF1p—which can bind to RNA, DNA, and itself in linked copies called multimers—accumulates into clusters of hundreds of molecules called condensates.

As more ORF1p molecules build up, they eventually envelop the LINE-1 RNA, which makes more binding sites available for the entire cluster to attach to DNA.

"Our study provides crucial insight into how a genetic element that has come to make up a large part of human DNA can successfully invade the nucleus to copy itself," said Liam J. Holt, Ph.D., associate professor in the Department of Biochemistry and Molecular Pharmacology, and the Institute for Systems Genetics, at NYU Grossman School of Medicine.

"These findings on the precise mechanisms behind LINE-1 insertion lay the foundations for the design of future therapies to prevent LINE-1 replication."

The work also suggests that the LINE-1 condensate acts as a delivery vehicle to bring its RNA into proximity of the right sequences (rich in the DNA bases adenine and thymine) on DNA where the retrotransposon tends to insert, say the study authors. Packaged in its condensates, LINE-1 is thought to evade mechanisms that exclude large particles from the nucleus during mitosis as a cellular defense against viruses.

"LINE-1 condensates have a remarkable feature in that their DNA binding ability emerges only when the ratio of ORF1p copies to RNA is high enough in the condensates," added Dr. Holt. "Moving forward, we will be looking to see if other condensates undergo functional changes as the ratios between their components change."

More information: Sarah Zernia et al, LINE-1 ribonucleoprotein condensates bind DNA to enable nuclear entry during mitosis, *Science Advances* (2025). DOI: [10.1126/sciadv.adt9318](https://doi.org/10.1126/sciadv.adt9318). www.science.org/doi/10.1126/sciadv.adt9318

Journal information: *Science Advances*, [bioRxiv](#)

Provided by [NYU Langone Health](#)

New ancestral component found in DNA of Japanese people

Researchers from the RIKEN Center reveal a third Northeast Asian ancestry component challenging established dual-structure model.

From RIKEN 12/05/25 (first released 07/05/24)

A research group led by scientists from the RIKEN Center for Integrative Medical Sciences in Japan have used whole-genome sequencing to unravel the complex ancestry of the Japanese population.

The analysis supports an earlier study that proposed that the Japanese population originated from admixtures of three ancestral groups, challenging the long-held dual-structure model, and also provides new evidence of Neanderthal and Denisovan influences in the population.

The study, published in *Science Advances*, started with the group performing whole-genome sequencing on 3,256 samples from the Biobank Japan—a large collection of samples collected from hospitals in Japan.

The samples were chosen to reflect the population distribution of Japanese throughout the archipelago, from Hokkaido in the northeast to Okinawa and the other Ryukyu islands in the south.

The first finding was that the Japanese population can be optimally divided into three clusters, with different concentrations in Okinawa, Northeastern Japan, and Western Japan.

While it was previously believed that the current Japanese people are mainly descended either from the indigenous Jomon population or other East Asians, principally Han Chinese, the research group found that there is also a Northeast Asian ancestry, which is likely composed of people from the Korean peninsula or from early non-Jomon Japanese populations.

They found that Jomon ancestry was most dominant in Okinawa, where it made up 28.5 percent of the sampled people's DNA, though it also made up roughly 19 percent in Northeastern Japan and 12 percent in Western Japan, and was slightly higher in the south of Japan, closest to Okinawa.

The East Asian ancestry, generally understood to be from China, was most common in Western Japan, gradually decreasing to the east, while the Northeast Asian lineage was most common in Northeastern Japan, decreasing to the west.

To see whether these findings could provide insights into clinically relevant genetic variants, they examined two well-known pathogenic variants associated with hereditary breast cancer.

The first, a variant of the *BRCA1* gene, is only found in Japanese populations, and is more common in the east than the west of the country.

This implied that it arose in Japanese people with Northeast Asian ancestry and then spread westward.

The other, a variant of the *BRCA2* gene, is more common in the west, and is also found in China and Korea, leading to the conclusion that this variant was likely brought into Japan from continental Asia.

The study also offered insights into gene sequences derived from Neanderthals and Denisovans—extinct human lineages that existed together with modern humans and left us genes through a process known as introgression, a gradual movement of genes from one lineage into another through hybridization.

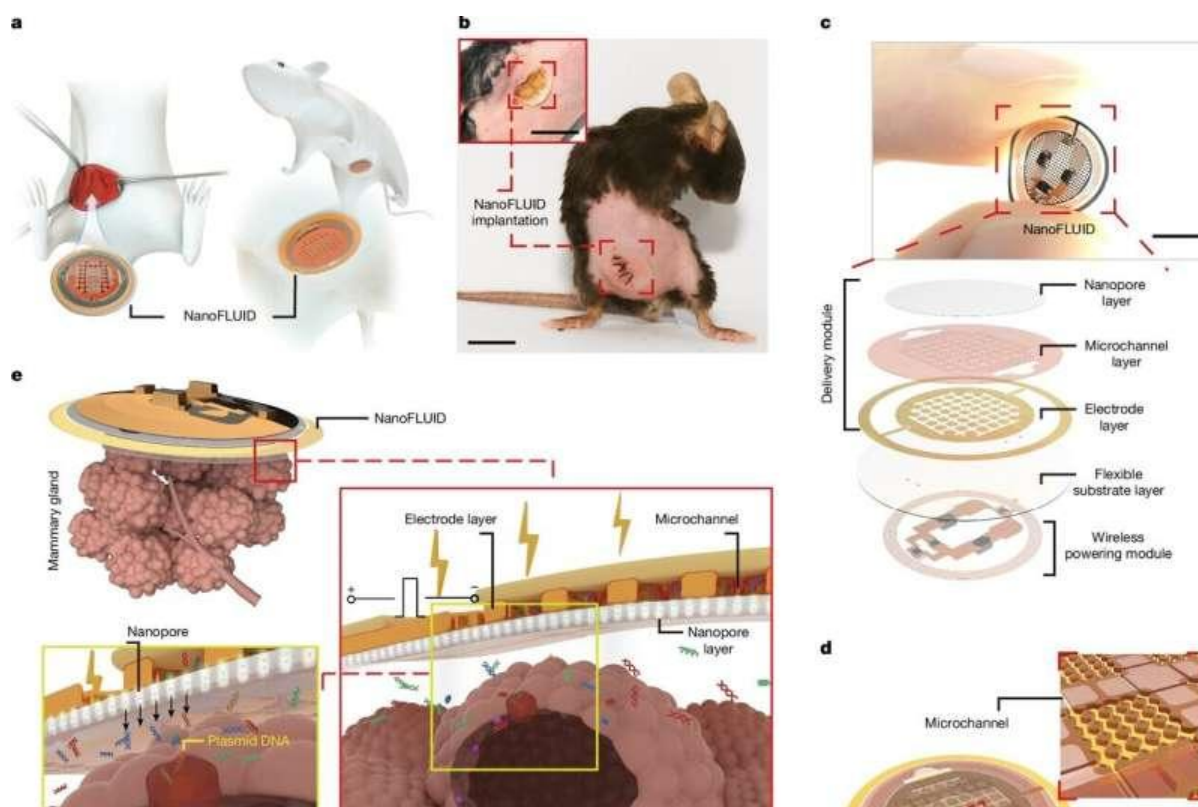
Specifically, they found gene sequences associated with type 2 diabetes and height derived from Denisovans, and while they mostly confirmed previous studies regarding gene introgressions from Neanderthals, they also found an interesting link to another gene associated with type 2 diabetes, which might affect sensitivity to semaglutide, an oral agent used to treat the disease.

According to Chikashi Terao, leader of the research group, “Though our findings were interesting because of the new insights they have given us into the origins of the Japanese people, we also believe that our work will serve as a reference for future genetic research beyond the Japanese population, as it could be used in areas such as personalized medicine.”

MAY 6, 2025

An electronic band-aid that delivers therapy directly to organs

by [Bob Yirka](#) , Phys.org



Credit: *Nature* (2025). DOI: 10.1038/s41586-025-08943-x

A team of biomedical engineers from China and the U.S. has developed a thin patch resembling a band-aid that can be applied to an internal organ to directly deliver therapeutic drugs. In their paper [published](#) in the journal *Nature*, the group describes the factors that went into the development of their patch, its construction and its capabilities.

There is a great need for a method to deliver drugs directly to organs rather than through the bloodstream, where they are dispersed throughout the body, causing undesirable side effects. Such a device would allow the direct targeting of tumors or be able to assist with organ repair. To date, efforts to make such a device have not fared well due to a variety of issues.

In this new research, the team in China says that they have found a way around these hurdles and have developed a wireless, battery-free thin [patch](#) that delivers drugs directly to an ailing organ.

The researchers describe their device as a nanofluid "band-aid" that can serve as a highway of sorts for [drug delivery](#)—it has integrated electronics that allow for micro-nano processing, which is used to generate a wireless power supply. The power assists in creating pores of access into organs and for sending drugs through them.

The patch attaches directly to a targeted organ, where it can perforate individual cell membranes using low voltage applied via an [electric field](#), delivering drugs directly to the cells in a desired part of an organ.

The research team has already tested their patch and found success with treating breast tumors and liver injuries. They note that it also offers feedback, which allows doctors to monitor organ repair and [tumor](#) reduction or even watch for new tumor development. The team claims that the patch has already been used to identify the eukaryotic enzyme DUS2 as a lung-specific metastasis driver in a mouse model.

More information: Dedong Yin et al, A battery-free nanofluidic intracellular delivery patch for internal organs, *Nature* (2025). DOI: [10.1038/s41586-025-08943-x](https://doi.org/10.1038/s41586-025-08943-x)

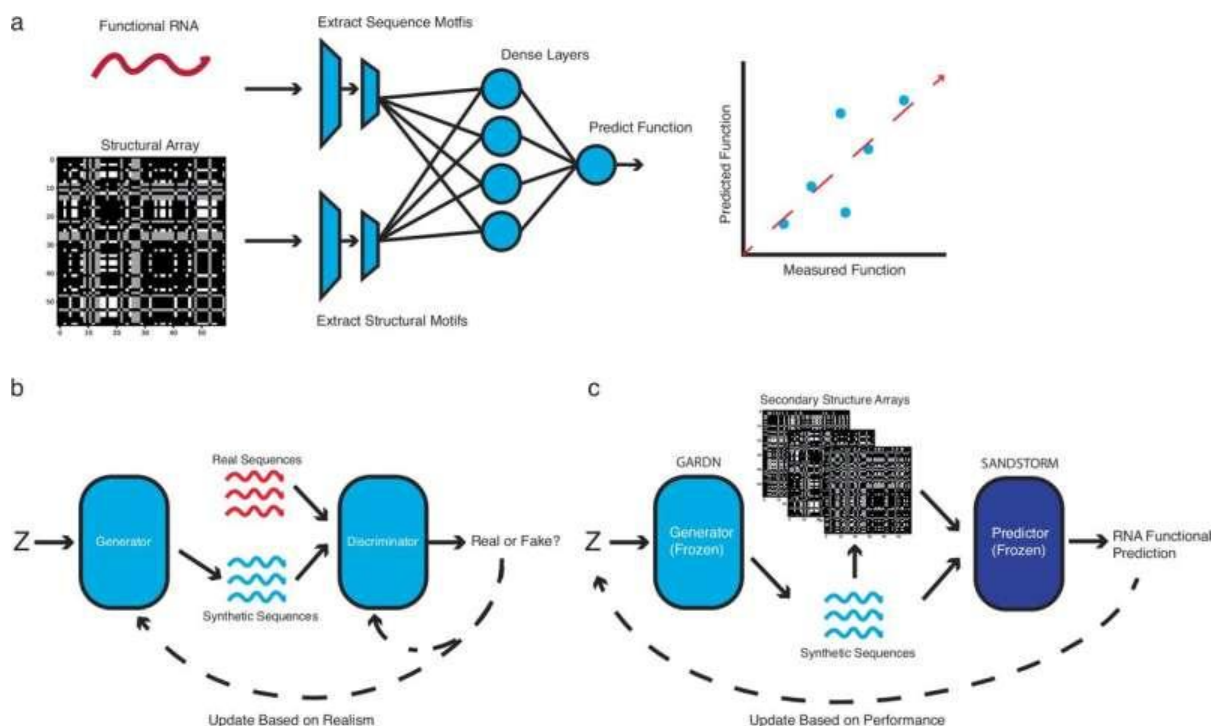
Journal information: [Nature](#)

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MAY 14, 2025

Q&A: A generative AI technique for designing RNA with improved function

by [Boston University](#)



Overview of the SANDSTORM and GARDN models. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-59389-8

Ribonucleic acid, also called RNA, is a molecule present in all living cells. It plays a critical role in transmitting genetic instructions from DNA and creating proteins. With the power to execute a plethora of functions, the little RNA "messenger" has led to important innovations across therapeutics, diagnostics, and vaccines, and made us rethink our understanding of life itself.

A team of researchers from Boston University's Biological Design Center and the Department of Biomedical Engineering recently made significant steps forward in the development of the next generation of computational RNA tools. They recently [published](#) a study in *Nature Communications* describing a generative AI technique for designing different types of RNA molecules with improved function.

Much like a [large language model](#) that can be used to compose entirely new texts, the model can compose new RNA sequences tailored for specific tasks in the cell or in a diagnostic assay. Their research has shown that it's possible to predict and generate RNA sequences that have specific functions across a broad array of potential applications.

In this Q&A, Dr. Alex Green, Associate Professor of Biomedical Engineering at BU, discusses the power of sequence and structure of RNA molecules (SANDSTORM) and Generative Adversarial RNA Design Networks (GARDN) as new tools in developing diagnostic and therapeutic RNAs with improved functions.

Why are you interested in engineering RNA with novel functions?

RNA engineering has tremendous potential because RNA is the only system in the body that both encodes genetic information and has diverse functional activity across a broad array of cellular processes. Engineered RNAs have applications in gene editing for research or therapeutic purposes, diagnostics, and synthetic biological systems.

Additionally, RNA engineering could provide a simpler and more streamlined approach to ensure cells produce the right amount of protein at the right time, which has tremendous potential in enabling novel protein-based therapeutics and targeted therapies.

The Green lab focuses on engineering RNA in a programmable way so it can function as a device to achieve a specific end goal. For instance, we work on designing RNAs that are active in cancer cells to produce a therapy, but are completely silent if they encounter a healthy cell, which minimizes unwanted side effects.

What have been the challenges to date in realizing the potential of RNA engineering?

A key challenge has been the need to synthesize and screen RNA in experimental systems, which can be both time-consuming and cost/resource intensive. Several computational tools have been developed to overcome the challenges of experimental approaches, but they all use different coding platforms and architectures, which makes it very difficult to integrate them.

Additionally, most of these existing methods have been designed to predict the function of specific types of RNAs, which means there isn't a single tool that can be broadly applied to answer all the questions and make all the predictions we'd like to make.

How do SANDSTORM and GARDN overcome these challenges?

SANDSTORM is a deep ML approach that incorporates information about RNA sequence and RNA secondary structure to predict the function of diverse classes of RNAs. We can use SANDSTORM neural networks—which learn and improve over time as we get more data—to predict the functional activity of the ends of RNA molecules (which play important roles in RNA stability, trafficking, and translation), parts of the RNA that interact with ribosomes, and RNAs used in CRISPR diagnostics.

GARDN is a generative adversarial network architecture, which is a system tasked with generating realistic examples of functional RNA and discriminating between realistic and unrealistic examples.

When we combine SANDSTORM with GARDN, we have a powerful system that can generate and select RNA sequences that provide desired functions while also being highly computationally efficient. Fewer parameters are needed for training and prediction compared with other computational approaches, which makes the system faster and related workflows easier.

A graduate student can use this system on their personal computer, as Aidan Riley, a Ph.D. student in my lab who championed the work, can attest. In fact, Aidan was a driver for this project because he wanted to use ML to screen and test engineered RNA faster and more efficiently, and his background in ML played a critical role in the ultimate design of the system.

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What are the next steps in this research?

To date we have demonstrated the utility of SANDSTORM and GARDN in engineering the ends of RNA molecules (known as the 5-prime and 3-prime ends). Part of our current focus is on designing the coding region between the two ends. Toward this end, we are merging these computational tools with other developments at BU, including self-amplifying RNA technology and more specific delivery of therapeutics. Self-amplifying RNA technology is a more efficient way to generate the RNAs we want to evaluate in experimental systems.

Further down the road, we also want to engineer RNA to improve the efficiency of protein production, which could have important implications in enabling new targeted therapies and making the production of therapeutic proteins more efficient.

In what ways might this research help further the development of vaccines or drug therapies, or in the treating of diseases?

This research can help make vaccines and therapies smarter and more effective. Using our models, we are finding that we can significantly increase the amount of payload protein that an mRNA generates. This is valuable since it can lead to more potent treatments or it can be used to reduce the amount of RNA that is required for the therapy, lowering costs and potentially reducing side effects.

We also use the models to design RNAs that only activate in response to different biomarkers that they detect. This capability could be used to develop therapies that only activate in specific tissues or in tumor cells only, for example.

How could biotech companies potentially benefit from the knowledge gained by this research?

Our technology could be used to help biotech companies develop RNA drug candidates much faster and more efficiently. Training new machine learning models often requires testing tens of thousands of different candidates, which is expensive and time-consuming. With SANDSTORM, we've found that we can generate effective models from only a few hundred test sequences, which is considerably smaller than I thought would be possible. For small biotech companies in particular, this cost and time benefit could be decisive in getting a new drug to market.

More information: Aidan T. Riley et al, Generative and predictive neural networks for the design of functional RNA molecules, *Nature Communications* (2025). DOI: [10.1038/s41467-025-59389-8](https://doi.org/10.1038/s41467-025-59389-8)

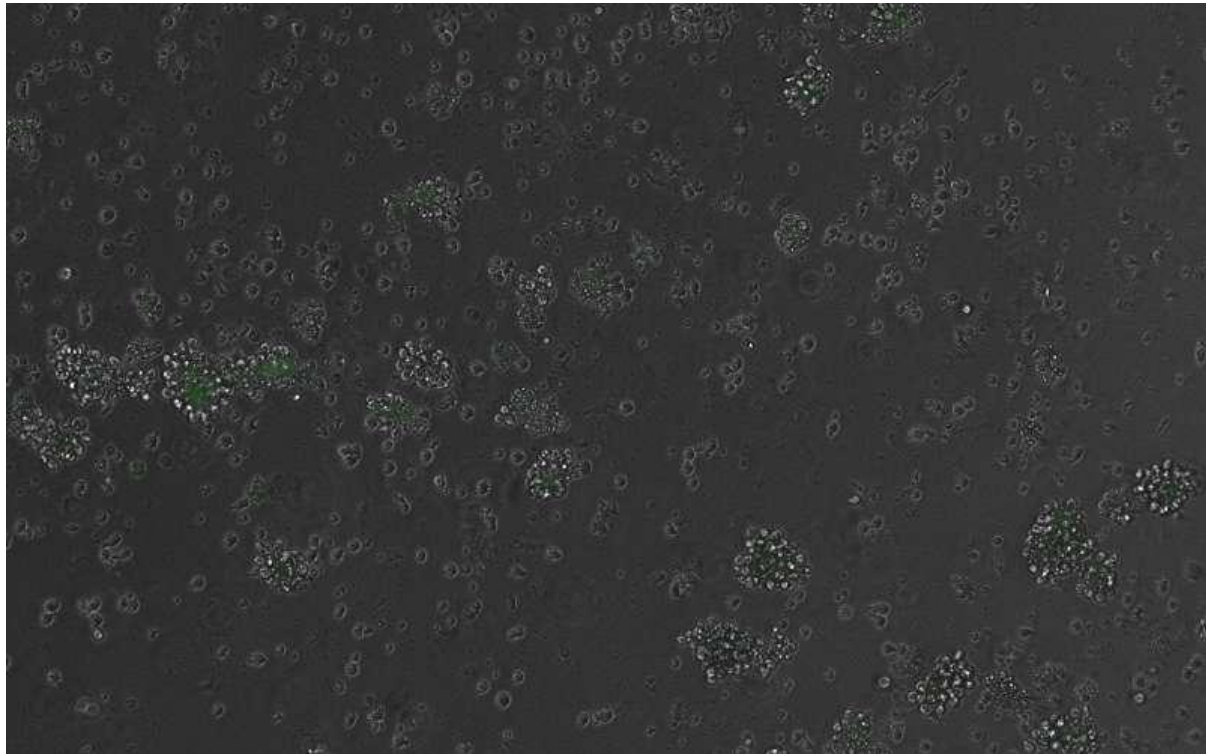
Journal information: [Nature Communications](#)

Provided by [Boston University](#)

MAY 8, 2025

AI-designed DNA controls genes in healthy mammalian cells for first time

by [Center for Genomic Regulation](#)



Cells where fluorescent reporter gene is activated by the AI-generated enhancers. Credit: Aina Bernal Martínez/Centro de Regulación Genómica

A study [published](#) in the journal *Cell* marks the first reported instance of generative AI designing synthetic molecules that can successfully control gene expression in healthy mammalian cells.

Researchers at the Center for Genomic Regulation (CRG) created an AI tool which dreams up DNA regulatory sequences not seen before in nature. The model can be told to create synthetic fragments of DNA with custom criteria, for example, "switch this gene on in [stem cells](#) which will turn into red-blood-cells but not platelets."

The model then predicts which combination of DNA letters (nucleotide bases: A, T, C, G) are needed for the [gene expression](#) patterns required in specific types of cells. Researchers can then chemically synthesize the roughly 250-letter DNA fragments and add them to a virus for delivery into cells.

As a proof-of-concept, the authors of the study asked the AI to design synthetic fragments which activate a gene coding for a [fluorescent protein](#) in some cells while leaving gene

expression patterns unaltered. They created the fragments from scratch and dropped them into mouse blood cells, where the sequence fused with the genome at random locations. The experiments worked exactly as predicted.

"The potential applications are vast. It's like writing software but for biology, giving us new ways of giving instructions to a cell and guiding how they develop and behave with unprecedented accuracy," says Dr. Robert Frömel, first author of the study who carried out the work at the Center for Genomic Regulation (CRG) in Barcelona.

The study could lead to new ways for gene-therapy developers to boost or dampen the activity of genes only in the cells or tissues that need adjusting. It also paves the way for new strategies to fine-tune a patient's genes and make treatments more effective and reduce side effects.

The work marks an important milestone in the field of generative biology. To date, advances in the field have largely benefited [protein design](#), helping scientists create entirely new enzymes and antibodies faster than ever before. However, many human diseases stem from faulty gene expression that is cell-type specific, for which there might never be a perfect protein drug candidate.

Gene expression is controlled by regulatory elements like enhancers, tiny fragments of DNA which switch genes on or off. To fix faulty gene expression, researchers can comb through genomes looking for naturally-existing enhancers that happen to suit their needs, limiting themselves to the sequences evolution has produced.

AI-generated enhancers can help engineer ultra-selective switches that nature has not yet invented. They can be designed to have exactly the on/off patterns required in specific types of cells, a level of fine-tuning which is crucial for creating therapies that avoid unintended effects in healthy cells.

However, the development of AI models requires lots of high-quality data, which has been historically lacking for enhancers. "To create a language model for biology, you have to understand the language cells speak. We set out to decipher these grammar rules for enhancers so that we can create entirely new words and sentences," explains Dr. Lars Velten, corresponding author of the study and researcher at the Center for Genomic Regulation (CRG).

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The authors of the study created huge volumes of biological data to build their AI model by carrying out thousands of experiments with lab models of blood formation. They studied both enhancers and transcription factors, proteins also involved in controlling gene expression.

Until now, scientists studying enhancers and transcription factors have typically used cancer cell lines because they are easier to work with. The researchers worked with healthy cells

instead because it's more representative of human biology. Their work helped uncover subtle mechanisms that shape our immune system and blood cell production.

Over five years, the team synthesized more than 64,000 synthetic enhancers, each carefully designed to test different arrangements and strengths of binding sites for 38 different transcription factors. It's the largest library of synthetic enhancers ever built in blood cells to date.

Once inserted into the cells, the team tracked exactly how active each synthetic enhancer became across seven stages of blood-cell development. They discovered that while many enhancers activate genes in one type of cell, they repress genes in another.

Most enhancers worked like a volume dial, turning gene activity up or down. Surprisingly, certain combinations acted like on/off switches. The scientists call this "negative synergy," meaning two factors that usually turn a gene on individually could effectively shut that gene down when they occur together.

The data from the experiments were crucial in setting out the design principles of the machine learning model. Once the model had enough measurements of how each synthetic enhancer changed gene activity in real cells, it could predict new designs that yield on/off outcomes, even if these [enhancers](#) had never existed in nature.

The study was designed to determine if a technology can work in practice before committing to larger-scale research. The researchers have only scratched the surface. Both humans and mice have an estimated 1,600 [transcription factors](#) regulating their genomes.

The work was carried out by Lars Velten, Robert Frömel, Julia Rühle, Aina Bernal Martínez, Chelsea Szu-Tu and Felix Pacheco Pastor, all members of Lars Velten's research group at the Center for Genomic Regulation.

Rosa Martinez Corral from the Barcelona Collaboratorium, a joint initiative between the CRG and EMBL-Barcelona, also took part.

More information: Design principles of cell state specific enhancers in hematopoiesis, *Cell* (2025). DOI: [10.1016/j.cell.2025.04.017](https://doi.org/10.1016/j.cell.2025.04.017). [www.cell.com/cell/fulltext/S0092-8674\(25\)00449-0](https://www.cell.com/cell/fulltext/S0092-8674(25)00449-0)

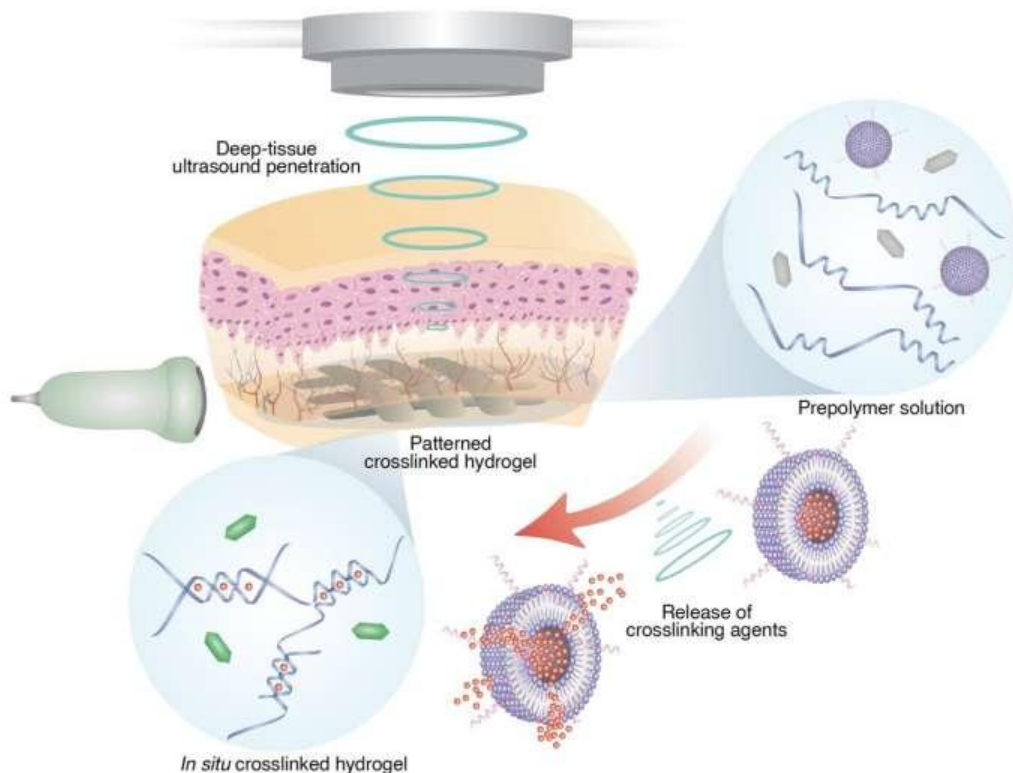
Journal information: *Cell*

Provided by [Center for Genomic Regulation](#)

MAY 8, 2025

In vivo 3D printing using sound holds promise for precise drug delivery, wound healing and more

by [California Institute of Technology](#)



A schematic of the DISP (deep tissue in vivo sound printing) platform developed by a team led by Caltech. The technique combines ultrasound with low-temperature-sensitive liposomes loaded with crosslinking agents. The liposomes were embedded in a polymer solution containing the monomers of the desired polymer, an imaging contrast agent that would reveal when the crosslinking had occurred (here they used gas vesicles), and the cargo they hoped to deliver—a therapeutic drug, for example. Additional components can be included, such as cells and conductive materials like carbon nanotubes or silver. The composite bioink was then injected directly into the body. By using focused ultrasound to increase the temperature in a targeted area by a few degrees, the scientists were able to have the liposomes release their contents exactly where they were needed. Credit: Elham Davoodi and Wei Gao

Imagine that doctors could precisely print miniature capsules capable of delivering cells needed for tissue repair exactly where they are needed inside a beating heart.

A team of scientists led by Caltech has taken a significant step toward that ultimate goal, having developed a method for 3D-printing polymers at specific locations deep within living animals. The technique relies on sound for localization and has already been used to print [polymer](#) capsules for selective drug delivery as well as glue-like polymers to seal internal wounds.

Previously, scientists have used [infrared light](#) to trigger polymerization, the linking of the basic units, or monomers, of polymers within living animals.

"But infrared penetration is very limited. It only reaches right below the skin," says Wei Gao, professor of medical engineering at Caltech and a Heritage Medical Research Institute Investigator. "Our new technique reaches the deep tissue and can print a variety of materials for a broad range of applications, all while maintaining excellent biocompatibility."

Gao and his colleagues report their new in vivo [3D-printing technique](#) in the journal *Science*.

Along with bioadhesive gels and polymers for drug and cell delivery, the paper also describes the use of the technique for printing bioelectric hydrogels, which are polymers with embedded conductive materials for use in the internal monitoring of physiological vital signs, as in electrocardiograms (ECGs). The lead author of the study is Elham Davoodi, an assistant professor of mechanical engineering at the University of Utah, who completed the work while a postdoctoral scholar at Caltech.

The origin of a novel idea

Wanting to figure out a way to realize deep tissue in vivo printing, Gao and his colleagues turned to ultrasound, a platform that is widely used in biomedicine for deep tissue penetration. But they needed a way to trigger crosslinking (binding of monomers) at a specific location and only when desired.

They came up with a novel approach: Combine ultrasound with low-temperature-sensitive liposomes. Such liposomes, spherical cell-like vesicles with protective fat layers, are often used for [drug delivery](#). In the new work, the scientists loaded the liposomes with a crosslinking agent and embedded them in a polymer solution containing the monomers of the polymer they wanted to print, an imaging contrast agent that would reveal when the crosslinking had occurred, and the cargo they hoped to deliver—a therapeutic drug, for example.

Additional components could be included, such as cells and conductive materials like carbon nanotubes or silver. The composite bioink was then injected directly into the body.

Raise the temperature just a touch to trigger printing

The liposome particles are low-temperature sensitive, which means that by using focused ultrasound to raise the temperature of a small targeted region by about 5 degrees Celsius, the scientists can trigger the release of their payload and initiate the printing of polymers.

"Increasing the temperature by a few degrees Celsius is enough for the liposome particles to release our crosslinking agents," says Gao. "Where the agents are released, that's where localized polymerization or printing will happen."

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The team uses gas vesicles derived from bacteria as an imaging contrast agent. The vesicles, air-filled capsules of protein, show up strongly in ultrasound imaging and are sensitive to chemical changes that take place when the liquid monomer solution crosslinks to form a gel network. The vesicles actually change contrast, detected by ultrasound imaging, when the transformation takes place, allowing scientists to easily identify when and precisely where polymerization crosslinking has occurred, enabling them to customize the patterns printed in live animals.

The team calls the new technique the deep tissue in vivo sound printing (DISP) platform.

When the team used the DISP platform to print polymers loaded with doxorubicin, a chemotherapeutic drug, near a bladder tumor in mice, they found substantially more tumor cell death for several days as compared to animals that received the drug through direct injection of drug solutions.

"We have already shown in a small animal that we can print drug-loaded hydrogels for tumor treatment," Gao says. "Our next stage is to try to print in a larger animal model, and hopefully, in the near future, we can evaluate this in humans."

The team also believes that machine learning can enhance the DISP platform's ability to precisely locate and apply focused ultrasound.

"In the future, with the help of AI, we would like to be able to autonomously trigger high-precision printing within a moving organ such as a beating heart," Gao says.

More information: Elham Davoodi et al, Imaging-guided deep tissue in vivo sound printing, *Science* (2025). DOI:

[10.1126/science.adt0293](https://doi.org/10.1126/science.adt0293). www.science.org/doi/10.1126/science.adt0293

Xiao Kuang, Replicating a tissue with sound waves, *Science* (2025). DOI: [10.1126/science.adx2433](https://doi.org/10.1126/science.adx2433). www.science.org/doi/10.1126/science.adx2433

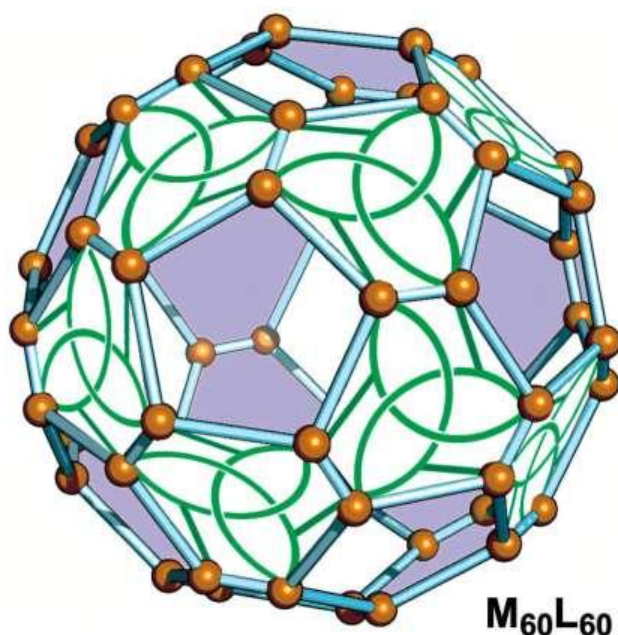
Journal information: [Science](#)

Provided by [California Institute of Technology](#)

MAY 9, 2025

Self-assembled dodecahedral nanostructure features 60 metal ions and peptide ligands

by [Institute of Science Tokyo](#)



- **Dodecahedral spatial graph** (60-crossings)
- **Goldberg polyhedron** ($T = 3$)

Graphical abstract. Credit: *Chem* (2025). DOI: 10.1016/j.chempr.2025.102555

Controlling the topology and structure of entangled molecular strands is a key challenge in molecular engineering, particularly when attempting to create large nanostructures that mimic biological systems. Examples found in nature, such as virus capsids and cargo proteins, demonstrate the remarkable potential of such architectures. However, methods for constructing large hollow nanostructures with precise geometric control have remained elusive—until now.

A research team led by Associate Professor Tomohisa Sawada from the Institute of Science Tokyo, Japan, has successfully constructed a molecular spherical shell structure with the geometric topology of a regular dodecahedron.

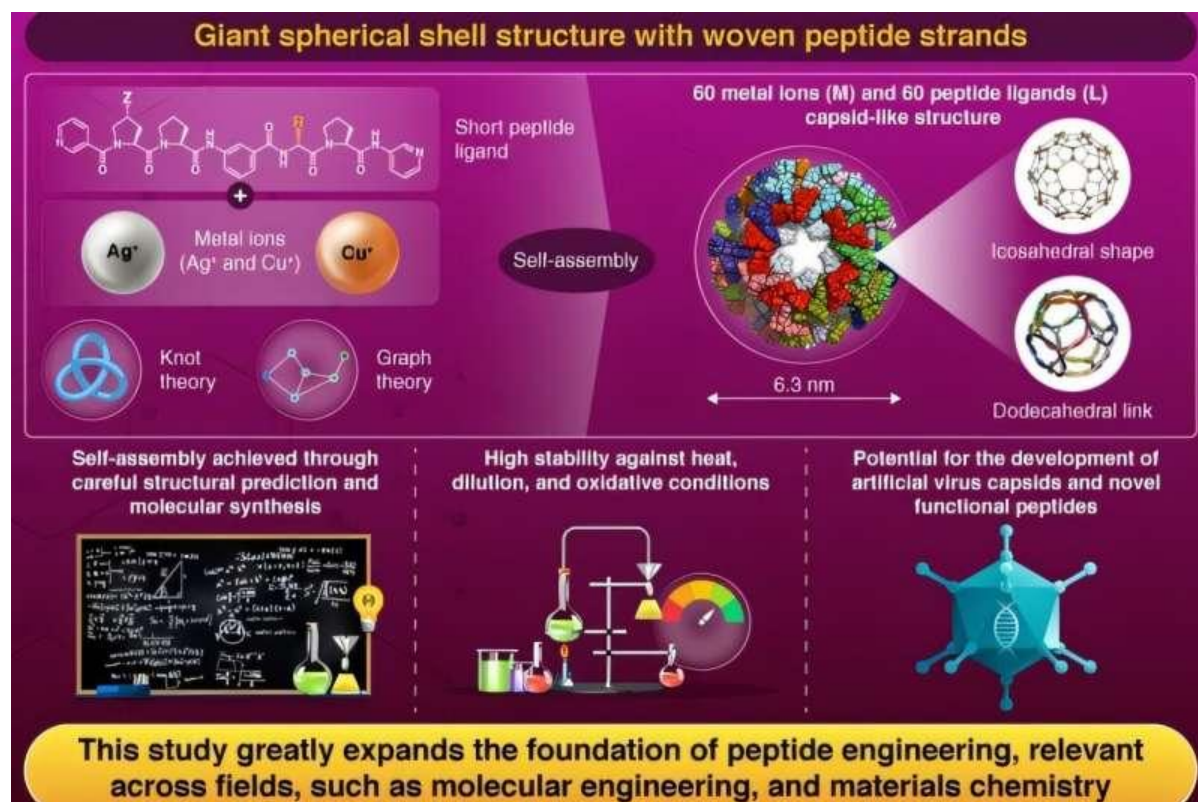
This groundbreaking work, which was published online in the journal [Chem](#), describes how the researchers created this large structure, bearing an outer diameter of 6.3 nanometers, through the entanglement of peptides with [metal ions](#).

"The synthesis of this highly [complex structure](#) was based on geometric considerations and predictions, leading to the proposal of a new concept: the geometric control of chemical structures," explains Sawada.

The team's approach combined two distinct mathematical frameworks, namely knot theory and [graph theory](#), to predict and then achieve the self-assembly of an unprecedented dodecahedral link with an entanglement of 60 crossings, composed of 60 metal ions and 60 peptide ligands (or $M_{60}L_{60}$).

The researchers had previously created smaller structures with tetrahedral and cubic links. However, a more complex dodecahedral link emerged after they introduced further modifications to the peptide sequence during attempts to functionalize $M_{24}L_{24}$, a smaller cubic link.

X-ray crystallographic analysis revealed that the resulting $M_{60}L_{60}$ metal-peptide shell contains an inner cavity of approximately 4.0 nanometers (approximately $34,000 \text{ \AA}^3$), which is large enough to encapsulate macromolecules such as proteins or nanomaterials.



Researchers develop a large dodecahedral structure through the self-assembly of metal ions and peptides, with potential implications in drug delivery systems and molecular transportation. Credit: Dr. Tomohisa Sawada / Institute of Science Tokyo, Japan

Beyond its impressive structural complexity, the M₆₀L₆₀ shell exhibited remarkable stability against heat, dilution, and oxidative conditions, which the researchers attributed to its unique entangled network structure.

