

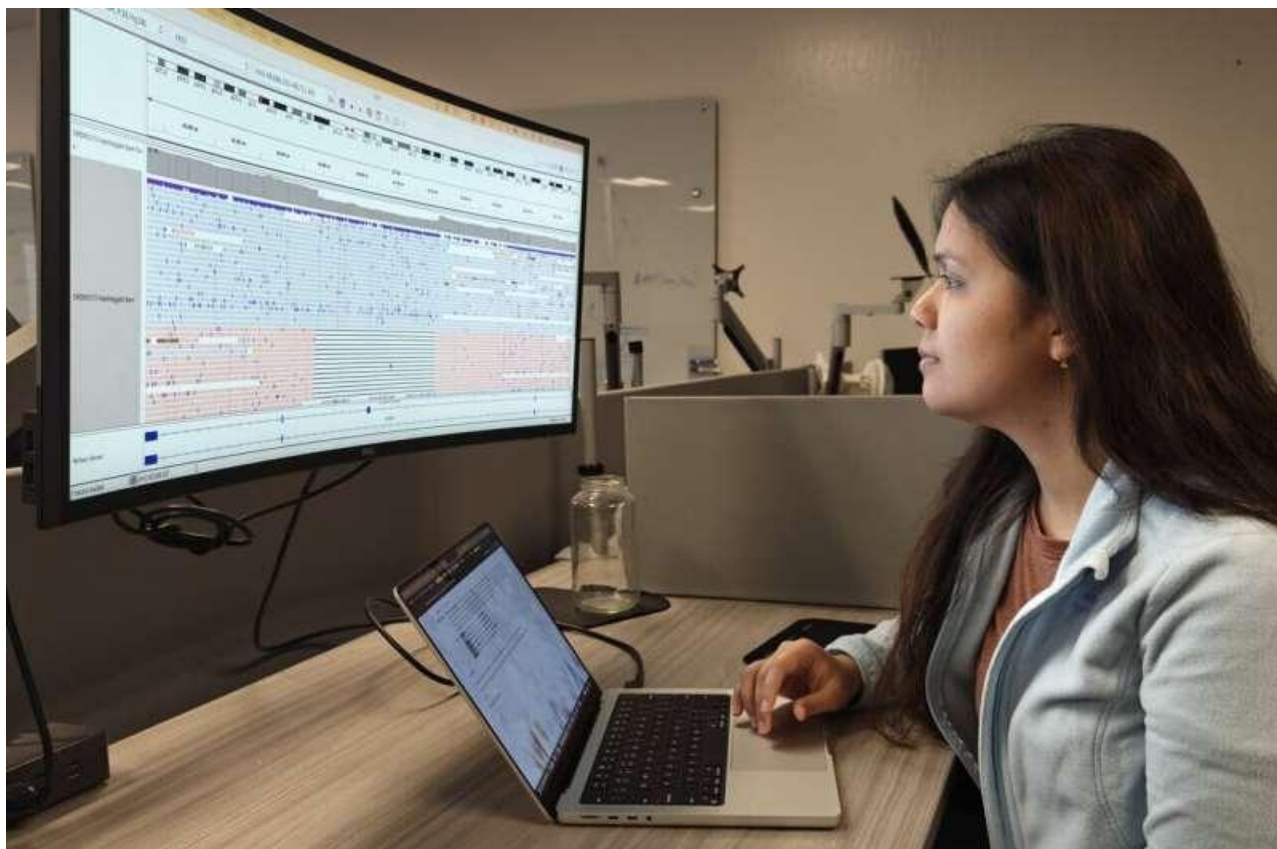
GENOMICS BIOTECH VOL 5



JANUARY 24, 2025

Long read sequencing reveals more genetic information while cutting time and cost of rare disease diagnoses

by [University of California - Santa Cruz](#)



Ph.D. student Shloka Negi analyzes long-read sequencing data in the UC Santa Cruz Computational Genomics lab. Credit: Shloka Negi, University of California - Santa Cruz

One in every 10 people worldwide is impacted by a rare genetic disease but about 50% of them remain undiagnosed despite rapid increases in genetic technology and testing. Even when a person does have access to testing, the process of getting a diagnosis can take about five years or more, which is sometimes too late for patients, who are often children, to start the right treatment.

This is partly because current clinical testing uses a method called short-read sequencing, which cannot access information in certain regions of the genome and so may miss crucial evidence to help make a diagnosis.

But UC Santa Cruz researchers are pushing forward research on a cutting-edge alternative method, called long-read sequencing, which can provide a more comprehensive dataset for finding variation, eliminate the need for multiple specialized tests, and streamline the diagnosis of rare diseases.

A new study shows that long-read sequencing has the potential to improve the rate of diagnosis while reducing the time to diagnosis from years to days—in a single test and at a much lower cost.

The study was [published](#) in *The American Journal of Human Genetics* and led by core members of the UCSC Genomics Institute Professor of Biomolecular Engineering (BME)

Benedict Paten and Associate Professor of BME Karen Miga, as well as former UCSC postdoctoral scholar Jean Monlong.

"Rare diseases are something that people have been struggling to diagnose for so many years, and if we have a sequencing technology which streamlines diagnostic testing, I think that will be a huge contribution—and that is what we tested as part of this paper," said Shloka Negi, a UC Santa Cruz BME Ph.D. student who is the paper's first author.

"Today, the diagnostic yield of genetic sequencing is frustratingly low," Paten said. "One likely cause is the incomplete sequencing methods used in clinical practice. In this work, we test the hypothesis that new, more comprehensive long-read sequencing can generate additional information useful for genetic diagnosis.

"We were excited to discover numerous additional potentially interesting genetic variants and epigenetic signals in our cohort. While it is still early days, there is great promise in this information, and it will take time for the community to interpret and fully understand much of this new information."

Finding rare disease

This study focused on rare monogenic diseases, which are those caused by a disruption to a single gene.

Scientists diagnose genetic diseases by searching through their genetic material to find variants—differences in a gene that may prevent it from functioning properly. The typical approach for finding these variants uses a technique called short-read sequencing, which reads the genetic base pairs—combinations of adenine (A), cytosine (C), guanine (G), and thymine (T)—in sequences of about 150–250 at a time.

The limitation of short-read sequencing, however, is that it can miss crucial information in certain regions of the genome, like patterns of base pairs that are much longer than just 250 base pairs. It also can't perform "phasing," the process of determining which variants are inherited from the mother and which are from the father.

This can help clinicians discover from whom variants are inherited; for example, if two variants are inherited from the same parent, one from each parent, or not inherited at all. This can be a very useful piece of information for genetic diagnoses, especially when parental data is not available.