The team also demonstrated that the capsid's surface could be modified with various functional groups while maintaining its [structural integrity](#), opening pathways for customization based on specific needs.

These features make M₆₀L₆₀ a promising platform for various applications, including drug delivery systems and molecular transportation.

"Considering the diversity and modifiability of peptide structures, our method is overwhelmingly advantageous compared to DNA origami technology in terms of functionalizing structures," highlights Sawada.

"Moreover, since our approach involves theoretical prediction and trial-and-error experiments, sometimes astonishing structures far beyond our expectations are obtained—this is the essence of chemistry."

Overall, this research represents a significant step forward in understanding how to construct artificial virus capsid-like structures.

"Our findings significantly expand the foundation of peptide engineering and are anticipated to have immense effects across various fields, including molecular self-assembly, materials chemistry, and mathematical theories," concludes Sawada.

The researchers are now aiming for even more ambitious structures, envisioning M₁₈₀L₁₈₀ and M₂₄₀L₂₄₀ assemblies with 180 and 240 crossings, respectively, as their next challenges.

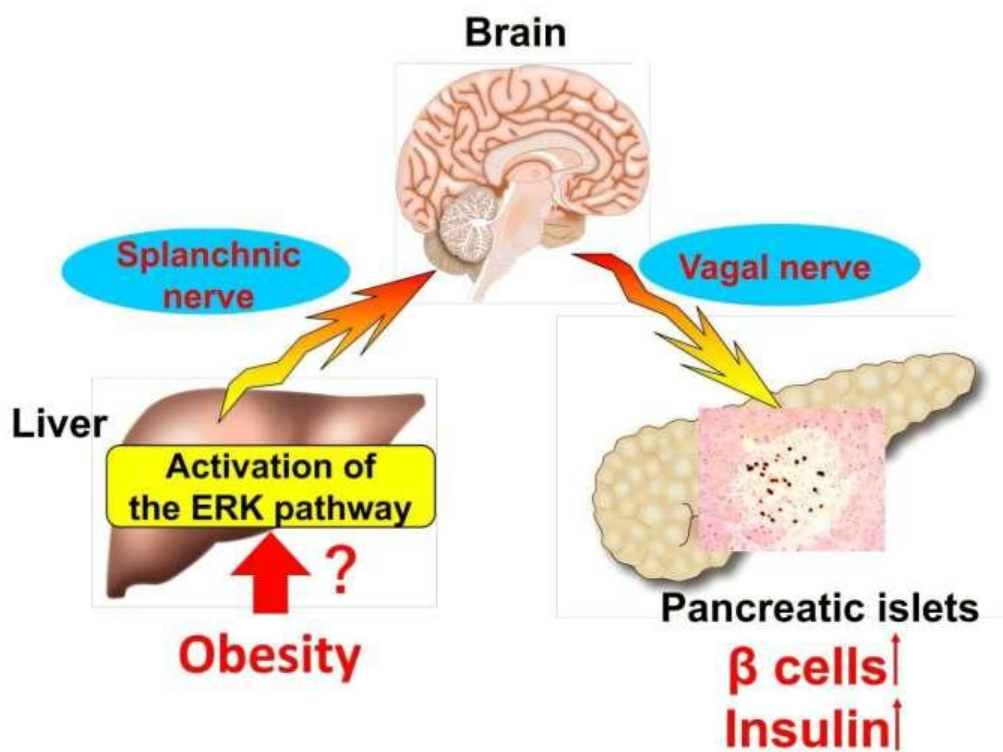
More information: Yuuki Inomata et al, An M60L60 metal-peptide capsid with a 60-crossing woven network, *Chem* (2025). DOI: [10.1016/j.chempr.2025.102555](https://doi.org/10.1016/j.chempr.2025.102555)

Journal information: [Chem](#)

Provided by [Institute of Science Tokyo](#)

Colonic inflammation may explain missing link between obesity and β -cell proliferation

by [Tohoku University](#)



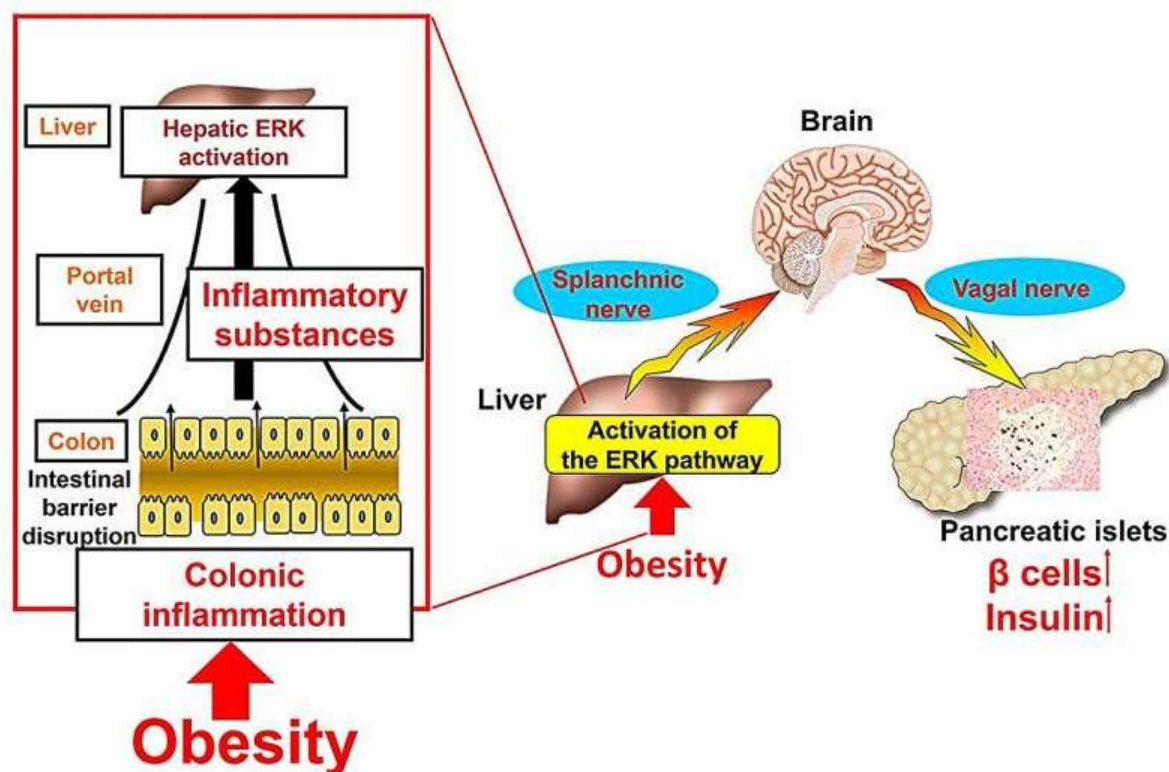
The neuronal relay system originating in hepatic ERK activation, consisting of afferent splanchnic nerves from the liver to the brain and efferent vagal nerves from the brain to the pancreas that promotes adaptive β -cell proliferation during obesity development. Credit: *JCI Insight* (2025). DOI: 10.1172/jci.insight.183864

Researchers at the Tohoku University Graduate School of Medicine have uncovered a key primary step in the hepatic ERK pathway that leads to increased insulin production.

While their [previous work](#) focused on aspects of the signaling pathway from the liver to the pancreas, this new study shows an even earlier step that begins in the colon when it is inflamed—triggered by [obesity](#). The work has revealed a novel role the gastrointestinal tract plays in regulating [glucose homeostasis](#).

The research is [published](#) in the journal *JCI Insight*.

Insulin is a hormone produced by β -cells in the pancreas. You can think of insulin as a key that unlocks cells to let glucose enter from the blood, so it can be used as energy. However, individuals with obesity can become insulin-resistant, which causes the pancreas to secrete more insulin to try to keep up. This occurs through an inter-organ neuronal signal relay originating in the hepatic ERK pathway.



Findings in the present study. Colonic inflammation and resultant intestinal barrier disruption induced hepatic ERK pathway activation, thereby promoting adaptive β -cell proliferation through the inter-organ neuronal relay system from the liver to the pancreas. The liver senses the state of obesity through colonic inflammation, and colonic inflammation serves as the first trigger of β -cell proliferation during obesity development. Credit: *JCI Insight* (2025). DOI: 10.1172/jci.insight.183864

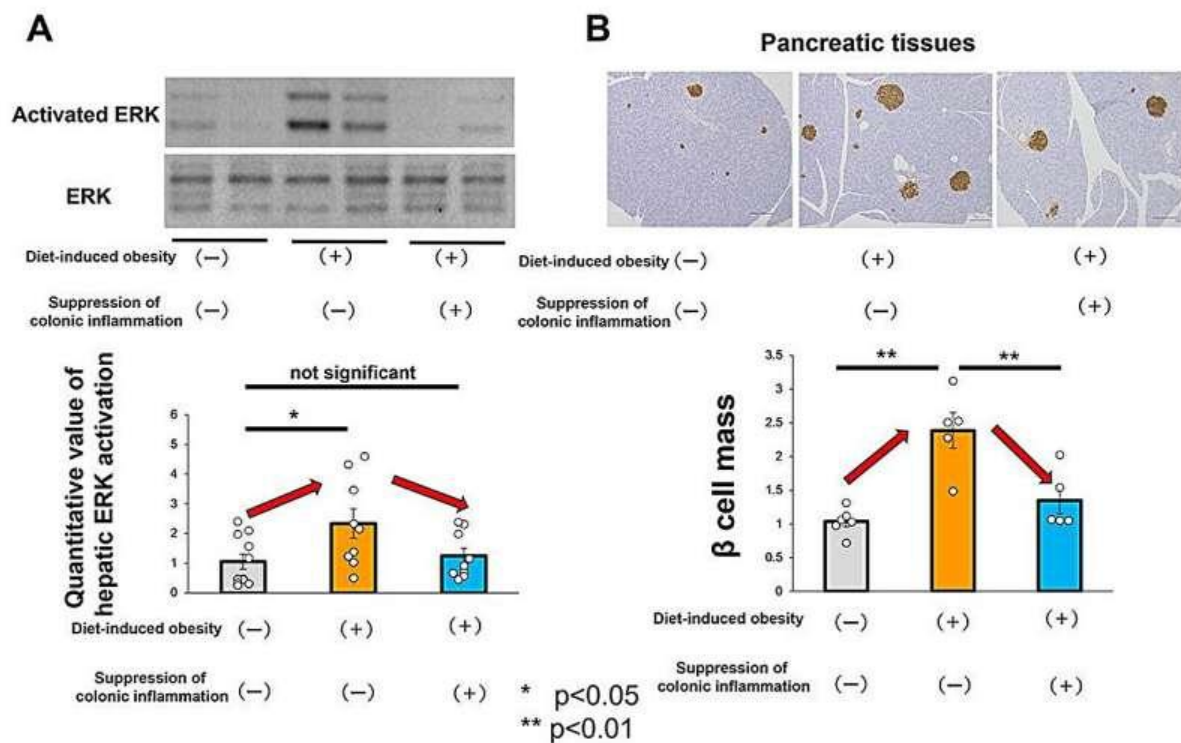
Due to the close relationship between obesity and the onset of diabetes, understanding this pathway in depth could help develop new ways to treat or prevent this condition.

"The goal of this study was to define how obesity in particular triggers this cascade," says Junta Imai (Tohoku University). "We theorized that it had to do with inflammation in the colon, since pro-inflammatory factors can play an excitatory role in the hepatic ERK pathway."

The researchers developed a thorough series of experiments to determine if colonic inflammation due to obesity could impact the hepatic ERK pathway. First, the research group analyzed mice without obesity that had been given a drug to cause inflammation in

the colon. They found that simply causing inflammation in the colon activates the ERK pathway in the liver, stimulates the neuronal relay pathway, and increases the number of β -cells even in mice without obesity.

Next, by analyzing colons of mice in which obesity was induced by a high-calorie diet, they found that colonic inflammation, along with both hepatic ERK pathway activation and increased β -cells, occurred in these obese mice.



Activation of the hepatic ERK pathway and enhancement of β -cell proliferation during obesity development were suppressed by prevention of colonic inflammation. A. Quantitative value of hepatic ERK activation in lean mice, obese mice without suppression of colonic inflammation and obese mice with suppression of colonic inflammation. B. Beta cell mass of lean mice, obese mice without suppression of colonic inflammation and obese mice with suppression of colonic inflammation. Credit: *JCI Insight* (2025). DOI: 10.1172/jci.insight.183864

"An exciting finding was when we tried to treat the **obese mice** with colon inflammation by lowering their inflammation, it actually stopped the ERK pathway in the liver from activating," explains Imai. "Despite the fact the mouse was still obese, targeting colon inflammation was exactly what was needed to alter the ERK pathway."

This research unveils a missing link in the **pathway**, determining that the **liver** senses the state of obesity through colonic inflammation, and colonic **inflammation** serves as the first trigger of β -cell proliferation during obesity development.

These achievements will lead to advancements in understanding the mechanism behind β -cell proliferation in order to maintain normal blood glucose levels. In addition, it is

anticipated that this research may help progress the development of treatments and prevention methods for diabetes.

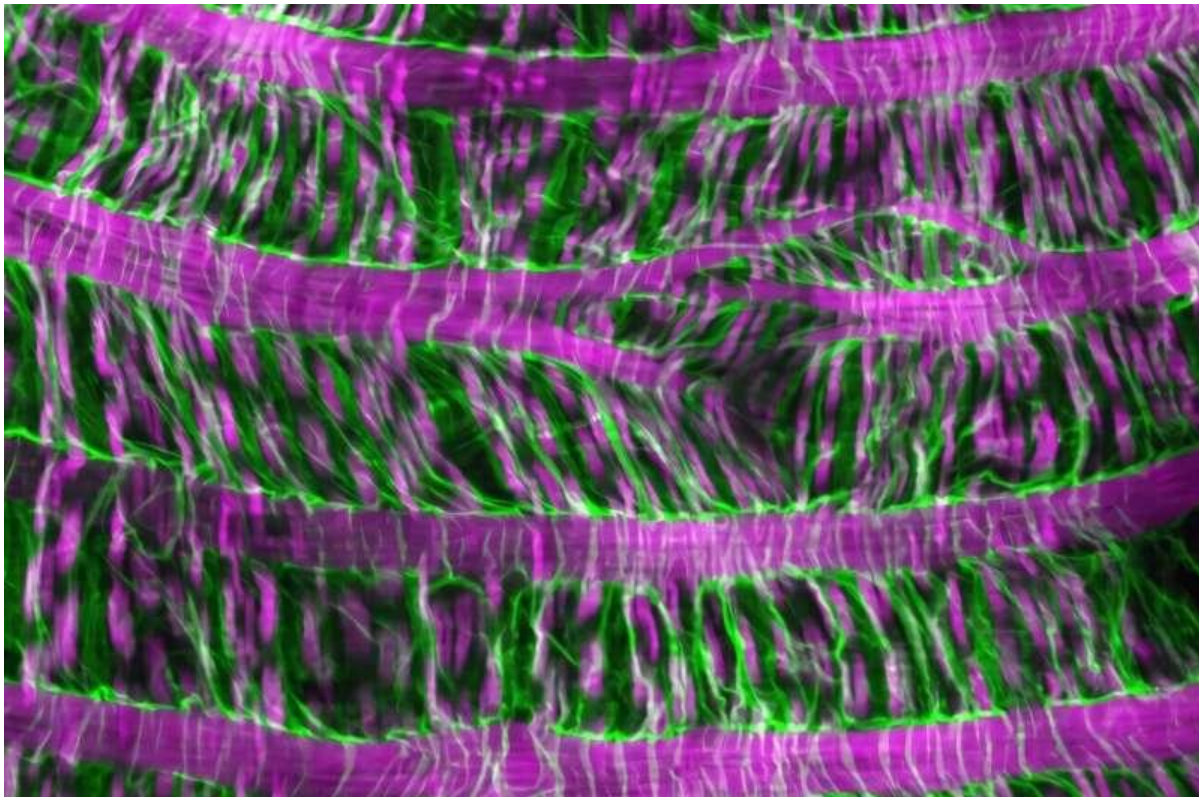
More information: Haremaru Kubo et al, Colonic inflammation triggers β cell proliferation during obesity development via a liver-to-pancreas interorgan mechanism, *JCI Insight* (2025). DOI: [10.1172/jci.insight.183864](https://doi.org/10.1172/jci.insight.183864)

Journal information: *JCI Insight*
Provided by [Tohoku University](#)

MAY 12, 2025

How tissues detect and repair damage to the body's hidden support system

by Alexandra Scammell, [Vanderbilt University](#)



Surface view of a fruit fly gut basement membrane (green) and muscles (magenta). This image from the study won the American Society for Matrix Biology 2024 Image Award. Credit: *Developmental Cell* (2025). DOI: [10.1016/j.devcel.2025.02.011](https://doi.org/10.1016/j.devcel.2025.02.011)

A new study by Vanderbilt investigators has uncovered a previously unknown biological mechanism: how tissues detect and respond to damage in basement membranes, the thin layers of extracellular matrix that surround and support nearly every organ in the body.

The research, [published](#) in *Developmental Cell*, is the first to show how local cells sense and respond to changes in basement membrane stiffness caused by damage—and how they activate a previously unknown set of "matrix mender" cells to repair the tissue. The results of this study have far-reaching implications, as basement membrane damage plays a role in numerous diseases, including diabetes, dementia, and cancer.

Basement membranes are extracellular matrices—flat sheets of protein and carbohydrate—that are essential for tissue architecture and function. But like all tissues, they are subject to damage. Until now, how the body notices and heals damage to these basement membranes has remained a mystery.

"Virtually nothing was known about how the damaged matrix is detected and repaired," researcher Andrea Page-McCaw said. "Basement membranes lie outside cells, and we wanted to know how cells know when the membranes are damaged and how they get repaired."

Page-McCaw, Stevenson Professor and professor of cell and developmental biology, led the research along with a recent graduate student from her lab, Aubrie Stricker.

Studying basement membranes is challenging, however, because they are best studied in an intact animal. If you remove them from the animal, Page-McCaw said, you change their organization and their relationship to other cells and fluids. For this study, the team worked entirely on living organisms and performed precise genetic manipulations in [fruit flies](#), preserving the natural environment of basement membranes and allowing the team to study how they function in real time.

Page-McCaw and Stricker employed advanced in vivo imaging techniques to observe basement membrane dynamics within the fruit flies' intact digestive systems. To sort through the complex imaging data they collected, the researchers used automated [image analysis](#) methods, which enabled precise quantification of the changes in tissue stiffness.

"Vandy has a highly collaborative atmosphere, and we were able to get help with automated image analysis from our colleague Shane Hutson," said Page-McCaw. Hutson is a professor of physics.

The authors uncovered three key results:

- Local cells monitor basement membrane integrity by sensing mechanical stiffness—essentially using touch to detect injury.
- Piezo channels, special proteins in cells that can sense physical pressure or stretch, detect the stiffness. When they feel mechanical force, they send signals that help cells respond.
- When Piezo channels detect damage, their activity triggers the generation of new cells—dubbed "matrix menders"—whose job is to fix the local [basement membrane](#).

"It was a very exciting day when Aubrie discovered that Piezo is required for the matrix menders to appear," Page-McCaw said.

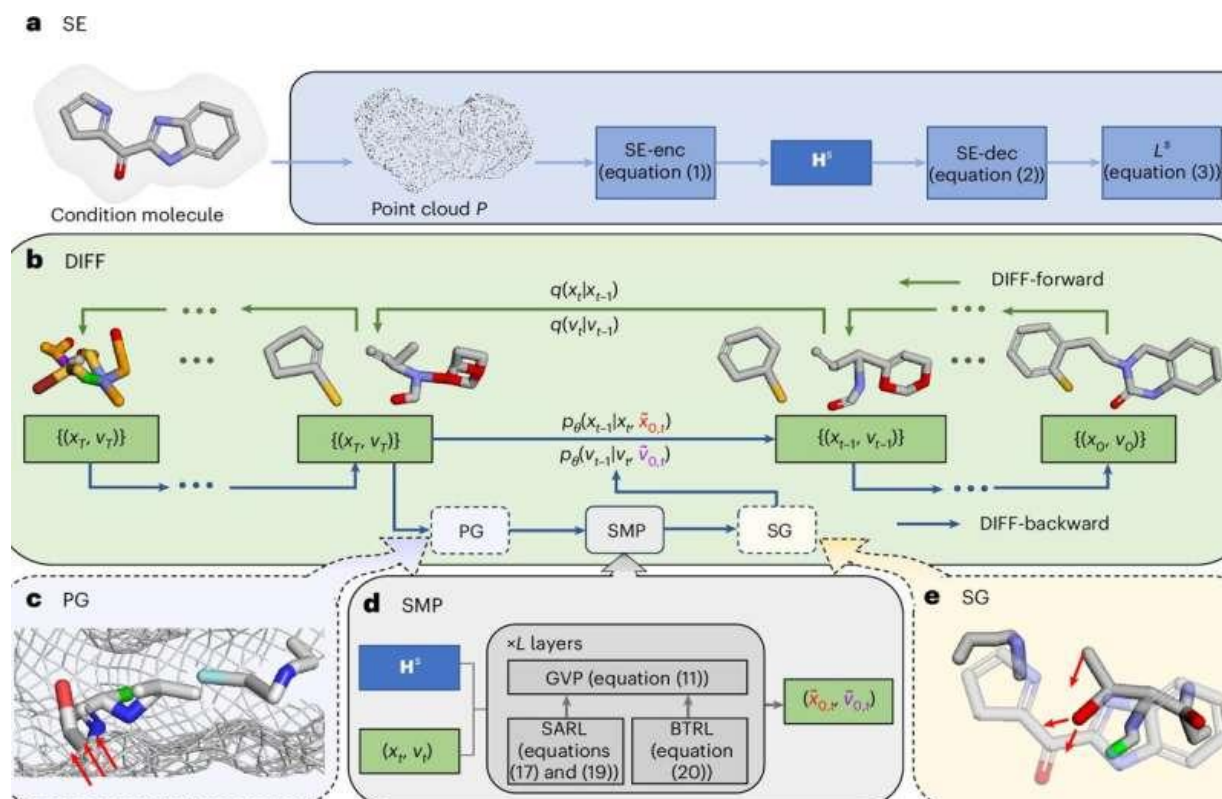
Although the research was conducted on fruit flies, the implications extend to human health. Understanding how the body detects and repairs such damage may lead to new therapeutic approaches in regenerative and [sports medicine](#), and in various diseases such as diabetes, dementia, and cancer.

Although the researchers have determined the role of the Piezo channels in sensing damage, the team hopes to determine which cell type uses them to sense stiffness. They hypothesize that [stem cells](#)—often found in close contact with basement membranes—might be cells involved in repair. If so, it could reshape our understanding of how stem cells maintain tissue integrity across the body.

More information: Aubrie M. Stricker et al, Piezo-dependent surveillance of matrix stiffness generates transient cells that repair the basement membrane, *Developmental Cell* (2025). DOI: [10.1016/j.devcel.2025.02.011](https://doi.org/10.1016/j.devcel.2025.02.011)
Journal information: *Developmental Cell*
 Provided by [Vanderbilt University](#)

MAY 12, 2025

Generative AI is on track to shape the future of drug design by [Ohio State University](#)



Model overview of DiffSMol. Credit: *Nature Machine Intelligence* (2025). DOI: [10.1038/s42256-025-01030-w](https://doi.org/10.1038/s42256-025-01030-w)

Using advanced artificial intelligence, researchers have developed a novel method to make drug development faster and more efficient.

In a new paper, Xia Ning, lead author of the study and a professor of biomedical informatics and computer science and engineering at The Ohio State University, introduces DiffSMol, a generative AI model capable of generating realistic 3D structures of small molecules that can serve as promising [drug candidates](#).

The study is [published](#) in *Nature Machine Intelligence*.

DiffSMol works by analyzing the shapes of known ligands—molecules that bind to [protein targets](#)—and using these shapes as conditions to generate novel 3D molecules that better bind to the protein targets. Study results showed that when used to create molecules with the potential to quicken the drug-making process, DiffSMol has a 61.4% [success rate](#), outperforming prior research attempts that achieved success about 12% of the time.

"By using well-known shapes as a condition, we can train our model to generate novel molecules with similar shapes that don't exist in previous chemical databases," said Ning.

Once DiffSMol learns the shapes of these ligands, the team's model can also tailor those new molecules to encourage certain binding characteristics. According to the paper, this suggests the model could modify them to have more favorable drug-like properties, altering aspects like their synthesizability or toxicity.

It takes about a decade for a drug to be developed and brought to market, but shortening that time could open up new paths to develop novel pharmaceuticals and agrochemical agents for use in many different industries. Chiefly, compared to existing [computational methods](#) used to design drugs, DiffSMol takes only one second to generate a [single molecule](#), said Ziqi Chen, co-author of the study and a former doctoral student in computer science and engineering at Ohio State.

"Generative AI models have the potential to substantially expedite this process and improve cost efficiency," said Chen.

To demonstrate DiffSMol's abilities, researchers conducted [case studies](#) on molecules used in two crucial drug targets, one called cyclin-dependent kinase 6 (CDK6), which can regulate cell cycles and disrupt cancer growth, and neprilysin (NEP), which is used in therapies aimed at slowing the progression of Alzheimer's. Their results revealed that the molecules DiffSMol created would likely be very effective, said Ning.

"It's very encouraging for us to find molecules with even better properties than known ligands," she said. "It indicates that our developed models have great potential in identifying good drug candidates."

The researchers also made DiffSMol's code available for other scientists to use.

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At the moment, DiffSMol is still only able to generate new molecules based on shapes of previously known ligands, which is a limitation the team hopes to overcome in future work. Further research will also be aimed at improving the model's ability to learn from complex molecule data and generate molecules that exhibit a wider range of potential interactions.

Despite the need for more testing, the team anticipates that continued leaps in AI will one day allow their work to reach new heights, partly due to AI's global rise in popularity.

"Nowadays, people are applying these advanced models to molecule generation, to chemistry, to nearly all science areas," said Ning. "This area grows really fast and I don't see it slowing down anytime soon."

More information: Ziqi Chen et al, Generating 3D small binding molecules using shape-conditioned diffusion models with guidance, *Nature Machine Intelligence* (2025). DOI: [10.1038/s42256-025-01030-w](https://doi.org/10.1038/s42256-025-01030-w)

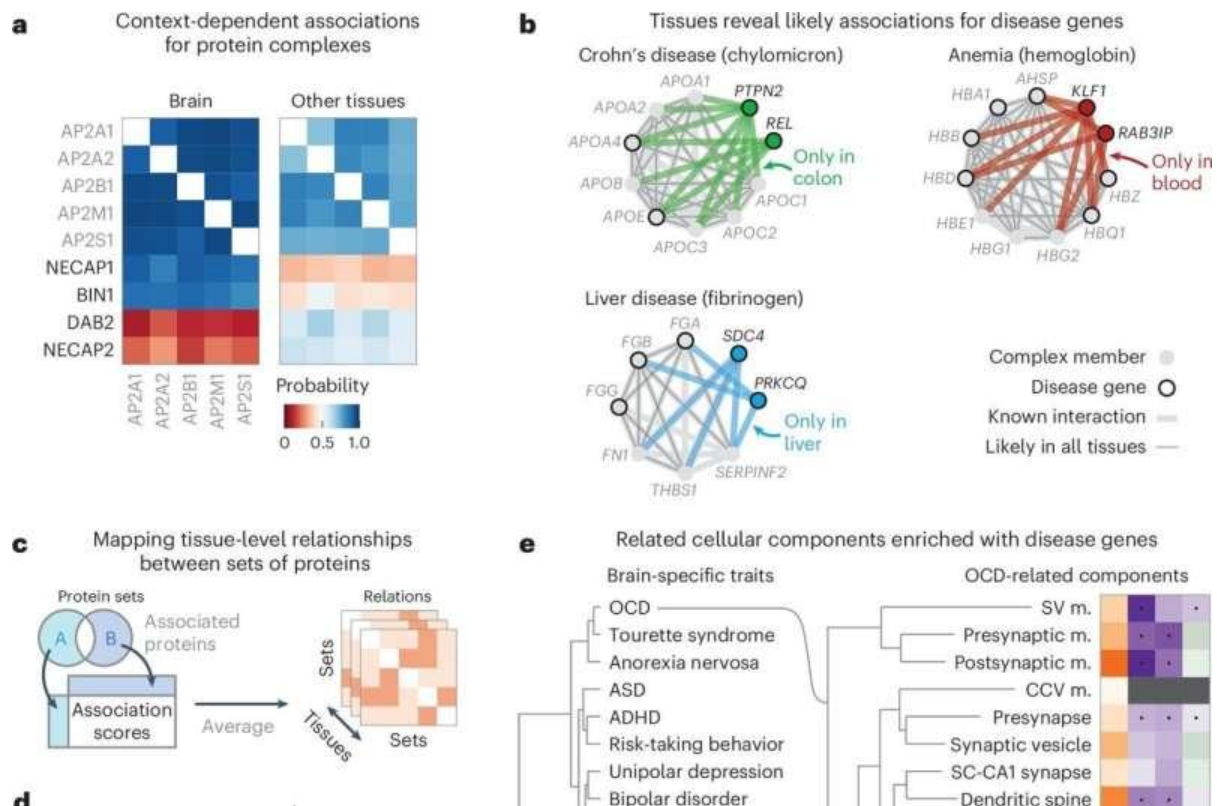
Journal information: [Nature Machine Intelligence](#)

Provided by [The Ohio State University](#)

MAY 12, 2025

New atlas provides deeper understanding of which proteins work together in specific tissues

by Peter Rüegg, [ETH Zurich](#)



Association scores define relationships between protein sets. Credit: *Nature*

Biotechnology (2025). DOI: 10.1038/s41587-025-02659-z

The human body and its organs are composed of a wide variety of cell types. Although all cells contain the same genes, they function very differently—partly because protein interactions differ between cells.

Researchers at ETH Zurich have now created an atlas showing which proteins work together in which tissues. These findings will help to identify disease genes more precisely and develop drugs that act specifically where they are needed and nowhere else. The work is [published](#) in the journal *Nature Biotechnology*.

Proteins seldom work alone, but in teams: They interact with other proteins, for example, by forming complexes or along biochemical signaling cascades.

In order to better understand how cells function in different tissues or organs of the body, scientists must first find out which proteins are working together and how their coordination differs from cell type to cell type. "If we know the specific protein interactions, we can better understand what distinguishes a liver cell from a brain cell," says Pedro Beltrao, professor at the Institute of Molecular Systems Biology at ETH Zurich.

Sifting through huge data sets

However, it is not yet sufficiently established which of these protein interactions occur universally throughout the body or are specific to a particular tissue. One reason for this is that systematically investigating protein interactions by way of laboratory experiments is expensive, time-consuming, and complicated.

Consequently, Beltrao and his colleagues opted for bioinformatics and tapped existing data collections on the proteome (the totality of all proteins present in a cell at a given time).

In their study, the ETH researchers combed through proteome data from over 7,800 human biopsies. Based on these huge data sets, the researchers then inferred tissue-specific protein interactions in eleven different tissue types.

Every fourth interaction is tissue-specific

The ETH researchers found that every fourth protein interaction is indeed tissue-specific. For example, one interaction may occur only in liver tissue, but not in the other ten tissue types examined. Beltrao attributes most of the differences between tissues to [cellular components](#) that are specific to cell types. Cellular compartments are distinct areas within a cell where certain activities take place—which is where some protein interactions occur.

A particularly high number of tissue-specific protein interactions occur in the brain and its neural connections (synapses). In order to examine the protein teams in synapses, Beltrao and his colleagues used data collected by ETH Professor Bernd Wollscheid in his laboratory.

Better drugs targeting specific areas

The findings are also valuable for pharmaceutical research. Knowledge of organ-specific protein interactions helps researchers to better understand disease mechanisms and identify [disease genes](#) to improve [drug development](#).

"Proteins engaging in teamwork usually also influence the same disease," Beltrao explains. "So if we can say which proteins work together exclusively in [nerve cells](#), for example, we can better define the genes involved in the disease."

Today's drugs can have a broad spectrum of activity, and as a result, incur undesirable side effects in parts of the body beyond the therapeutic target. The findings from this study may

help researchers to search for active substances that act on proteins in a specific organ or [tissue](#). This will increase drug safety thanks to specificity.

More information: Diederik S. Laman Trip et al, A tissue-specific atlas of protein–protein associations enables prioritization of candidate disease genes, *Nature*

Biotechnology (2025). DOI: [10.1038/s41587-025-02659-z](https://doi.org/10.1038/s41587-025-02659-z)

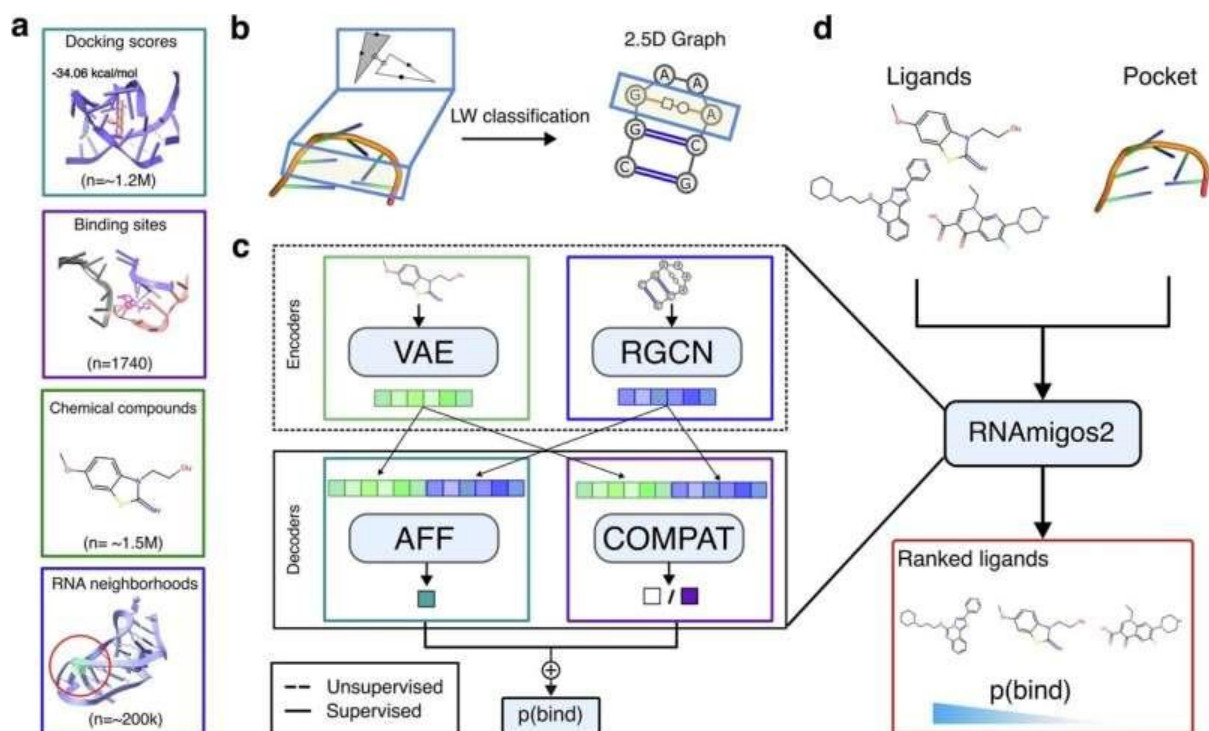
Journal information: [Nature Biotechnology](#)

Provided by [ETH Zurich](#)

MAY 12, 2025

Q&A: AI speeds up search for RNA-targeting drugs, opening new therapeutic possibilities

by Lorena Infante Lara, [Vanderbilt University](#)



Overview of the RNAmigos2 compound screening pipeline, including the datasets used, the models used to learn RNA-ligand interactions, and more. This image is Figure 1 from the paper. Credit: [Carvajal-Patiño, Mallet, et al.](#)

The majority of RNAs in each of our cells don't code for any of the thousands of proteins that make up our bodies. Instead, noncoding RNAs have critical roles in many biological processes—such as gene expression—making them ideal targets for a variety of ailments,

including cancers. Despite that, the first RNA-targeting therapeutic in the market was launched only five years ago, and the vast majority of all Food and Drug Administration–approved drugs target proteins.

Targeting ncRNAs with drugs presents a much larger therapeutic opportunity than targeting proteins, but the currently available drug discovery tools are slow and computationally intensive.

At Vanderbilt University, Assistant Professor of Molecular Physiology and Biophysics and core member of the Center for Applied AI in Protein Dynamics Carlos Oliver is working with collaborators to unlock the untapped potential of ncRNAs, as they are a promising family of targets for the development of novel small-molecule therapeutics. Oliver's work was [published](#) in *Nature Communications* and was completed in collaboration with researchers at McGill University in Montreal, Canada, and the École des Mines de Paris in Paris, France.

We sat down with Oliver to discuss targeting RNAs in medicine, the problems with current technologies, RNAmigos2, and the implications of the team's findings.

What issue/problem does your research address?

Our research addresses the challenge of discovering small-molecule drugs that target RNA, a promising yet underexplored frontier in medicine. While most drugs target proteins, only a tiny fraction of RNA has been harnessed beyond the small portion that codes for proteins, despite RNA's critical role in diseases like cancer and viral infections.

Traditional drug screening methods, like molecular docking, are too slow and computationally intensive to efficiently explore RNA's vast potential, limiting progress in this field.

What was unique about your approach to the research?

We developed RNAmigos2, a deep-learning tool that accelerates RNA-targeted drug screening by 10,000 times compared to traditional docking, which is physics-based and computationally expensive. RNAmigos2 uses a novel combination of coarse-grained 3D RNA modeling, synthetic docking data for training, and RNA-specific self-supervision to overcome the scarcity of RNA-ligand data. Unlike prior methods, it was rigorously validated on in vitro data it had never encountered during training, proving its real-world reliability.

What were your top three findings?

1. RNAmigos2 ranks [active compounds](#) in the top 2.8% of candidates across diverse RNA targets in the Protein Data Bank [the single repository of information about the 3D structures of proteins, [nucleic acids](#), and complex assemblies], matching or surpassing docking accuracy while running in seconds instead of hours.

2. Our tool works synergistically with more fine-grained docking software by rapidly suggesting promising compounds for further validation. With a hybrid approach, we improve the discovery efficiency in all testing RNAs.
3. In a blind test, RNAmigos2 screened 20,000 compounds in minutes against unseen RNA riboswitches from an in vitro microarray. It achieved a 2.93-fold enrichment of active molecules at the top 1% and improved the diversity of hits over those obtained by docking.

What do you hope will be achieved with the research results in the short term?

We hope RNAmigos2, [freely available as an open-source tool](#), will transform early-stage RNA drug discovery. By enabling researchers to rapidly screen large compound libraries and pinpoint promising candidates, it could streamline lab testing and accelerate the development of RNA-targeted therapies for clinical trials within the next few years.

What are your highest translational aspirations that might result from this research?

Our long-term vision is to unlock RNA as a primary drug target, revolutionizing treatment for complex diseases. We aspire to see RNAmigos2 contribute to new therapies for conditions such as cancer, genetic disorders, and [viral infections](#) in which RNA's regulatory roles are pivotal—potentially expanding the druggable space and advancing precision medicine over the next decade.

Who or what made the difference in your research?

Our team merged RNA biology, deep learning, and cheminformatics expertise, and this diverse collaboration was the backbone of our success. Public resources like the Protein Data Bank and the ChEMBL database, alongside tools like rDock, provided critical data and benchmarks. Incremental steps, such as refining the 2.5D graph representation of RNA structures and tweaking neural network designs, steadily built our breakthrough.

Where is this research taking you next?

As the state-of-the-art in structure-based RNA drug discovery, RNAmigos2 sets the stage for further innovation. I will be working to integrate it with binding site–prediction tools to identify RNA targets at the genome level and to build partnerships with experimental groups for deeper validation. With our open-source code, datasets, and model weights, global researchers can enhance its accuracy, apply it to new RNA families, and drive the next wave of RNA therapeutics.

More information: Juan G. Carvajal-Patiño et al, RNAmigos2: accelerated structure-based RNA virtual screening with deep graph learning, *Nature Communications* (2025). DOI: [10.1038/s41467-025-57852-0](https://doi.org/10.1038/s41467-025-57852-0)

Provided by [Vanderbilt University](#)

With AI, researchers predict the location of virtually any protein within a human cell

a

PC2

PC1

Localization

- Actin filaments
- Aggresome
- Cell junctions
- Centriole satellite
- Centrosome
- Cytoskeletal bridge
- Cytoskeletal bundle
- Cytosol
- Endoplasmic reticulum
- Ethosomes
- Focal adhesion site
- Golgi apparatus
- Intermediate filaments
- Kinetochore
- Lipid droplets
- Lysosomes
- Mitochondrial end
- Mitochondrion
- Mitotic chromosome
- Mitotic spindle
- No staining
- Nuclear bodies
- Nuclear envelope
- Nuclear speckles
- Nucleol
- Nucleolar fibrillar center
- Nucleolar rim
- Nucleoplasm
- Nucleus
- Peroxisomes
- Plasma membrane
- Ribbs & Rings
- Vesicles

Nuclear localization

- Nucleoplasm
- Cytosol
- Nucleoplasm + Cytosol

PC2

PC1

A protein located in the wrong part of a cell can contribute to several diseases, such as Alzheimer's, cystic fibrosis, and cancer. But there are about 70,000 different proteins and protein variants in a single human cell, and since scientists can typically only test for a handful in one experiment, it is extremely costly and time-consuming to identify proteins' locations manually.

A new generation of computational techniques seeks to streamline the process using [machine-learning models](#) that often leverage datasets containing thousands of proteins and their locations, measured across multiple cell lines. One of the largest such datasets is the Human Protein Atlas, which catalogs the subcellular behavior of over [13,000 proteins in more than 40 cell lines](#). But as enormous as it is, the Human Protein Atlas has only explored about 0.25% of all possible pairings of all proteins and cell lines within the database.

Now, researchers from MIT, Harvard, and the Broad Institute have developed a new computational approach that can efficiently explore the remaining uncharted space. Their method can predict the location of any protein in any human cell line, even when both protein and cell have never been tested before.

The paper is [published](#) in *Nature Methods*.

The technique goes one step further than many AI-based methods by localizing a protein at the single-cell level, rather than as an averaged estimate across all the cells of a specific type. This single-cell localization could pinpoint a protein's location in a specific cancer cell after treatment, for instance.

The researchers combined a protein language model with a special type of computer vision model to capture rich details about a protein and cell. In the end, the user receives an image of a cell with a highlighted portion indicating the model's prediction of where the protein is located. Since a protein's localization is indicative of its functional status, this technique could help researchers and clinicians more efficiently diagnose diseases or identify drug targets, while also enabling biologists to better understand how complex biological processes are related to protein localization.

"You could do these protein-localization experiments on a computer without having to touch any lab bench, hopefully saving yourself months of effort. While you would still need to verify the prediction, this technique could act like an initial screening of what to test for experimentally," says Yitong Tseo, a graduate student in MIT's Computational and Systems Biology program and co-lead author of a paper on this research.

Tseo is joined on the paper by co-lead author Xinyi Zhang, a graduate student in the Department of Electrical Engineering and Computer Science (EECS) and the Eric and Wendy Schmidt Center; Yunhao Bai of the Broad Institute of MIT and Harvard; and senior authors Fei Chen, an assistant professor at Harvard and a member of the Broad Institute, and Caroline Uhler, the Andrew and Erna Viterbi Professor of Engineering in EECS and the Institute for Data, Systems, and Society (IDSS), who is also director of the Eric and Wendy Schmidt Center at the Broad Institute and a researcher at MIT's Laboratory for Information and Decision Systems (LIDS).

Collaborating models

Many existing protein prediction models can only make predictions based on the protein and cell data on which they were trained or are unable to pinpoint a protein's location within a single cell.

To overcome these limitations, the researchers created a two-part method for prediction of unseen proteins' subcellular location, called PUPS.

The first part utilizes a protein sequence model to capture the localization-determining properties of a protein and its 3D structure based on the chain of amino acids that forms it.

The second part incorporates an image inpainting model, which is designed to fill in missing parts of an image. This computer vision model looks at three stained images of a cell to gather information about the state of that cell, such as its type, individual features, and whether it is under stress.

PUPS joins the representations created by each model to predict where the protein is located within a single cell, using an image decoder to output a highlighted image that shows the predicted location.

"Different cells within a cell line exhibit different characteristics, and our model is able to understand that nuance," Tseo says.

A user inputs the sequence of amino acids that form the protein and three cell stain images—one for the nucleus, one for the microtubules, and one for the endoplasmic reticulum. Then PUPS does the rest.

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A deeper understanding

The researchers employed a few tricks during the training process to teach PUPS how to combine information from each model in such a way that it can make an educated guess on the protein's location, even if it hasn't seen that protein before.

For instance, they assign the model a secondary task during training: to explicitly name the compartment of localization, like the cell nucleus. This is done alongside the primary inpainting task to help the model learn more effectively.

A good analogy might be a teacher who asks their students to draw all the parts of a flower in addition to writing their names. This extra step was found to help the model improve its general understanding of the possible cell compartments.

In addition, the fact that PUPS is trained on proteins and cell lines at the same time helps it develop a deeper understanding of where in a cell image proteins tend to localize.

PUPS can even understand, on its own, how different parts of a protein's sequence contribute separately to its overall localization.

"Most other methods usually require you to have a stain of the protein first, so you've already seen it in your training data. Our approach is unique in that it can generalize across proteins and cell lines at the same time," Zhang says.

Because PUPS can generalize to unseen proteins, it can capture changes in localization driven by unique protein mutations that aren't included in the Human Protein Atlas.

The researchers verified that PUPS could predict the subcellular location of new proteins in unseen [cell lines](#) by conducting lab experiments and comparing the results. In addition, when compared to a baseline AI method, PUPS exhibited on average less prediction error across the proteins they tested.

In the future, the researchers want to enhance PUPS so the model can understand protein-[protein](#) interactions and make localization predictions for multiple proteins within a cell. In the longer term, they want to enable PUPS to make predictions in terms of living human tissue, rather than cultured cells.

More information: Xinyi Zhang et al, Prediction of protein subcellular localization in single cells, *bioRxiv* (2024). DOI: [10.1101/2024.07.25.605178](https://doi.org/10.1101/2024.07.25.605178)

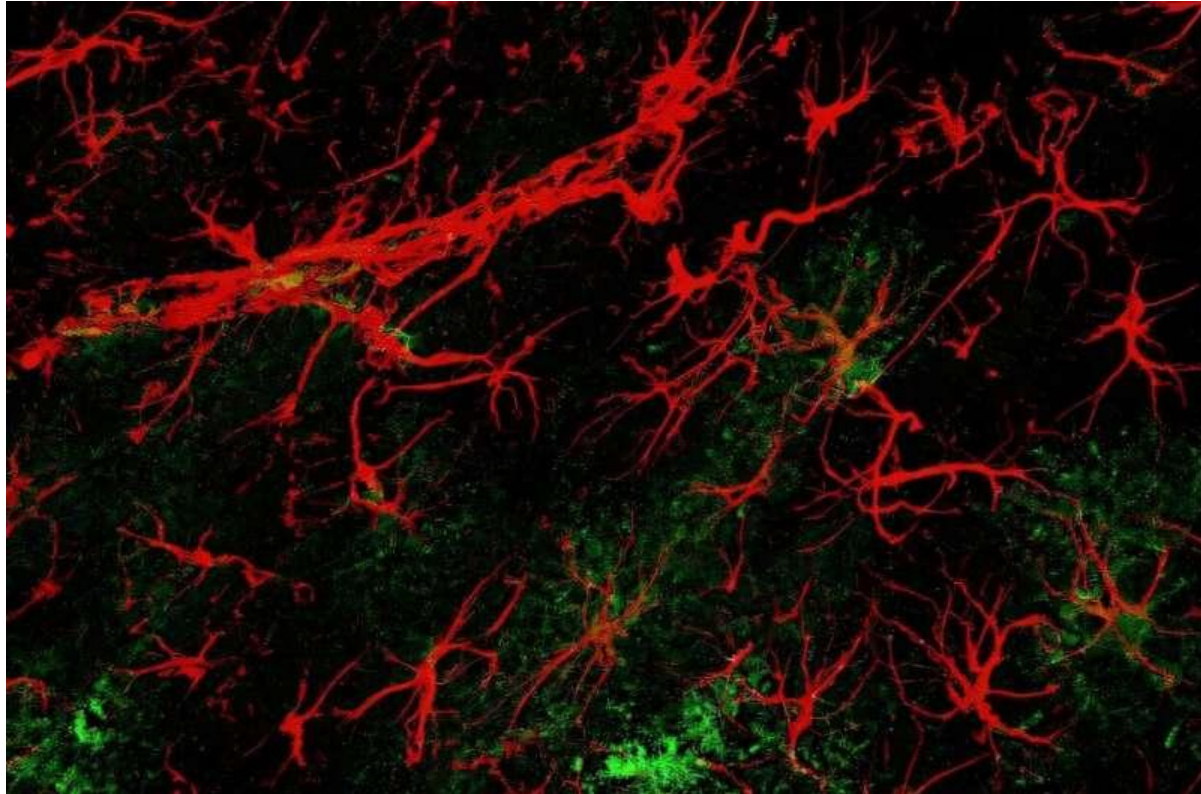
Xinyi Zhang et al, Prediction of protein subcellular localization in single cells, *Nature Methods* (2025). DOI: [10.1038/s41592-025-02696-1](https://doi.org/10.1038/s41592-025-02696-1) , www.nature.com/articles/s41592-025-02696-1

Journal information: [Nature Methods](#) , [bioRxiv](#)
Provided by [Massachusetts Institute of Technology](#)

MAY 13, 2025

Molecule reverses cognitive deficits associated with aging and dementia in animal tests

by Maria Fernanda Ziegler, [FAPESP](#)



Rodent hippocampal astrocytes (in red) overexpressing hevin (in green). Credit: Felipe Cabral-Miranda and Ana Paula Bergamo Araujo

In Brazil, researchers from the Federal University of Rio de Janeiro (UFRJ) and collaborators from the University of São Paulo (USP) have discovered that a molecule called Hevin can reverse cognitive impairment. The study, conducted in mice, showed that this glycoprotein produced by brain cells (astrocytes) is able to increase the connections between neurons (synapses) in aged rodents and in animal models of Alzheimer's disease.

"Hevin is a well-known molecule involved in neural plasticity. It's naturally secreted by cells in the central nervous system that support the functioning of neurons and are known as astrocytes. We found that the overproduction of Hevin is capable of reversing cognitive deficits in aged animals by improving the quality of synapses in these rodents," says Flávia Alcantara Gomes, head of the Cellular Neurobiology Laboratory at the UFRJ Institute of Biomedical Sciences.

The study is [published](#) in the journal *Aging Cell*.

It is important to note that there is still a long way to go before a molecule involved in the process of reversing cognitive impairment becomes a drug. This is a basic science study in mice.

Another aspect to consider is the need to ensure that this compound can cross the [blood-brain barrier](#), which would require efforts to design molecules with this property and the same therapeutic potential.

"Of course, in the future it'll be possible to develop drugs that have the same effect as Hevin. For now, however, the fundamental benefit of this work is a deeper understanding of the cellular and molecular mechanisms of Alzheimer's disease and the aging process," says Gomes.

"The originality lies in understanding the role of the astrocyte in this process. We've taken the focus away from neurons, shedding light on the role of astrocytes, which we've shown could also be a target for new treatment strategies for Alzheimer's disease and [cognitive impairment](#)."

Evidence-based hypothesis

By observing public data, the researchers found that Hevin levels in the brain of Alzheimer's patients decrease compared to healthy individuals of the same age.

With this information and using a recombinant viral vector, the group at the UFRJ Institute of Biomedical Sciences overexpressed Hevin in astrocytes from aged animals and in transgenic animal models of Alzheimer's disease.

In addition, the set of proteins produced by the [brain cells](#) (brain proteome) of these animals was also analyzed. Comparing the animals with and without Hevin overproduction, the researchers found that 89 proteins were differentially expressed.

This stage of the work was carried out in the "Redox Proteomics Core" Multiuser Laboratory of the Center for Redox Processes in Biomedicine (Redoxoma)—a FAPESP Research, Innovation and Dissemination Center (RIDC) based at the University of São Paulo's Institute of Chemistry (IQ-USP).

"The synapse depends on proteins to release a chemical signal from one neuron to another. Proteomic analysis showed that Hevin reinforcement in astrocytes regulates different groups of proteins involved in synapses. We observed an increase in synapses, or in other words, a closer connection between neurons and, consequently, better cognitive performance," explains Danilo Bilches Medinas, professor at the IQ-USP Department of Biochemistry.

Amyloid plaques

In addition to identifying the potential of Hevin to reverse cognitive deficits in rodents through behavioral testing, the researchers also observed that overexpression of the molecule in astrocytes did not affect the deposition of beta-amyloid plaques in the hippocampus—a hallmark of Alzheimer's disease that has been the focus of disease studies and a target for drug development.

"To our surprise, although the cognitive deficit was reversed in Alzheimer's model animals, there was no change in the content of the plaques. This highlights the complexity of the disease in terms of having a multifactorial mechanism. This is illustrated by older people who have plaque formation but show no symptoms of the disease," says Felipe Cabral-Miranda, a biomedical scientist at the UFRJ Institute of Biomedical Sciences and first author of the study.

"Although there's still no consensus among researchers, I work with the hypothesis that the formation of beta-amyloid plaques isn't the cause of Alzheimer's. And the results of the study, by providing proof of concept for a molecule that can reverse [cognitive decline](#) without affecting beta-[amyloid plaques](#), support the hypothesis that these, although involved in the mechanisms of the pathology, aren't enough to cause Alzheimer's," he adds.

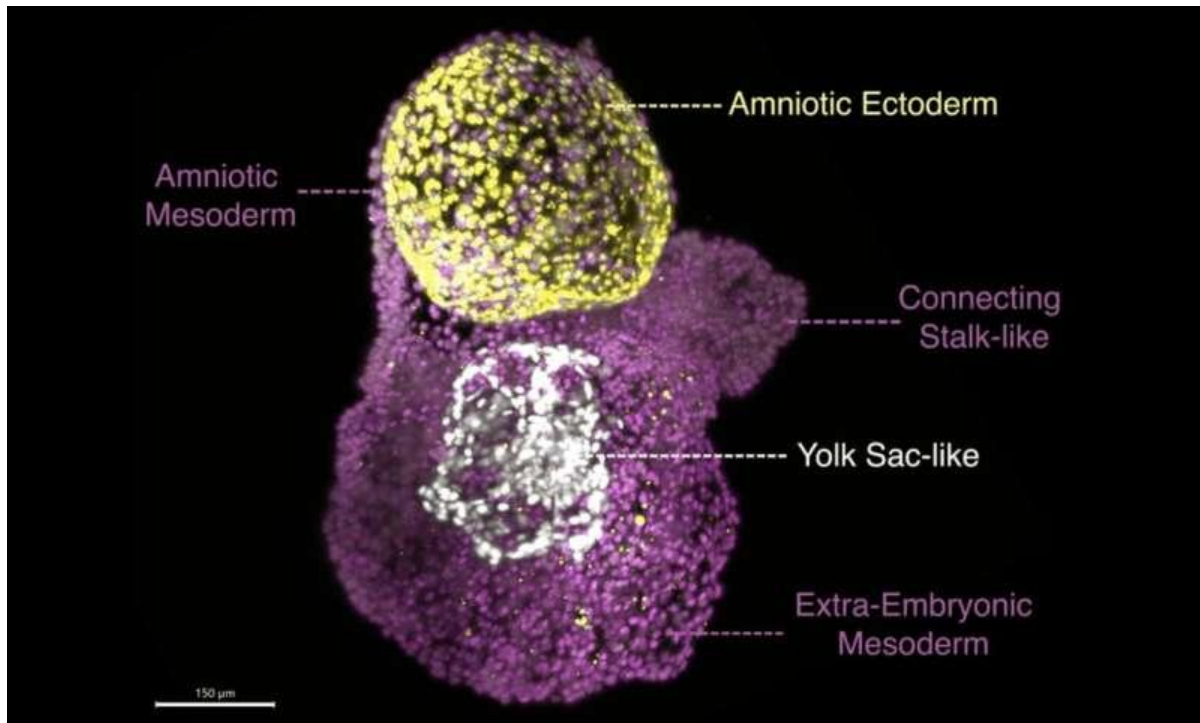
More information: Felipe Cabral-Miranda et al, Astrocytic Hevin/SPARCL-1 Regulates Cognitive Decline in Pathological and Normal Brain Aging, *Aging Cell* (2025). DOI: [10.1111/accel.14493](https://doi.org/10.1111/accel.14493)

Journal information: [Aging Cell](#)
Provided by [FAPESP](#)

MAY 15, 2025

Stem cell model replicates human amniotic sac development past two weeks

by [The Francis Crick Institute](#)



Microscopy image of a PGA at day eight showing the early tissues supporting the embryo, including the amniotic sac and the yolk sac-like structures, surrounded by (extra-embryonic) mesoderm tissue. Credit: Gharibi, B. (2025). *Cell*.

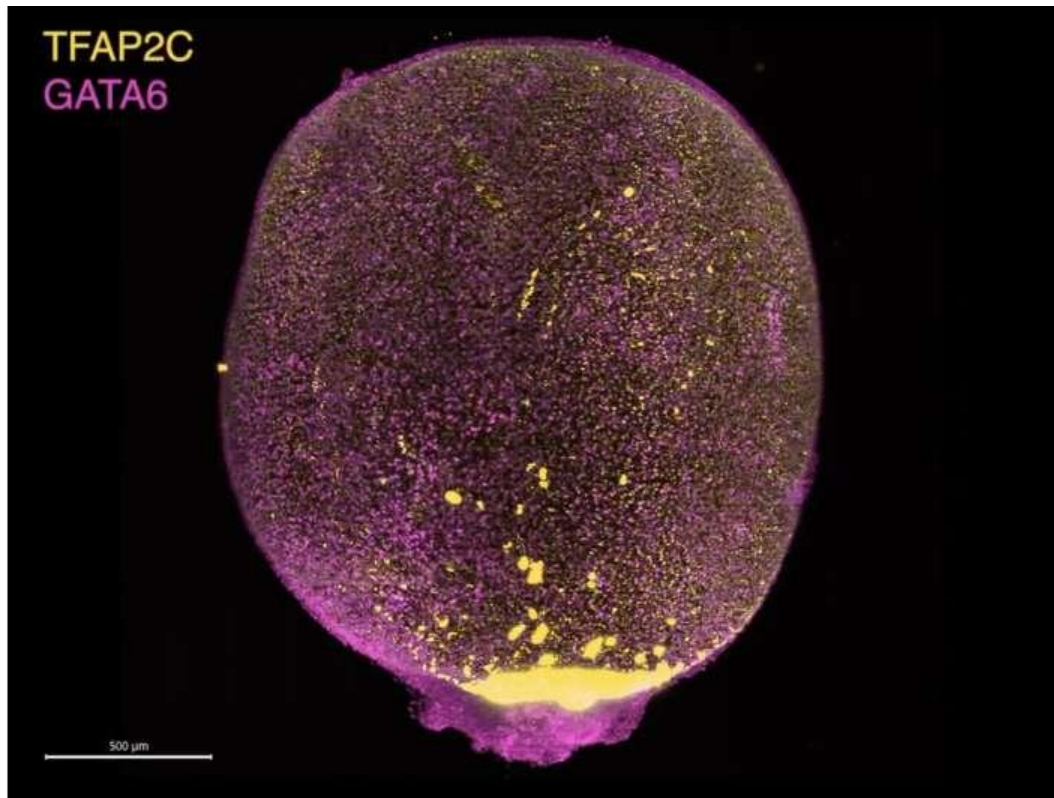
Researchers at the Francis Crick Institute have developed a new stem cell model of the mature human amniotic sac, which replicates development of the tissues supporting the embryo from two to four weeks after fertilization. This is the first model of amniotic sac development after two weeks.

As described in research [published](#) in *Cell*, the new model can be used to study the origin and function of the human amnion and help identify previously unknown ways the amniotic sac might support [embryonic development](#). It also holds promise for medical procedures that make use of the amniotic membrane.

The amnion is a protective membrane that balloons into a sac containing [amniotic fluid](#), which leaves the body when the mother's waters break before labor. Until recently, its major

role was thought to be surrounding and protecting the baby, cushioning it against shocks and allowing nutrients to pass before the placenta forms.

Researchers haven't been able to study the amnion in detail because current stem cell embryo models don't typically capture later stages of human development and, for ethical reasons, human embryos can't be studied after fourteen days.



Microscopy image of a PGA at day 18 showing that PGAs are composed of two different cell populations (magenta, the extra-embryonic mesoderm and yellow, the amniotic endoderm). Credit: Gharibi, B. (2025). *Cell*

Replicating the amniotic sac

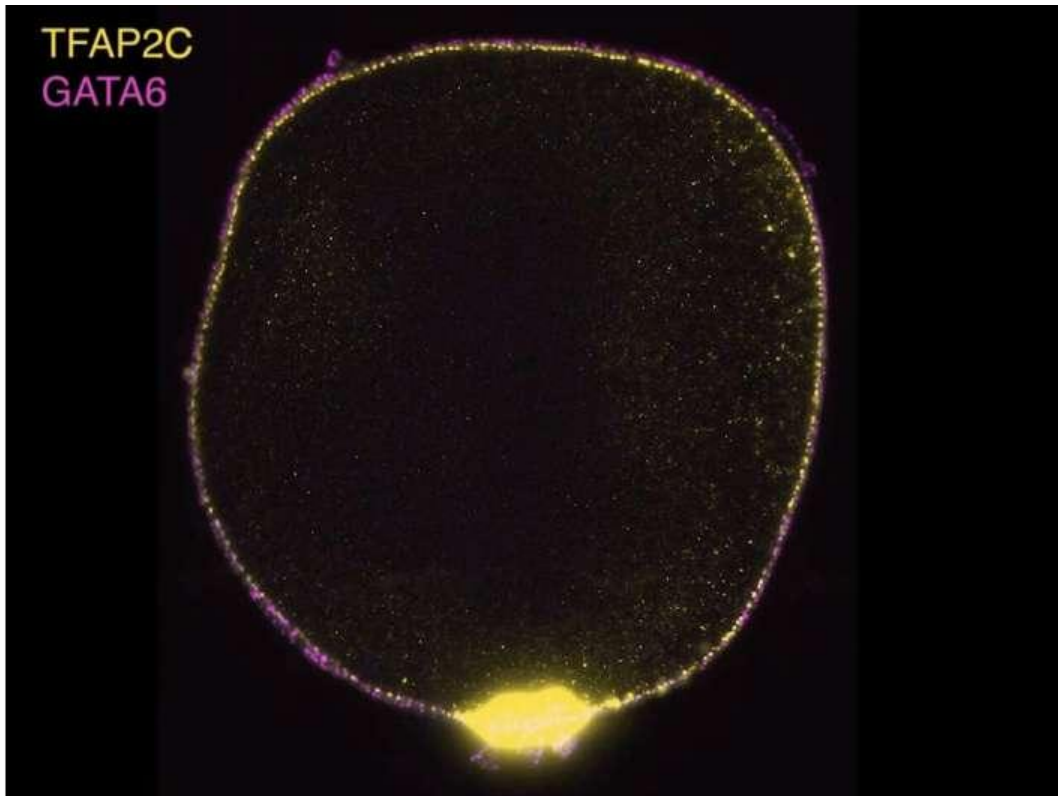
The team at the Crick created a new 3D model—called a post-gastrulation amnioid (PGA)—which closely resembles the human amnion and other supportive tissues after gastrulation (when the embryo's cells organize into layers that will form tissues and organs).

They did this by culturing [human embryonic stem cells](#) in a series of steps with just two chemical signals over 48 hours, after which the cells organized themselves into the inner and outer layers of the amnion.

A sac-like structure formed by day 10 in over 90% of the PGAs. These gradually expanded in size over 90 days, without being given any further signals. The cell composition in the models showed remarkable similarity to the human amniotic sac, and the fluid within PGAs mimicked the contents of human amniotic fluid.

Crosstalk between the amnion and the embryo

Using genetic manipulation techniques, the researchers found a transcription factor (a gene which switches other genes on or off) called GATA3 caused impaired growth of amnion tissue if switched off in PGAs.



Microscopy image of a PGA showing it is a two-membrane sac. The inner membrane represents amniotic endoderm cells and the outer extra-embryonic mesoderm cells. The dark space in the middle represents the fluid within PGAs. Credit: Gharibi, B. (2025). *Cell* Conversely, when they boosted GATA3 in [embryonic stem cells](#), the cells developed an amniotic sac-like structure without being given any other signals. These experiments showed that GATA3 is necessary to kick-start amnion development.

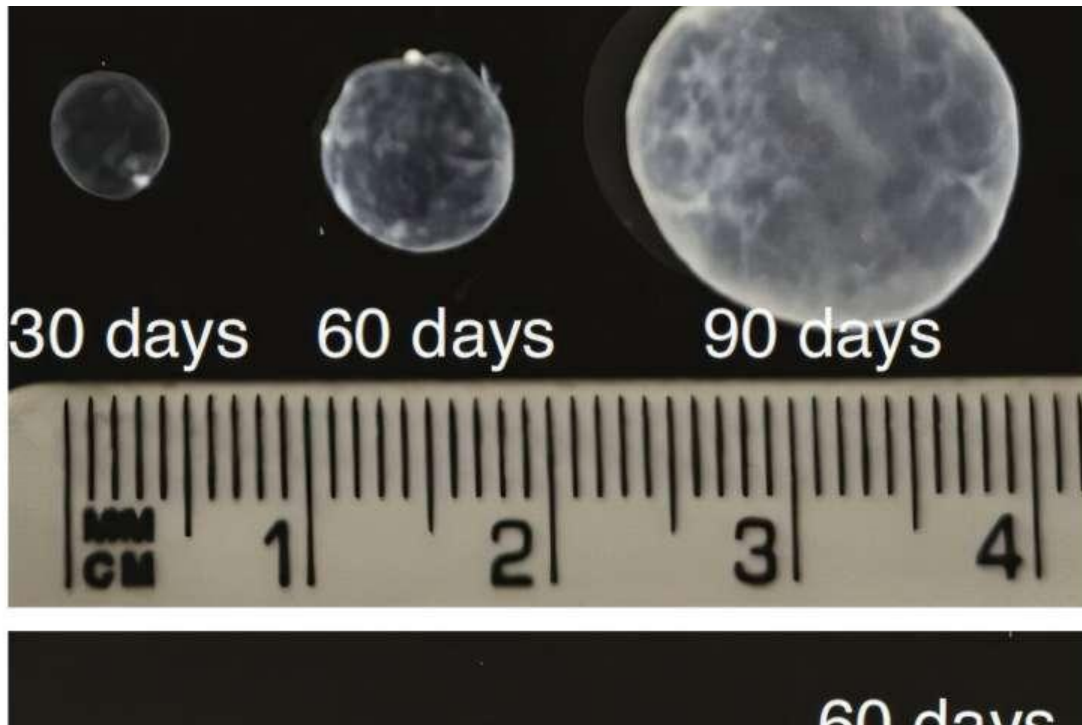
Finally, the team asked if the amniotic tissues help the embryonic cells develop and specify rather than just protect them. They mixed PGA cells with embryonic stem cells that had not been treated, and saw that untreated cells developed amniotic sac-like structures, showing that signals from the amnion might indeed communicate with embryonic cells..

A new approach for medical procedures

Due to its regenerative, anti-inflammatory and antimicrobial properties, the amniotic sac membrane can be donated by people who have had elective c-sections, to be used for medical procedures like reconstructing the cornea in the eye, repairing the uterus lining or treating burns and ulcers.

Because transplanted tissue relies on donations, the team believes PGAs could provide an alternative source of amniotic membranes, which could even be grown from a patient's own cells.

The researchers are now working with Crick's Translation team to explore the potential of using PGAs in the clinic, as well as delving further into understanding the communication between the amniotic sac and the embryonic cells.



- In the study, the majority of PGAs grew to roughly the same size and were able to survive more than 90 days. Credit: Gharibi, B. (2025). *Cell*



- PGAs (translucent spheres) are large enough to be visible inside the flask. Credit: Gharibi, B. (2025). *Cell*
-

Shifting our view of the amnion

Silvia Santos, Group Leader of the Quantitative Stem Cell Biology Laboratory at the Crick and senior author, said, "Early human development is still a black box due to ethical and technical constraints, but our new model gives some visibility during this critical time, without needing to use [human embryos](#)."

"This work shifts our view of the amnion as just a protective structure: it's actively talking to the embryo and promoting its growth. We're also excited about the potential of PGAs as a fast, cheap and scalable way to provide amniotic membranes for medical use."

Borzo Gharibi, Principal Laboratory Research Scientist in the Quantitative Stem Cell Biology Laboratory at the Crick and first author, said, "We were originally investigating how embryonic cells form their identity, and then our research took a very interesting turn, leading to the development of PGAs."

"This model replicates the mature human amnion for the first time, closely mimicking the structural and functional traits of the human amniotic sac with high reproducibility. This gives researchers a tool to investigate later stages of human development and the functions of tissues supporting the embryo."

This project was made possible through close collaboration with the Genomics, Metabolomics, and Proteomics teams at the Crick.

More information: Post-gastrulation amnioids as a stem cell-derived model of human extra-embryonic development, *Cell* (2025). DOI:

[10.1016/j.cell.2025.04.025](https://doi.org/10.1016/j.cell.2025.04.025). [www.cell.com/cell/fulltext/S0092-8674\(25\)00458-1](https://www.cell.com/cell/fulltext/S0092-8674(25)00458-1)

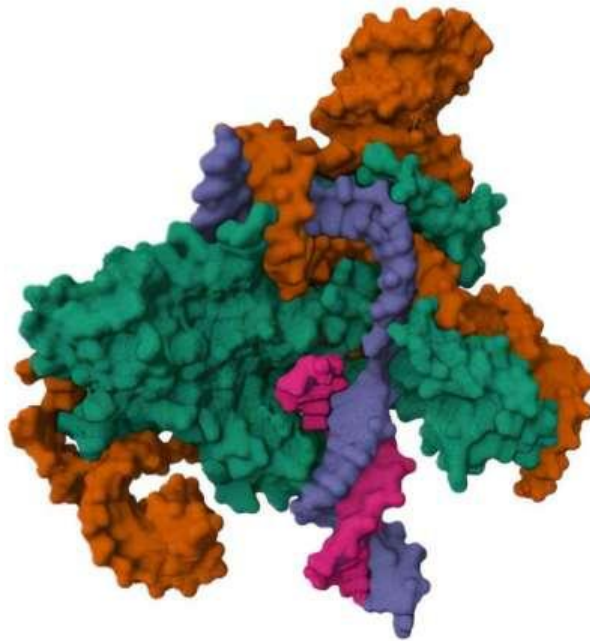
Journal information: *Cell*

Provided by [The Francis Crick Institute](#)

MAY 15, 2025

Cas9 ancestor engineered into a compact genome editing tool

by Jennifer Michalowski, [Broad Institute of MIT and Harvard](#)



PDB ID 7UTN IscB (green) bound to DNA (purple and pink) and RNA (orange). Credit: RCSB.org

Scientists at the McGovern Institute and the Broad Institute of MIT and Harvard have reengineered a compact RNA-guided enzyme they found in bacteria into an efficient, programmable editor of human DNA. The engineered protein, called NovalscB, can be adapted to make precise changes to the genetic code, modulate the activity of specific genes, or carry out other editing tasks. Because its small size simplifies delivery to cells, NovalscB's developers say it is a promising candidate for developing gene therapies to treat or prevent disease.

The study was led by McGovern Institute investigator and Broad Institute core member Feng Zhang, who is also the James and Patricia Poitras Professor of Neuroscience at MIT and a Howard Hughes Medical Institute investigator. Zhang and his team reported their [work](#) in the journal *Nature Biotechnology*.

Compact tools

NovalscB is derived from a bacterial DNA cutter that belongs to a family of proteins called IscBs, which Zhang's lab discovered in 2021. IscBs are a type of OMEGA system, the evolutionary ancestors to Cas9, which is part of the bacterial CRISPR system that Zhang and others have developed into powerful genome-editing tools. Like Cas9, IscB enzymes cut DNA at sites specified by an RNA guide. By reprogramming that guide, researchers can redirect the enzymes to target sequences of their choosing.

IscBs had caught the team's attention not only because they share key features of CRISPR's DNA-cutting Cas9, but also because they are a third of its size. That would be an advantage for potential gene therapies: Compact tools are easier to deliver to cells, and with a small enzyme, researchers would have more flexibility to tinker, potentially adding new functionalities without creating tools that were too bulky for [clinical use](#).

From their initial studies of IscBs, researchers in Zhang's lab knew that some members of the family could cut DNA targets in [human cells](#). None of the bacterial proteins worked well enough to be deployed therapeutically, however. The team would have to modify an IscB to ensure it could edit targets in human cells efficiently without disturbing the rest of the genome.

To begin that engineering process, Soumya Kannan, a graduate student in Zhang's lab who is now a junior fellow at the Harvard Society of Fellows, and postdoctoral fellow Shiyong Zhu first searched for an IscB that would make a good starting point. They tested nearly 400 different IscB enzymes that can be found in bacteria. Ten were capable of editing DNA in human cells.

Even the most active of those would need to be enhanced to make it a useful genome editing tool. The challenge would be increasing the enzyme's activity, but only at the sequences specified by its RNA guide. If the enzyme became more active, but indiscriminately so, it would cut DNA in unintended places. "The key is to balance the improvement of both activity and specificity at the same time," Zhu explained.

Zhu noted that bacterial IscBs are directed to their target sequences by relatively short RNA guides, which makes it difficult to restrict the enzyme's activity to a specific part of the genome. If an IscB could be engineered to accommodate a longer guide, it would be less likely to act on sequences beyond its intended target.

To optimize IscB for human genome editing, the team leveraged information that graduate student Han Altae-Tran, who is now a postdoctoral fellow at the University of Washington, had learned about the diversity of bacterial IscBs and how they evolved. For instance, the

researchers noted that IscBs that worked in human cells included a segment they called REC, which was absent in other IscBs.

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They suspected the enzyme might need that segment to interact with the DNA in human cells. When they took a closer look at the region, structural modeling suggested that by slightly expanding part of the protein, REC might also enable IscBs to recognize longer RNA guides.

Based on these observations, the team experimented with swapping in parts of REC domains from different IscBs and Cas9s, evaluating how each change impacted the protein's function. Guided by their understanding of how IscBs and Cas9s interact with both DNA and their RNA guides, the researchers made additional changes, aiming to optimize both efficiency and specificity.

In the end, they generated a protein they called NovalscB, which was over 100 times more active in human cells than the IscB they had started with and that had demonstrated good specificity for its targets.

Kannan and Zhu constructed and screened hundreds of new IscBs before arriving at NovalscB—and every change they made to the original protein was strategic. Their efforts were guided by their team's knowledge of IscBs' natural evolution as well as predictions of how each alteration would impact the protein's structure, made using an artificial intelligence tool called AlphaFold2.

Compared to traditional methods of introducing random changes into a protein and screening for their effects, this rational engineering approach greatly accelerated the team's ability to identify a protein with the features they were looking for.

The team demonstrated that NovalscB is a good scaffold for a variety of genome editing tools. "It biochemically functions very similarly to Cas9, and that makes it easy to port over tools that were already optimized with the Cas9 scaffold," Kannan said. With different modifications, the researchers used NovalscB to replace specific letters of the DNA code in human cells and to change the activity of targeted genes.

Importantly, the NovalscB-based tools are compact enough to be easily packaged inside a single adeno-associated virus (AAV)—the vector most commonly used to safely deliver gene therapy to patients. Because they are bulkier, tools developed using Cas9 can require a more complicated delivery strategy.

Demonstrating NovalscB's potential for therapeutic use, Zhang's team created a tool called OMEGAoff that adds chemical markers to DNA to dial down the activity of specific genes. They programmed OMEGAoff to repress a gene involved in cholesterol regulation, then used AAV to deliver the system to the livers of mice, leading to lasting reductions in cholesterol levels in the animals' blood.

The team expects that NovalscB can be used to target genome editing tools to most human genes, and look forward to seeing how other labs deploy the new technology. They also hope others will adopt their evolution-guided approach to rational protein engineering. "Nature has such diversity and its systems have different advantages and disadvantages," Zhu says. "By learning about that natural diversity, we can make the systems we are trying to engineer better and better."

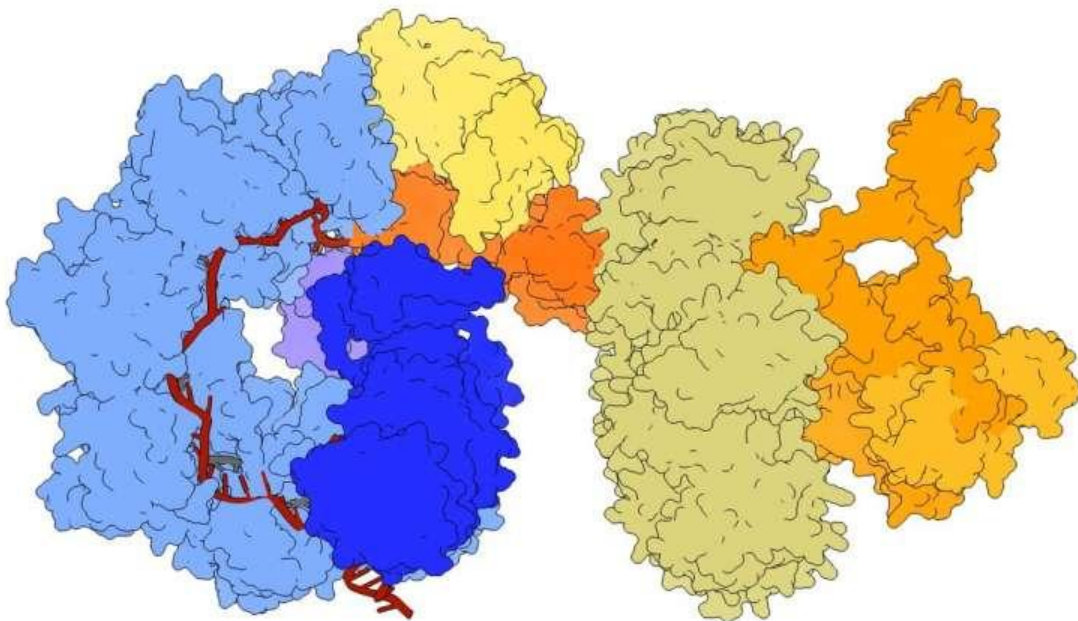
More information: Soumya Kannan et al, Evolution-guided protein design of IscB for persistent epigenome editing in vivo, *Nature Biotechnology* (2025). DOI: [10.1038/s41587-025-02655-3](https://doi.org/10.1038/s41587-025-02655-3)

Journal information: [Nature Biotechnology](#)
Provided by [Broad Institute of MIT and Harvard](#)

MAY 15, 2025

Advanced gene editor enables more precise insertion of complete genes

by [Columbia University Irving Medical Center](#)



The multiple components of the evoCAST gene editor grasping a strand of DNA (red).
Credit: George Lampe (Columbia University Irving Medical Center)

Ask scientists which gene-editing tool is most needed to advance gene therapy, and they'd probably describe a system that's now close to realization in the labs of Samuel Sternberg at Columbia University Vagelos College of Physicians and Surgeons and David Liu at the Broad Institute of MIT and Harvard.