In contrast, long-read sequencing can read lengthy stretches of DNA at once, eliminating gaps that may lead scientists and clinicians to miss important information about gene variation. Long-read sequencing also provides direct phasing data as well as information about methylation, a chemical process in DNA that causes genes to be "turned on or off," and can contribute to disease.

"Long-read sequencing is going to be a lot better in certain cases, and we are taking steps to prove that," Negi said.

Leading in methods

UC Santa Cruz Genomics Institute researchers have a rich history of innovation and expertise in long-read sequencing and are actively developing methods to optimize sequencing and analysis for a wide range of health research applications. Many of the techniques researchers developed to achieve feats, such as the [first truly complete "telomere-to-telomere" reference genome](#), are now being used to improve patient outcomes.

"Reinforcing earlier findings, we found that the benefits of using long-read sequencing were increased substantially by using a complete, so-called 'telomere-to-telomere' reference genome in place of the existing incomplete but widely used genomic reference," Miga said.

"We anticipate that pangenomes—references that represent diverse human variation—will extract even more benefit from new long-read sequencing technologies."

Paten and Miga's labs partnered with clinicians to work on the cases of 42 patients with rare diseases—some of whom received a diagnosis via short-read methods or other specialized testing, and some of whom were still undiagnosed. In some cases, the researchers had access to parental genetic information, but in others, they did not.

Long-read sequencing of the patients was led by the Miga Lab using nanopore sequencing, a method for long-read sequencing [pioneered at UCSC](#), to achieve highly accurate, end-to-end reads of the patients' genomes for about \$1,000 per sample.

The genomic data was analyzed using computational methods developed in Paten's lab to find small and large variants, phasing data, and methylation data, all using one pipeline called the [Napu pipeline](#). The analysis process takes around a day or less, depending on the computer processing speed, and costs \$100.

Solving cases

After sequencing and analyzing the patient data, the researchers found that long-reads provided a more exhaustive dataset as compared to what can be derived with short-read sequencing.

Long-read sequencing delivered conclusive diagnosis for 11 of the 42 patients in the cohort, providing everything that was known from the short-read data as well as additional information, including additional rare candidate variants, long-range phasing, and methylation—all in a single, cost-efficient, and rapid protocol.

The 11 diagnosed cases included four of congenital adrenal hypoplasia (a rare condition where the adrenal glands are enlarged and fail to function properly). The gene responsible for this disease is in a particularly challenging region of the genome—it can't be characterized with short read [sequencing technology](#), and the current clinical test is cumbersome and incomplete.

"To solve these cases, we developed a new pangenomic tool that integrates new high-quality assemblies like the 'telomere-to-telomere' reference genome," said Monlong, who began this project as a postdoctoral scholar in Paten's lab and continued in his current position at INSERM in France.

"We were excited to see that we could find and phase the pathogenic variants of all four patients suffering from this disease in our cohort. In the future, it might offer a rapid and comprehensive clinical test. We know many rare diseases involve regions of the human genome that have been historically difficult to study, so our results encourage us to extend our approach to more of those diseases that have been at a standstill for a long time."

In addition, two cases involved disorders of sex development, while one rare case of Leydig cell hypoplasia affected male sexual development due to underdeveloped Leydig cells in the testes. Additionally, four cases of neurodevelopmental disorders, each representing long and challenging diagnostic odysseys, were finally resolved.

"Long read sequencing is likely the next best test for unsolved cases with either compelling variants in a single gene or a clear phenotype," Negi said. "It can serve as a single diagnostic test, reducing the need for multiple clinical visits and transforming a years-long diagnostic journey into a matter of hours."

On average, each patient had 280 genes (including some Mendelian disease genes, which are linked to inherited disorders caused by [single-gene](#) mutations) with significant protein-coding regions uniquely covered by long reads and undetected by short reads.

"There's so much more of the genome that the long reads can unlock," Negi said. "But, it will take some time until we can fully interpret this new information revealed by long reads. This data has been absent from our clinical databases, which were built using short-read analysis and mapping to the standard reference."

"We showed that long reads are uncovering about 5.8% more of the telomere-to-telomere genome that short reads simply couldn't access."

Other UC Santa Cruz researchers involved in this research include Brandy McNulty, Ivo Violich, Joshua Gardner, Todd Hillaker, and Sara O'Rourke.

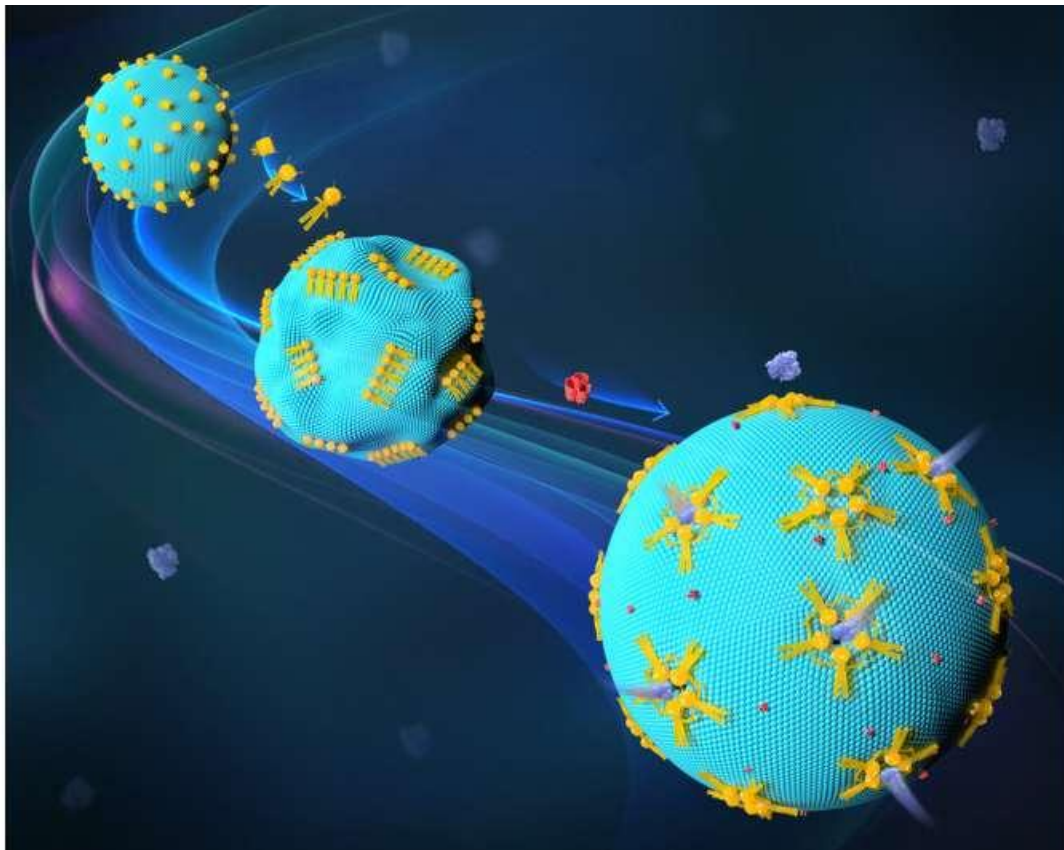
More information: Advancing long-read nanopore genome assembly and accurate variant calling for rare disease detection, *The American Journal of Human Genetics* (2025). DOI: [10.1016/j.ajhg.2025.01.002](https://doi.org/10.1016/j.ajhg.2025.01.002). [www.cell.com/ajhg/fulltext/S0002-9297\(25\)00002-3](https://www.cell.com/ajhg/fulltext/S0002-9297(25)00002-3)