The gene editor—called evoCAST—goes a long way toward solving a problem that has confounded the development of gene therapies from the field's beginnings: How to add long stretches of DNA to defined locations in the [human genome](#) without creating unwanted modifications.

The latest iteration of the editor, which utilizes complex enzymes found in bacteria, can be programmed to insert an entire gene—or multiple genes—into a specific location in the human genome with an efficiency suitable for gene therapy. Details of the editor are described in a [paper](#) published in *Science*.

The need for an advanced gene editor

CRISPR-Cas, viruses, and other editing systems have enabled dozens of genetic medicines now being developed for patients, but all current methods have drawbacks. Some methods are precise but only make small corrections. Viruses, the most frequently used method in gene therapy, can insert complete genes, but do so randomly while activating immune responses.

A tool like evoCAST could make gene therapy more reliable and efficient, particularly for diseases like cystic fibrosis and hemophilia that are caused by any one of thousands of different mutations.

"Hundreds to thousands of different mutations in the CFTR gene can cause [cystic fibrosis](#), for example, so an inordinate number of distinct gene-editing drugs would be needed to ensure each patient could be treated," says Sternberg. "Instead, something like evoCAST could enable a single gene therapy that inserts a complete and healthy gene into the patient's genome.

"There's more work to be done, but evoCAST represents a milestone in the development of these systems for permanently installing a complete, healthy gene, regardless of the underlying genetic defect."

The new system could also enable simpler and more accurate gene editing in other medical and research applications, including the production of CAR T-cell therapies for cancer treatment, and transgenic cell lines and model organisms needed for biomedical research.

New editor developed from 'jumping genes'

evoCAST is based on a natural system the Sternberg lab discovered several years ago in bacteria that allows genes to jump into new locations in the bacterial genome. (Jumping genes—also known as transposons—can benefit a species by generating genetic diversity).

The lab recognized that several features of CASTs (CRISPR-associated transposases) made them attractive as potential gene editing systems. One advantage is the ability to insert large pieces of DNA without breaking the chromosome in the process, which can introduce serious, unintended errors. Another is the system's "programmability," which directs insertions to any location in the genome specified by the researcher.

Adapting the bacterial system for use in human cells proved challenging. Sternberg's graduate student, George Lampe, successfully developed the system to work in human cells, but early versions of the technology functioned with low efficiency.

Sternberg had expected the difficulty. "CAST systems exist to help mobile genes jump around the genome over evolutionary timescales. They're not under [selective pressure](#) to act efficiently, so we reasoned there would be a greater need to squeeze more activity out of these systems compared to CRISPR-Cas9, which evolved into a very potent and efficient system to save bacteria from viral infections."

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Artificial evolution improves gene editing

Instead of guessing what changes could improve their system, Sternberg and Lampe turned to David Liu, a molecular biologist and organic chemist at Harvard and the Broad Institute, who established a laboratory technique, PACE, that accelerates the evolution of proteins. Lampe pushed the performance of the system to a point that made PACE a viable option, and Isaac Witte and Simon Eitzinger, two graduate students in Liu's lab, moved the system into PACE, which enabled hundreds of rounds of evolution to be performed with minimal intervention.

"PACE turbocharges evolution and improves enzymes beyond what researchers can typically accomplish with targeted, rationally designed modifications," Lampe says. "The mutations acquired through PACE vastly improved the performance of the entire CAST system."

After hundreds of evolutionary generations, the new evoCAST system is able to edit 30% to 40% of cells, a huge increase from the original system's lower editing rates.

Next steps

The evoCAST system has already achieved efficiencies that are suitable for some gene editing and [gene therapy](#) applications, and the researchers are looking to begin testing their system in more relevant model systems.

At the same time, the team is continuing to make improvements, including changes to other evoCAST components, to further improve editing efficiencies.

But one of the biggest challenges right now for evoCAST, and other large DNA editing tools under development, is delivery.

"How do we actually get these tools and their payloads into the cells or tissues of interest?" Sternberg says. "That's a challenge that many of us in the field are facing."

More information: Isaac P. Witte et al, Programmable gene insertion in human cells with a laboratory-evolved CRISPR-associated transposase, *Science* (2025). DOI: [10.1126/science.adt5199](https://doi.org/10.1126/science.adt5199). www.science.org/doi/10.1126/science.adt5199

Journal information: *Science*

Provided by [Columbia University Irving Medical Center](#)

MAY 15, 2025

World's first patient treated with personalized CRISPR gene editing therapy

by [Children's Hospital of Philadelphia](#)

In a historic medical breakthrough, a child diagnosed with a rare genetic disorder has been successfully treated with a customized CRISPR gene editing therapy by a team at Children's Hospital of Philadelphia (CHOP) and Penn Medicine.

The infant, KJ, was born with a rare metabolic disease known as severe carbamoyl phosphate synthetase 1 (CPS1) deficiency. After spending the first several months of his life in the hospital, on a very restrictive diet, KJ received the first dose of his bespoke therapy in February 2025, between six and seven months of age.

The treatment was administered safely, and he is now growing well and thriving.

The case is detailed in a study published in [The New England Journal of Medicine](#) and was presented at the [American Society of Gene & Cell Therapy](#) Annual Meeting in New Orleans.

This landmark finding could provide a pathway for gene-editing technology to be successfully adapted to treat individuals with rare diseases for whom no [medical treatments](#) are available.

"Years and years of progress in gene editing and collaboration between researchers and clinicians made this moment possible, and while KJ is just one patient, we hope he is the first of many to benefit from a methodology that can be scaled to fit an individual patient's needs," said Rebecca Ahrens-Nicklas, MD, Ph.D., director of the Gene Therapy for Inherited

Metabolic Disorders Frontier Program (GTIMD) at Children's Hospital of Philadelphia and an assistant professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania.

CRISPR (clustered regularly interspaced short palindromic repeats)-based gene editing can precisely correct disease-causing variants in the human genome.

Gene-editing tools are incredibly complex and nuanced, and up to this point, researchers have built them to target more common diseases that affect tens or hundreds of thousands of patients, such as the two diseases for which there currently are U.S. Food and Drug Administration-approved therapies, [sickle cell disease](#) and beta thalassemia.

However, relatively few diseases benefit from a "one-size-fits-all" gene editing approach since so many disease-causing variants exist. Even as the field advances, many patients with rare genetic diseases—collectively impacting millions of patients worldwide—have been left behind.

A collaborative effort

Ahrens-Nicklas and Kiran Musunuru, MD, Ph.D., the Barry J. Gertz Professor for Translational Research at Penn's Perelman School of Medicine, who are co-corresponding authors on the published report, began collaborating to study the feasibility of creating customized gene-editing therapies for individual patients in 2023, building upon many years of research into rare metabolic disorders, as well as the feasibility of gene editing to treat patients.

Ahrens-Nicklas and Musunuru decided to focus on urea cycle disorders. During the normal breakdown of proteins in the body, ammonia is naturally produced.

Typically, our bodies know to convert the ammonia to urea and then excrete that urea through urination. However, a child with a urea cycle disorder lacks an enzyme in the liver needed to convert ammonia to urea. Ammonia then builds up to a toxic level, which can cause organ damage, particularly in the brain and the liver.

After years of preclinical research with similar disease-causing variants, Ahrens-Nicklas and Musunuru targeted KJ's specific variant of CPS1, identified soon after his birth. Within six months, their team designed and manufactured a base editing therapy delivered via lipid nanoparticles to the liver in order to correct KJ's faulty enzyme.

In late February 2025, KJ received his first infusion of this experimental therapy, and since then, he has received follow-up doses in March and April 2025. In the new paper, the researchers, along with their academic and industry collaborators, describe the customized CRISPR [gene editing](#) therapy that was rigorously yet speedily developed for administration to KJ.

As of April 2025, KJ had received three doses of the therapy with no serious side effects. In the short time since treatment, he has tolerated increased dietary protein and needed less nitrogen scavenger medication. He has also been able to recover from certain typical childhood illnesses like rhinovirus without ammonia building up in his body. Longer follow-up is needed to fully evaluate the benefits of the therapy.

"While KJ will need to be monitored carefully for the rest of his life, our initial findings are quite promising," Ahrens-Nicklas said.

"We want each and every patient to have the potential to experience the same results we saw in this first patient, and we hope that other academic investigators will replicate this method for many rare diseases and give many patients a fair shot at living a healthy life," Musunuru said.

"The promise of gene therapy that we've heard about for decades is coming to fruition, and it's going to utterly transform the way we approach medicine."

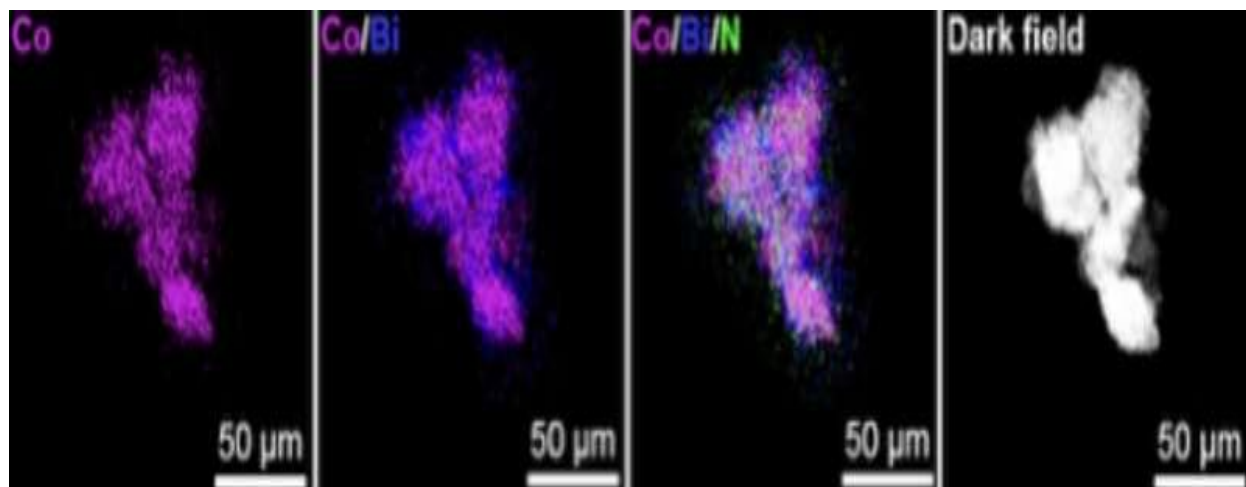
More information: Musunuru et al, Patient-Specific In Vivo Gene Editing to Treat a Rare Genetic Disease, *New England Journal of Medicine* (2025). DOI: [10.1056/NEJMoa2504747](https://doi.org/10.1056/NEJMoa2504747)

Journal information: [New England Journal of Medicine](#)
Provided by [Children's Hospital of Philadelphia](#)

MAY 18, 2025

Nanoparticle-cell interface enables electromagnetic wireless programming of mammalian transgene expression

by [Ingrid Fadelli](#), Phys.org



The nanoparticles are composed of multiferric cores (Cobalt ferrite and Bismuth ferrite which responsive to magnetic field) and chitosan outer layers (which is rich in positive amino group for translocate nanoparticles to cytoplasm and shields the bioenvironment from the nanoparticles). Credit: Lin et al.

Recent technological advances are fueling the development of cutting-edge technologies that can monitor and control physiological processes with high precision. These include devices that could control the expression of genes within living organisms, without requiring invasive surgeries or procedures.

Researchers at ETH Zurich recently introduced a new method that enables the electromagnetic programming of the wireless expression regulation (EMPOWER) of transgenes in mammals, via the interfacing of [nanoparticles](#) and cells.

Their proposed approach, outlined in a paper [published](#) in *Nature Nanotechnology*, could help to treat [chronic conditions](#), including diabetes, while also opening new possibilities for research in synthetic biology and regenerative medicine.

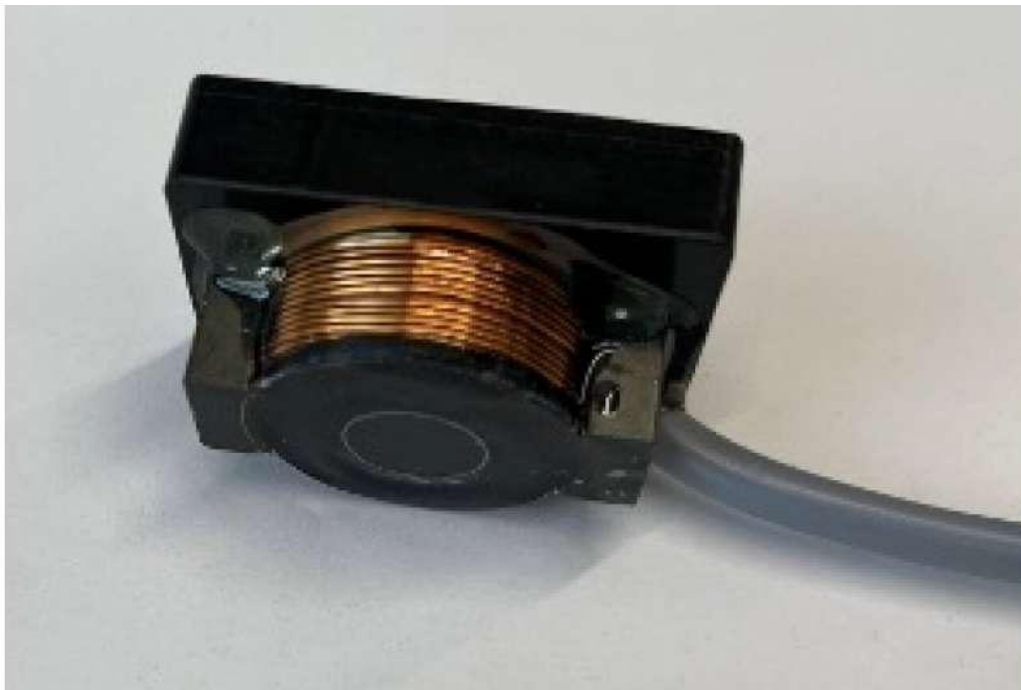
"Our recent study is all about tackling the ongoing challenge in biomedicine of precisely and non-invasively controlling therapeutic gene expression within living organisms," Martin Fussenegger, senior author of the paper, told Phys.org.

"I understand that conventional methods can be a bit tricky. Either they require invasive procedures, or they might not be as precise or robust as we'd like. This inspired us to use magnetic fields for wireless control, taking advantage of their ability to penetrate biological tissues safely and effectively without direct contact or invasive devices."

The main objective of the recent study by Fussenegger and their colleagues was to devise a safe and robust approach to reliably control the amount of a therapeutic protein produced by mammals from a distance. The method they introduced in their paper relies on nanoparticles made of multiferroic materials, which were coated with a biocompatible polymer called chitosan.

"When these nanoparticles are stimulated by a low-frequency [magnetic field](#), they generate biosafe levels of reactive oxygen species (ROS) within the [cell cytoplasm](#)," explained Fussenegger. "We engineered [mammalian cells](#) to include a genetic circuit that's sensitive to these ROS signals, using the cellular KEAP1/NRF2 pathway. When ROS are detected, it's like a signal to NRF2 proteins to get busy, and they work together to bring selected therapeutic proteins, like insulin, to life."

A key advantage of the nanoparticle-cell interface introduced by Fussenegger and his colleagues is that it enables [precise control](#) over when and where one wants a gene to be expressed. In addition, the method is gentle and non-invasive, as it does not require demanding procedures or high-energy stimulation. Compared to other previously proposed nanoparticle-based methods for the wireless control of gene expression, the team's approach is highly bio-compatible and requires lower nanoparticle dosages, while also minimizing off-target effects. To demonstrate its potential, the researchers tested it on a mouse model of diabetes. The stimulated insulin release can be achieved by a single-coil



generated electromagnetic field with an E-shaped iron core at a plane 3–5 mm from the coil surface, which matches the depth of subcutaneous implantation in mice. Credit: Lin et al.

"In this experiment, we exposed mice to a weak electromagnetic field (1 kHz, 21 mT) for just three minutes each day," said Fussenegger.

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"This controlled their insulin secretion really well and kept their [blood glucose](#) levels normal during the whole study. We're so excited to share the most significant achievement of our study: we've successfully connected wireless electromagnetic controls to natural transgene expression in mammalian cells via intracellular nanoparticles as interfacial magnetic receivers."

The nanoparticles utilized by the researchers were introduced in the cytoplasm, the jelly-like substance that surrounds the nucleus in cells. This allowed the nanoparticles to communicate with the cells, leveraging chemical reactive oxygen species (ROS), a class of reactive oxygen-containing molecules naturally produced in cells.

"This was true even when the nanoparticles were interacting directly with the proteins," said Fussenegger. "Our construction is great because it gets the cells working together, and it does this without disrupting the integrity of engineered cells. This helps us get the results we need, but without any of the problems."

The nanoparticle-cell interface devised by this team of researchers could have highly valuable medical applications. Notably, the approach utilizes a very weak electromagnetic field (below 1 kHz) and low power (21 mT), while stimulating cells for a very short time (three minutes).

"This is much weaker than the levels used in clinical MRI scans," said Fussenegger. "Our approach could thus be highly valuable for managing chronic diseases, as it would let us adjust therapy remotely and dynamically. This would eliminate the need for repeated injections, invasive implants or systemic drug administration."

In the future, the team's approach for remotely controlling transgene expression could be tested and implemented in clinical settings. The researchers are now exploring the potential application of their method in the fields of oncology, neurology and regenerative medicine, while also working on improving their nanoparticle-based system.

"In our next studies, we're going to focus on making our system even more sensitive, biocompatible and efficient," added Fussenegger.

"We're also planning to make some improvements to the electromagnetic stimulation equipment. We want to make it more compact so it's easier to use in a clinical setting.

"We're looking forward to doing even more in the future. We're going to use this platform for other chronic diseases. We're also going to explore alternative genetic circuits. And we're going to get the technology ready for preclinical and clinical evaluation."

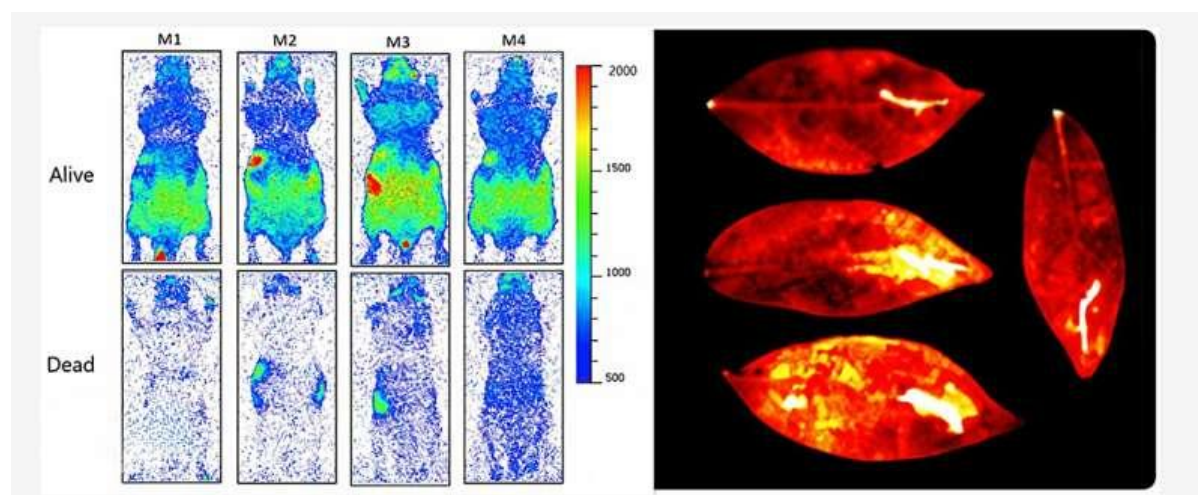
More information: Zhihua Lin et al, Electromagnetic wireless remote control of mammalian transgene expression, *Nature Nanotechnology* (2025). DOI: [10.1038/s41565-025-01929-w](https://doi.org/10.1038/s41565-025-01929-w)
Journal information: [Nature Nanotechnology](#)

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MAY 17, 2025

Living beings emit a faint light that extinguishes upon death, according to a new study

by [Sanjukta Mondal](#) , Phys.org

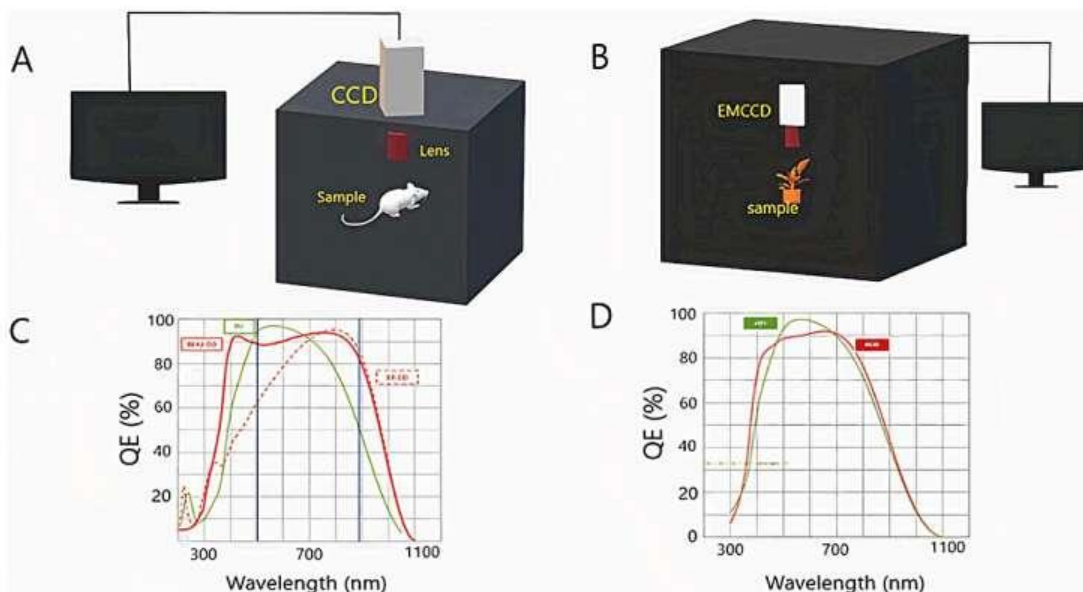


Credit: *The Journal of Physical Chemistry Letters* (2025). DOI: [10.1021/acs.jpcllett.4c03546](https://doi.org/10.1021/acs.jpcllett.4c03546)
The light of someone's life might not be just another person, but light in the literal sense. According to a recent study by researchers from University of Calgary, every living system emits light without requiring external excitation due to a biological phenomenon known as ultraweak photon emission (UPE).

In [mice](#), UPE was linked to vitality as live mice emitted significantly higher UPE intensity compared to recently dead mice. In plants, however, UPE varied depending on exposure to stress factors like temperature changes, injury and chemical treatments, as [reported](#) in *The Journal of Physical Chemistry Letters*.

Living organisms are compact biochemical labs where complex chemical reactions keep the system up and running. Cellular metabolism, a series of chemical reactions that fuel life-sustaining processes, produces a group of highly reactive oxygen-containing molecules produced as a natural byproduct called [reactive oxygen species](#) or ROS.

Studies suggest that ROS plays a central role in UPE. When organisms encounter stress, they activate biochemical pathways that generate ROS, which act as signaling molecules in the [cellular stress response](#). However, excessive ROS production can lead to [oxidative stress](#), overwhelming the cell's antioxidant defenses. This oxidative stress can induce electron excitation and transfer processes, ultimately resulting in UPE.

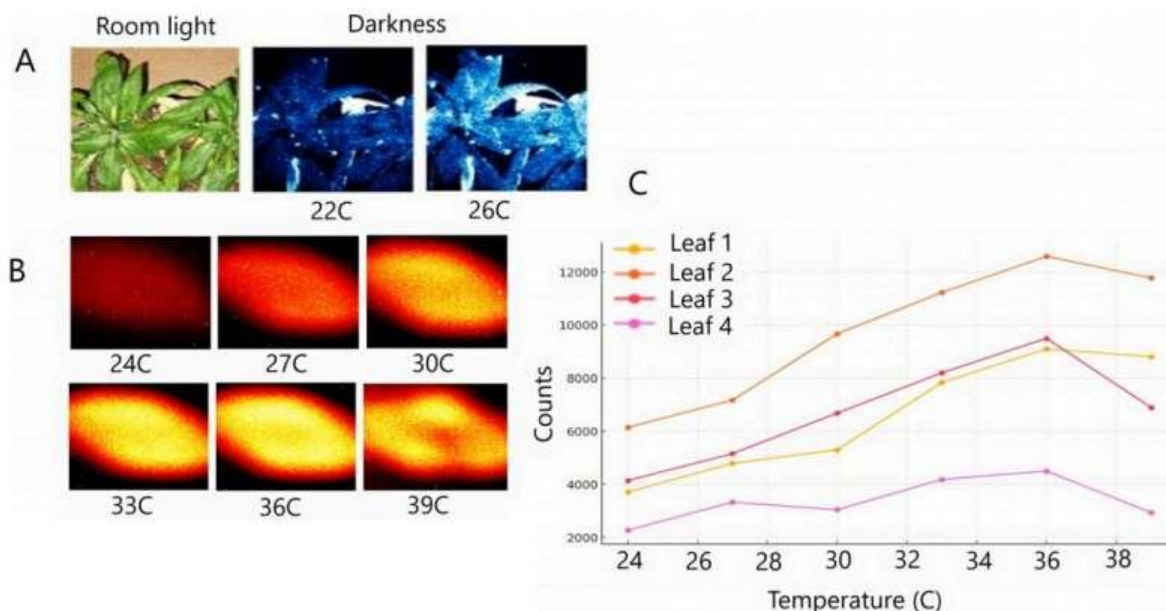


High-sensitivity EMCCD and CCD cameras for imaging UPE in dark, controlled environments. Credit: *The Journal of Physical Chemistry Letters* (2025). DOI: 10.1021/acs.jpclett.4c03546

Unlike bioluminescence, which produces high-intensity light visible to the naked eye, UPE, also known as biophoton emission, is a spontaneous release of extremely low-intensity light that is invisible to the human eye and falls within the spectral range of 200–1,000 nm. This faint light has been detected in a wide range of life forms—from [single-celled organisms](#) and bacteria to plants, animals, and even humans.

Despite being so widely observed, not much is known about the impact of mortality and stress factors on UPE. Furthermore, the ability to monitor UPE in response to stress factors and injuries could be a powerful, non-invasive tool for diagnostics and medical research.

The researchers used advanced imaging techniques to explore the biological significance of UPE by directly comparing emissions in living versus dead animals, while also systematically visualizing the effects of temperature, injury, and chemical treatments on UPE in plants.



Effect of the temperature on the intensity of UPE in plants. Credit: *The Journal of Physical Chemistry Letters* (2025). DOI: 10.1021/acs.jpcllett.4c03546

To carry out the experiments, the researchers designed ultradark enclosures to eliminate environmental light interference. They then used an Electron-Multiplying Charge-Coupled Device (EMCCD) camera for imaging plants and a Charge-Coupled Device (CCD) camera with IVIS system to image UPE changes in mice.

The results revealed that despite both groups having the same body temperature of 37°C, the live mice showed robust emissions, whereas the UPE from the euthanized mice was nearly extinguished. In plants, an increase in temperature and injuries led to an increase in UPE intensity. Injured sites were consistently brighter than uninjured parts—a change in the former was observed once the site received any chemical treatment.

This study establishes that UPE can act as a sensitive indicator of vitality in animals and of stress responses in plants. The researchers suggest that these findings could catalyze the application of UPE imaging as a non-invasive technique for both basic biological research and clinical diagnostics.

More information: V. Salari et al, Imaging Ultraweak Photon Emission from Living and Dead Mice and from Plants under Stress, *The Journal of Physical Chemistry Letters* (2025). DOI: [10.1021/acs.jpcllett.4c03546](https://doi.org/10.1021/acs.jpcllett.4c03546)

Journal information: [Journal of Physical Chemistry Letters](#)

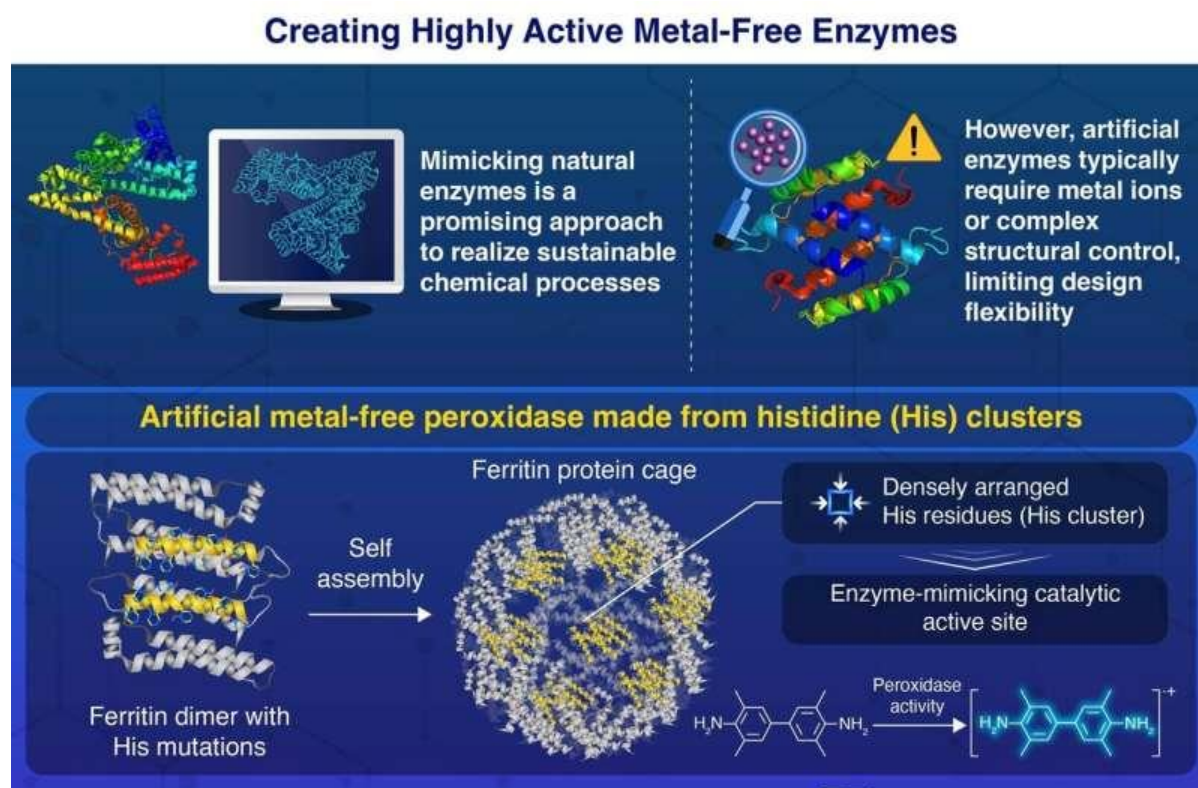
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MAY 19, 2025

Designing efficient artificial enzymes with self-assembling protein cages

by [Institute of Science Tokyo](#)

edited by [Gaby Clark](#), reviewed by [Robert Egan](#)



Researchers at Institute of Science Tokyo have developed a highly active artificial peroxidase enzyme using histidine clusters within a ferritin protein cage—without requiring metal ions. This innovation mimics natural enzymes and achieves over 80 times greater catalytic efficiency than traditional oligohistidine assemblies, opening new avenues for sustainable chemical production, biomaterials, and environmental remediation. Credit: Professor Takafumi Ueno from Institute of Science Tokyo

Natural enzymes are remarkable molecular machines that enable all sorts of essential biochemical reactions. For decades, scientists have sought to create artificial versions of these catalysts for industrial and biomedical applications. However, they have struggled to match nature's efficiency and simplicity. This, in turn, has hindered the development of environmentally friendly catalysts for sustainable chemistry.

Creating [artificial enzymes](#) typically requires either cofactors or complex structural arrangements that precisely position reactive groups in three-dimensional space. These requirements constrain design flexibility, often resulting in enzymes that underperform

compared to their natural counterparts. Finding simpler approaches that don't sacrifice catalytic power has remained an elusive goal in the field of biocatalysis.

Against this backdrop, a research team led by Professor Takafumi Ueno from the Institute of Science Tokyo, Japan, reported a novel approach to enzyme design using [protein](#) nanocages. Their paper, [published](#) in *Angewandte Chemie* on April 24, 2025, demonstrates how precisely arranged histidine [amino acids](#) inside a ferritin protein cage can function as a highly effective metal-free peroxidase—an enzyme that drives oxidation reactions using hydrogen peroxide as a reactant.

The researchers engineered the ferritin cage by introducing histidine residues and a series of targeted mutations. By taking advantage of ferritin's ability to self-assemble into protein cages, they created clusters of histidine residues on the cage's inner surface. These histidine clusters act as catalytic centers, mimicking peroxidase activity that promotes reactions between hydrogen peroxide and 3,3', 5,5'-tetramethylbenzidine substrate.

"The engineered ferritin variant showed approximately 80 times higher reaction efficiency compared to conventional oligohistidine assemblies," remarks Prof. Ueno.

The team's innovative approach demonstrates that the proper spatial arrangement of simple amino acids can eliminate the need for metal cofactors in certain enzymatic reactions. Through careful positioning of these amino acids at the interfaces of the ferritin cage, the team produced a confined reaction environment that significantly enhanced [catalytic activity](#).

Using [molecular dynamics simulations](#), they revealed how the ferritin cage confines reactants in close proximity to the histidine clusters, explaining the dramatic enhancement in catalytic efficiency.

"Based on theoretical calculations, we confirmed that this high activity is further enhanced by a 'confined environment effect' within the protein [cage](#), which concentrates reactants and facilitates their interaction," says Prof. Ueno.

These exciting findings unlock new possibilities for protein cages in metal-free catalytic systems, which could find applications in sustainable chemical production, biomaterials development, and environmental remediation. "This research represents a major advancement in artificial enzyme design and environmentally friendly catalysis, paving the way for the development of sustainable biocatalysts," concludes Prof. Ueno.

In the near future, further studies in this field could lead to high-performance bioinspired catalysts. By refining the spatial design of catalytic residues and exploring other self-assembling protein frameworks, researchers may develop a broader range of metal-free enzymes tailored for specific industrial or biomedical tasks.

Such advances would not only improve catalytic efficiency but also reduce reliance on rare or toxic metals, making green chemistry more accessible and practical for real-world applications across various sectors.

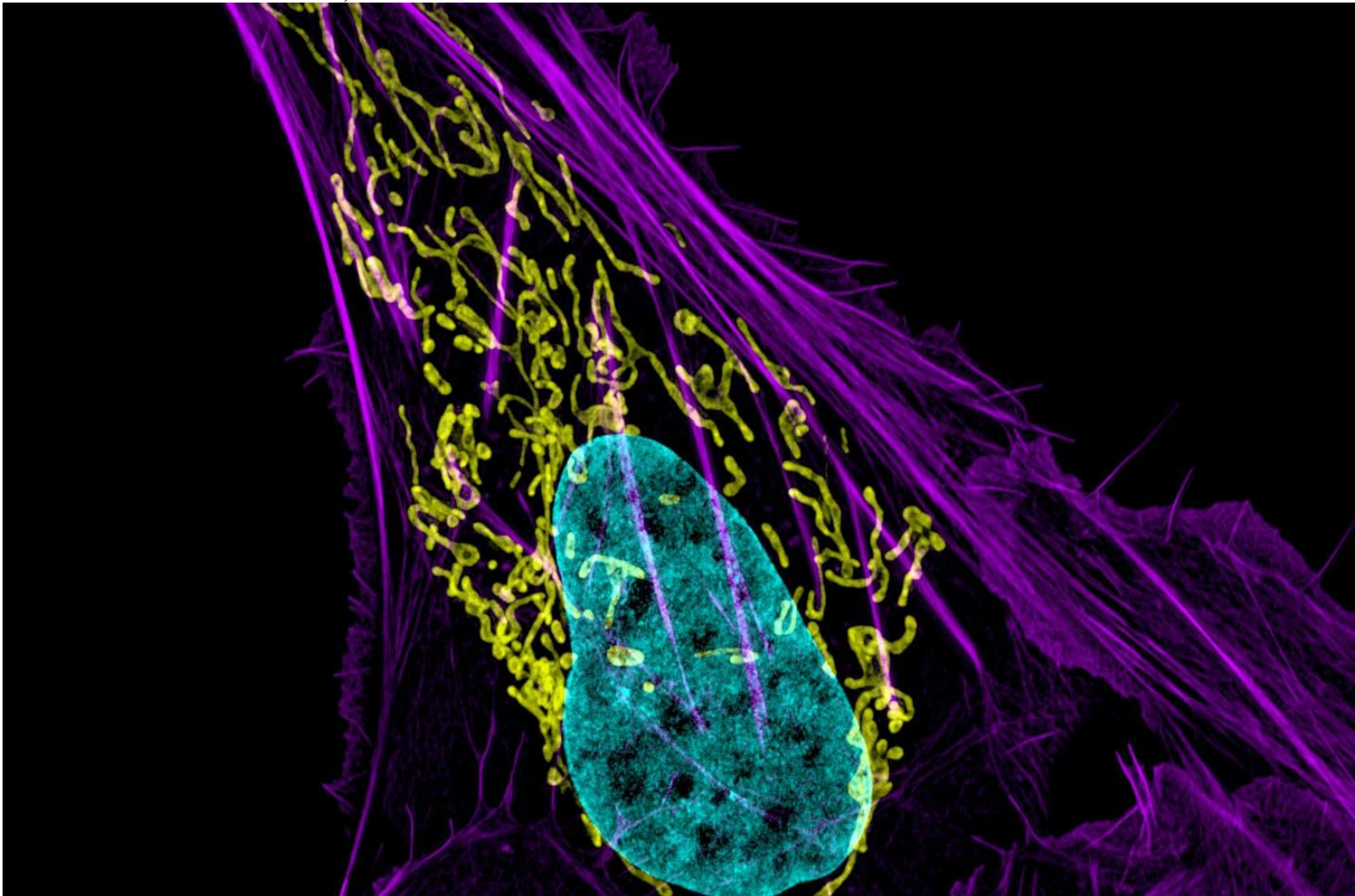
More information: Jiaxin Tian et al, An Artificial Metal-Free Peroxidase Designed Using a Ferritin Cage for Bioinspired Catalysis, *Angewandte Chemie International Edition* (2025). DOI: [10.1002/anie.202504608](https://doi.org/10.1002/anie.202504608)

Journal information: [Angewandte Chemie International Edition](#) , [Angewandte Chemie](#)
Provided by [Institute of Science Tokyo](#)

Light-induced gene therapy successfully kills cancer cells

Scientists develop a light-activated mitochondrial therapy that targets cancer cells, showing promise in treating glioblastoma and breast cancer.