Journal information: [American Journal of Human Genetics](#)

JANUARY 13, 2025

DNA nanorobots that can alter artificial cells offer a new tool for synthetic biology

[University of Stuttgart](#)



Reconfigurable DNA nanorobots that are working on the surface of synthetic cells. Credit: 2nd Physics Institute, University of Stuttgart

The shape and morphology of a cell play a key role in the biological function. This corresponds to the principle of "form follows function," which is common in modern fields of design and architecture. The transfer of this principle to artificial cells is a challenge in synthetic biology. Advances in DNA nanotechnology now offer promising solutions. They allow the creation of novel transport channels that are large enough to facilitate the passage of therapeutic proteins across cell membranes.

In this emerging field, Prof. Laura Na Liu, Director of the 2nd Physics Institute at the University of Stuttgart and Fellow at the Max Planck Institute for Solid State Research (MPI-FKF), has developed an innovative tool for controlling the shape and permeability of lipid membranes in synthetic cells. These membranes are made up of [lipid bilayers](#) that enclose an aqueous compartment and serve as simplified models of biological membranes. They are useful for studying membrane dynamics, protein interactions, and lipid behavior.

The work is [published](#) in *Nature Materials*.

A milestone in the application of DNA nanotechnology

This new tool may pave the way for the creation of functional synthetic cells. The work of Laura Na Liu aims to significantly influence the research and development of new therapies. Liu and her team have succeeded in using signal-dependent DNA nanorobots to enable programmable interactions with synthetic cells.

"This work is a milestone in the application of DNA nanotechnology to regulate cell behavior," Liu says.

The team works with giant unilamellar vesicles (GUVs), which are simple, cell-sized structures that mimic living cells. Using DNA nanorobots, the researchers were able to influence the shape and functionality of these synthetic cells. GUV deformations induced by the conformation change from the s-DRs to e-DRs after adding unlocking DNA strands. b, Control experiment by adding randomly-sequenced DNA strands. Credit: *Nature Materials* (2025). DOI: 10.1038/s41563-024-02075-9

New transport channels for proteins and enzymes

DNA nanotechnology is one of Laura Na Liu's main research areas. She is an expert in DNA origami structures—DNA strands that are folded by means of specifically designed shorter DNA sequences, so-called staples. The team of Liu used DNA origami structures as reconfigurable nanorobots that can reversibly change their shape and thereby influence their immediate environment in the micrometer range.

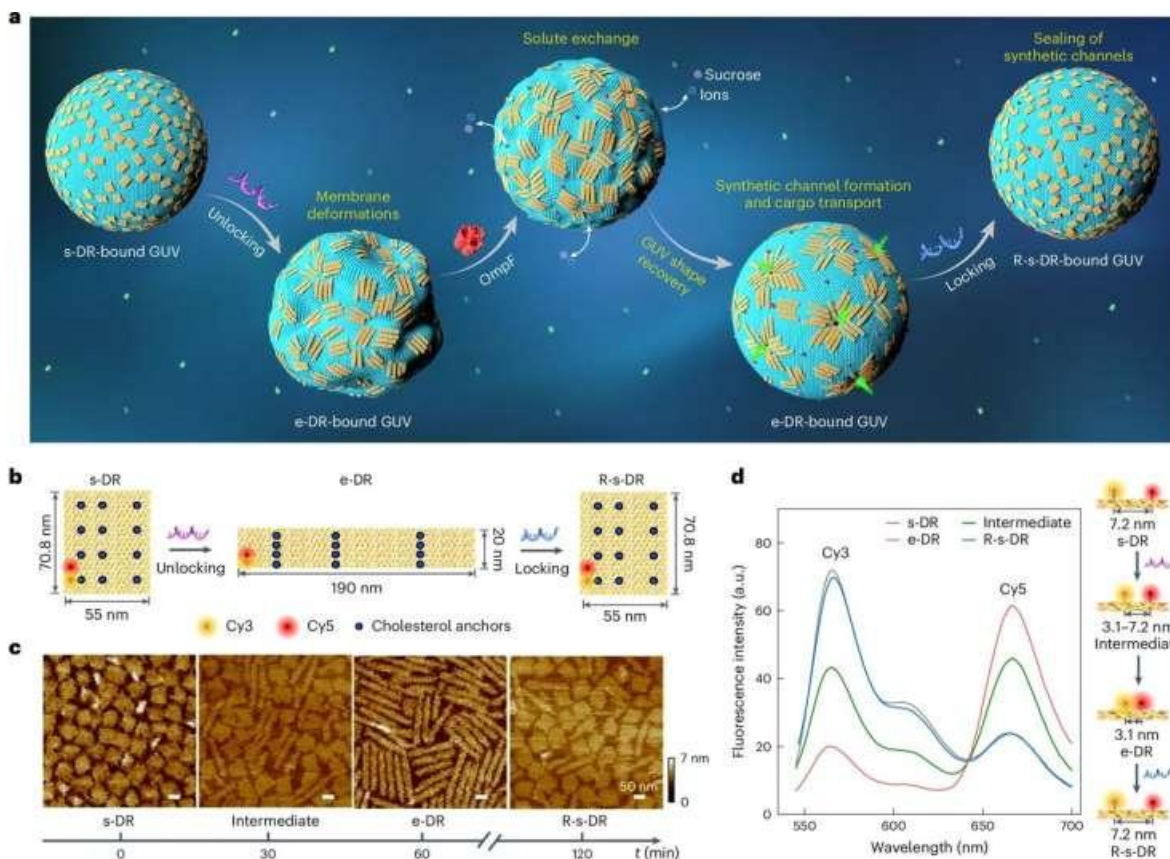
The researchers found that the transformation of these DNA nanorobots can be coupled with the deformation of the GUVs and the formation of synthetic channels in the model GUV membranes. These channels allowed large molecules to pass through the membrane and can be resealed if necessary.

Fully artificial DNA structures for biological environments

"This means that we can use DNA nanorobots to design the shape and configuration of GUVs to enable the formation of transport channels in the membrane," says Prof. Stephan Nussberger, who is a co-author of this work.

"It is extremely exciting that the functional mechanism of the DNA nanorobots on GUVs has no direct biological equivalent in living cells."

The new work raises new questions: Could synthetic platforms—such as DNA nanorobots—be designed with less complexity than their biological counterparts, which would nevertheless function in a biological environment?



Reconfigurable DNA rafts working on lipid membranes. Credit: *Nature Materials*, DOI: 10.1038/s41563-024-02075-9

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Understanding disease mechanisms and improving therapies

The new study is an important step in this direction. The system of cross-membrane channels, created by DNA nanorobots, allows efficient passage of certain molecules and substances into the cells. Most importantly, these channels are large and can be programmed to close when needed.

When applied to living cells, this system can facilitate the transportation of therapeutic proteins or enzymes to their targets in the cell. It thus offers new possibilities for the administration of drugs and other therapeutic interventions.

"Our approach opens up new possibilities to mimic the behavior of living cells. This progress could be crucial for future therapeutic strategies," says Prof. Hao Yan, one of the co-authors of this work.

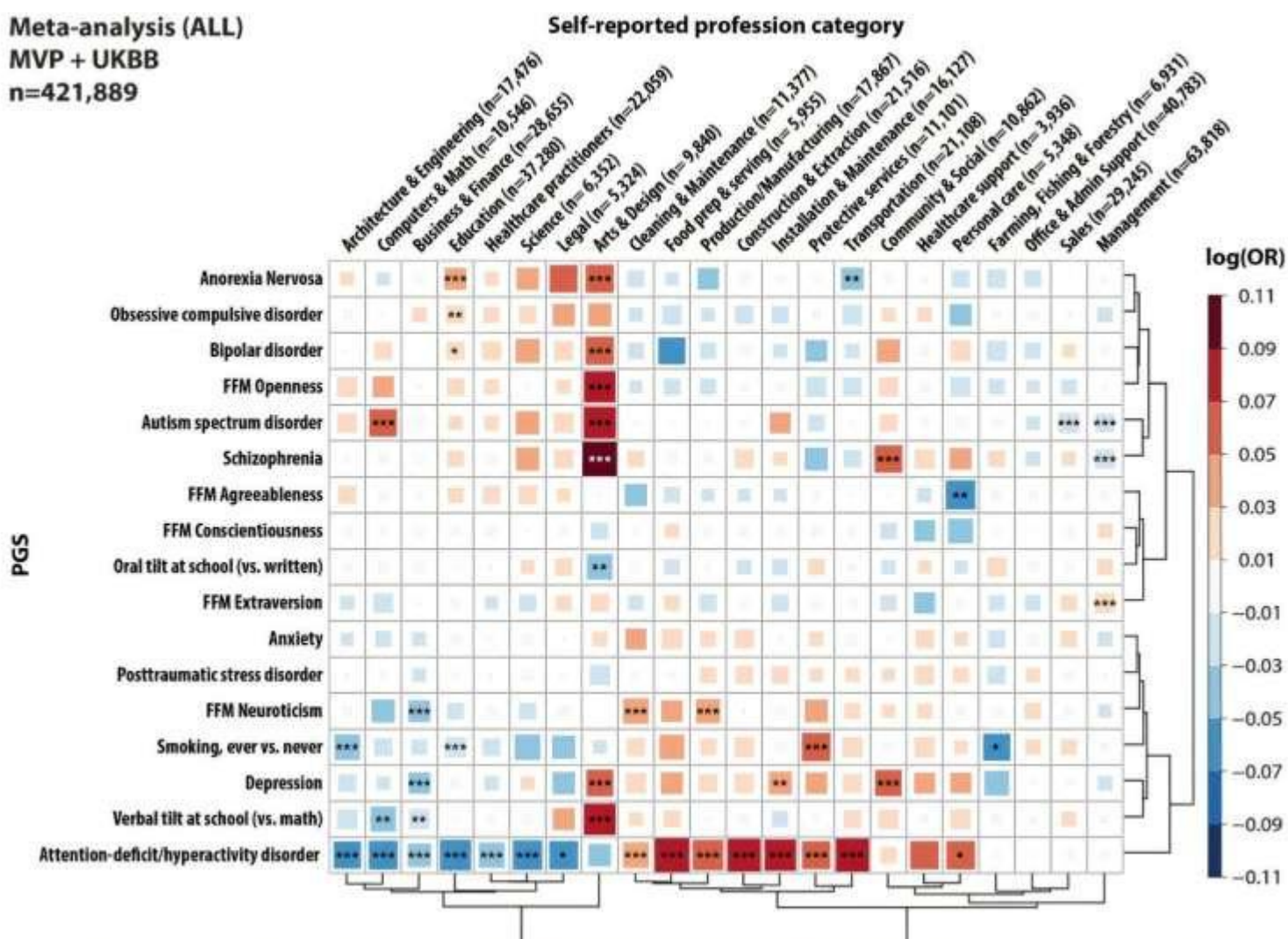
More information: Sisi Fan et al, Morphological transformation and formation of membrane channels in synthetic cells through reconfigurable DNA nanotubes, *Nature Materials* (2025). DOI: [10.1038/s41563-024-02075-9](https://doi.org/10.1038/s41563-024-02075-9) www.nature.com/articles/s41563-024-02075-9

Journal information: [Nature Materials](#)
Provided by [University of Stuttgart](#)

Study explores link between people's professions and their genetic predisposition to neuropsychiatric traits

by Ingrid Fadelli , Medical Xpress

Meta-analysis (ALL)
MVP + UKBB
n=421,889



Matrix of meta-analyzed PGS-profession association estimates. Meta-analysis (fixed-effect inverse-variance weighted) of associations between neuropsychiatric trait PGS and distinct profession categories in all individuals (ALL; n = 421,889) of European ancestry, as

estimated by logistic regression in both cohorts (MVP and UKBB; $\text{professioni} \sim \text{PGSj} + \text{age} + \text{age}^2 + \text{sex} + \text{ancestral PC1 to PC20} + \text{genotyping batch}$ (needed only for UKBB), for each of the 374 PGSj-profession pairs). Plotted natural logarithm of odds ($\log(\text{OR})$) denoted by both color and size, with statistical significance denoted by stars (***, ** and * correspond to Bonferroni-adjusted two-tailed p values of association equal or less than 0.001, 0.01 and 0.05 respectively). Most profession categories (20/22) were significantly associated with at least one neuropsychiatric PGS, with the highest number of associations found for ADHD (15), depression (4), autism spectrum disorder (ASD) (4) and smoking, ever vs. never (4). "Health care support" and "office & admin support" were the only profession categories with no significant association with neuropsychiatric trait PGS. Dendrograms for PGS and professions were derived from hierarchical clustering analysis with Ward's method. Credit: Voloudakis et al. (*Nature Human Behaviour*, 2024).