Published Dec 16, 2024



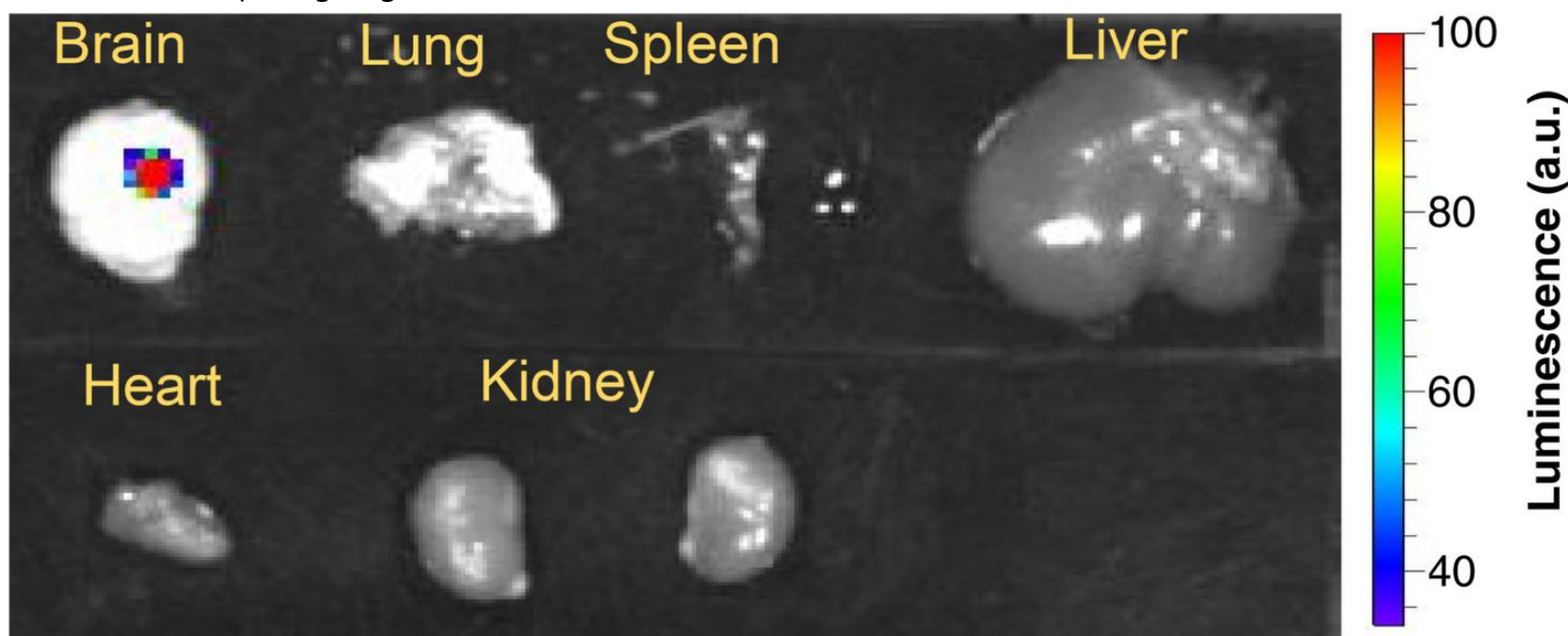
Researchers unveiled a groundbreaking mitochondrial therapy that uses internal bioluminescence to target and destroy cancer cells. (CREDIT: Dylan Burnette and Jennifer Lippincott-Schwartz, NICHD)

Mitochondria, the cell's energy centers, play a vital role in regulating cellular processes, including growth and survival. Their unique structure and function have made them a promising target in the [battle against cancer](#).

Mitochondrial genetics and metabolism are deeply involved in cancer progression—from aiding cell motility and invasion to modulating the tumor microenvironment. Despite these insights, developing mitochondrial-targeted therapies remains a challenge.

Numerous treatments targeting [mitochondria](#), such as mitocans and mitochondriotoxics, aim to disrupt specific signaling pathways. These approaches often focus on proteins like hexokinase or Bcl2 family proteins. However, their long-term efficacy is limited due to the unpredictability of mutations in cancer cells. This has hindered the clinical success of mitochondrial therapies.

One innovative approach to tackling cancer involves targeting the inner mitochondrial membrane (IMM). Maintaining its electrical potential gradient, known as $\Delta\Psi_m$, is critical for mitochondrial function. When $\Delta\Psi_m$ dissipates, it triggers cell death, making it a compelling target for cancer treatment.



Ex vivo IVIS imaging confirmed mLumiOpto expression in GBM xenografts but not in normal organs. (CREDIT: Cancer Research)

Previous methods to disrupt $\Delta\Psi_m$, such as chemical uncouplers or genetic modifications, often lacked specificity or caused irreversible side effects, limiting their utility.

A groundbreaking advancement in this field is mitochondrial optogenetics (mOpto). By introducing light-gated channelrhodopsins into mitochondria, researchers achieved

controlled $\Delta\Psi_m$ depolarization and induced [cell death](#). However, the need for external light sources to activate this mechanism limited its application to surface-level tumors. Building on this, scientists have developed mitochondrial luminoptogenetics (mLumiOpto), which uses an internal light source. This approach combines cationic channelrhodopsin (CoChR), a protein activated by blue light, with nanoluciferase (NLuc), a bioluminescent enzyme.

The genes encoding these molecules are selectively expressed in [cancer cells](#) using a cancer-enhanced promoter. Once delivered to cancer cells, NLuc generates light that activates CoChR, causing mitochondrial collapse and cell death.

Related Stories

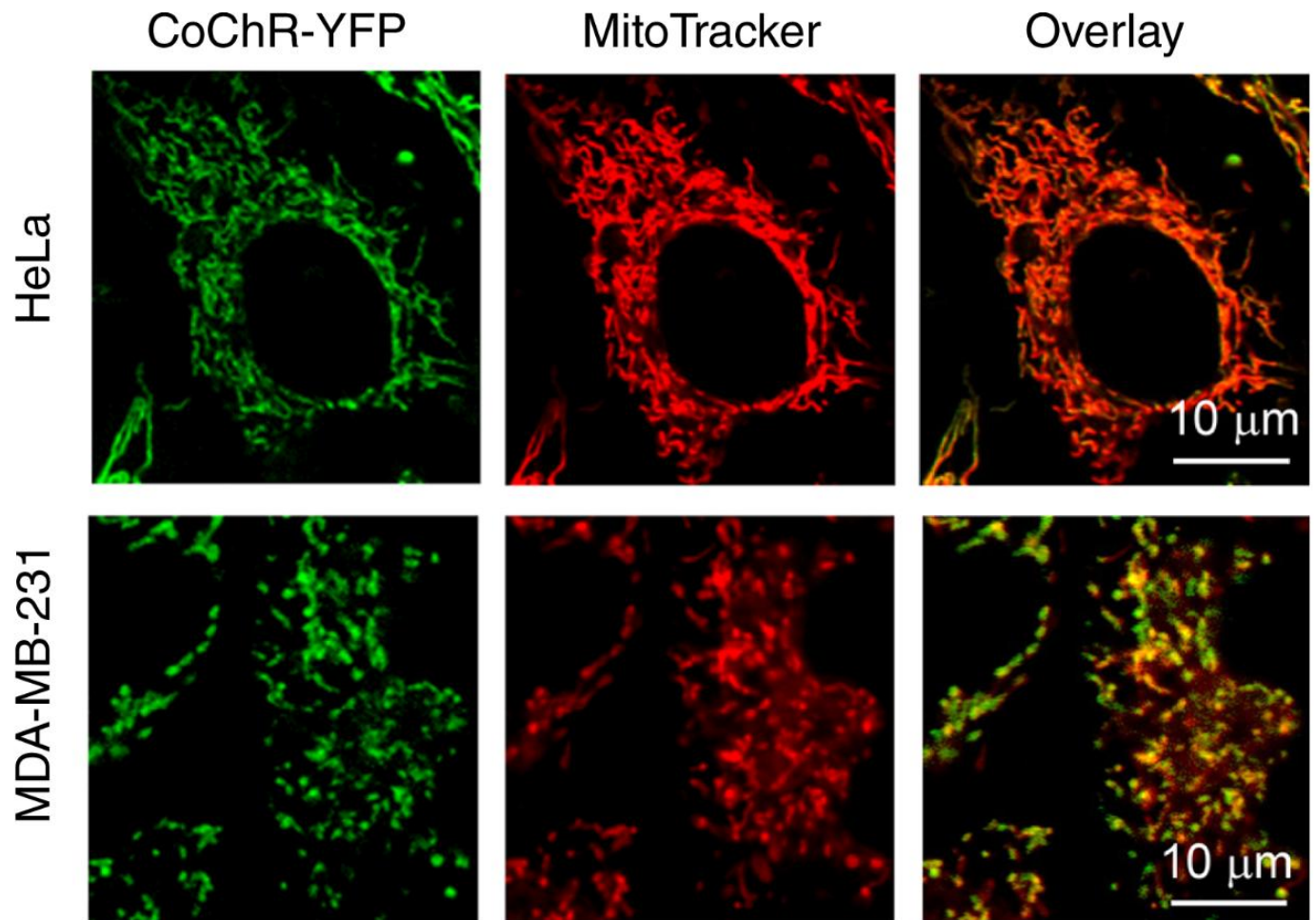
- [New anticancer drugs could significantly improve immunotherapy](#)
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- [Breakthrough immunotherapy drug revolutionizes pancreatic cancer treatment](#)

To deliver this gene therapy, researchers used a modified adeno-associated virus (AAV) combined with a monoclonal antibody. This delivery system ensures that the therapy targets cancer cells while sparing healthy tissue.

The virus is encapsulated in nanocarriers derived from human cells, enhancing its stability and effectiveness. The monoclonal [antibody](#) further improves specificity by binding to receptors on cancer cell surfaces.

The therapeutic potential of mLumiOpto was tested in preclinical mouse models of glioblastoma and triple-negative breast cancer. These aggressive cancers are notoriously difficult to treat. The results were promising.

In glioblastoma models, mLumiOpto significantly reduced tumor size and extended survival. Imaging studies confirmed that the effects were limited to [cancerous tissues](#), with no detectable damage to healthy cells.



Confocal images showing high-level mitochondrial CoChR expression in HeLa and MDA-MB-231 cells, indicated by strong overlap of eYFP (fused to CoChR) and MitoTracker dye. (CREDIT: Cancer Research)

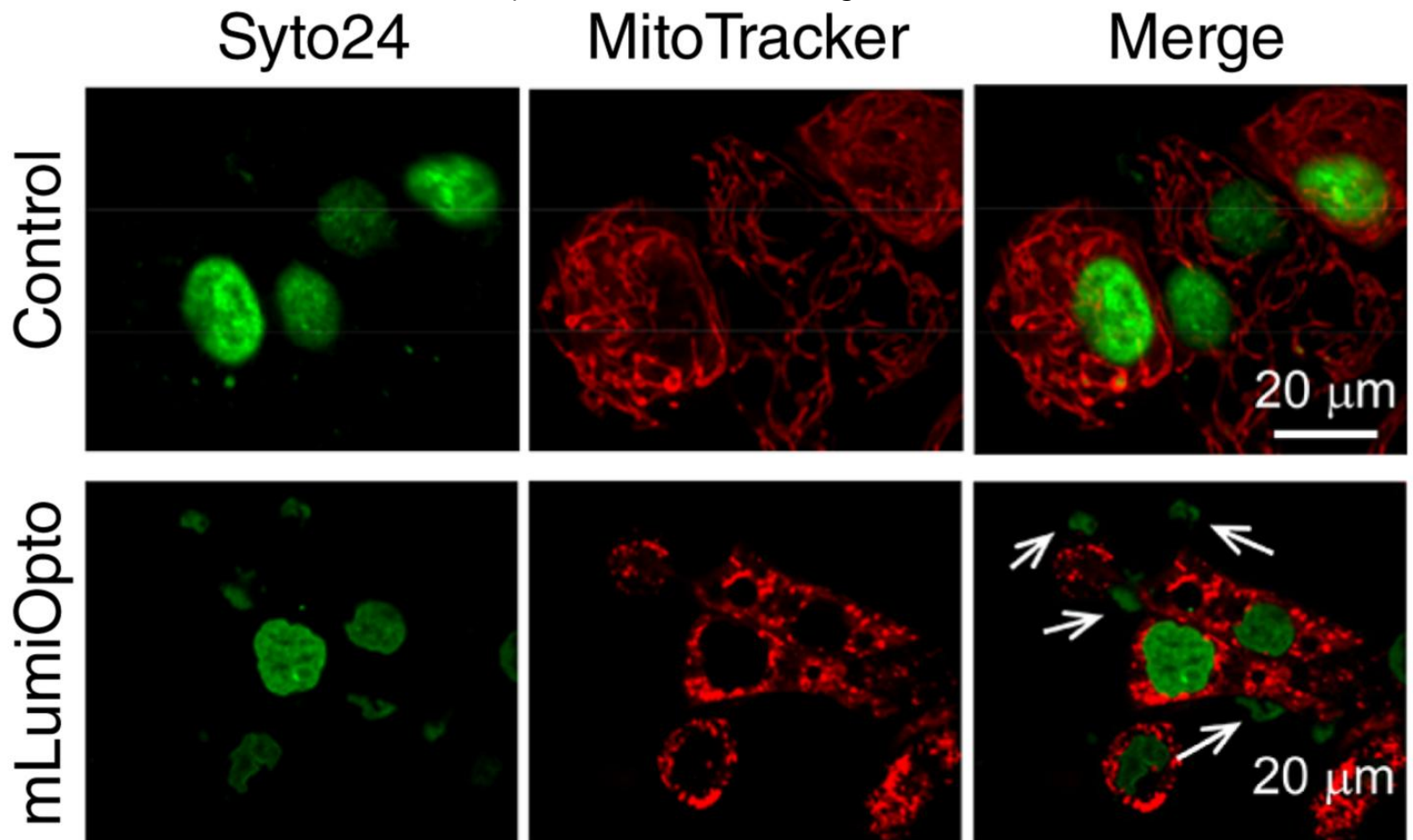
"We disrupt the membrane so mitochondria cannot work functionally to produce energy or work as a signaling hub. This causes programmed cell death followed by DNA damage – our investigations showed these two mechanisms are involved and kill the cancer cells," explained Lufang Zhou, co-lead author and professor at [The Ohio State University](#).

Zhou's research team collaborated with X. Margaret Liu, a chemical engineering professor specializing in nanoparticle-based therapies. Together, they refined the AAV delivery system, ensuring its stability and cancer specificity.

Liu's expertise in creating targeted anti-cancer therapies was instrumental in designing the delivery particles, which resemble naturally occurring extracellular vesicles in human blood. "This construction assures stability in the human body because this particle comes from a [human cell](#) line," Liu noted.

Beyond its direct effects, the therapy also appears to stimulate the immune system. The monoclonal antibody triggers an immune response within the tumor microenvironment,

potentially enhancing its therapeutic effects. This dual action—targeted cell death and immune activation—could prove invaluable in treating resistant cancers.



Syto24 staining revealed mLumiOpto-induced substantial DNA damage. (CREDIT: Cancer Research)

"Our approach targets mitochondria directly, using external genes to activate a process that kills cells. That's an advantage, and we've shown we can get a very good result in killing different types of cancer cells," Zhou said.

His team's earlier [studies](#) had shown that disrupting the IMM's electrical charge could be achieved using light-activated proteins. The mLumiOpto system builds on this by creating light from within the cells, making it viable for clinical use.

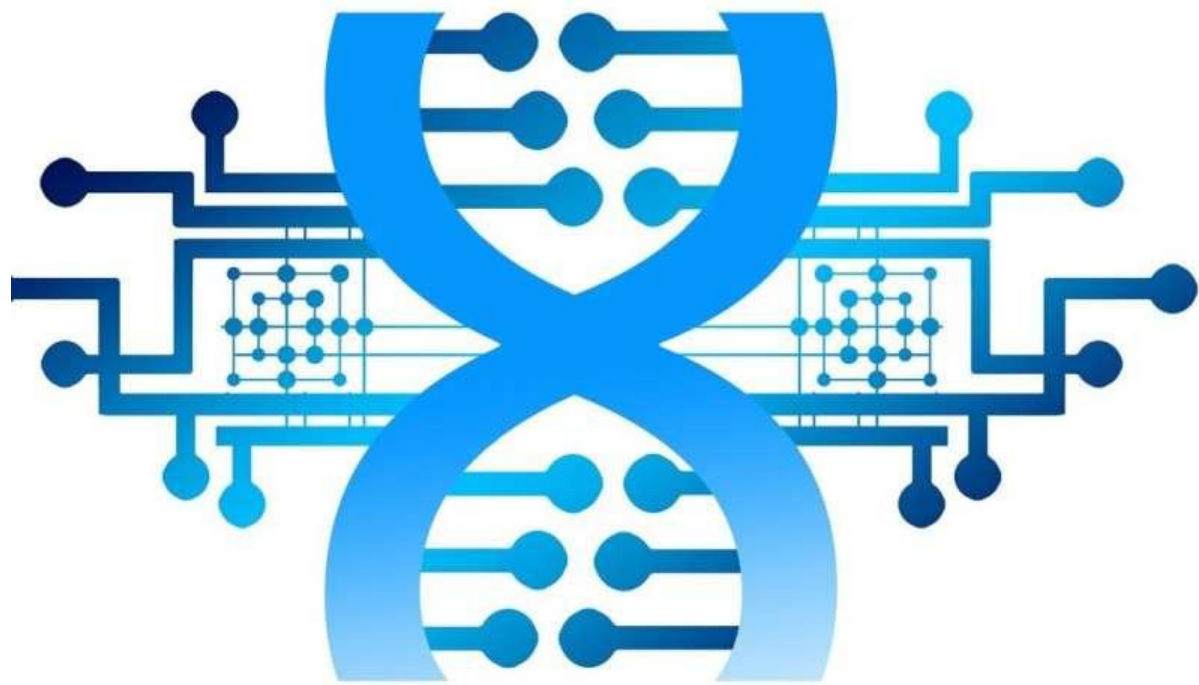
The researchers' success lies not only in developing the therapy but also in proving its efficacy across multiple cancer types. In triple-negative breast cancer models, the treatment reduced [tumor burden](#) and prolonged survival. The technology's versatility and precision make it a promising candidate for further research and clinical trials.

Ohio State University has filed a provisional patent for the mLumiOpto

MAY 22, 2025

An artificial protein that moves like something found in nature

by [University of California, San Francisco](#) edited by [Sadie Harley](#), reviewed by [Robert Egan](#)



Credit: Pixabay/CC0 Public Domain

Proteins catalyze life by changing shape when they interact with other molecules. The result is a muscle twitching, the perception of light, or a bit of energy extracted from food. But this crucial ability has eluded the growing field of AI-augmented protein engineering.

Now, researchers at UCSF have shown it is possible to make new proteins that move and change [shape](#) like those in nature. This ability will help scientists engineer proteins in powerful new ways to treat disease, clean up pollution, and increase crop yields.

"This study is the first step on a path that will lead far beyond biomedicine, into agriculture and the environment," said Tanja Kortemme, Ph.D., professor of bioengineering and senior author of the study, which appears in [Science](#).

Scientists have been engineering rigid proteins—proteins that can't move or change shape—since the 1980s. These proteins were first used in commercial products like cleaning solutions.

More recently, they've been employed to produce blockbuster medicines like artificial insulin, GLP-1 weight-loss drugs, and antibody treatments for cancer and inflammation.

While important, these immovable molecules can't match the potential of proteins that can swivel, twist, and morph in complicated ways and then return to their original shape, said Kortemme, who is also an investigator at the Chan-Zuckerberg BioHub San Francisco.

She said the most important proteins to emulate for medical uses are those that regulate processes like metabolism, [cell division](#), and other basic life functions. These powerful proteins are the targets of nearly one in three FDA-approved drugs. They facilitate communication within or between cells by changing from one shape into another, and then back again, like an on-off switch.

An overwhelming problem

Designing such stable yet dynamic forms requires [computational power](#) and artificial intelligence that didn't exist until a few years ago.

The challenge was huge, so Kortemme and graduate student Amy Guo began with something small: giving a simple natural protein the ability to move in a new way. Guo then made part of the protein swing so it could bind to calcium, a common way that proteins change shape.

"We wanted to devise a [design method](#) that could be applied in lots of situations, so we focused on creating a movable part that does what many natural proteins do," she said. "The hope is that this movement could also be added to static artificial proteins to expand what they can do, too."

Guo's next step was to generate a virtual library of thousands of possible shapes that the protein could take. She picked two stable shapes for the protein: one that could bind calcium and another that couldn't.

Then, she zoomed in on specific areas of the virtual protein to look at how the atoms in it were interacting. The work, which began before the pandemic, accelerated once the [artificial intelligence](#) program AlphaFold2 became available. Guo used it to make the movable part twist and capture the calcium, and then untwist to set it free.

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The moment of truth came when the researchers tested their model in a computer simulation. They teamed up with Mark Kelly, Ph.D., a pharmaceutical chemist at UCSF who uses [nuclear magnetic resonance](#) to visualize the atoms in a protein.

"I was amazed that the simulations showed it working exactly like we'd expected it to," Guo said. "That really gives me confidence that this was for real, that we really did it."

In the medical realm, movable engineered proteins could be used in biosensors that change shape in response to signals of disease, triggering an alert. Or they could be used as medicinal proteins that are tailored to work with a person's unique body chemistry.

Shapeshifting proteins could also be designed to break down plastics or help plants resist climate-related stresses like drought or pests. They could even be used to make metal that can repair itself when it cracks.

"The possibilities are truly endless," Guo said.

More information: *Science* (2025). DOI: [10.1126/science.adr7094](https://doi.org/10.1126/science.adr7094)

Journal information: [Science](#)

Provided by [University of California, San Francisco](#)

MAY 26, 2025

How rapid DNA repair in plants protects genomes from internal threats

by Rebecca Vaßen, [Max Planck Society](#) edited by [Lisa Lock](#), reviewed by [Robert Egan](#)



The flowers of tobacco plants have five petals. In this plant, grown from a single tobacco cell that experienced an EGT event, flowers have four or three petals, which is likely the consequence of a mutation and/or instability in the nuclear genome. Credit: MPI-MP/Enrique Gonzalez-Duran

Scientists have uncovered a critical role for rapid DNA repair in maintaining genome stability. A new study reveals that repair of double-strand breaks (DSBs) in nuclear DNA in plants serves as a powerful safeguard against the integration of foreign DNA from chloroplasts—a phenomenon that, while important for evolution, can be highly destabilizing to the genome. The research expands our knowledge about plant genome evolution and also has relevance to the medical field.

The [findings](#), presented by Dr. Enrique Gonzalez-Duran and Prof. Dr. Ralph Bock from the Max Planck Institute of Molecular Plant Physiology in *Nature Plants*, shed new light on endosymbiotic gene transfer (EGT)—an ongoing evolutionary process in which genes from organelles such as chloroplasts and mitochondria are relocated into the nuclear genome.

While successful gene transfers help the nucleus to better coordinate its function with that of the organelles, they also pose risks: Mutations arising from DNA insertion can disrupt essential nuclear genes and provoke harmful rearrangements.

The team of researchers discovered that the DSB repair machinery has a key role in controlling the frequency of gene transfer. To investigate how plants control EGT, the team focused on the DSB repair pathways—known entry points for organellar DNA. Using genetically engineered [tobacco plants](#) and a previously developed screening system for EGT events, the researchers selectively inactivated two different DSB repair pathways and monitored more than 650,000 seedlings for new EGT events.

The results were striking: disabling either of the two repair pathways led to a dramatic increase in gene transfers from chloroplasts to the nucleus—in some cases up to 20-fold.

The researchers propose a new model to explain their results: Under normal conditions, plants rapidly repair DSBs in their nuclear DNA, effectively sealing these vulnerable sites before organellar DNA can enter. In this way, the DNA repair machinery serves as a molecular "gatekeeper."

However, when one repair pathway is defective, the other pathways can compensate to some extent, but repair proceeds more slowly. This delay leaves DSBs exposed for longer, thus creating more opportunities for chloroplast DNA to integrate. The result is a surge in EGT events, often accompanied by genome rearrangements and increased instability.

"The magnitude of the effect suggests that rapid DNA repair is essential for plants to maintain long-term genome stability," explains Dr. Enrique Gonzalez-Duran, first author of the study.

Implications beyond plants

Although the work was carried out in tobacco plants, the team believes the mechanism uncovered is likely universal across eukaryotes. "These DNA repair pathways are conserved in animals and fungi," says Prof. Dr. Ralph Bock, director of the institute and co-author. "Our findings could explain similar genome instability mechanisms in other organisms, including humans. Further research is needed to clarify this."

The research opens new avenues for understanding how organellar DNA contributes to mutations in the nuclear genome. It may even have relevance for human health, and in particular to [cancer biology](#), where mitochondrial DNA insertions and genome instability are known molecular triggers of tumor initiation.

"Our discovery provides fundamental insights into genome protection and the risks of gene transfer," adds Gonzalez-Duran. "It reveals how crucial fast DNA repair is—not just to fix damage, but also to defend the integrity of the [genome](#) itself."

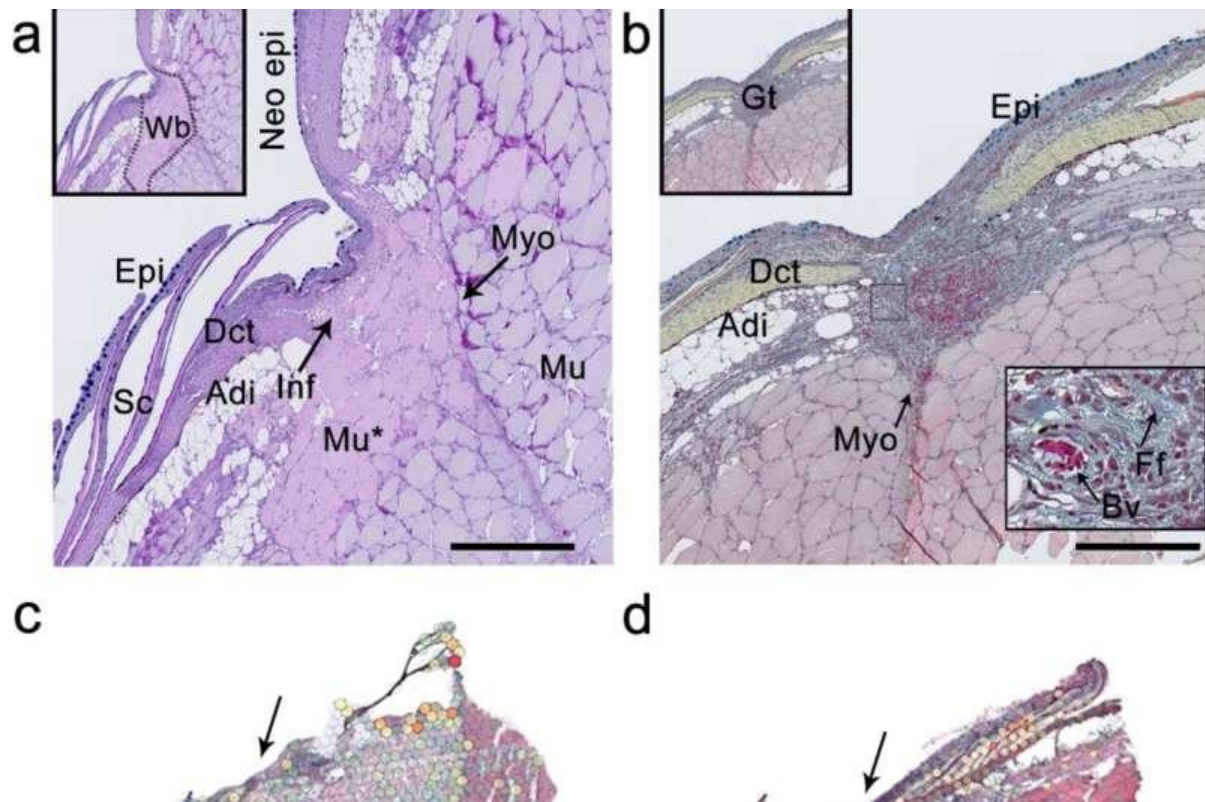
More information: Enrique Gonzalez-Duran et al, Suppression of plastid-to-nucleus gene transfer by DNA double-strand break repair, *Nature Plants* (2025). DOI: [10.1038/s41477-025-02005-w](https://doi.org/10.1038/s41477-025-02005-w)

Journal information: [Nature Plants](#)
Provided by [Max Planck Society](#)

MAY 27, 2025

Discovery offers new insights into skin healing in salmon

by [University of Stirling](#) edited by [Lisa Lock](#), reviewed by [Andrew Zinin](#)



Wound healing in Atlantic salmon. Credit: *BMC Biology* (2025). DOI: [10.1186/s12915-025-02196-w](https://doi.org/10.1186/s12915-025-02196-w)

University of Stirling scientists have discovered cells in the skin of Atlantic salmon that offer new insights into how wounds heal, tissues regenerate, and cellular transitions support long-term skin health.

By understanding how [skin cells](#) remodel and heal tissue, researchers hope to develop new strategies to enhance tissue integrity and reduce non-healing wounds, potentially improving salmon farming mortality rates.

Research led by Dr. Rose Ruiz Daniels of the University's Institute of Aquaculture uncovered the previously unknown population of stem cells.

Published in *BMC Biology*, the [study](#), "Transcriptomic characterization of transitioning [cell types](#) in the skin of Atlantic salmon," reveals that fibroblast-like stem cells—known as mesenchymal stromal cells (MSCs)—play a central role in the remodeling phase of wound healing, which is critical for restoring skin integrity following injury.

Using advanced cell profiling technologies—single-nucleus RNA sequencing and spatial transcriptomics—the researchers profiled skin cells during a wound healing time course.

Dr. Rose Ruiz Daniels said, "We found MSCs at both the wound site and in intact skin, suggesting these [adult stem cells](#) are a stable and functional part of salmon skin, and likely to be involved in maintaining its barrier and structural properties.

"These cells become more transcriptionally active during the remodeling stage of healing and show signs of differentiating into multiple tissue types including bone and fat.

"This hints at a broader regenerative capacity in fish skin than previously understood, potentially linking repair processes in the skin to those in deeper tissues like muscle, scales, and connective tissue."

MSC-like cells are well characterized in mammals, but this study suggests that in teleost fish such as salmon, these cells may retain higher pluripotency—or stemness—meaning they can take on a wider range of regenerative roles.

This raises the possibility that fish skin regeneration may operate through more flexible cellular pathways than in terrestrial vertebrates.

The study also maps the spatial niches of various MSC subclusters, laying the groundwork for future studies aimed at manipulating these cells to improve tissue repair, resilience, and overall fish health.

Dr. Ruiz Daniels added, "These findings have potentially far-reaching implications for aquaculture. Barrier tissue health, particularly of the skin and gills, is a major challenge in Atlantic [salmon](#) farming and a leading cause of mortality in sea cages.

"There is an urgent need for innovative biotechnological approaches to enhance fish health, as aquaculture also faces mounting challenges from climate change, including heightened disease risks and increased thermal uncertainties.

"By understanding how skin cells remodel and heal tissue, we hope to develop new strategies to enhance [tissue](#) integrity and reduce non-healing wounds at barrier tissues."

This study is a collaborative effort across institutions including the University of Stirling, the Roslin Institute, Nofima, and the University of Prince Edward Island.

More information: R. Ruiz Daniels et al, Transcriptomic characterization of transitioning cell types in the skin of Atlantic salmon, *BMC Biology* (2025). DOI: [10.1186/s12915-025-02196-w](https://doi.org/10.1186/s12915-025-02196-w)

Journal information: [BMC Biology](#)
Provided by [University of Stirling](#)

JUNE 3, 2025

CRISPR gene editing in blood stem cells linked to premature aging effects: Study offers solutions

by Fondazione Telethon edited by [Sadie Harley](#), reviewed by [Robert Egan](#)



Credit: Unsplash/CC0 Public Domain

Scientists at the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), Milan, have found that gene editing using CRISPR-Cas9 in combination with AAV6 vectors can trigger inflammatory and senescence-like responses in blood stem cells, compromising their long-term ability to regenerate the blood system.

The study, [published](#) in *Cell Reports Medicine*, outlines new strategies to overcome this hurdle, improving both the safety and efficacy of [gene-editing](#)-based therapies for inherited blood disorders.

The research was led by Dr. Raffaella Di Micco, group leader at SR-Tiget, New York Stem Cell Foundation Robertson Investigator and Associate Professor at the School for Advanced Studies (IUSS) of Pavia, in collaboration with Professor Luigi Naldini, Director of SR-Tiget, and several European research partners.

Unmasking senescence as a hidden challenge in gene editing

Homology-directed repair (HDR)-based gene editing in hematopoietic stem and [progenitor cells](#) (HSPCs) holds great promise for the treatment of genetic blood diseases.

Despite significant advances in HDR-based gene editing, translating these approaches into safe and effective clinical therapies for patients remains a major challenge. While the technology shows strong potential in laboratory settings, achieving reliable, durable outcomes in human [hematopoietic stem cells](#)—without compromising their function—has indeed proven difficult.

The team of Di Micco at SR-Tiget discovered that CRISPR-Cas9 editing, especially when using AAV6 vectors to deliver the repair template, activates a strong DNA damage response (DDR) and inflammatory signals driven by p53 and IL-1/NF-κB pathways. This leads to inflammation and a senescence-like state that reduces the regenerative capacity of the edited cells post-transplantation.

"We found that a fraction of gene-edited hematopoietic stem cells shows signs of premature aging," explains Dr. Di Micco. "This reduces their ability to regenerate blood cells after transplantation, which can limit the long-term success and therapeutic benefit of [gene therapy](#)."

"We were surprised by the persistence of senescence-like features even months after transplantation," says Dr. Anastasia Conti, first author of the study and Project Leader in Dr. Di Micco's lab. "Our findings suggest that stem cells retain a 'memory' of the genetic engineering process. These adverse effects are not just transient stress responses—they can lead to lasting impairments in stem cell function."

Mitigating senescence for superior performance of genetically-engineered cells

To counteract this adverse effect, the researchers tested two complementary strategies: transient p53 inhibition and the use of anti-inflammatory agents, particularly Anakinra—a clinically approved IL-1 receptor antagonist.

"Both approaches significantly reduced senescence markers in edited HSPCs and improved their ability to regenerate a healthy, diverse blood system in preclinical models. Importantly, Anakinra also reduced potential genotoxic events, such as large deletions and translocations, suggesting a safer profile compared to p53 inhibition alone," says Dr. Conti.

"Our study shows that modulating the inflammatory and senescence-related response during gene editing can preserve the fitness of edited [hematopoietic stem](#) cells and enable more stable and polyclonal hematopoietic reconstitution in the long-term," concludes Dr. Di Micco.

"These findings help explain setbacks observed in recent clinical trials involving HDR-based gene editing in [blood stem cells](#) and offer a concrete path to enhance outcomes. The strategies proposed could be especially valuable for diseases requiring long-term correction and stem cell engraftment, such as immunodeficiencies or bone marrow failure syndromes."

More information: Senescence and inflammation are unintended adverse consequences of CRISPR-Cas9/AAV6 mediated gene editing in hematopoietic stem cells, *Cell Reports Medicine* (2025). DOI: [10.1016/j.xcrm.2025.102157](https://doi.org/10.1016/j.xcrm.2025.102157). [www.cell.com/cell-reports-medi ... 2666-3791\(25\)00230-7](https://www.cell.com/cell-reports-medicine/2666-3791(25)00230-7)

Journal information: [Cell Reports Medicine](#)

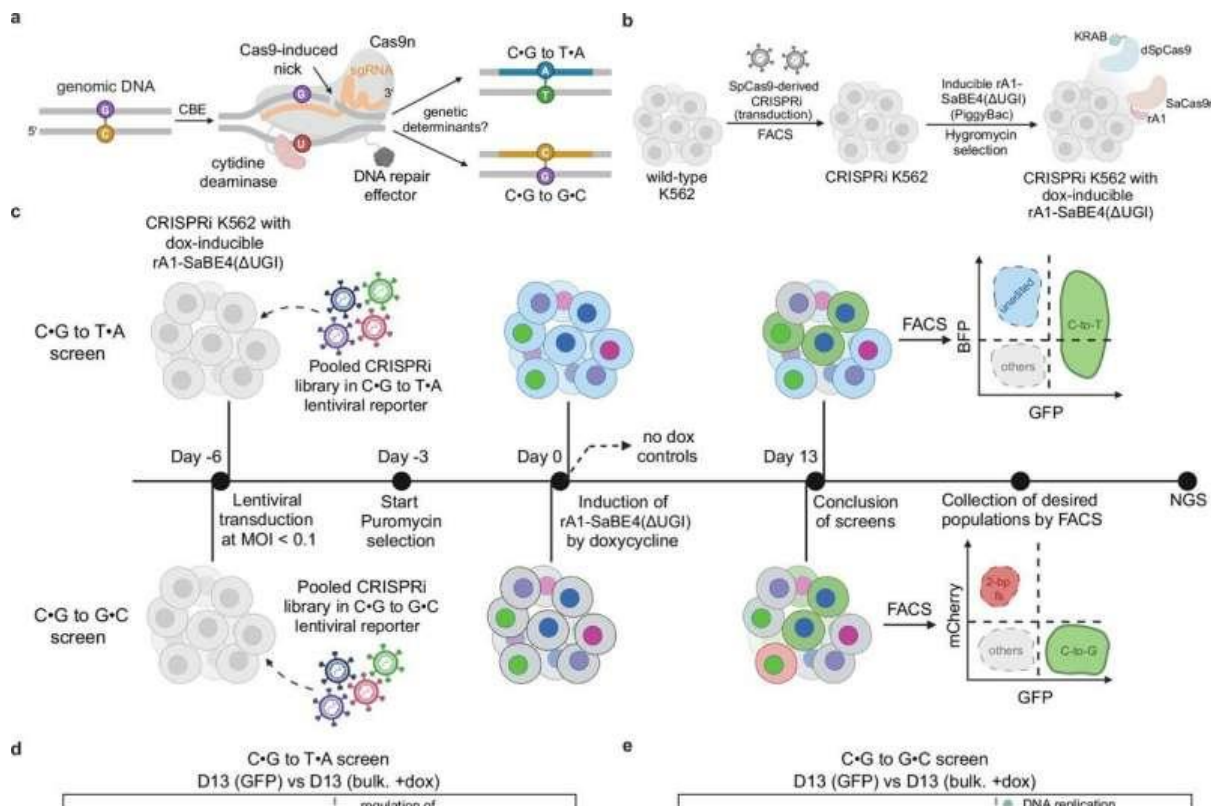
Provided by Fondazione Telethon

JUNE 4, 2025

Manipulating DNA repair proteins to improve gene editing outcomes

by Michelle Franklin, [University of California - San Diego](#)

edited by [Gaby Clark](#), reviewed by [Robert Egan](#)



Development and implementation of CRISPRi screens for identifying genes involved in processing cytosine base editing intermediates. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-59948-z

You may have seen it in the news recently: a baby in Pennsylvania with a rare genetic disorder was healed with a personalized treatment that repaired his specific genetic mutation. The treatment was created using a form of gene editing called base editing—a method created by Alexis Komor when she was a postdoctoral scholar in molecular biologist David Liu's group at Harvard University.

Since that work was published in 2016, Komor, who is now an associate professor of chemistry and biochemistry at the University of California San Diego, has continued to study base-editing tools to better understand and further develop their capabilities. Her latest

research, published in [Nature Communications](#), outlines the way certain DNA repair proteins can be manipulated to produce desired outcomes.

Our genomic DNA is comprised of four bases—cytosine (C), thymine (T), guanine (G) and adenosine (A). These bases join together into approximately 3 billion different base pairs, arranged in a double-helix structure.

Humans are 99.9% identical in their genetic makeup, while the remaining 0.1% accounts for any difference between one person and another. Where one person has a C base, another person might have a T base. There are millions of genetic variations possible between any two people, and although many are harmless, others can lead to debilitating or terminal genetic diseases.

For many people with genetic diseases, [gene editing](#) is their only hope of a cure.

Gene editing is traditionally done using CRISPR-Cas9 to make a physical change in the DNA. A guide RNA directs the Cas9 protein to a specific DNA location, where Cas9 completely severs the DNA—called a double stranded break. There are many proteins within the cell that can detect DNA damage and then fix it through a process called a repair pathway.