Polygenic scores (PGS) are metrics used to estimate the genetic predisposition of people to developing specific mental health conditions, personality traits or diseases. In recent years, these metrics have often been used to investigate the intricate connections between genes and environmental factors.

Researchers at the JJ Peters VA Medical Center, Icahn School of Medicine at Mount Sinai and other institutes recently carried out a study aimed at determining whether neuropsychiatric [polygenic scores](#) could predict the professional categories that individuals belong to. Their findings, [published](#) in *Nature Human Behaviour*, suggest that these scores weakly predict the professional category that people belong to.

"Neuropsychiatric disorders are both common and highly heritable, yet they remain heavily stigmatized," Georgios Voloudakis, first author of the paper, told Medical Xpress.

"We were inspired to examine whether certain genetic variants that increase the risk of developing these disorders might also offer potential benefits in specific contexts—a 'trade-off' that could help explain why these common variants persist in populations."

The key objective of the recent work by Voloudakis and his colleagues was to investigate the complex ways in which genetic factors shape people's individual traits and societal outcomes. Specifically, they wished to determine whether PGS scores hinting at a predisposition for specific [neuropsychiatric disorders](#), such as autism spectrum disorder (ASD) or schizophrenia, are predictors of the membership to specific professional categories (e.g., "computers & math," "arts & design," etc.).

"In addition to looking at potential advantages, we also wanted to explore any disadvantages or barriers that individuals with a higher genetic predisposition to neuropsychiatric traits might face," said Voloudakis.

"For example, we found that some attention-deficit/hyperactivity disorder (ADHD)-related associations are significantly mediated by educational attainment—a key driver of career pathways. This implies that systemic biases in education can disproportionately affect individuals with a higher genetic predisposition for ADHD, even if they never receive an actual diagnosis."

Voloudakis and his colleagues wished to better understand possible systemic biases that could preferentially lead specific individuals to particular fields, while precluding them the opportunity to approach other careers, as this could inform interventions aimed at reducing inequities in educational and professional contexts. In addition, the researchers set out to investigate the extent to which genetic predispositions can predict professional outcomes.

"Ever since the first preimplantation genetic diagnosis in 1990, and popularized notions from the 1997 sci-fi film 'GATTACA,' society has grappled with the idea that genetic profiles could predetermine life trajectories, including career success," said Voloudakis. "By investigating genetic predispositions for neuropsychiatric traits, our aim was to move beyond speculation and quantify these influences in large, real-world datasets."

To determine whether a slightly higher predisposition for specific psychiatric traits was aligned with a person's profession, the researchers analyzed data collected as part of two of the world's largest biobanks. One of these is the Million Veteran Program (MVP), which is run in the US, while the other is the UK Biobank (UKBB), collected in the UK.

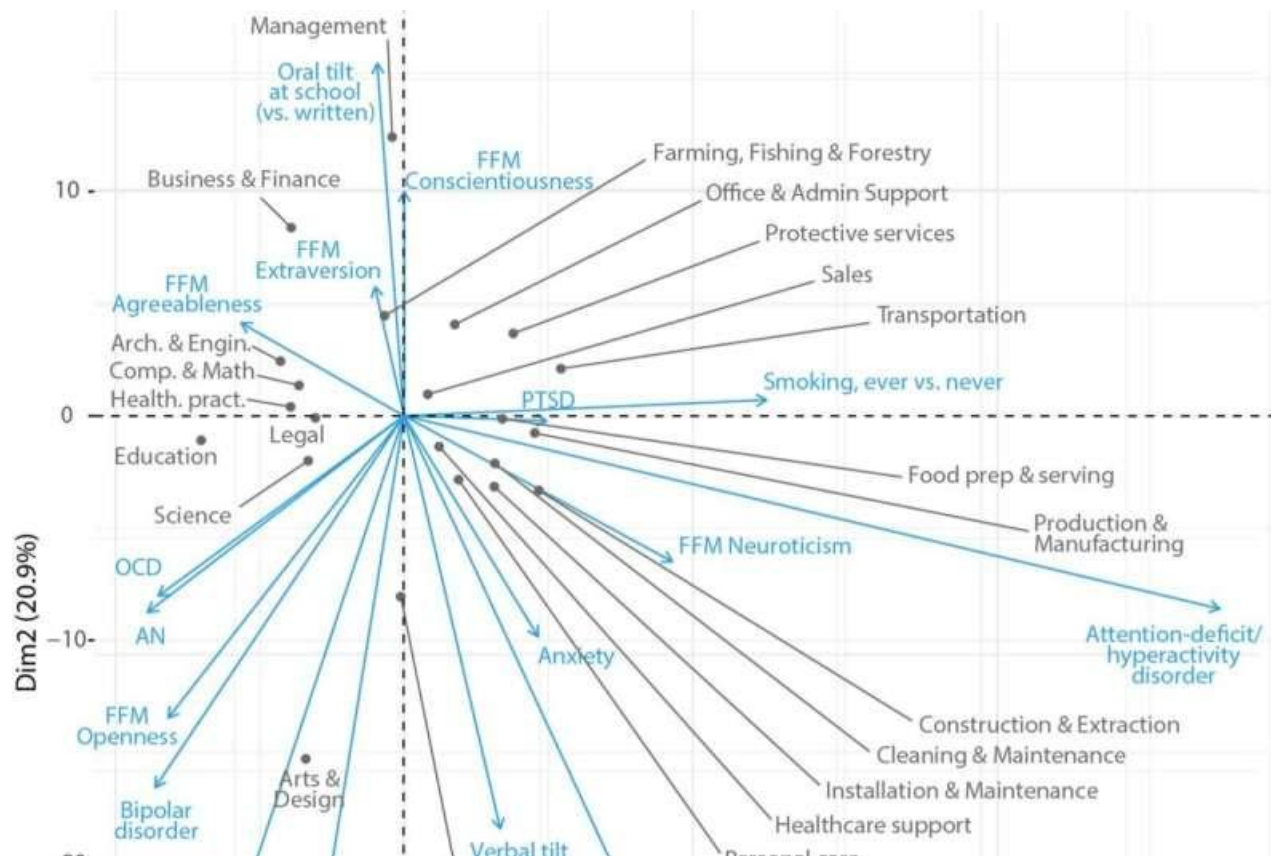
"In MVP, participants reported their occupation(s) in a survey (they could pick more than one category), and we analyzed each occupation category separately," explained Voloudakis.

"In UKBB, on the other hand, people's primary occupation was recorded during an interview. We then did careful work to match up these reported jobs into common categories across both studies (for example, 'arts & design,' 'health care,' etc.). Notably, we only looked at individuals who had reached age 30 or older when they reported their jobs (to capture a reasonably settled career path)."

Voloudakis and his colleagues used past genetic studies to create PGSs for 421,889 individuals whose data was collected as part of either the MVP or UKBB projects.

As current methods for calculating PGSs rely on large-scale prior genetic studies which are currently almost exclusively available for people of European ancestry, the researchers decided to only include individuals with a European background in their study, for which PGS can be reliably estimated.

"Our next step was to link genetics to professions," said Voloudakis. "For each profession category (e.g., 'arts & design') in each study, we checked whether the PGS for a certain psychiatric trait was linked to membership in that profession. In other words, we tried to determine if having a slightly higher PGS for a specific psychiatric disorder corresponded to a greater likelihood, on average, to be in a particular field."



Principal Component Analysis (PCA) biplot for neuropsychiatric trait PGS and professions. PCA was performed using estimates from all PGS-profession pairs. More than 76% of variance at the population level was captured by Dim1 (56.4%; mainly driven by ADHD) and Dim2 (20.9%; mostly driven by psychotic and mood disorders). Loadings for each neuropsychiatric PGS (cyan) and normalized scores for each profession (gray) are shown on Dim1 (x-axis) and Dim2 (y-axis). Of note, PGS loading magnitude also depends on source GWAS power and that should be taken into account when comparing loading magnitude between traits. Credit: Voloudakis et al.

The researchers analyzed the scores they derived and the professional categories that people belonged to using statistical models known as logistic regressions, while also accounting for factors like age and sex, which are known to influence people's career choices.

Notably, they replicated the analyses by additionally excluding individuals that were diagnosed with neuropsychiatric disorders to see if the same findings apply to those who only had a genetic predisposition for specific neuropsychiatric traits.

"We ran these analyses separately in MVP and UKBB to see if the patterns matched," said Voloudakis. "We found that, although the effects were small, they were significant and quite similar between the two studies. We then combined (meta-analyzed) the results from both groups to strengthen our findings and confirm that these small effects were consistent."

Overall, the researchers' analyses revealed that neuropsychiatric PGS have a significant impact on people's professional endeavors, yet this effect is small. Overall, the variation explained by genetic scores is far less than 1% for most professions.

"Even if these effects are small, because we studied so many people, we could reliably detect them," said Voloudakis. "These findings don't mean we can predict someone's job based on their genetics. Rather, they highlight subtle group-level trends. On average, people with a higher PGS for certain traits might be slightly more likely to end up in certain jobs."

The researchers found that the "tiny genetic signals" influencing people's professional outcomes are both reproducible and consistent. Nonetheless, they are not strong enough to determine what a particular individual's career path will be, as other factors (e.g., environment, education, interests and opportunities) play a far greater role in determining people's profession.

"A major takeaway is that while we do see statistically significant associations between several neuropsychiatric traits and professional categories, each trait's polygenic score (PGS) explains less than 0.4% of the variation in whether a person enters a particular profession," said Voloudakis. "In other words, there is a real but weak genetic signal in these career placements."

Interestingly, the researchers found that both age and sex played a far greater role in determining the professions that individuals will pursue compared to neuropsychiatric PGSs. Age accounted for approximately 21% of the observed variance in profession, while sex accounted for 7%.

"Our findings emphasize that demographic and [social factors](#) far outweigh genetic predisposition when it comes to occupational outcomes," explained Voloudakis.

"Finally, they indicate that neuropsychiatric PGS does not—and almost certainly will not—serve as a reliable tool to predict or determine someone's career path. Environmental, social, and personal factors continue to play a much larger role in shaping individual outcomes than any single genetic measure."

The results of this recent study suggest that while a genetic predisposition for specific traits is associated with choices in professions, this association is far too weak to use PGS to predict people's professional categories. Nonetheless, these scores could be useful for research exploring broad social contexts, in which genetic, environmental and systemic factors interact, shaping people's individual outcomes.

"We now plan to continue exploring how genetic variations, known as risk variants, associated with neuropsychiatric disorders can influence multiple aspects of health and behavior—a phenomenon known as pleiotropy," said Voloudakis.

"These genetic variations may not only contribute to specific psychiatric conditions but could also impact broader areas, such as cognitive abilities, emotional regulation, and other key mental functions."

In their next studies, Voloudakis and his colleagues plan to continue exploring the link between PGS and specific aspects of people's lives, experiences and skills. This could help them to shed new light on the sophisticated biological mechanisms connecting genetics and mental health.

"Our ultimate goal is to use this knowledge within a computational psychiatry framework, which combines advanced data analysis and modeling techniques, to gain deeper insights into how these [genetic factors](#) shape mental health and cognition," added Voloudakis. "This approach could help pave the way for more precise and personalized treatments in the future."

More information: Georgios Voloudakis et al, Neuropsychiatric polygenic scores are weak predictors of professional categories, *Nature Human Behaviour* (2024). [DOI: 10.1038/s41562-024-02074-5](https://doi.org/10.1038/s41562-024-02074-5).