Normally, these pathways take the two broken ends of the DNA and fuse them back together, called a ligation. With CRISPR-Cas9, as the number of breaks and repairs increases, so do unwanted insertions and deletions, called indels. When this happens, the DNA strand no longer matches the original and the editing process ends.

The basics of base editing

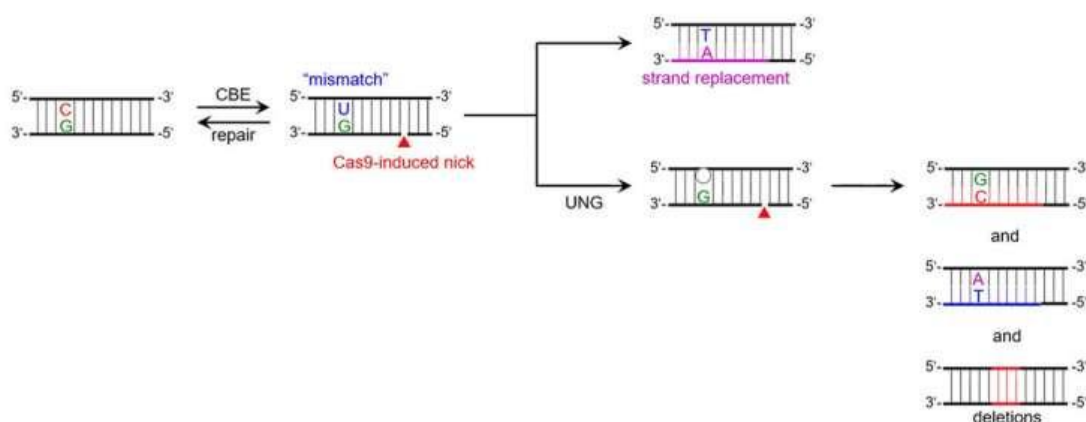
As a postdoc, Komor found a way to achieve gene-editing with higher efficiencies and a lower incidence of indels by avoiding double-stranded breaks. She called this new class of tools "base editing" because it chemically changes a DNA base one letter at a time.

"With base editing, not only do we achieve a better outcome, but the steps leading to the outcome are also improved," stated Komor. "Double-stranded breaks can be toxic and can cause [cell death](#). They can also cause larger-scale genomic rearrangements because you're physically cutting up the DNA. Base editors avoid that."

Komor developed two tools, an adenine base editor (ABE), which converts an A base to G base, and a cytosine base editor (CBE), which converts a C base to a T base. Base editors make conversions through an intermediary. In the case of CBEs, the cytosine is first converted to uracil, a nucleic acid found in RNA. During repair, the DNA reads the uracil as thymine.

Although there's no double-stranded break, base editors do create a nick in one strand. An enzyme is attached to the Cas9 and chemically changes the base. CBEs can have a 90-95% conversion rate with minimal unwanted byproducts.

We know the base editor works, but how? That's the main question Komor's group wanted to answer. They wondered how the uracil was being handled by the cell. What role does the nick play? How do all of the different proteins in the cell affect the editing outcomes?



A

schematic showing the cytosine base editing intermediate and the various outcomes that can occur when the UNG protein is active. Credit: Alexis Komor / UC San Diego

One particular protein called uracil N-glycosylase (UNG) finds and deletes uracils. When that protein is present, the incidence of unwanted outcomes rose. When UNG was inhibited, CBE efficiency increased. But Komor's group didn't have a full understanding of the process.

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To uncover the answer, the team used a technique called gene knockdown, which turns down a gene's ability to express itself. They did this for every single different DNA repair or processing protein in the human genome—2,015 proteins in total.

Then they used green fluorescent protein markers to identify cells containing the desired edits, either C to T mutations or the UNG-affected C to G edits, while discarding the UNG-affected edits they didn't want.

They did this work using a CRISPRi screen, which takes a guide RNA to a gene of interest and reduces its expression. Komor's CRISPRi cells had two guide RNAs—one to activate the fluorescent protein maker with the CBE and one directed to knock down the specific repair protein. All told, Komor had a library of around 12,000 different guide RNA combinations for the CRISPRi screen.

Once they collected all the cells that had fluoresced green, they sequenced the guide RNAs to see which genes were knocked down (and therefore their expression was detrimental to base editing).

They discovered that a ligase called Lig3 inhibited base editing. Ligases attached the ends of broken DNA strands back together and when Lig3 was present, CBE editing was lower.

"We think that the Lig3 can sneak in and seal that nick back together. Then we don't have a chance for that uracil to be turned into a thymine anymore," stated Komor. "It's like the Lig3 is working against us."

They also found a [repair pathway](#) called mismatch repair that actually helped cytosine base editing. The MutS-alpha protein complex, a component of mismatch repair, is composed of two proteins and is expressed throughout a cell's lifetime. When it was knocked down, conversions of C to T dropped. Komor thinks it's because MutS-alpha recognizes the uracil intermediate and helps convert it to thymine.

Why all the fuss? If the tool works, does it matter why? Yes, says Komor.

"These base editing tools are good, but they're not perfect," she stated. "If we can better understand how they're functioning in the cell, that will help us understand how we can improve their efficiency or even create new types of base editors."

Komor also notes that it's important to understand how these tools work for safety reasons. Does base editing activate an unforeseen cellular response? Is there DNA damage or cell death? The more we know about the mechanisms of the [base editors](#) and how cells respond, the better positioned we are to observe and stop unintended consequences.

"That's one of the reasons this work was supported by the National Science Foundation. This is basic science—understanding why things are the way they are and how they function in certain environments," Komor said.

Often it takes decades to see the real-world impact of basic science research, but Komor's base editing techniques were being deployed in hospitals in much shorter time. She notes that, to date, at least 10 people have been saved using CBE. Additionally, there are several clinical trials underway, meaning it's likely that number will increase greatly in the coming years.

More information: Sifeng Gu et al, Elucidating the genetic mechanisms governing cytosine base editing outcomes through CRISPRi screens, *Nature Communications* (2025). DOI: [10.1038/s41467-025-59948-z](https://doi.org/10.1038/s41467-025-59948-z)

Journal information: [Nature Communications](#)
Provided by [University of California - San Diego](#)

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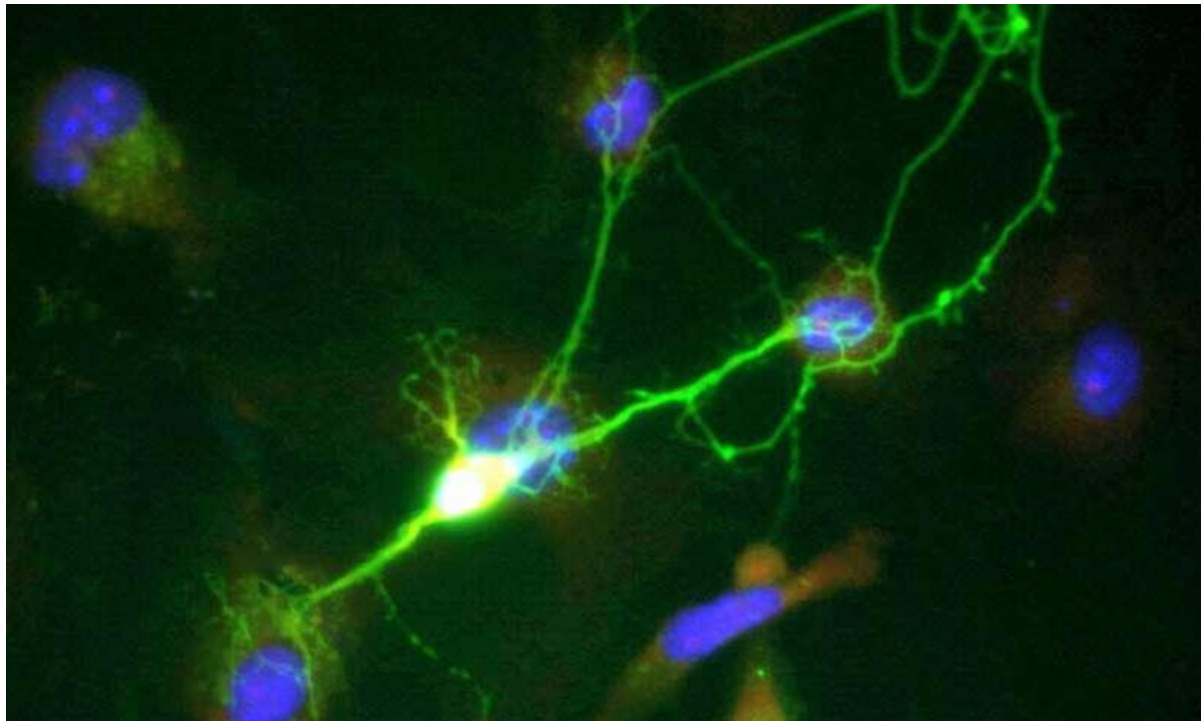
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JUNE 4, 2025

Research challenges conventional theories of how cells detect electrical fields

by Laurie Fickman, [University of Houston](#)

edited by [Lisa Lock](#), reviewed by [Robert Egan](#)



Credit: Public Domain

The human body is a veritable cellular highway with up to 37 trillion cells traveling about and carrying out all essential life functions, from taking in nutrients and converting them to energy, to repairing a skinned knee. In large part, cells get their marching orders from electric fields influencing their functions.

In fact, new evidence from the University of Houston suggests that cells are incredibly sensitive to [electrical fields](#), much more so than older scientific theories suggest.

"Our research challenges long-held assumptions about the limits of cellular electrical sensing and explains how cells detect electric fields with remarkable sensitivity," reports Yashashree Kulkarni, Bill D. Cook Professor of Mechanical and Aerospace Engineering at

UH in an article [published](#) in the *Proceedings of the National Academy of Sciences*. Kulkarni supervised the work of graduate student Anand Mathew, who led the research.

For decades, scientists thought cells couldn't detect very weak electric fields because of "thermal noise"—tiny random movements caused by heat. It's like trying to hear a whisper during a loud rock concert: the background noise drowns it out. Scientists believed this "noise floor" set the limit for what cells could possibly sense.

Kulkarni and Mathew's study presents a compelling new explanation: active matter within the [cell membrane](#) can push the system out of equilibrium, enabling heightened electrical sensitivity.

"Biological membranes are not passive," said Kulkarni. "They are embedded with [active proteins](#) and other components that continuously consume energy, creating dynamic, nonequilibrium environments. Our findings show that these active processes can fundamentally change the way cells respond to mechanical and electrical stimuli."

The researchers created a new theoretical model using nonequilibrium [statistical mechanics](#)—a type of science that studies systems always using energy. The new model helps explain how electromechanical membranes in cells move and change in their active, energy-filled environment.

Their analysis shows that these energy-consuming processes can lead to a dramatic increase in electrical sensitivity—offering a theoretical model that aligns with experimental observations in many biological systems.

"Understanding how cells can actively respond to their environment could inform the development of next-generation [medical devices](#), biosensors, and therapies for various diseases," said Mathew. "By harnessing the concept of active matter, we can begin to design systems that mimic or even exceed the sensing capabilities found in nature."

More information: Anand Mathew et al, Active matter as the underpinning agency for extraordinary sensitivity of biological membranes to electric fields, *Proceedings of the National Academy of Sciences* (2025). DOI: [10.1073/pnas.2427255122](https://doi.org/10.1073/pnas.2427255122)

Journal information: [Proceedings of the National Academy of Sciences](#)
Provided by [University of Houston](#)

JUNE 4, 2025

First genetic 'toggle switch' for plants paves the way for smarter farming

by [Colorado State University](#)

edited by [Stephanie Baum](#), reviewed by [Robert Egan](#)



CSU Professor June Medford, research scientist Tessema Kassaw (right), and Professor Ashok Prasad discuss plants in a lab within the Biology Building in May 2025. Credit: Colorado State University Walter Scott, Jr. College of Engineering

Researchers at Colorado State University have developed a tool that can be used to switch a plant's key genetic traits on or off at will. The breakthrough was [recently published](#) in *ACS Synthetic Biology* and represents the first time that a synthetic genetic "toggle switch" has been used in a full-grown plant.

Synthetic biologists design and build new segments of DNA that can then be inserted into living organisms to work like circuits in electronics or a computer. Just as a switch is used to turn a lightbulb on or off in an electric circuit, the team's "toggle" turns genes on and off when an external signal is applied. Up until now, the genetic toggle switch has only been used in [single-celled organisms](#) such as bacteria. The work at CSU is led by professors

June Medford from the Department of Biology and Ashok Prasad from the Department of Chemical and Biological Engineering.

Medford said the [interdisciplinary research](#) has plenty of practical applications, particularly in agriculture where a switch could be used to better time the ripening of fruit, for example.

She added that any number of traits could eventually be regulated with this tool. The challenge is inserting it into fully developed living organisms.

"The multicellular nature of a plant—its roots, tissues, vegetative and [reproductive organs](#)—makes it a complex challenge that we are finally able to overcome," she said. "This work is a promising initial step to programming plants to do all sorts of useful things that were not possible before."

The paper describes the team's work to synthesize relevant plant DNA parts and then design a potential genetic "toggle" system around the two key genes within them using mathematical modeling. This approach helped the team to mix and match possible combinations on the computer, until they found an effective combination. From there, the team began transforming plants with the chosen DNA sequences and tracked results over a 12-day period to quantify the changes.

Medford said it was a long and iterative process towards the proof of concept the paper now demonstrates.

"As biologists, we understand biology really well, and we partner with folks like Professor Prasad and his team, who are experts at developing the algorithms—this allows us to find the key signals amid the noise," said Medford.

"This project is a true marriage between quantitative research and mathematical modeling to predictably engineer a plant's abilities for any number of needs. Our work also opens the possibility that in the future, genetic circuitry design like this could be automated through machine learning, speeding the process."

Notably, the research shows that these circuits function across the whole plant and can be used to regulate shoots and cells across different parts of the life cycle. Prasad said that means these switches could be used to engage different plant functions in support of food security or materials development.

"In the face of unpredictable and unseasonable climates, farmers could control the state of their crops by 'turning on' a switch that promotes drought tolerance, or one that helps plants like pumpkins grow earlier in the season and then retain size and nutrition," Prasad said. "The applications for this breakthrough are nearly endless for humanity and the environment."

More information: Tessema K. Kassaw et al, Genetic Toggle Switch in Plants, *ACS Synthetic Biology* (2025). DOI: [10.1021/acssynbio.4c00777](https://doi.org/10.1021/acssynbio.4c00777)

Journal information: [ACS Synthetic Biology](#)

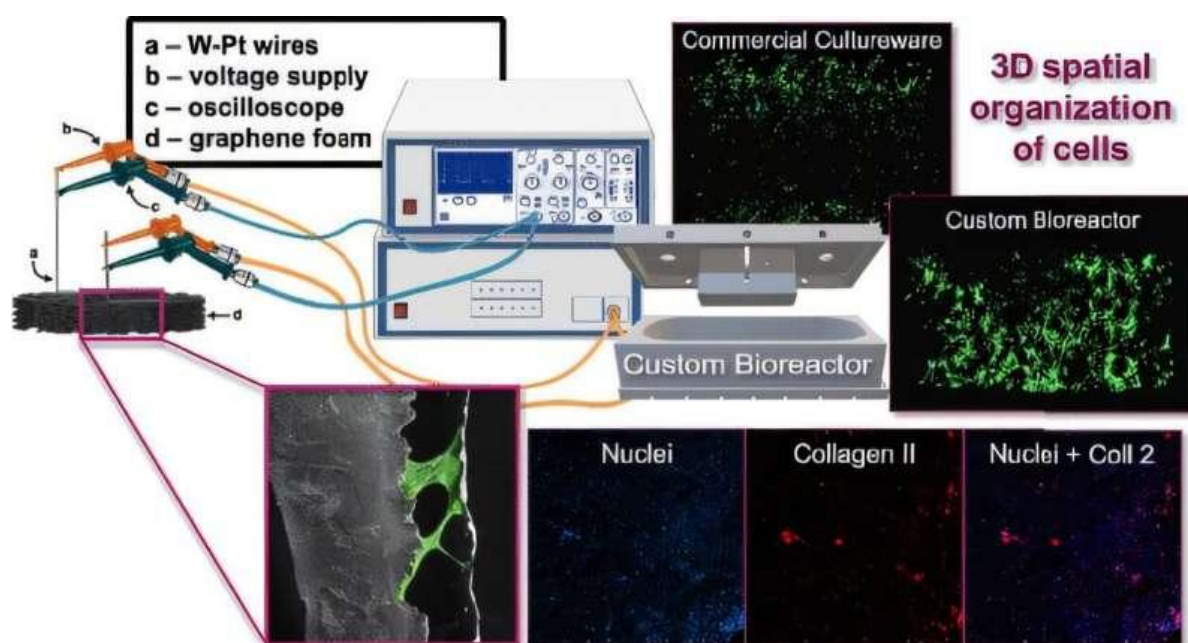
Provided by [Colorado State University](#)

JUNE 4, 2025

Graphene foam supports lab-grown cartilage for future osteoarthritis treatments

by [Boise State University](#)

edited by [Stephanie Baum](#), reviewed by [Robert Egan](#)



Credit: *ACS Applied Materials & Interfaces* (2025). DOI: 10.1021/acsami.5c02628
Boise State University researchers have developed a new technique and platform to communicate with cells and help drive them toward cartilage formation. Their work leverages a 3D biocompatible form of carbon known as graphene foam and is [featured](#) on the cover of *Applied Materials and Interfaces*.

In this work, the researchers aim to develop new techniques and materials that can hopefully lead to new treatments for osteoarthritis through [tissue engineering](#). Osteoarthritis is driven by the irreversible degradation of hyaline cartilage in the joints, which eventually leads to pain and disability, with complete joint replacement being the standard clinical treatment. Using custom-designed and 3D-printed bioreactors with electrical feedthroughs, they were able to deliver brief daily electrical impulses to cells being cultured on 3D graphene foam.

The researchers discovered that applying direct [electrical stimulation](#) to ATDC5 cells adhered to the 3D graphene foam bioscaffolds significantly strengthens their [mechanical properties](#) and improves [cell growth](#)—key metrics for achieving lab-grown cartilage. ATDC5 cells are a murine chondrogenic progenitor cell line well studied as a model for cartilage tissue engineering.

Additionally, their specialized setup allowed full submersion of the 3D graphene foam scaffold, enhancing cell attachment and integration within its porous structure—highlighting a promising approach for improving engineered tissues using an electrical stimulus through conductive biomaterials.

"One of the biggest challenges in applying direct electrical stimulation to stem cells is achieving repeatable delivery while monitoring the electrical environment and mapping that back to specific cellular responses," said Mone't Sawyer, lead author of the study. "Our system introduces a modular and scalable platform that enables [high-throughput](#), scaffold-coupled electrical stimulation with precise control—opening new possibilities for understanding how electrical cues influence tissue formation."

Osteoarthritis ranks as a world-leading cause of pain and disability, currently affecting over 595 million individuals—more than double the 256 million afflicted individuals recorded in 1990. The [economic burden](#) is large, with global costs exceeding \$460 billion annually, including health care expenses, lost productivity, and disability-related costs. In the U.S. alone, OA accounts for \$65 billion in direct and indirect costs, with over 1 million joint replacements performed each year to manage severe cases.

"Mone't's work is providing new fundamental insights into the role of materials and electrical stimuli in communicating with [stem cells](#)," said Prof. David Estrada of the Micron School of Materials Science and Engineering. "I believe this work is setting the stage for greater understanding of the human electrobiome; that is, the role of electric charge and transport across different length scales and ultimately in cell fate to tissue function."

More information: Mone't Sawyer et al, Direct Scaffold-Coupled Electrical Stimulation of Chondrogenic Progenitor Cells through Graphene Foam Bioscaffolds to Control the Mechanical Properties of Graphene Foam–Cell Composites, *ACS Applied Materials & Interfaces* (2025). DOI: [10.1021/acsami.5c02628](https://doi.org/10.1021/acsami.5c02628)

Journal information: [ACS Applied Materials and Interfaces](#)
Provided by [Boise State University](#)

JUNE 4, 2025

A new blood-based epigenetic clock for aging focuses on intrinsic capacity

by Buck Institute for Research on Aging

edited by [Sadie Harley](#), reviewed by [Robert Egan](#)

A team of international researchers has developed a new biological age "clock" that estimates how well someone is aging, not just how "old" they or their various organs might be. The IC Clock, which is described in a study in *Nature Aging*, measures intrinsic capacity (IC), the sum of six key functions that determine healthy aging: mobility, cognition, mental health, vision, hearing and nutrition/vitality.

"Maintaining function during the [aging process](#) is what matters to older adults. Function should inform [medical care](#) instead of focusing on getting patients to some disease-free state," said senior author David Furman, Ph.D., Buck associate professor and director of the Buck Bioinformatics and Data Science Core.

The World Health Organization (WHO) developed the concept of intrinsic capacity and recognized its decline with aging as a condition in 2022 in the International Classification of Diseases ICD-11.

The IC Clock was developed by scientists at the Buck, IHU HealthAge (France) in collaboration with the French INSERM and Universite de Montpellier, reflecting a growing alliance between US and European researchers to advance the science of healthy longevity.

Collaborators began developing the IC Clock by utilizing data from the INSPIRE-T cohort consisting of 1,000 individuals (ages 20 to 102) in and around Toulouse, France with follow-up over four years out of 10, so far.

In addition to data based on physical and cognitive function as well as lifestyle factors, researchers also had access to biospecimens including blood, urine, saliva, and dental plaque that are collected annually.

The IC Clock uses DNA methylation, a molecular signal found in blood or saliva, to assess IC noninvasively. After training the new model on data from the INSPIRE-T cohort, the team

validated it using the Framingham Heart Study, a long-term, ongoing cardiovascular cohort study of residents of the city of Framingham, Massachusetts.

Furman says the IC Clock, which factors in all of the currently recognized hallmarks of aging, outperformed all first- and second-generation aging clocks in predicting overall mortality.

He also noted that the research found links between higher IC Clock scores and better immune system performance, reduced inflammation and healthier lifestyle choices, suggesting that this measure taps into the core biology of aging and could be useful in the assessment of longevity-promoting interventions.

Furman's team is developing a dried-blood spot solution for the IC Clock, which would reduce the need for labor-intensive clinic visits, making the IC Clock useful for assessing functional decline in low-and-middle income countries.

"If we can offer a scalable, affordable molecular level tool to assess functional decline, the IC Clock could help clinicians, researchers, and [policy makers](#) better identify at-risk individuals and tailor interventions that promote a longer, healthier life," he said.

While WHO has adopted a decline in IC as a diagnostic for aging, the US FDA has yet to tackle the issue, creating what some see as a bottleneck in efforts to get clinical treatments approved to address biological aging. Furman thinks the IC Clock could provide a way to end the long-standing argument as to whether aging should be classified as a disease.

"We hope the IC Clock will ultimately enable the FDA to approve treatments that would improve health and function in older adults."

The IC Clock will be utilized in the [XPRIZE Healthspan competition](#). The Buck and colleagues from Hospital-University Institute of HealthAge at the University of Toulouse have been named semifinalists for the seven-year, \$101 million global competition, which is aimed at revolutionizing how we approach human aging.

Competing teams are tasked with developing and testing modalities that restore muscle, cognition, and immune function by a minimum of 10 years, with an ambitious goal of 20 years, in persons aged 50–80 years, in one year or less.

The Buck-Toulouse team is proposing a hybrid intervention that combines taking a daily ketone ester with a personalized intervention called ICOPE-INTENSE, which spans exercise, cognitive training, nutrition and more.

The IC Clock will be used to track and analyze responses among participants. ICOPE-INTENSE is the most robust non-drug intervention to date designed to improve Intrinsic Capacity.

More information: A Novel Blood-Based Epigenetic Clock for Intrinsic Capacity Predicts Mortality and is Associated with Clinical, Immunological and Lifestyle Factors, *Nature Aging* (2025). DOI: [10.1038/s43587-025-00883-5](https://doi.org/10.1038/s43587-025-00883-5)

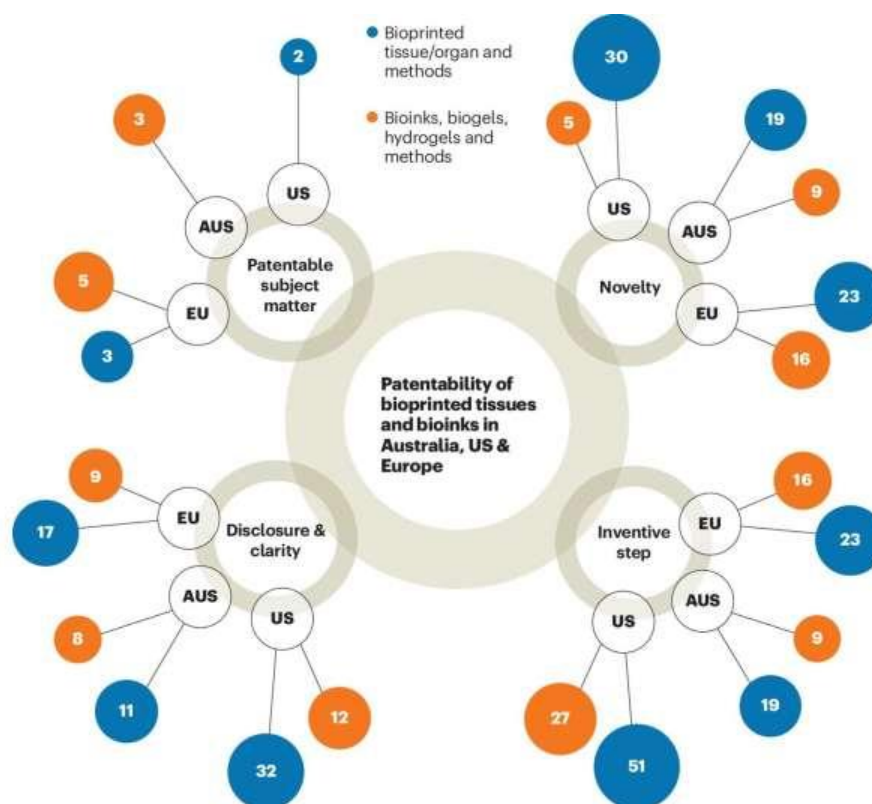
Journal information: *Nature Aging*

Provided by [Buck Institute for Research on Aging](#)

JUNE 6, 20

3D bioprinting is booming but patent laws may be holding it back

by [University of Queensland](#) edited by [Sadie Harley](#), reviewed by [Andrew Zinin](#)



A

comparative network visualization of types of objections received by patent applications claiming bioprinted tissues/organs, bioinks and related sub-technologies. Credit: *Nature Biotechnology* (2025). DOI: [10.1038/s41587-025-02661-5](https://doi.org/10.1038/s41587-025-02661-5)

The use of 3D printers to create living tissues and organs is revolutionizing medicine—but University of Queensland research reveals the legal system is struggling to keep up as the technology races ahead.

Lead researcher Dr. Pratap Devarapalli from UQ's Law School said there are about 1,850 Australians on the [organ transplant](#) waiting list, with bioprinting emerging as a promising solution if supported by clear and flexible global patent laws.

"Patent law hasn't kept pace with what's scientifically possible," Dr. Devarapalli said.

"The implications extend beyond medicine to fundamental questions about innovation policy.

"Ironically, the more realistic and medically useful a bioprinted organ is, the harder it becomes to patent because laws often require it to be clearly different from what exists in nature."

The [research](#) was published in *Nature Biotechnology* and in Dr. Devarapalli's [book](#).

In 2025, the bioprinting market is estimated at \$5.5 billion and is projected to reach \$20 billion by 2034.

Patents give inventors temporary protection from copying and without them companies may be less willing to invest, slowing down progress in developing lifesaving medical tools and treatments.

The research compares how major jurisdictions, including the US, Europe and Australia, assess the patentability of bioprinted inventions.

Dr. Devarapalli said the lack of consistency across borders creates legal uncertainty, especially when ethical concerns intersect with innovation.

"For instance, some patent offices may reject applications on the grounds that bioprinted tissues could resemble early-stage [human embryos](#), invoking moral objections in decision making," he said.

Australia has adopted a new classification regulating bioprinted devices containing [human cells](#) as '[medical devices](#) with biological components.'

Dr. Devarapalli said this progress brought Australia's framework in line with European and US standards.

"While this requires stricter oversight, it also provides clearer pathways to commercialization," he said.

"There needs to be balance between incentivizing funding research and the greater good."

Dr. Devarapalli will travel to Geneva this month to present on the topic at the United Nations.

More information: Pratap Devarapalli et al, 3D bioprinting innovation and the patentability hurdle, *Nature Biotechnology* (2025). DOI: [10.1038/s41587-025-02661-5](https://doi.org/10.1038/s41587-025-02661-5)

Journal information: [Nature Biotechnology](#)

Provided by [University of Queensland](#)

JUNE 10, 2025

CRISPR-Cas13 allows selective modification of desired RNA in living cells

by [The Korea Advanced Institute of Science and Technology \(KAIST\)](#)

edited by [Sadie Harley](#), reviewed by [Robert Egan](#)

Development of hyperactive variant eNAT10 through NAT10 protein engineering. By engineering the NAT10 protein, which performs RNA acetylation in human cells, based on its domain and structure, eNAT10 was developed, showing approximately a 3-fold increase in RNA acetylation activity compared to the wild-type enzyme. Credit: *Nature Chemical Biology* (2025). DOI: [10.1038/s41589-025-01922-3](https://doi.org/10.1038/s41589-025-01922-3)

RNA gene scissors (CRISPR-Cas13) are gaining significant attention as a next-generation gene therapy with fewer side effects. They can suppress infection by eliminating viral RNA, such as in coronaviruses, or regulate the expression of disease-causing genes.

KAIST researchers have developed the world's first technology that can precisely locate and acetylate (chemically modify) only the desired RNA among countless RNA molecules (molecules crucial for transmitting genetic information and producing proteins) within cells. This is expected to be a key technology that could open a new chapter in RNA-based therapies.

This research was [published](#) in *Nature Chemical Biology*.

Professor Won Do Heo's research team in the Department of Biological Sciences has developed an innovative technology capable of acetylating specific RNA in the human body using the CRISPR-Cas13 system, an RNA gene scissors system gaining attention in the field of gene regulation and RNA-based technology.

RNA can undergo changes in its properties and functions through a process called "[chemical modification](#)"—a gene regulation process where specific chemical groups are added, altering the properties and roles of RNA without changing its nucleotide sequence.

One such chemical modification is cytidine acetylation (N4-acetylcytidine). Until now, the precise function of this chemical modification within cells has not been clearly understood. In particular, there has been ongoing debate about whether this modification truly exists in human mRNA (RNA that produces proteins) and what role it plays.

To overcome these limitations, the research team developed a "targeted RNA acetylation system (dCas13-eNAT10)" by combining Cas13, gene scissors that precisely target desired RNA, with a hyperactive variant of NAT10 (eNAT10), an enzyme that acetylates RNA. In essence, they created a "targeted RNA modification technology" that precisely selects and acetylates only the desired RNA.

Acetylation of various RNA in cells using dCas13-eNAT10 fusion protein. Utilizing the CRISPR-Cas13 system, which can precisely target specific RNA through guide RNA, a dCas13-eNAT10 fusion protein was created, demonstrating its ability to specifically acetylate various endogenous RNA at different locations within cells. Credit: *Nature Chemical Biology* (2025). DOI: 10.1038/s41589-025-01922-3

The research team demonstrated that the targeted RNA acetylation system, guided by guide RNA that locates specific RNA within cells, can introduce acetylation chemical modifications to desired RNA. Through this, they confirm that protein production increases in messenger RNA (mRNA) that has undergone acetylation chemical modification.

Furthermore, the research team, using the developed system, revealed for the first time that RNA acetylation facilitates the translocation of RNA from the cell nucleus to the cytoplasm. This study demonstrates the possibility that acetylation chemical modification can also regulate intracellular RNA "localization."

The research team also proved that the developed technology could precisely control RNA acetylation within an animal's body by delivering the targeted RNA acetylation system to the liver of experimental mice via AAV (adeno-associated virus), a widely used viral vector in gene therapy.

This is the first case to show that RNA chemical modification technology can be extended to in vivo applications. This achievement is evaluated as opening up possibilities for application in RNA-based gene therapy technology.

In vivo delivery of targeted RNA acetylation system. The targeted RNA acetylation system was encoded in an AAV vector, commonly used in gene therapy, and delivered intravenously to adult mice, showing that target RNA in liver tissue was specifically acetylated according to the guide RNA.

Credit: *Nature Chemical Biology* (2025). DOI: 10.1038/s41589-025-01922-3

Professor Won Do Heo, who previously developed COVID-19 treatment technology using RNA gene scissors and technology to activate RNA gene scissors with light, stated, "Existing RNA chemical modification research faced difficulties in controlling specificity, temporality, and spatiality. However, this new technology allows selective acetylation of desired RNA, opening the door for accurate and detailed research into the functions of RNA [acetylation](#)."

"The RNA chemical modification technology developed in this study can be widely used as an RNA-based therapeutic agent and a tool for regulating RNA functions in living organisms in the future."

More information: Jihwan Yu et al, Programmable RNA acetylation with CRISPR–Cas13, *Nature Chemical Biology* (2025). DOI: [10.1038/s41589-025-01922-3](https://doi.org/10.1038/s41589-025-01922-3)

Journal information: [Nature Chemical Biology](#)

JUNE 10, 2025

Chimera approach overcomes mitochondrial barrier to alter protein production in living cells

by Universitätsmedizin Göttingen edited by [Sadie Harley](#), reviewed by [Robert Egan](#)

Mitochondrial network in cells. Credit: stefan jakobs (umg/fraunhofer)

Mitochondria supply the body with the energy currency adenosine triphosphate (ATP), which drives all bodily activities. For ATP production, the mitochondria consume around

95% of the oxygen inhaled. This process takes place in the so-called respiratory chain in the mitochondria, which is built of numerous individual proteins.

Malfunctions in the respiratory chain lead to serious and often [fatal diseases](#) that can affect [skeletal muscle](#) and nerve cells, as well as the heart.

Mitochondria have their own genetic material, mitochondrial DNA, or mtDNA for short. This is required for the production of 13 central proteins of the respiratory chain. Many of the mitochondrial hereditary diseases are caused by defects in the mtDNA, which lead to a loss of function of the respiratory chain and thus to a disruption of the cell's [energy supply](#).

How the mtDNA is read and translated into proteins has not yet been sufficiently clarified. The reason for this is that there are currently no techniques available to influence protein production in mitochondria.

Researchers led by Prof. Dr. Peter Rehling, director of the Department of Cellular Biochemistry at the University Medical Center Göttingen (UMG) and member of the Göttingen Cluster of Excellence "Multiscale Bioimaging: From Molecular Machines to Networks of Excitable Cells" (MBExC), are now one step further: they have succeeded in developing a new technology that can be used to alter protein production in the mitochondria of living cells.

The results of the study are [published](#) in *Science*. The knowledge gained with the help of this new technology makes it possible to understand the fundamental principles of cellular energy production and thus also to draw conclusions about the development of mitochondrial diseases.

The study in detail

The process of producing key respiratory chain proteins in the mitochondria is very complex. Defects in the process can lead to a variety of disorders, including cardiovascular disorders and disorders of the nervous system. "In order to understand the molecular mechanisms of protein production in mitochondria, we need experimental approaches that enable us to influence the individual steps of the process," says Prof. Rehling, senior author of the publication.

"Such technologies help us to understand how disturbances of a biological process challenge the cells. We can also use them to investigate how the cells react to such challenges in order to compensate for them." Until now, however, experimental strategies for investigating protein production in mitochondria have been lacking.

Established techniques, such as CRISPR, which can be used to specifically alter genetic material, do not work in mitochondria, as the mitochondrial membrane represents an insurmountable barrier for the gene scissors.

Targeted deactivation of proteins in living cells

The new technique developed by researchers in Göttingen overcomes the mitochondrial barrier. They use a chemically modified small protein fragment known as a chimera. It contains the necessary information, a kind of "zip code," to enter the mitochondria. Once there, it interferes specifically in the process of protein production.

In order for a protein to be made, a copy of the genetic material, in this case the mtDNA, must first be created. This copy contains the blueprint of the protein to be produced. The chimera was constructed in advance in such a way that it specifically attaches itself to the blueprint of a selected protein, thereby blocking the further steps in the production of a functional protein. In this way, it is possible to investigate how the cell's metabolism changes when certain proteins are no longer produced.

The researchers were also able to influence protein production in the mitochondria of heart muscle and liver cells. "With the help of the new technology, it is now possible for the first time to investigate how cells react to very specific disturbances in protein production," says Dr. Luis Daniel Cruz-Zaragoza, group leader at the Institute of Cell Biochemistry at the UMG and first author of the study.

"This opens up completely new possibilities for gaining insights into the development of mitochondrial diseases and developing new therapies on this basis."

More information: Luis Daniel Cruz-Zaragoza et al, Silencing mitochondrial gene expression in living cells, *Science* (2025). DOI: [10.1126/science.adr3498](https://doi.org/10.1126/science.adr3498)

Journal information: [Science](#)

Provided by Universitätsmedizin Göttingen

JUNE 10, 2025

S100A1: A potential new biomarker for frailty in older patients with heart disease

by Ina Henkel, [University of Potsdam](#) edited by [Gaby Clark](#), reviewed by [Robert Egan](#)

Gait Speed was determined using the 5-meter walk test. Credit: David Ausserhofer, DIfE
Frailty is a condition characterized by increased vulnerability and decline in physical function. It's a growing concern in the aging population, particularly among those with heart disease.

A multidisciplinary research team led by the German Institute of Human Nutrition Potsdam-Rehbruecke (DIfE), the Faculty of Health Sciences (FGW) at the University of Potsdam and

Deutsches Herzzentrum der Charité has now identified the gene S100A1 as a potential biomarker and therapeutic target in muscle tissue of older patients with heart disease, offering the potential to counteract mobility loss and [muscle weakness](#) early on. The findings were [published](#) in the *Journal of Cachexia, Sarcopenia and Muscle*.

Frailty, also known as frailty syndrome, is emerging as a significant health challenge for the aging population. It is characterized by increased susceptibility to falls, hospitalizations, complications after surgery, and a general decline in physical function.

Limited physical performance is a crucial factor in frailty among [older adults](#) with cardiovascular disease. To optimize health and functional treatment outcomes for this patient group, a better understanding of the underlying biological mechanisms is essential.

Therefore, this study focused on identifying [gene expression patterns](#) linked to different levels of frailty in older patients undergoing [cardiac surgery](#), offering new insights that could help guide more personalized treatment strategies.

Co-led by PD Dr. Heike Vogel from DIfE as well as PD Dr. Annett Salzwedel and Prof. Dr. Heinz Völler from the FGW at the University of Potsdam, and in close collaboration with the Deutsches Herzzentrum der Charité (PD Dr. Simon Sündermann) and other partner institutions, a total of 63 patients over 70 years of age were examined. These patients were hospitalized for cardiac surgery or transcatheter aortic valve implantation (TAVI).

Before the procedures, the researchers assessed the patients for three frailty phenotypes: gait speed, handgrip strength, and overall mobility.

During cardiac surgery, tissue samples were taken from the thigh muscle to perform a comprehensive gene expression analysis and to capture molecular changes in [skeletal muscle](#) using bioinformatics.

The researchers also utilized data from a separate cohort of older, healthy individuals and investigations in cell culture and animal models to validate the identified findings.

S100A1, a novel determinant of physical frailty. Credit: *Journal of Cachexia, Sarcopenia and Muscle* (2025). DOI: 10.1002/jcsm.13846

Key gene S100A1 in focus

The research team identified ten genes whose altered expression was associated with all three frailty phenotypes through gene expression analyses. The gene S100A1 emerged as particularly significant due to its key role in both skeletal and cardiac muscle function.

Individuals with poor muscle strength and impaired mobility showed markedly lower levels of S100A1 in muscle samples. Correspondingly, the validation cohort showed that higher S100A1 blood levels correlated with better grip strength.

A functional link was also demonstrated. Experiments in muscle cells confirmed that reduced S100A1 expression leads to impaired muscle development. Animal models showed that genetically determined higher S100A1 levels correlated with increased muscle mass, and that regular exercise further enhances gene expression.

Maintaining mobility and quality of life in old age

"For the first time, we have been able to demonstrate a correlation between reduced gene expression of S100A1 in muscle tissue and frailty phenotypes," explains doctoral candidate Omar Baritello from the FGW.

Study head Heike Vogel emphasized the importance of the findings: "We believe that S100A1 plays a central role in maintaining muscle health, and that it could be key to preventing frailty."

The research offers valuable insight into the biological processes that drive age-related frailty and highlights S100A1 as a potential biomarker for identifying older adults at risk. Moreover, the gene may represent a novel therapeutic target to help preserve muscle strength and mobility in elderly patients with cardiovascular disease.

Future research efforts will focus on validating S100A1 as a clinical marker and investigating its therapeutic utility. This includes developing diagnostics that can measure S100A1 levels and exploring strategies to modulate S100A1 expression, such as targeted muscle training or pharmacological interventions.

"This study brings us closer to the goal of not only understanding [frailty](#) better but also recognizing it early and actively counteracting it—and thereby improving the quality of life and safety of older people," says Vogel.

More information: Omar Baritello et al, Transcriptomic Signature of Frailty in Older Patients With Cardiovascular Disease Undergoing Cardiac Surgery or TAVI, *Journal of Cachexia, Sarcopenia and Muscle* (2025). DOI: [10.1002/jcsm.13846](https://doi.org/10.1002/jcsm.13846)
Provided by [University of Potsdam](#)

JUNE 11, 2025

Mouse stem cell lines offer new window into autism's genetic associations

by [Kobe University](#) edited by [Stephanie Baum](#), reviewed by [Robert Egan](#)

Cell models (pictured are neurons produced from human embryonic stem cells) allow studying how changes in the genes affect the shape and function of the cell. Credit: Nomura Jun

To study the genetic causes of autism spectrum disorder, a Kobe University research team has created a bank of 63 mouse embryonic stem cell lines containing the mutations most strongly associated with the disorder. The achievement was made possible by developing a new and more efficient method for changing the genome of embryonic stem cells.

Although it is well understood that genetics influence the development of [autism spectrum disorder](#), no one has yet been able to pinpoint the precise cause and mechanism. To study the biological background of diseases, researchers use models: Cell models allow us to study how changes in the genes affect the shape and function of the cell, while animal models show how the change in its cellular components affects health and behavior.

Despite significant differences between mice and humans, many disease-causing genes are very similar and cause similar conditions across these species.

"One of the problems, however, is the lack of a standardized biological model to study the effects of the different mutations associated with autism spectrum disorder. This makes it difficult to find out, for example, whether they have common effects or what is specific to certain cell types," explains Kobe University neuroscientist Takumi Toru.

Thus, twelve years ago, Takumi and his team embarked on a journey to change that. Being experts in studying mouse models of the disorder, they combined a conventional manipulation technique for mouse [embryonic stem cells](#)—cells that can be made to develop into almost any kind of cell in the body—with the then-newly discovered, highly specific and easy-to-handle CRISPR gene editing system.

This new method proved highly efficient in making genetic variants of these cells and allowed the Kobe University team to produce a bank of 63 mouse embryonic stem cell lines of the genetic variants most strongly associated with autism spectrum disorder.

In the journal *Cell Genomics*, Takumi and his team have now published research showing that they were able to develop their cells into a broad range of cell types and tissues, and even generate adult mice with their genetic variations. The analysis of these alone proved that their cell lines were adequate models for studying autism spectrum disorder. However, the [cell lines](#) also allowed them to conduct large-scale data analyses to clearly identify genes that are abnormally active, and in which [cell types](#) this is the case.

One of the things the [data analysis](#) brought to light is that autism-causing mutations often result in neurons being unable to eliminate misshapen proteins. "This is particularly interesting since the local production of proteins is a unique feature in neurons, and a lack of quality control of these proteins may be a causal factor of neuronal defects," explains Takumi.

The Kobe University neuroscientist expects that his team's achievement, which has been made available to other researchers and can be flexibly integrated with other lab techniques and adjusted to other targets, will be an invaluable resource for the scientific community studying [autism](#) and trying to find drug targets.

He adds, "Interestingly, the genetic variants we studied are also implicated in other neuropsychiatric disorders such as schizophrenia and bipolar disorder. So, this library may be useful for studying other conditions as well."

More information: ES cell models of autism with copy number variations reveal cell-type-specific translational vulnerability, *Cell Genomics* (2025). DOI: [10.1016/j.xgen.2025.100877](https://doi.org/10.1016/j.xgen.2025.100877)
Journal information: [Cell Genomics](#)
Provided by [Kobe University](#)

JUNE 11, 2025

Boosting precision gene editing: Autophagy shifts DNA repair toward homologous recombination

by [National Research Council of Science and Technology](#)

edited by [Sadie Harley](#), reviewed by [Robert Egan](#)

Illustration showing how autophagy induction increases the efficiency of precise gene editing. Credit: Korea Research Institute of Chemical Technology (KRICT)
Precision gene editing is crucial for treating genetic diseases, as it enables targeted correction of specific mutations. A Korean research team has become the first in the world

to significantly enhance the low efficiency of a key genome editing mechanism—known as homologous recombination (HR)—by inducing autophagy, a natural process within cells.

The study is [published](#) in the journal *Nucleic Acids Research*.

Dr. Hye Jin Nam's team at the Korea Research Institute of Chemical Technology (KRICT), in collaboration with Professors Dong Hyun Jo and Sangsu Bae at Seoul National University College of Medicine, found that [autophagy](#) induction via nutrient deprivation or mTOR inhibition markedly enhances the efficiency of HR-based CRISPR–Cas9 gene editing up to three-fold.

The technique was also successfully validated in patient-derived cells carrying genetic mutations and in live animal models, marking a major step toward applying this method in therapeutic settings.

CRISPR–Cas9 technology works by creating double-strand breaks (DSBs) in DNA to enable gene editing. However, most of these breaks are repaired through an error-prone process called nonhomologous end joining (NHEJ), which often introduces unintended mutations.

In contrast, [homologous recombination](#) (HR) is a more accurate form of DNA repair—but it occurs infrequently, making precision editing difficult. Previous efforts to enhance HR activity, such as modulating the [cell cycle](#) or inhibiting NHEJ, have been limited by toxicity and poor compatibility across diverse systems.

Suspecting that autophagy might promote the use of HR over error-prone repair pathways, the research team investigated its effect on gene editing.

When autophagy was triggered—either by nutrient starvation or treatment with mTOR inhibitors—the efficiency of HR-based editing increased by 1.4 to 3.1 times across various target genes and DNA insert sizes. In contrast, cells unable to undergo autophagy showed no such improvement, highlighting autophagy's essential role in promoting precise genome repair.

Autophagy induction significantly enhances the efficiency of precise gene editing in both living organisms and patient-derived cells. In both models, autophagy activation led to an approximately three-fold increase in editing efficiency. Credit: Korea Research Institute of Chemical Technology (KRICT)

Even alternate versions of CRISPR, such as nickase Cas9 (nCas9) and dead Cas9 (dCas9), showed improved editing performance under autophagic conditions.

This suggests that the strategy is widely applicable across different gene editing platforms. Further analysis revealed that autophagy enhanced the accumulation of HR-associated DNA repair proteins within the Cas9 complex, which may help direct repair activity toward more precise outcomes.

In experiments using patient-derived cells carrying mutations in the MPZL2 gene—linked to hearing loss—the method led to increased expression of the corrected gene up to three-fold.

The research team also tested the approach in mouse models. When gene editing was performed in the mouse retina, autophagy induction led to about a three-fold improvement in editing efficiency. This confirms that the strategy works not only in cultured cells but also in living organisms.

This study is the first to demonstrate that autophagy can enhance the accuracy of genome editing both in human cells and in animal models. The findings suggest a new path forward for gene therapies, offering a safer and more effective way to precisely rewrite faulty genetic sequences.

Dr. Nam stated, "Leveraging autophagy to enhance homologous recombination represents a breakthrough strategy to overcome key limitations in current gene editing technologies."

KRICT President Young-Kuk Lee added, "This achievement significantly improves both the efficiency and safety of genome editing and marks an important milestone in the advancement of precision therapeutics."

More information: Hye Jin Nam et al, Autophagy induction enhances homologous recombination-associated CRISPR–Cas9 gene editing, *Nucleic Acids Research* (2025). DOI: [10.1093/nar/gkaf258](https://doi.org/10.1093/nar/gkaf258)

Journal information: [Nucleic Acids Research](#)

Provided by [National Research Council of Science and Technology](#)

JUNE 11, 2025

DHEA-S hormone linked to shorter lifespan in men, but not women

by [The City University of New York](#) edited by [Gaby Clark](#), reviewed by [Andrew Zinin](#)

A new genetic [study](#) suggests that higher levels of the hormone dehydroepiandrosterone sulfate (DHEA-s) are associated with a shorter lifespan in men, but show no significant effect on the lifespan of women.

The research, led by CUNY SPH Professor Mary Schooling, used a Mendelian randomization approach, leveraging [genetic data](#) from large European cohorts to minimize confounding factors. The paper is published in the journal *Nutrition, Metabolism and Cardiovascular Diseases*.

"Gold standard" evidence, i.e., from randomized controlled trials, about the effects of DHEA supplements on blood pressure or lifespan is very limited, with most of the evidence for blood pressure concerning [women](#), and no evidence available for lifespan. To address this gap, Professor Schooling and Dr. Jie V. Zhao from the University of Hong Kong assessed how having genetically higher DHEA-s affected blood pressure and lifespan.

The researchers found genetically higher DHEA-s increased blood pressure and reduced lifespan in men, but not in women.

"Given that DHEA-s is a precursor of testosterone, our finding is consistent with a recent [warning](#) from the FDA that testosterone products may increase [blood pressure](#) in men," says Schooling. "Our findings about DHEA-s also likely reducing [lifespan](#) in men raises questions about the labeling and availability of DHEA over the counter in the United States."

More information: C Mary Schooling et al, Dehydroepiandrosterone sulfate on lifespan in men and women using Mendelian randomization, *Nutrition, Metabolism and Cardiovascular Diseases* (2025). DOI: [10.1016/j.numecd.2025.104128](https://doi.org/10.1016/j.numecd.2025.104128)
Provided by [The City University of New York](#)

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JUNE 11, 2025

How AI can be integrated seamlessly into pathological diagnosis

by [Friedrich–Alexander University Erlangen–Nurnberg](#)

edited by [Lisa Lock](#), reviewed by [Robert Egan](#)

Operational modalities of the integration framework. Credit: *Genome Medicine* (2025). DOI: [10.1186/s13073-025-01484-y](https://doi.org/10.1186/s13073-025-01484-y)

Algorithms from artificial intelligence (AI) are being used more and more frequently, including for medical diagnosis. However, their potential is barely being tapped in a number of areas. A collaborative project from Universitätsklinikum Erlangen (UKER) at Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) and Gravina Hospital in Caltagirone (Italy) is showing that it does not need to be that way.

The researchers are demonstrating how AI can be seamlessly integrated into [clinical practice](#) in a fully digitized department of [pathology](#). Their findings have now been [published](#) in the journal *Genome Medicine*.

Each year, more than 1.4 million people in Germany are treated in hospital for cancer. When a tumor is surgically removed, the tissue is usually examined in the department of pathology: which type of cancer is it exactly? Is the growth malignant? Should chemotherapy be offered, and if so, with which medication?

AI algorithms can help pathologists find the answers to these and other questions, for example, by highlighting malignant transformation in digitized tissue samples. However, their full potential often still remains untapped today. This is due in part to examination methods: while an MRI or ultrasound scan can produce [digital images](#) that can be assessed directly using AI, that is not the case with a tissue sample.

"Until now, samples have mainly been examined using microscopes," explains PD Dr. Fulvia Ferrazzi, who leads the working group for bioinformatics and computer-assisted pathology at the Department of Nephropathology and at the Institute of Pathology at UKER. "Digitizing histopathological samples to obtain high-resolution images remains an exception."

The Department of Pathology at Gravina Hospital in Caltagirone in Italy is already a step ahead—they routinely digitize all [tissue samples](#). "The problem here is not the availability of digital data," comments Miriam Angeloni, who is pursuing a doctoral degree in Ferrazzi's working group.

"Rather, there has been no way of analyzing these data automatically using deep learning models until now." This is the reason why AI tools are not yet routinely integrated into [clinical diagnosis](#). "We investigated how we could integrate the use of these tools more smoothly."

How does a fully digitized department of pathology work?

When a tissue sample arrives in the pathology laboratory in Gravina Hospital, it goes through several processing steps. As a rule, several extremely thin specimens are prepared, fixed on thin glass slides and dyed with various chemicals. Next, high-resolution digital images are produced of these slides. Employees can access these images directly via the laboratory information system (LIS). The diagnosis is then made not like normal using a microscope but on a computer screen instead.

During their collaborative project, the researchers have developed a procedure that automatically integrates AI analysis into their workflow. As soon as new scans are entered in the LIS, all information required for the analysis is automatically transferred to a server with various AI models. There, the suitable algorithms are selected depending on the dyeing method that was used and the tissue from which the sample was taken. In addition to this standard procedure, the pathologists are also able to select an "on demand" analysis directly from the LIS.

Improved integration is hoped to improve the accuracy of the algorithms

The results of the analysis are then returned to the LIS. There, the algorithms' predictions can be shown as "heatmaps." These colored superimpositions can be used, for example, to indicate malignant regions on the digitized tissue sample.

"Together with our collaboration partners we hope to use the workflow we have developed to provide clinical validation of the integrated deep learning models," explains Ferrazzi. The aim is to continue to improve the algorithms' accuracy in future. "We also hope that our collaboration project will encourage the integration of deep learning models into routine diagnostics for other departments of pathology."

More information: Miriam Angeloni et al, Closing the gap in the clinical adoption of computational pathology: a standardized, open-source framework to integrate deep-learning models into the laboratory information system, *Genome Medicine* (2025). DOI: [10.1186/s13073-025-01484-y](https://doi.org/10.1186/s13073-025-01484-y)

Journal information: [Genome Medicine](#)

MIT engineers uncover a surprising reason why tissues are flexible or rigid

Watery fluid between cells plays a major role, offering new insights into how organs and tissues adapt to aging, diabetes, cancer, and more.

Jennifer Chu | MIT News Publication Date: June 20, 2025

Water makes up around 60 percent of the human body. More than half of this water sloshes around inside the cells that make up organs and tissues. Much of the remaining water flows in the nooks and crannies between cells, much like seawater between grains of sand.

Now, MIT engineers have found that this “intercellular” fluid plays a major role in how tissues respond when squeezed, pressed, or physically deformed. Their findings could help scientists understand how cells, tissues, and organs physically adapt to conditions such as aging, cancer, diabetes, and certain neuromuscular diseases.

In a [paper](#) appearing today in *Nature Physics*, the researchers show that when a tissue is pressed or squeezed, it is more compliant and relaxes more quickly when the fluid between its cells flows easily. When the cells are packed together and there is less room for intercellular flow, the tissue as a whole is stiffer and resists being pressed or squeezed.

The findings challenge conventional wisdom, which has assumed that a tissue’s compliance depends mainly on what’s inside, rather than around, a cell. Now that the researchers have shown that intercellular flow determines how tissues will adapt to physical forces, the results can be applied to

understand a wide range of physiological conditions, including how muscles withstand exercise and recover from injury, and how a tissue's physical adaptability may affect the progression of aging, cancer, and other medical conditions.

The team envisions the results could also inform the design of artificial tissues and organs. For instance, in engineering artificial tissue, scientists might optimize intercellular flow within the tissue to improve its function or resilience. The researchers suspect that intercellular flow could also be a route for delivering nutrients or therapies, either to heal a tissue or eradicate a tumor.

“People know there is a lot of fluid between cells in tissues, but how important that is, in particular in tissue deformation, is completely ignored,” says Ming Guo, associate professor of mechanical engineering at MIT. “Now we really show we can observe this flow. And as the tissue deforms, flow between cells dominates the behavior. So, let's pay attention to this when we study diseases and engineer tissues.”

Guo is a co-author of the new study, which includes lead author and MIT postdoc Fan Liu PhD '24, along with Bo Gao and Hui Li of Beijing Normal University, and Liran Lei and Shuainan Liu of Peking Union Medical College.

Pressed and squeezed

The tissues and organs in our body are constantly undergoing physical deformations, from the large stretch and strain of muscles during motion to the small and steady contractions of the heart. In some cases, how easily tissues adapt to deformation can relate to how quickly a person can recover

from, for instance, an allergic reaction, a sports injury, or a brain stroke. However, exactly what sets a tissue's response to deformation is largely unknown.

Guo and his group at MIT looked into the mechanics of tissue deformation, and the role of intercellular flow in particular, following a study they published in 2020. In that study, they focused on tumors and observed the way in which fluid can flow from the center of a tumor out to its edges, through the cracks and crevices between individual tumor cells. They found that when a tumor was squeezed or pressed, the intercellular flow increased, acting as a conveyor belt to transport fluid from the center to the edges. Intercellular flow, they found, could fuel tumor invasion into surrounding regions.

In their new study, the team looked to see what role this intercellular flow might play in other, noncancerous tissues.

“Whether you allow the fluid to flow between cells or not seems to have a major impact,” Guo says. “So we decided to look beyond tumors to see how this flow influences how other tissues respond to deformation.”

A fluid pancake

Guo, Liu, and their colleagues studied the intercellular flow in a variety of biological tissues, including cells derived from pancreatic tissue. They carried out experiments in which they first cultured small clusters of tissue, each measuring less than a quarter of a millimeter wide and numbering tens of thousands of individual cells. They placed each tissue cluster in a custom-designed testing platform that the team built specifically for the study.

“These microtissue samples are in this sweet zone where they are too large to see with atomic force microscopy techniques and too small for bulkier devices,” Guo says. “So, we decided to build a device.”

The researchers adapted a high-precision microbalance that measures minute changes in weight. They combined this with a step motor that is designed to press down on a sample with nanometer precision. The team placed tissue clusters one at a time on the balance and recorded each cluster’s changing weight as it relaxed from a sphere into the shape of a pancake in response to the compression. The team also took videos of the clusters as they were squeezed.

For each type of tissue, the team made clusters of varying sizes. They reasoned that if the tissue’s response is ruled by the flow between cells, then the bigger a tissue, the longer it should take for water to seep through, and therefore, the longer it should take the tissue to relax. It should take the same amount of time, regardless of size, if a tissue’s response is determined by the structure of the tissue rather than fluid.

Over multiple experiments with a variety of tissue types and sizes, the team observed a similar trend: The bigger the cluster, the longer it took to relax, indicating that intercellular flow dominates a tissue’s response to deformation.

“We show that this intercellular flow is a crucial component to be considered in the fundamental understanding of tissue mechanics and also applications in engineering living systems,” Liu says.

Going forward, the team plans to look into how intercellular flow influences brain function, particularly in disorders such as Alzheimer’s disease.

“Intercellular or interstitial flow can help you remove waste and deliver nutrients to the brain,” Liu adds. “Enhancing this flow in some cases might be a good thing.”

“As this work shows, as we apply pressure to a tissue, fluid will flow,” Guo says. “In the future, we can think of designing ways to massage a tissue to allow fluid to transport nutrients between cells.”

JUNE 17, 2025

How hair follicles sense their environment

by Olivia Dimmer, [Northwestern University](#) edited by [Lisa Lock](#), reviewed by [Robert Egan](#)

Northwestern Medicine scientists have discovered how cells responsible for hair growth perceive physical forces in their environment and utilize that information to regulate their growth, according to a study [published](#) in *Science Advances*.

Hair follicle [stem cells](#) (HF-SCs) are long-lived cells within the hair follicle that are responsible for [hair growth](#) and regeneration throughout a person's life. In many tissues, including hair follicles, stem cells spend most of their time in a quiet, resting state. Understanding how they maintain this state is crucial for developing therapies for hair loss and [wound healing](#), said Rui Yi, Ph.D. and the Paul E. Steiner Research Professor of Pathology and professor of Dermatology.

"The question is how cells sense [mechanical force](#) and how they translate that force into signals to tell them what to do, which has not previously been clear," said Yi, the senior author of the study.

In the study, Yi and his collaborators observed HF-SCs in mice and found that the stem cells used the ion channel PIEZO1 to detect mechanical forces, like the tension between cells or pressure from surrounding tissue. PIEZO1 is a mechanosensitive ion channel, meaning it opens in response to physical force and allows [calcium ions](#) to flow into the cell.

Next, using advanced imaging techniques, the investigators analyzed the flow of calcium into the cells. HF-SCs are connected to each other through a protein called E-cadherin, which acts like molecular Velcro. The investigators found that when E-cadherin is pulled with a force of about 20 piconewtons (a trillionth of a Newton), PIEZO1 becomes activated.

This activation causes tiny bursts of calcium—called "calcium flickers"—to enter the cell. These calcium signals help keep the stem cells in their resting state.

When investigators deleted the PIEZO1 gene in these stem cells, the cells received fewer calcium signals and were more likely to exit their dormant state. This suggests that PIEZO1 is essential for maintaining the balance between rest and growth in HF-SCs, Yi said.

Using single-cell genomic analysis, the team also identified a network of genes controlled by PIEZO1. Two key players in this network are AP1 and NFATC1—genes that code for [transcription factors](#) that help regulate genes involved in cell structure and adhesion. These genes help reinforce the unique mechanical environment that HF-SCs need to stay dormant.

PIEZO1's job seems to be sensing how strong the force is around the stem cell, and then triggering the stem cell to express even more of the genes to make sure the mechanical property is maintained, according to Yi.

The findings open up new possibilities for manipulating stem cell behavior in [regenerative medicine](#) and aging research, Yi said.

"Mechanical force sensing and the downstream regulation are really important to controlling [hair follicle](#) stem cell activities," Yi said. "When we get older, the frequency of hair growth decreases. We want to know whether we can leverage some of our findings by manipulating specific mechanical forces to change stem cell behavior to stimulate their division or activation."

While the study was conducted with mice, Yi said he hopes to confirm the findings in humans.

"The study was just done in mice as a proof of principle," he said. "Maybe one day we can start to treat human [hair loss](#) disorders."

More information: Jingjing Wang et al, PIEZO1-mediated calcium signaling reinforces mechanical properties of hair follicle stem cells to promote quiescence, *Science Advances* (2025). DOI: [10.1126/sciadv.adt2771](https://doi.org/10.1126/sciadv.adt2771)

Journal information: [Science Advances](#)

Provided by [Northwestern University](#)

JUNE 18, 2025

Biohybrid molecule uses light-driven electrons to efficiently produce hydrogen

by [Ruhr University Bochum](#) edited by [Lisa Lock](#), reviewed by [Robert Egan](#)

Structures of the active site cofactor of [FeFe]-hydrogenases, the diiron site mimic employed here, and of *C. reinhardtii* PetF (CrPetF). Credit: *Advanced Science* (2025). DOI: 10.1002/advs.202501897

Natural hydrogen-producing enzymes are large and extremely sensitive to oxygen. This makes it difficult to use them for the applied production of green hydrogen. Researchers from the Photobiotechnology group at Ruhr University Bochum and partners at the University of Potsdam, Germany, have found a way to bypass this problem: They transferred the iron-containing catalytic center of one such enzyme—[FeFe]-hydrogenase—into a ferredoxin.

This small biomolecule acts as an electron carrier in all living organisms. The artificial biohybrid can efficiently produce hydrogen using electrons from light-powered biological systems. The researchers [published](#) their findings in the journal *Advanced Science* on June 17, 2025.

Shortcut to hydrogen production

Hydrogen is considered a clean energy carrier of the future, but it remains difficult to produce it sustainably. Natural enzymes known as hydrogenases are highly efficient, hydrogen-producing biocatalysts, but they are not yet being used industrially. With 600 [amino acids](#), they are very large and complex, and often extremely sensitive to oxygen. They also require highly energetic electrons that should also be sustainably produced.

[FeFe]-hydrogenases use an iron-containing molecule to produce hydrogen. This cofactor functions similarly to a platinum catalyst and can be chemically synthesized. However, as an isolated molecule it is inert and requires the [protein](#) environment to achieve maximum effectiveness.

Simplifying the biocatalyst

The researchers from Ruhr University Bochum wanted to simplify the highly complex hydrogenase biocatalyst to facilitate its integration into industrial processes. In some microalgae, hydrogenases are supplied with electrons provided by photosynthesis. The small protein ferredoxin, which also contains iron, transfers the electrons. Ferredoxin itself receives the electrons directly from the photosynthetic electron transport chain.

"We asked the biologically somewhat crazy question of whether we can't just find a shortcut and let ferredoxin produce hydrogen," explains Vera Engelbrecht, one of the two lead authors of the study. To her great surprise, the researchers were able to identify ferredoxins that could produce hydrogen in combination with the hydrogenase cofactor.

"However, we had to circumvent the biological synthesis pathways," explains Yiting She, the other lead author. "Only specific ferredoxins could collaborate with the cofactor. It was a difficult but exciting journey to discover this."

Successful interaction between protein and catalyst

The biohybrid's high activity surprised the researchers. "We know that the interaction between protein and cofactor in natural [FeFe]-hydrogenases is finely tuned," explains Professor Thomas Happe, who supervised the project. In cooperation with partners from the University of Potsdam, the new ferredoxin hydrogenase was characterized spectroscopically and with quantum-mechanical calculations.

"It seems that the ferredoxin protein provides a chemically favorable environment for the hydrogenase catalyst," concludes Happe. In order to achieve this, the natural cofactor of the ferredoxin must be replaced with the hydrogenase cofactor via complex synthesis pathways.

"Despite this, the new protein can still receive electrons from photosynthesis components," says Yiting She. This is thus an important feasibility study for a small, artificial metalloenzyme that imitates natural, light-powered hydrogenases but with fewer components and smaller scaffolds.

More information: Yiting She et al, Hydrogen-Producing Catalysts Based on Ferredoxin Scaffolds, *Advanced Science* (2025). DOI: [10.1002/adv.202501897](https://doi.org/10.1002/adv.202501897)

Journal information: [Advanced Science](#)

Provided by [Ruhr University Bochum](#)

JUNE 18, 2025

Hidden role of hydrogen—study reveals how atom position controls molecular breakdown pathways

by [Polish Academy of Sciences](#) edited by [Gaby Clark](#), reviewed by [Robert Egan](#)

Bromine and hydrogen play unexpected roles in the dissociation dynamics of triazole anions. The findings provide new insights into the behavior of transient negative ions. Photo taken thanks to the ActiveZone fitness club. Credit: Source IPC PAS, Grzegorz Krzyzewski

Imidazoles and triazoles are essential chemical compounds used in many medicines, including drugs used to defeat various pathogen-induced infections and cancer. Besides these applications, both imidazoles and triazoles are used not only in humans but also to protect crops against fungi.

However, despite their high effectiveness, they can easily end up in water or soil, leading to environmental pollution and uncontrolled development of fungi resistant to fungicides. Removing these chemicals from the environment is far from easy for the high stability of the compounds.

Therefore, novel ways to degrade imidazoles and triazoles are widely studied to improve and deeply understand the mechanisms that stand behind the bonds breaking in both compounds, especially in developing effective wastewater treatment. To control the structure of obtained [molecules](#) under the application of external stimuli, mechanistic insight for detailed description on a molecular level is needed.

A recent study [published](#) in the *Journal of the American Chemical Society* by an international research team, led by Dr. Dariusz Piekarski from the Institute of Physical Chemistry, Polish Academy of Sciences and Dr. Jaroslav Kočíšek from the Czech Academy of Sciences presents significant advancements for molecular chemistry, revealing the role of [hydrogen](#) and bromine in the dissociation dynamics of triazole anions. Researchers show in detail how to break these molecules using low-energy electrons.

When a compound like triazole captures one of these low-energy electrons, it forms a short-lived charged version of itself that finally breaks up. But not all triazoles undergo such a reaction in the same way. This process depends on the [molecular structure](#), especially the position of hydrogen atoms.

In the present study, researchers looked at two versions of a bromine-substituted triazole. Researchers employed dissociative electron attachment (DEA) to study the behavior of the specific site in two nearly identical molecules, like 3-bromo-1H-1,2,4-triazole and 3-bromo-4H-1,2,4-triazole (4HBrT) that differ only in the position of one hydrogen atom, under the exposition to low-energy electrons.

By combining the [empirical studies](#) with sophisticated theoretical calculations based on the potential energy surfaces, molecular dynamics, and analytic continuation methods, they tracked the atom's position change and the lifetimes of transient negatively charged molecules with remarkable precision.

Such combining of experiments with quantum chemistry shows that hydrogen position change has a direct influence on the molecular dynamics after an interaction with low-energy electrons, where even a single electron induces subtle structural differences, resulting in dramatically different molecular dynamics.

Hydrogen position controls the character of the resonant states. While the singly occupied molecular orbital SOMO of 1HBrT is highly symmetric with a short lifetime against both dissociation of bromine or loss of electron, the 4HBrT SOMO state is asymmetric, resulting in induced dance of the bromine atom around the rest of the molecule.

Abstract Credit: *Journal of the American Chemical Society* (2025). DOI: 10.1021/jacs.4c18446

Quantum chemical calculations show that bromine migrates more easily when the hydrogen is in the 4-position than an 80 times lighter hydrogen atom, forming a stable noncovalent complex around the triazole ring. The hydrogen position defines whether the bromine atom will move around a molecule or break away directly during a molecular breakup reaction.

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For 4HBrT, the dissociation of the bromine atom proceeds via a delayed mechanism, where the bromine forms temporarily weakly bonded species, stabilizing the transient negative ion and elongating its lifetime. This results in an intermediate metastable state before hydrogen bromide (HBr) is formed.

In contrast, the 1HBrT, a different position of the H-atom facilitates easy and direct cleavage of the C–Br bond, allowing bromine to dissociate without interaction with the remaining triazole ring structure.

The research findings provide new insights into the behavior of transient negative ions and could have far-reaching implications for pharmaceutical development and environmental chemistry. They found that the bromine atom not only makes it easier for the molecule to grab an electron, but also helps stabilize different forms of the molecule, depending on where the hydrogen is placed in the ring via different timescale-lived resonant states called transient negative ions.

"Like two keys that at first glance look the same but open completely different doors," explains Dr. Piekarski.

This "roaming" of bromine completely reverses the molecular breaking patterns, facilitating the release of hydrogen bromide HBr, whereas, in the 1H-form, the direct bromine dissociation dominates. This fundamental scientific achievement challenges conventional chemical knowledge in several ways, not only for the bromine orbiting around a molecule.

More surprisingly, [bromine](#) roaming happens in negative charge states prior to the electron auto-detachment process. Second, the study reveals that even a tiny shift in the position of the hydrogen atom can completely alter this reaction pathway. Third, it shows that Br⁻ ions can form weak, noncovalent bonds around the triazole ring, creating a much more stable complex that holds the electrons much longer than expected.

"The idea that we can control the movement of heavy atoms through something as simple as placing hydrogen in a given position is exciting and offers new possibilities for chemical design," remarks Dr. Piekarski.

Now, it is possible to steer halogenated molecular targets' breakups in desired directions just by positioning hydrogen atoms. These findings point out how even subtle structural differences can guide chemical reactions in unexpected directions. Their study opens new directions for controlled molecular manipulation in chemistry and [material science](#), demonstrating the value of low-energy electron studies in probing dynamic molecular behavior.

The demonstrated work points to a pathway for more effective breakdown of stable, pollution-prone compounds in the environment and an understanding of how drug-like molecules behave under certain conditions, which is crucial for drug design. Future studies will explore whether similar phenomena occur while induced with different radiation sources and in other halogenated compounds.

More information: Smith Pataraprasitpon et al, Hydrogen Controls the Heavy Atom Roaming in Transient Negative Ion, *Journal of the American Chemical Society* (2025). DOI: [10.1021/jacs.4c18446](https://doi.org/10.1021/jacs.4c18446)

Journal information: [Journal of the American Chemical Society](#)
Provided by [Polish Academy of Sciences](#)

JUNE 23, 2025

Synthetic 'killswitch' uncovers hidden world of cellular condensates

by [Justin Jackson](#), Phys.org edited by [Sadie Harley](#), reviewed by [Robert Egan](#)

Researchers at the Max Planck Institute for Molecular Genetics have developed a novel synthetic micropeptide termed the "killswitch" to selectively immobilize proteins within cellular condensates, unveiling crucial connections between condensate microenvironments and their biological functions.

Biomolecular condensates are specialized regions inside cells, existing without membranes, where critical biochemical reactions occur. Their importance in health and disease is well established, including roles in cancer progression and viral infection.

Methods to precisely probe and manipulate condensates in living cells remain limited. Existing strategies lack specificity, either dissolving condensates indiscriminately or requiring artificial protein overexpression, which obscures the natural behavior of native cellular proteins.

In the study, "Probing condensate microenvironments with a micropeptide killswitch," [published](#) in *Nature*, the authors engineered a short hydrophobic micropeptide capable of specifically targeting and immobilizing proteins within naturally occurring cellular condensates. By tagging this killswitch peptide to small antibody fragments, they directed it precisely to condensates labeled with fluorescent proteins.

The Max Planck team initially characterized this killswitch in human osteosarcoma cells and then expanded their analyses to a variety of endogenous condensates across different cell types.

Using antibody fragments to specifically recruit the killswitch into targeted condensates labeled with [green fluorescent protein](#) (GFP), they systematically manipulated condensates, such as nucleoli, nuclear speckles, and chromocentres, as well as pathological condensates, including those formed by cancer-driving fusion proteins and adenoviral proteins.

Employing human and mouse cell lines, the researchers tested the effects of the killswitch across these diverse condensate types.

Utilizing fluorescence recovery after photobleaching (FRAP), a microscopy-based method that measures how quickly proteins within condensates move and exchange, they observed a marked immobilization of targeted proteins. For example, nucleoli showed reduced dynamics and altered protein composition upon killswitch recruitment.

Further exploration using advanced mass spectrometry revealed specific proteins excluded from nucleoli following killswitch exposure, leading to functional consequences such as diminished ribosomal protein mobility and a separation from critical ribosomal RNA components.

Beyond fundamental cellular condensates, the team also tested disease-linked condensates. In [cancer cells](#) driven by fusion oncoproteins, misfit proteins formed through erroneous gene combinations.

The killswitch dramatically reduced condensate mobility and altered their internal composition. Notably, in a mouse model of acute myeloid leukemia driven by the fusion protein NUP98::KDM5A, the killswitch substantially impaired leukemic cell proliferation, hinting at the therapeutic potential of targeting condensate properties.

Versatility of the killswitch extended into viral pathology. Researchers targeted condensates formed by adenovirus protein 52K, critical for viral particle assembly. Here, the killswitch not only immobilized these viral condensates but also prevented necessary viral structural proteins from accumulating, and substantially reduced the virus by more than 90%.

Through their innovative killswitch micropeptide, the researchers have introduced a universally adaptable method for manipulating endogenous condensates.

With this approach in the toolkit, researchers will be able to significantly enhance our understanding of how [condensate](#) microenvironments influence cellular function and disease, and probe novel avenues for future therapeutic interventions in cancer and viral diseases.

Written for you by our author [Justin Jackson](#), edited by [Sadie Harley](#), and fact-checked and reviewed by [Robert Egan](#)—this article is the result of careful human work. We rely on readers like you to keep independent science journalism alive. If this reporting matters to

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More information: Yaotian Zhang et al, Probing condensate microenvironments with a micropeptide killswitch, *Nature* (2025). DOI: [10.1038/s41586-025-09141-5](https://doi.org/10.1038/s41586-025-09141-5)

A 'killswitch' peptide solidifies protein droplets in living cells, *Nature* (2025). DOI: [10.1038/d41586-025-01875-6](https://doi.org/10.1038/d41586-025-01875-6)

Journal information: [Nature](#)

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JUNE 23, 2025

Lipid nanoparticles that engineer CAR T cells in vivo could unlock access for millions of autoimmune patients

by [Justin Jackson](#), Phys.org edited by [Sadie Harley](#), reviewed by [Robert Egan](#)

B cell depletion in lymph nodes and CAR expression in peripheral blood of cynomolgus monkey. CD20 immunohistochemistry of lymph nodes from two cynomolgus monkeys eight Capstan Therapeutics scientists demonstrate that lipid nanoparticles can engineer CAR T cells within the body without laboratory cell manufacturing and ex vivo expansion. The method using targeted lipid nanoparticles (tLNPs) is designed to deliver messenger RNA specifically to CD8⁺ T cells.

CAR T therapy has revolutionized the treatment of B-cell cancers, with lasting remissions in lupus, myositis, and leukemia and other B-cell-driven [autoimmune disorders](#). The method requires the use of a patient's own T cells, reengineering those T cells in a lab, growing the population of the modified cells and placing them back in the patient.

More than 20 million U.S. patients living with autoimmune conditions remain without access to the treatment as it depends on costly personalized lab processes, available at only a few specialized centers.

Capstan's lipid-nanoparticle drug is formulated once, then administered to many patients without tailoring the genetic payload for each recipient, making it a universal option without the specialty center price tag or access obstacles.

In the study, "In vivo CAR T cell generation to treat cancer and autoimmune disease," [published](#) in *Science*, researchers designed a lipid-nanoparticle delivery system to convert CD8⁺ T cells inside the body into transient anti-B-cell CAR T cells.

Experiments spanned humanized mice, primary human immune cells, and 22 cynomolgus monkeys given three doses of the therapeutic nanoparticle L829 (0.1–2.0 mg/kg).

A second cohort of 15 monkeys tested a two-dose schedule, and four additional animals examined steroid–antihistamine premedication. Pharmacokinetics, flow cytometry, imaging, and histology tracked CAR expression, B-cell counts, cytokines, and organ distribution.

Bioluminescent and fluorescent reporters confirmed reduced off-target expression in the liver and enhanced accumulation in spleen and [lymphoid tissues](#) compared with benchmark lipids used in mRNA vaccines. CD8-L829-tLNPs preferentially modified CD8⁺ T cells over CD4⁺ T cells, monocytes, and B cells.

CAR expression was detectable within six hours, declining by 72 hours. CAR T cells engineered in vivo exhibited antigen-specific cytotoxicity, cytokine production, proliferation, and serial killing capacity. Transfected T cells demonstrated effective clearance of CD19⁺ [target cells](#) in vitro.

In humanized mice, a single intravenous dose of 10 or 30 µg CD8-L829-tLNP-CD19 induced near-complete B cell depletion within three hours, with measurable CAR expression on CD8⁺ T cells persisting at 24 hours.

Nalm6 leukemia-bearing mice receiving the 30 µg dose exhibited near-total tumor clearance in four of five animals within two days of the first dose and complete clearance by the third day after treatment with a second dose.

In cynomolgus monkeys, two or three infusions of CD8-L829-tLNPs encoding an anti-CD20 CAR at 0.1 to 2.0 mg/kg resulted in rapid and profound B cell depletion across blood, spleen, and lymph nodes. CAR expression was observed in up to 85% of CD8⁺ T cells and 95% of CD8⁺ NK cells, with minimal expression in CD4⁺ populations. B cell repopulation began by day 21 and was characterized by a predominantly naive phenotype.