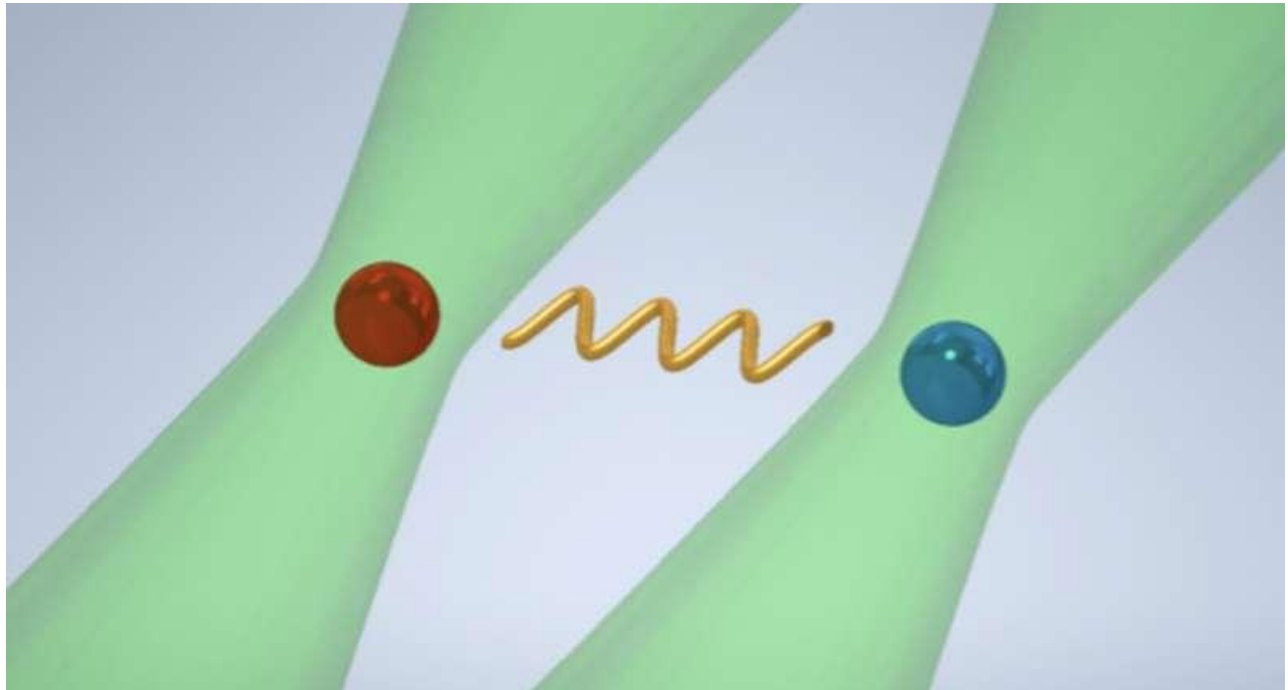
Journal information: [Nature Human Behaviour](#)

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JANUARY 15, 2025

Scientists achieve direct experimental realization of dual-type entangling gates

by Ingrid Fadelli , Phys.org



Using the same laser setup to entangle dual-type qubits. Credit: Chenxi Wang and Chuanxin Huang.

To develop scalable and reliable quantum computers, engineers and physicists will need to devise effective strategies to mitigate errors in their quantum systems without adding complex additional components. A promising strategy to reduce errors entails the use of so-called dual-type qubits.

These are qubits that can encode [quantum information](#) in a system across two different types of quantum states. These qubits could increase the flexibility of quantum computing architectures, while also reducing undesirable crosstalk between qubits and enhancing a system's operational fidelity.

Researchers at Tsinghua University and other research institutes in China recently realized an entangling gate between dual-type qubits in an experimental setting.

Their paper, [published](#) in *Physical Review Letters*, introduces a promising approach for realizing these gates, which could help to boost the performance of quantum computing systems without the need for additional hardware components.

"In ion trap quantum computation, recently it has been realized that encoding two types of qubits in the same ion species is a promising scheme, one type for carrying quantum information and the other type for auxiliary operations," Luming Duan, senior author of the paper, told Phys.org.

"A crucial gadget in this scheme is to entangle the qubits encoded in these two types. Although in principle one can first convert the qubits into the same type and then perform the same-type entangling gate, in practice it would lead to considerable overhead."

The main objective of this recent study by Duan and his colleagues was to directly and experimentally realize a dual-type entangling gate. The team achieved this using a single 532 nm laser system to drive Raman transitions, entangling dual-type qubits without employing any additional hardware.

"We carefully design multiple frequency components in the driving laser, such that they couple the two [qubit](#) types, one encoded in the hyperfine levels of one ion and the other encoded in the hyperfine levels of another ion, simultaneous to the collective spatial oscillation of the two ions," explained Duan.

"Using these collective oscillation modes as a quantum bus, we generate entanglement between the dual-type qubits."

The researchers evaluated their proposed approach's potential in a series of tests and found that it achieved entanglement between dual-type qubits encoded in the S and D manifolds of ions, respectively, with a remarkable Bell state fidelity of 96.3%. This performance is comparable to that achieved by same-type entangling gates (i.e., S-S or D-D gates).

"Using a single setup, we achieve dual-type and same-type entangling gates with similar gate performance," said Duan. "This suggests that there is no additional fundamental limitation in realizing a dual-type entangling gate, such that it can be applied in practical quantum circuits to help reduce the overhead of back-and-forth qubit type conversions."

The findings of this study could soon inspire other research groups to experiment with dual-type qubits to reduce errors in quantum systems without increasing their complexity. Meanwhile, Duan and his colleagues will continue building on their methods, to further boost the performance of the dual-type entangling gate they realized.

"We plan to upgrade the system for better stabilization of the optical paths and better locking of the trap frequency," added Duan.

"These will help improve the gate performance. We also plan to apply this dual-type entangling gate to demonstrate mid-circuit quantum state detection for [quantum error correction](#), and to demonstrate the functioning of a trapped-ion-based quantum network node."

More information: Chenxi Wang et al, Experimental Realization of Direct Entangling Gates between Dual-Type Qubits, *Physical Review Letters* (2025). [DOI: 10.1103/PhysRevLett.134.010601](https://doi.org/10.1103/PhysRevLett.134.010601). On arXiv: [DOI: 10.48550/arxiv.2410.05659](https://doi.org/10.48550/arxiv.2410.05659)
Journal information: [Physical Review Letters](#) , [arXiv](#)

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JANUARY 15, 2025

Octopus arms have segmented nervous systems to power extraordinary movements

by [University of Chicago](#)



Octopus bimaculoides. Credit: Cassady Olson

Octopus arms move with incredible dexterity, bending, twisting, and curling with nearly infinite degrees of freedom. New research from the University of Chicago revealed that the nervous system circuitry that controls arm movement in octopuses is segmented, giving these extraordinary creatures precise control across all eight arms and hundreds of suckers to explore their environment, grasp objects, and capture prey.

"If you're going to have a nervous system that's controlling such dynamic movement, that's a good way to set it up," said Clifton Ragsdale, Ph.D., Professor of Neurobiology at UChicago and senior author of the study.

"We think it's a feature that specifically evolved in soft-bodied cephalopods with suckers to carry out these worm-like movements."

The study, "Neuronal segmentation in cephalopod arms," was published January 15, 2025, in *Nature Communications*.

Each octopus arm has a massive nervous system, with more neurons combined across the eight arms than in the animal's brain. These neurons are concentrated in a large axial nerve cord (ANC), which snakes back and forth as it travels down the arm, every bend forming an enlargement over each sucker.

Octopus arms move with incredible dexterity, bending, twisting, and curling with nearly infinite degrees of freedom. Credit: Cassady Olson

Cassady Olson, a graduate student in Computational Neuroscience who led the study, wanted to analyze the structure of the ANC and its connections to musculature in the arms of the California two-spot octopus (*Octopus bimaculoides*), a small species native to the Pacific Ocean off the coast of California.