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Mild and transient elevations in liver enzymes and pro-inflammatory cytokines, including interleukin-6 and interferon-gamma, were recorded at higher doses. One animal in the 1.5 mg/kg group was euthanized due to clinical features consistent with immune effector cell-associated hemophagocytic lymphohistiocytosis. A compact two-dose regimen replicated depletion efficacy while reducing cytokine release.

Targeted [lipid nanoparticles](#) enable in vivo generation of functional CAR T cells without requiring ex vivo cell manipulation or integrating viral vectors.

Researchers at Capstan Therapeutics demonstrated that lipid nanoparticle formulations bearing mRNA and conjugated to CD8-targeting antibodies can program T cells directly inside the body, offering a platform that bypasses conventional manufacturing, lymphodepletion, and the costly infrastructure required for existing CAR T therapies.

As lipid nanoparticle therapeutics are commercially scalable and already validated in mRNA vaccines, this technology may represent a foundational shift toward broader clinical use of engineered immunotherapy from within the patient's body.

Written for you by our author [Justin Jackson](#), edited by [Sadie Harley](#), and fact-checked and reviewed by [Robert Egan](#)—this article is the result of careful human work. We rely on readers like you to keep independent science journalism alive. If this reporting matters to you, please consider a [donation](#) (especially monthly). You'll get an **ad-free** account as a thank-you.

More information: Theresa L. Hunter et al, In vivo CAR T cell generation to treat cancer and autoimmune disease, *Science* (2025). DOI:

[10.1126/science.ads8473](https://doi.org/10.1126/science.ads8473). www.science.org/doi/10.1126/science.ads8473

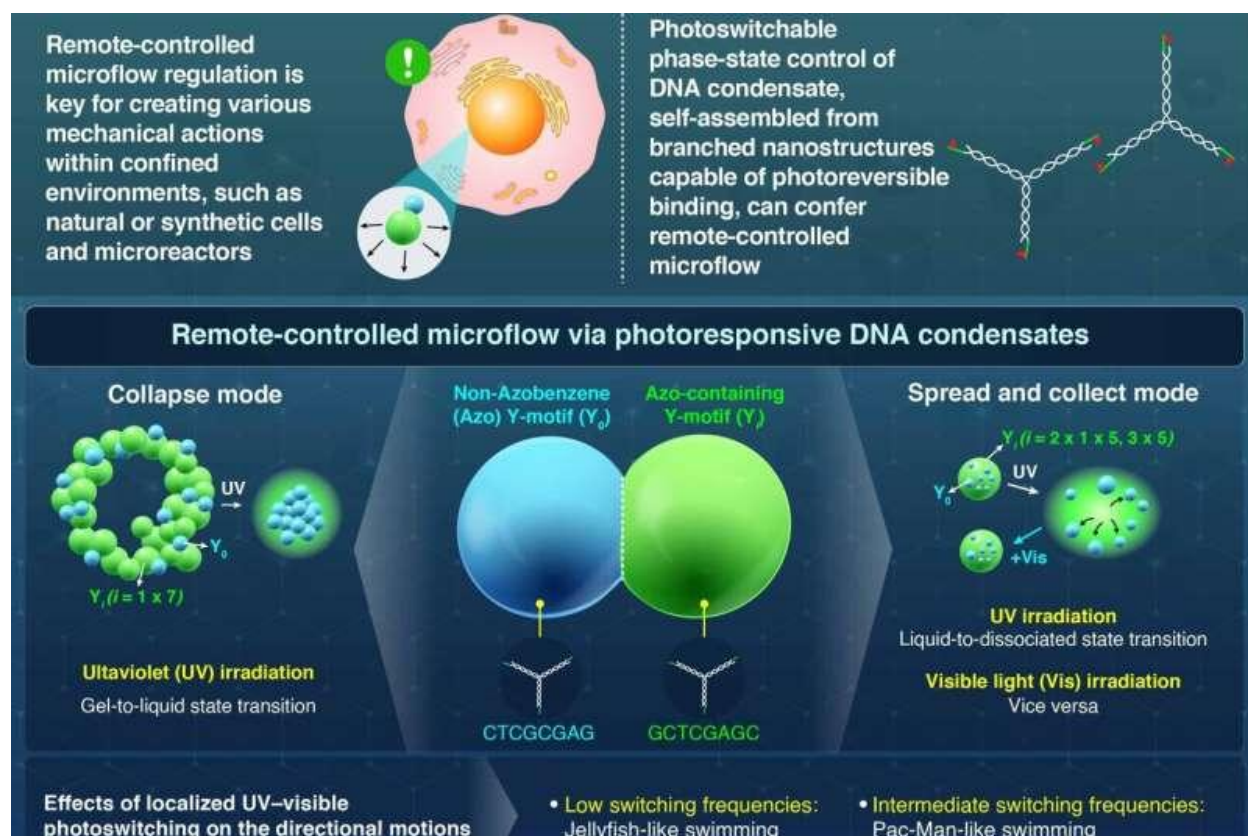
Journal information: [Science](#)

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JUNE 23, 2025

Photo-switchable DNA condensates enable remote-controlled microflow systems

by [Institute of Science Tokyo](#) edited by [Gaby Clark](#), reviewed by [Robert Egan](#)



In a recent study, scientists from Institute of Science Tokyo, Japan, have developed light-responsive DNA condensates that exhibit multi-modal mechanical actions. These novel micro-assemblies can be further developed for potential applications in fluid-based diagnostic chips and molecular computers. Credit: Institute of Science Tokyo

Remote-controlled microflow using light-controlled state transitions within DNA condensates has been reported by scientists from the Institute of Science Tokyo, Japan. By switching between ultraviolet light (UV) and visible light irradiation, the researchers demonstrated that the novel DNA motifs containing azobenzene can dissociate or reassemble. Furthermore, localized photo-switching within a DNA liquid condensate generated two distinct directional motions. This study can fuel the development of innovative fluid-based diagnostic chips and molecular computers.

Advancements in micro- and nano-scale fabrication technologies have given rise to diverse micrometer-sized entities such as microgels and liposomes, which are widely utilized in therapeutic formulations and microfluidic sensors. The precise control of the structure and function permits the adoption of micro-scale objects in various applications. However, the remote controllability of miniaturized fluidic objects has not yet been realized.

A recent study by scientists from the Institute of Science Tokyo (Science Tokyo), Japan, represents a significant step toward the development of remotely controllable microfluidic objects that are capable of performing mechanical actions. The research team comprised Professor Masahiro Takinoue and Specially Appointed Assistant Professor Hirotake Udono, both from the Department of Computer Science, along with Associate Professor Shin-ichiro M. Nomura from the Department of Robotics, Graduate School of Engineering, Tohoku University. Their research findings were published online in [Nature Communications](#) on May 14, 2025.

In their study, the researchers utilized photoresponsive DNA liquid condensates that contained azobenzene (Azo)—a photo-reactive compound. Three single-stranded DNA strands self-assembled via complementary base-pairing of nucleotides to form distinctive "Y"-shaped nanostructures (Y-motifs). Azobenzene was incorporated into the terminal overhangs of the Y-motif, or "sticky ends," to form photoresponsive DNA motifs.

"Previous studies have reported the photo-regulated state transitions of self-assembled DNA structures. However, no study has achieved any significant mechanical actions using them. Through our study, we have demonstrated remote-controlled microflow using photoresponsive DNA condensates," remarks Takinoue, highlighting the novelty of the present study.

By switching between [ultraviolet light](#) (UV) and visible light irradiation, the scientists demonstrated that the DNA motifs dissociate or reassemble reversibly. Interestingly, the light-induced changes in the motif binding state led to a reversible change in fluidity, from a gel to liquid or dissociated states, and vice versa.

To create microflows using the fabricated DNA motifs, a non-photoresponsive motif without azobenzene was crosslinked to a photoresponsive DNA structure. The sticky end of the non-photoresponsive motif contained an orthogonal DNA sequence.

"This cross-linking enabled mechanical actions by the photoresponsive DNA [condensate](#) on the non-photoresponsive DNA condensate," comments Takinoue.

Directional motions of DNA liquid condensates (composed of Y2x4) with localized UV–Vis photoswitching. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-59100-x During further experiments, the scientists discovered multiple modes in the photo-generated mechanical actions. Initially, a fast, diffusion-like outward spread of DNA condensates was detected when irradiated with UV light. Further, a UV-induced gel-to-liquid state transition called collapse mode was observed in condensates with a different DNA sequence.

Remarkably, by alternating between UV and [visible light](#), a 'spread and collect' mode signaling a reversible phase transition from a liquid-to-dissociated state, followed by reassembly into liquid DNA, was demonstrated by the researchers.

To show their application toward directional motion, an eagerly aspired robotic actuation, localized UV–visible photo-switching focusing on a fraction of the condensate was performed, resulting in two distinct directional motions of the DNA liquid condensates. "At lower switching frequencies, the DNA condensate can swim like a jellyfish, and at higher frequencies, the condensate can be pulled by its localized cycle flow, reminiscent of Pac-Man's motion," states Takinoue.

In summary, this study shines light on remote-controlled mechanical actions in DNA-based micro-assemblies. The potential applications of these novel DNA condensates include intelligent fluid-based diagnostic chips and fluid-type molecular computers.

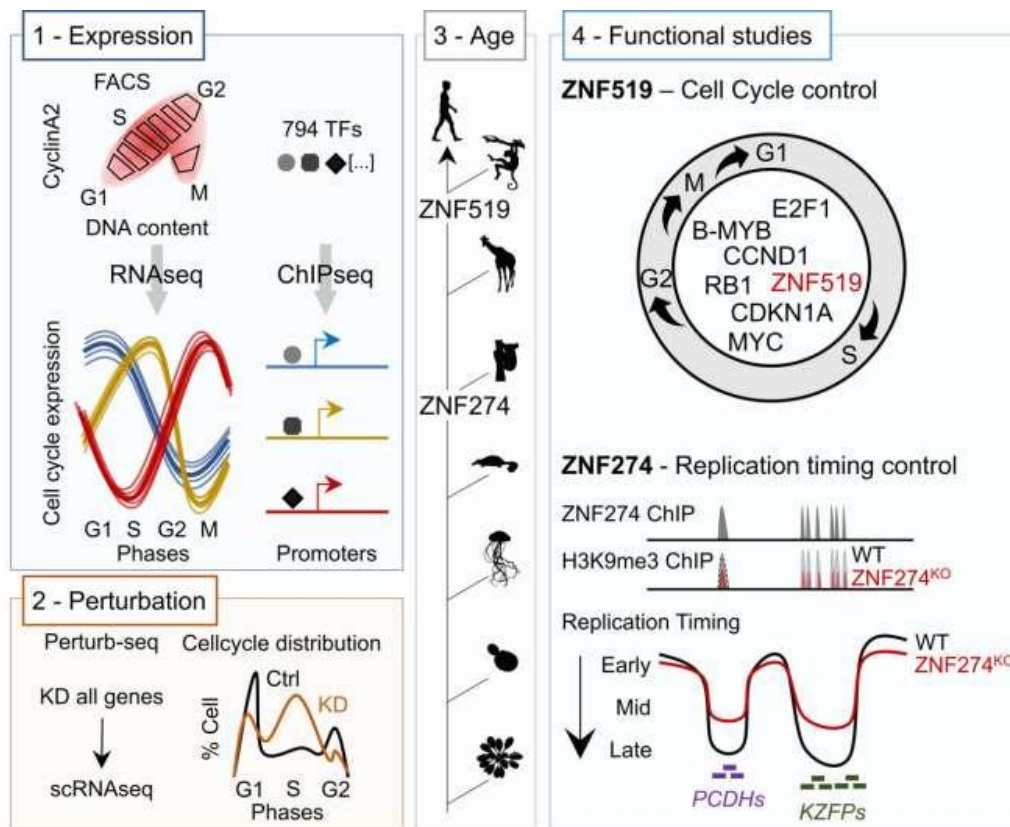
More information: Hirotake Udonon et al, Remote-controlled mechanical and directional motions of photoswitchable DNA condensates, *Nature Communications* (2025). DOI: [10.1038/s41467-025-59100-x](https://doi.org/10.1038/s41467-025-59100-x)

Journal information: [Nature Communications](#)
Provided by [Institute of Science Tokyo](#)

JUNE 23, 2025

New genes, old job: Recently evolved genes play key role in cell division, study finds

by [Ecole Polytechnique Federale de Lausanne](#) edited by [Gaby Clark](#), reviewed by [Robert Egan](#)



A graphical summary of the research. Credit: Pulver et al 2025.

Every day, our bodies perform around 330 billion cell divisions to keep us alive and functioning. These divisions rely on the cell cycle, which has been in place since the earliest bacteria. The principle is the same: double the cell's content, then split into two "daughter" cells.

However, in more complex organisms, the [cell cycle](#) has become increasingly sophisticated. This raises a question: What role do recently evolved genes play in regulating this fundamental process?

Two scientists with the group of Didier Trono at EPFL, Romain Forey and Cyril Pulver, set out to answer this question. Combining cell cycle biology with genomics, they investigated how gene activity changes across cell division. Working with their colleague, Alex Lederer, they created a detailed atlas of human cell cycle gene activity, which is now available to researchers and the public. The study itself is [published](#) in *Cell Genomics*.

The project was distinctively interdisciplinary, which is characteristic of research at EPFL. "Romain oversaw all of the wet lab experiments and brought in his cell cycle expertise, while I took care of the genomics analyses," says Cyril Pulver.

He adds, "However, we did not strictly adhere to those disciplinary boundaries, as key hypotheses, mathematical modeling and wet lab experiments were discussed and decided upon jointly. We are also indebted to Alex Lederer from the lab of Gioele La Manno, who performed a key analysis regarding the CRISPRi data, essentially positioning 1.9 million cells within the cell cycle according to their transcriptomes."

Starting with the atlas, the researchers focused on a special group of genes: those that produce [transcription factors](#)—proteins that control which genes are turned on or off. They found that some of these transcription factors, which help guide cells through the cell cycle and ensure everything happens at the right time, have emerged surprisingly recently.

Specifically, the study revealed that several recently evolved transcription factors regulate genes that are active during specific phases of the cell cycle. When some of these factors were knocked down, the cells got stuck at specific stages or lost their usual timing compared to the rest of the cell population, disrupting the orderly flow of division.

One standout was ZNF519, a gene found only in primates. Disabling it caused the cells to struggle with copying their DNA correctly—a critical step before division—and as a result, their growth slowed down. The team confirmed that ZNF519 directly binds to the DNA of key cell cycle [genes](#) and acts as a repressor.

Another protein, ZNF274, found in mammals but absent in older reptiles, fish etc., was found to have an additional impact: it regulates the moment at which specific chunks of the genome are duplicated prior to mitosis, a process linked to epigenome maintenance, 3D organization and nucleus organization.

"We contribute a comprehensive resource regarding human cell cycle gene expression and perturbations, which we hope will be of use to our colleagues worldwide," says Pulver.

The discovery shows that processes as ancient as [cell division](#) integrate new genetic players, some of which are specific to humans or our close relatives. This has implications for understanding diseases like cancer, where the cell cycle becomes dysregulated. It might also help explain why certain cancers or developmental disorders are more prevalent or behave differently in humans than other mammals.

More information: Cyril Pulver et al, Evolutionarily recent transcription factors partake in human cell cycle regulation, *Cell Genomics* (2025). DOI: [10.1016/j.xgen.2025.100923](https://doi.org/10.1016/j.xgen.2025.100923)

JUNE 23, 2025

Why regulations in plant gene editing are a must

by Lara Pacillo, [University of Adelaide](#) edited by [Lisa Lock](#), reviewed by [Andrew Zinin](#)



Credit: Unsplash/CC0 Public Domain

While some scientists argue that agricultural gene editing regulations are overly restrictive, a new paper from the University of Adelaide emphasizes the importance of clear regulations to ensure that new technologies are used safely and responsibly.

Published in *The Plant Journal*, the [Focused Review](#) was conducted by researchers Dr. Emily Buddle, Michail Ivanov and Professor Rachel Ankeny. It outlines how regulation plays a vital role in the innovation process by encouraging public involvement and building trust in emerging gene technologies.

"Regulatory decisions are not just about scientific facts or [economic benefits](#). They always involve value judgments, especially concerning safety, risk and societal benefits," Dr. Buddle explains.

"Plant scientists need to engage with diverse groups of people early and often throughout the innovation process to understand their concerns about new technologies. This engagement is a mutual learning process, not just a formality, as no single group has the expertise and capacity to shape regulation in isolation."

Dr. Buddle notes that while forms of gene-editing can make the same changes that could happen naturally in agriculture—a concept known as "scientific equivalency"—this does not translate to [public acceptance](#).

"What truly matters to the public is how the gene technology will be applied and what its perceived benefits are, rather than just whether it is gene-edited or genetically modified," she says.

"For example, our previous research has shown that people might be more accepting of gene editing that improves the crop's tolerance to drought rather than altering the nutritional qualities of the grain."

Gene editing is an [emerging technology](#) in agriculture and is increasingly being used to help crops better withstand environmental stressors such as drought and salinity. While no gene-edited plants are currently in commercial production in Australia, the development of new breeding technologies has reignited a long-standing global debate over how these technologies should be regulated.

Regulation refers to the laws, policies, licenses and guidelines that govern how people and organizations can use gene technology, where penalties apply if these rules are not followed. There is limited consistency around the world in how gene editing is regulated.

In Australia, [gene technology](#), including genetically modified and gene-edited crops, is regulated by the Office of the Gene Technology Regulator (OGTR). Under the "Gene Technology Act 2000" (Commonwealth), gene-edited crops were originally treated the same as genetically modified organisms.

However, amendments made in 2019 mean organisms modified using SDN-1 techniques—which involve making small, targeted changes to DNA without adding any foreign genetic material—are generally not regulated under the Act, as these changes are considered similar to those that could occur naturally or through traditional breeding.

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Ivanov says the review challenges some common criticisms in crop sciences.

"In our research experience, we often hear scientists working in agricultural genomics talk about regulation as problematic, emphasizing that regulation is a 'bottleneck' or a 'hurdle' that limits research and innovation in crop sciences," Ivanov says.

"However, we argue that calling regulation a 'bottleneck' depends on your perspective and what your goals are.

"We contend that regulation is actually an important part of the innovation process as it allows regulators and diverse publics to get involved in the research and assess whether a new technology is truly needed, desirable and beneficial outside of the lab or field.

"Instead of being a bottleneck, regulation can be seen as a filter as it helps remove elements of science and innovation that could cause problems or harms to society or the environment, making sure that new technologies align with societal expectations and values before they are widely used."

More information: Michail Ivanov et al, Regulation as key to fulfilling the promises of agricultural genomics: Going beyond bottlenecks in plant gene technology development, *The Plant Journal* (2025). [DOI: 10.1111/tpj.70277](https://doi.org/10.1111/tpj.70277)

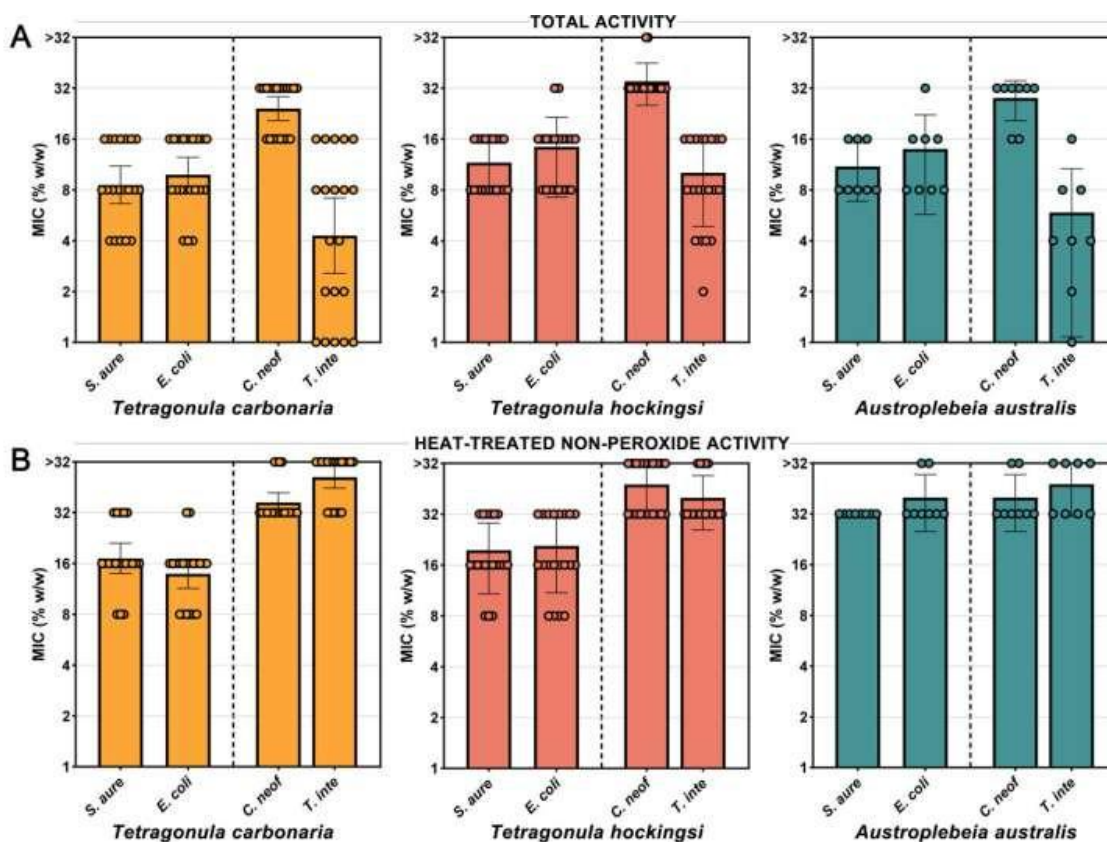
Journal information: [The Plant Journal](#)

Provided by [University of Adelaide](#)

JUNE 23, 2025

Native bee honey shows medical potential in fight against antibiotic resistance

by [University of Sydney](#) edited by [Lisa Lock](#), reviewed by [Andrew Zinin](#)



Total and heat-treated non-peroxide activity of stingless bee honey against bacteria and fungi. Credit: *Applied and Environmental Microbiology* (2025). DOI: 10.1128/aem.02523-24

Resistance to synthetic antibiotics poses a critical global health challenge. Various European honeybee and other natural products have been proposed as novel therapeutic agents to address this problem. However, little has been known about the potential of Australian native bee honey as an antimicrobial agent.

A study led by Dr. Kenya Fernandes from the University of Sydney has now demonstrated the remarkable antimicrobial properties of [honey](#) produced by three species of native Australian stingless bees: *Tetrasonula carbonaria*, *Tetrasonula hockingsi*, and *Austroplebeia australis*.

Commonly referred to as "sugarbag bees," the honey from these species has historically served as a food source. It is also a traditional remedy for ailments like itchy skin and sores among Indigenous communities in Australia.

The new research reveals stingless bee honey possesses antimicrobial properties that remain effective even after [heat treatment](#) and long-term storage. These distinctive features set it apart from honey from honeybees, highlighting its potential as a sustainable, natural agent for combating drug-resistant infections. The study has been [published](#) in *Applied and Environmental Microbiology*.

Dr. Fernandes said, "Given the growing medical challenge of antimicrobial resistance, our findings suggest stingless bee honey could complement, or provide a valuable alternative to, synthetic antibiotics."

Unlike honey from the European honeybee (*Apis mellifera*), which often relies on [hydrogen peroxide](#) for its antimicrobial effects, the honey from Australian stingless bees exhibits high levels of both hydrogen peroxide and non-peroxide activity—making it robust and versatile as a potential therapeutic agent.

The research found when hydrogen peroxide was removed the honey displayed antimicrobial activity, suggesting this is intrinsic to the honey itself.

Dr. Fernandes said, "Manuka honey from honeybees displays strong non-peroxide antimicrobial activity, which is one reason why its production has been a commercial success. However, that is largely reliant on the source of its nectar from specific myrtle plants (*Leptospermum*).

"In contrast, the persistent antimicrobial activity of heat-treated, non-peroxide honey from stingless Australian bees across diverse locations and nectar sources suggests there is something special about these bees, rather than just nectar, that plays a critical role here."

Co-author Professor Dee Carter said, "We discovered the [antimicrobial activity](#) is consistent across all sugarbag samples tested, unlike honeybee honey, which can vary significantly based on seasonal changes and floral sources."

The researchers hope this consistency could enhance the potential for commercial medical applications.

However, challenges remain concerning scalability. Each stingless beehive produces about half a liter of honey a year, presenting a challenge for large-scale production.

Co-author Dr. Ros Gloag said, "While the yield is small, these hives require less maintenance than traditional beehives, allowing beekeepers to manage larger numbers. With proper incentives, such as commercial value for the honey, it's feasible to cultivate more hives, providing a pathway for commercial scalability."

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Encouragingly, native stingless bee honey last year gained approval from Food Standards Australia New Zealand, paving the way for national and international commercialization. This regulatory support holds promise for the establishment of a niche market for high-value, small-quantity products.

The antimicrobial properties of stingless bee honey have garnered attention not only for their effectiveness but also for their potential stability over time. Furthermore, earlier studies have highlighted that microbes generally do not develop resistance to honey, unlike conventional antibiotics that often operate on a singular mechanism. This offers a compelling argument for incorporating stingless bee honey into therapeutic frameworks, the researchers say.

The research team aims to explore non-peroxide activity further to understand its sources and implications.

Dr. Fernandes said, "While we have yet to test the honeys against drug-resistant bacteria specifically, the presence of multiple antimicrobial factors significantly reduces the likelihood of resistance developing."

More information: Kenya E. Fernandes et al, Strong antimicrobial activity and unique physicochemical characteristics in honey from Australian stingless bees *Tetragonula carbonaria*, *Tetragonula hockingsi*, and *Austroplebeia australis*, *Applied and Environmental Microbiology* (2025). DOI: [10.1128/aem.02523-24](https://doi.org/10.1128/aem.02523-24)

Journal information: [Applied and Environmental Microbiology](#)
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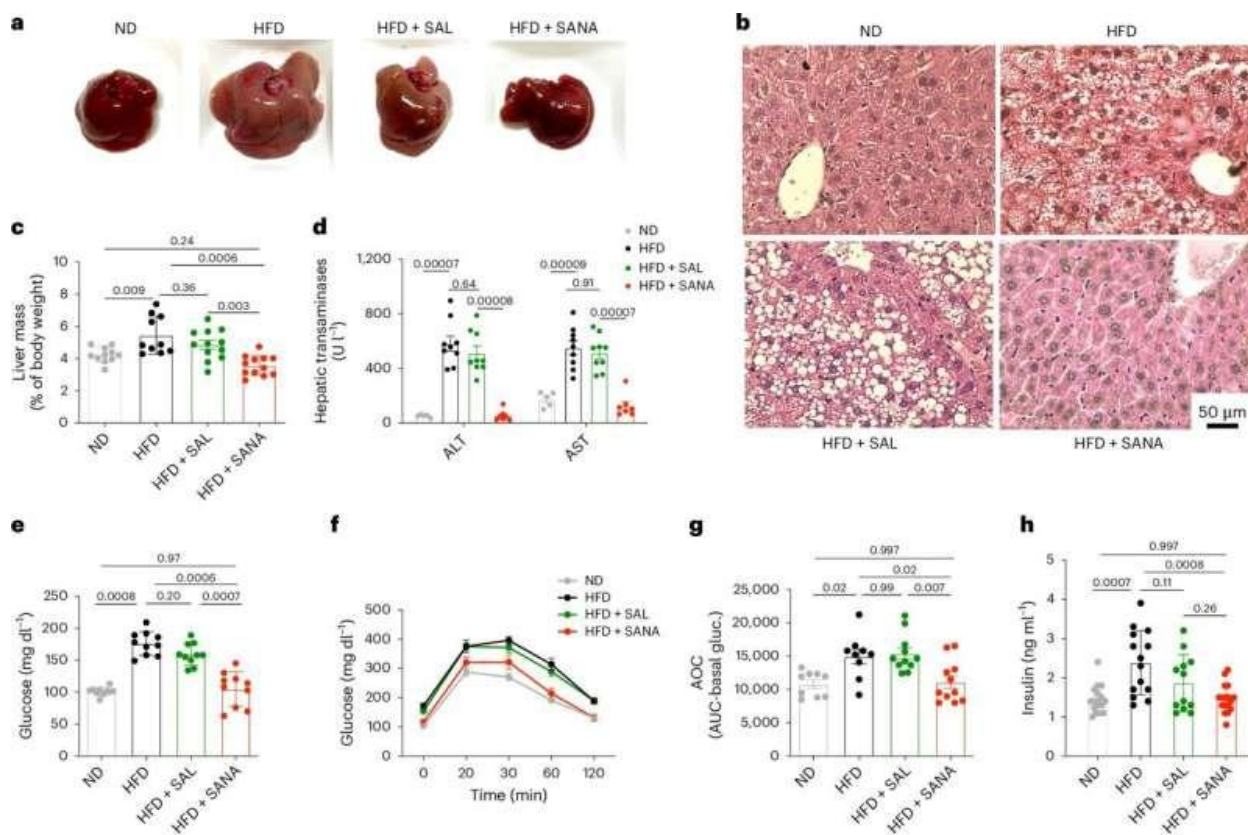
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JUNE 23, 2025

Experimental drug holds promise for controlling weight and blood sugar

by Karina Toledo, [FAPESP](#) edited by [Stephanie Baum](#), reviewed by [Robert Egan](#)



SANA protects against glucose intolerance and liver steatosis in response to DIO.

Credit: *Nature Metabolism* (2025). DOI: 10.1038/s42255-025-01311-z

An article [published](#) in the journal *Nature Metabolism* presents an experimental drug that stimulates adipose tissue cells to produce heat through a process known as thermogenesis, thereby promoting weight loss.

In animal tests, the compound prevented [fat accumulation](#) in response to a [high-fat diet](#), treated existing obesity, and reversed associated metabolic disorders, including insulin resistance. Preliminary results from clinical research indicate that the substance is safe and may have beneficial metabolic effects on humans.

"We observed [weight loss](#) and improved [blood sugar levels](#) in obese volunteers who participated in the phase 1 clinical trial. But this result isn't conclusive because it was a

small group, and the objective was to assess whether the compound is safe and well tolerated. We intend to start phase 2 of the study later this year, which is designed to test its effectiveness in treating obesity," says Carlos Escande, a researcher at the Pasteur Institute in Montevideo, Uruguay, and coordinator of the study.

The [experimental drug](#), currently called SANA (short for "salicylate-based nitroalkene"), is a derivative of salicylate, a [chemical compound](#) with analgesic and anti-inflammatory properties found naturally in plants and used to make drugs such as aspirin (acetylsalicylic acid). According to Escande, his group initially sought to develop an anti-inflammatory drug. To this end, they tested several chemical modifications to the salicylate molecule.

"We wanted the precursor we used to be as safe as possible. Salicylate is the drug that's been known the longest, and many people consume its derivatives daily. However, we observed that instead of protecting against inflammation, the molecule we synthesized protects against diet-induced obesity," says the researcher.

Two different models were used to test this effect in animals. In the first model, SANA was administered to mice alongside a high-fat diet, which prevented any weight gain. Meanwhile, the animals in the control group gained between 40% and 50% of their [body weight](#) over eight weeks.

In the second model, treatment began after the animals were obese. After three weeks, the mice had lost 20% of their body mass. There was also a reduction in blood sugar, improved insulin sensitivity, and a decrease in fat accumulated in the liver (a condition known as hepatic steatosis for which there is still no effective pharmacological treatment).

First in class

The next step was to investigate the mechanism of action of the substance. Nine Brazilian researchers collaborated on this task: Marcelo Mori, Pedro Vieira and Larissa Menezes dos Reis from the State University of Campinas (UNICAMP); William Festuccia and Luiz Osório Leiria from the University of São Paulo (USP); and Juliana Camacho-Pereira, Marina Santo Chichierchio, Gabriele Barbosa, and Leonardo de Souza from the Federal University of Rio de Janeiro (UFRJ).

The experiments showed that SANA specifically targets adipose tissue, activating thermogenesis through an unconventional mechanism. It can therefore be considered the first in a new class of anti-obesity drugs. It does not affect the central nervous or digestive systems or appetite.

As the authors explain, thermogenesis is typically mediated by a protein called UCP1, which is found within mitochondria (the organelles that generate energy for cells). UCP1 is activated in certain situations, such as exposure to cold. It then interferes with the synthesis of ATP (adenosine triphosphate), the cellular fuel. This causes the energy generated by cellular respiration to dissipate as heat. However, this is not the case with SANA.

The new drug causes adipocytes to use creatine, a compound formed by three [amino acids](#) (arginine, glycine, and methionine), as an energy source to produce heat without involving the UCP1 protein.

"We conducted tests with UCP1-deficient mice [genetically modified to not express the protein] and proved that SANA activates thermogenesis in these animals, even in the absence of UCP1 and under thermoneutral conditions, that is, without exposure to cold," says William Festuccia, a professor at the Biomedical Sciences Institute at USP.

According to the researcher, the observed impact on body temperature is small and does not pose a significant health risk.

"Older thermogenic agents, such as dinitrophenol, have an effect on the mitochondria of the entire body, causing a large increase in temperature and overloading the cardiovascular system, which needs to increase blood pressure for blood to reach the periphery and dissipate heat. But in the case of SANA, there's only action on the mitochondria of adipose tissue," he explains.

In experiments coordinated by Marcelo Mori at the Institute of Biology at UNICAMP, it was confirmed that SANA acts on enzymes involved in the so-called "creatine futile cycle," a thermogenic mechanism in which the amino acid compound is repeatedly converted into phosphocreatine and back into creatine, consuming ATP and releasing energy as heat.

"The fact that it's a small molecule and acts through a totally different mechanism allows SANA to be combined with other substances already used in the treatment of obesity, such as GLP-1 analogs [semaglutide and similar]," says Mori. "When we reduce food intake, our body tends to slow down its metabolism. To avoid this plateau effect, it'd be interesting to combine a molecule that inhibits appetite with another that promotes caloric expenditure."

Mori adds that although GLP-1 analogs are effective in combating obesity and controlling blood sugar, they also tend to promote lean mass loss, which is particularly problematic for the elderly. "That's why it's important to have alternatives," he concludes.

More information: Karina Cal et al, A nitroalkene derivative of salicylate, SANA, induces creatine-dependent thermogenesis and promotes weight loss, *Nature Metabolism* (2025). DOI: [10.1038/s42255-025-01311-z](https://doi.org/10.1038/s42255-025-01311-z)

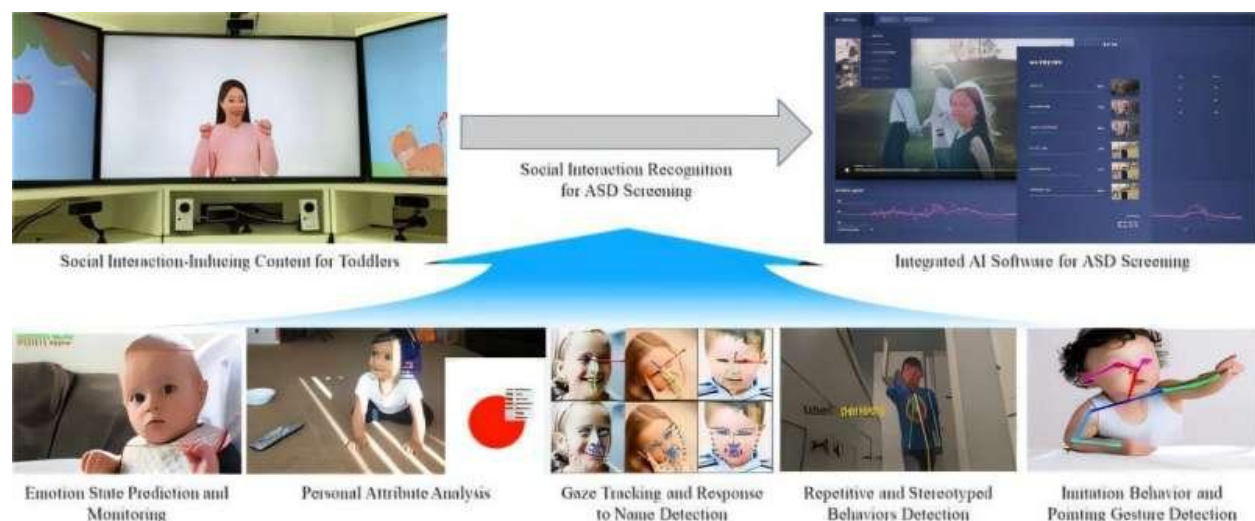
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AI technology for early screening of autism spectrum disorder developed

by [National Research Council of Science and Technology](#) edited by [Gaby Clark](#), reviewed by [Robert Egan](#)



Credit: Electronics and Telecommunications Research Institute (ETRI)
ETRI researchers have developed an artificial intelligence (AI) technique for the early screening of autism spectrum disorder (ASD). The technology is designed to detect early signs of ASD in children more quickly, which could expand opportunities for early screening and intervention and greatly improve accessibility.

Electronics and Telecommunications Research Institute (ETRI) announced that it has developed a "social interaction recognition AI" technology that can screen for [autism spectrum disorder](#) by analyzing "social interaction-inducing content" for infants and toddlers and video footage collected within six minutes of viewing it.

Autism spectrum disorder can be detected by observing certain behaviors and development, such as lack of social communication skills and restricted, repetitive behaviors. Early screening and intervention is critical for ASD, as early detection and appropriate medical intervention can have a positive impact on developmental outcomes.

However, due to a lack of experts, limited [social awareness](#), and constraints on time and resources, it is reported that it takes two to six years from symptom detection to actual diagnosis. The key symptoms of ASD can appear as early as 12 to 24 months of age, and in some cases even earlier, emphasizing the importance of [early screening](#) and intervention.

ETRI researchers collaborated with Prof. Yoo Hee-Jung's team from the Department of Psychiatry at Seoul National University Bundang Hospital to analyze the sensitivity of the screening index for ASD, based on data from 3,531 cases of infants and toddlers aged 42 months or younger. Based on this analysis, the researchers developed a scenario for observing infants and toddlers in which AI technology can be applied.

Based on this scenario, they developed the world's first "social interaction-inducing content" that can induce and observe various social responses, such as showing an interesting object, responding to a name, imitating behavior, pointing gesture, eye contact, etc.

Credit: Electronics and Telecommunications Research Institute (ETRI)

In addition, they developed a "Social Interaction Recognition AI" technology that captures the interaction processes of infants and toddlers watching the content with cameras and performs analysis of personal attributes, prediction and monitoring of emotion state, gaze tracking and response to name detection, detection of pointing gestures, detection of imitative and stereotypical behaviors, and etc.

The researchers established a living lab for screening of [autism](#) spectrum disorder at the Korea Institute of Robotics and Technology Convergence (KIRO) Seoul Center in 2020 and have been conducting observational tests and [data collection](#) on infants and toddlers for the past five years, thus advancing the technology of the field.

This technology is the world's first multidisciplinary, convergence-based [artificial intelligence](#) (AI) technology for the screening of autism spectrum disorder, overcoming the limitations of existing screening tools and presenting a new solution that enables more objective and quantitative evaluations.

It lowers the barrier to [mental health services](#), making it easier for preschools, childcare centers, developmental centers, and even homes to screen children as they interact with content.

It is expected to be used as a practical way to address the issue of early [screening](#) of infants and children by improving social awareness of autism spectrum disorders and activating preventive testing and early intervention.

Dr. Yoo Jang-Hee, Principal Researcher of the Social Robotics Research Section, said "We hope that this will help shorten the time between symptom detection and diagnosis, along with changing societal perceptions of autism. In addition, it is important for our research to solve hard problems, but we also hope that it will also contribute more to solving important problems like autism."

Provided by [National Research Council of Science and Technology](#)