She and her co-author Grace Schulz, a graduate student in Development, Regeneration and Stem Cell Biology, were trying to look at thin, circular cross-sections of the arms under a microscope, but the samples kept falling off the slides. They tried lengthwise strips of the arms and had better luck, which led to an unexpected discovery.

Using cellular markers and imaging tools to trace the structure and connections from the ANC, they saw that neuronal cell bodies were packed into columns that formed segments, like a corrugated pipe. These segments are separated by gaps called septa, where nerves and blood vessels exit to nearby muscles. Nerves from multiple segments connect to different regions of muscles, suggesting the segments work together to control movement.

Octopus bimaculoides. Credit: Cassady Olson

"Thinking about this from a modeling perspective, the best way to set up a control system for this very long, flexible arm would be to divide it into segments," Olson said. "There has to be some sort of communication between the segments, which you can imagine would help smooth out the movements."

Nerves for the suckers also exited from the ANC through these septa, systematically connecting to the outer edge of each sucker. This indicates that the nervous system sets up a spatial, or topographical, map of each sucker.

Octopuses can move and change the shape of their suckers independently. The suckers are also packed with sensory receptors that allow the octopus to taste and smell things that they touch—like combining a hand with a tongue and a nose. The researchers believe the "suckeroptopy," as they called the map, facilitates this complex sensory-motor ability.

To see if this kind of structure is common to other soft-bodied cephalopods, Olson also studied longfin inshore squid (*Doryteuthis pealeii*), which are common in the Atlantic Ocean.

These squid have eight arms with muscles and suckers like an octopus, plus two tentacles. The tentacles have a long stalk with no suckers, with a club at the end that does have suckers. While hunting, the squid can shoot the tentacles out and grab prey with the sucker-equipped clubs.

Using the same process to study long strips of the squid tentacles, Olson saw that the ANC in the stalks with no suckers are not segmented, but the clubs at the end are segmented the same way as the octopus. This suggests that a segmented ANC is specifically built for controlling any type of dexterous, sucker-laden appendage in cephalopods.

The squid tentacle clubs have fewer segments per sucker, however, likely because they do not use the suckers for sensation the same way octopuses do. Squid rely more on their vision to hunt in the open water, whereas octopuses prowl the [ocean floor](#) and use their sensitive arms as tools for exploration.



Octopus bimaculoides. Credit: Cassady Olson

While octopuses and squid diverged from each other more than 270 million years ago, the commonalities in how they control parts of their appendages with suckers—and differences in the parts that don't—show how evolution always manages to find the best solution.

"Organisms with these sucker-laden appendages that have worm-like movements need the right kind of nervous system," Ragsdale said.

"Different cephalopods have come up with a segmental structure, the details of which vary according to the demands of their environments and the pressures of hundreds of millions of years of evolution."

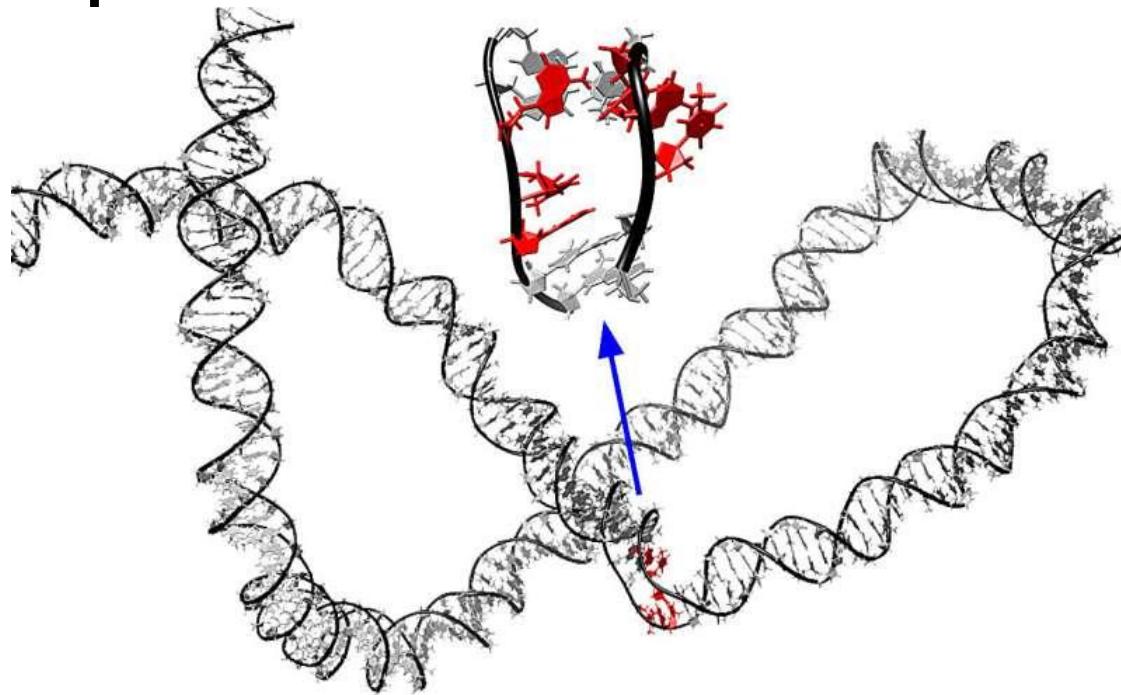
More information: Neuronal segmentation in cephalopod arms, *Nature Communications* (2025). DOI: [10.1038/s41467-024-55475-5](https://doi.org/10.1038/s41467-024-55475-5)

Journal information: [Nature Communications](#)

Provided by [University of Chicago](#)

FEBRUARY 4, 2025

Molecular simulations provide new insights into the dynamics of supercoiled DNA



Computer simulation showing the two DNA helix strands separating to form a "bubble" (in red). Credit: Agnes Noy. (*PRL*, 2025).

DNA (deoxyribonucleic acid), the molecular "blueprint" carrying the genetic instructions that influence the growth, development, reproduction and predispositions of individual humans, can undergo different types of mechanical stress inside cells. For instance, it can be twisted or stretched, impacting its overall structure and dynamics.

Researchers at the University of York recently explored how DNA behaves under torsion and tension using molecular dynamics simulations. These atomic-scale simulations yielded interesting new findings, which were [published](#) in a paper in *Physical Review Letters*.

"I have always been interested in studying how DNA behaves inside the cell," Dr. Agnes Noy, senior author of the paper, told Phys.org. "We are used to thinking of DNA as a relaxed 'perfect' [double helix](#), but the reality is far from that. Inside cells, DNA is

under/overtwisted, resulting in the formation of 'supercoiled' loops, resembling what can happen to long cords or garden hoses in our homes."

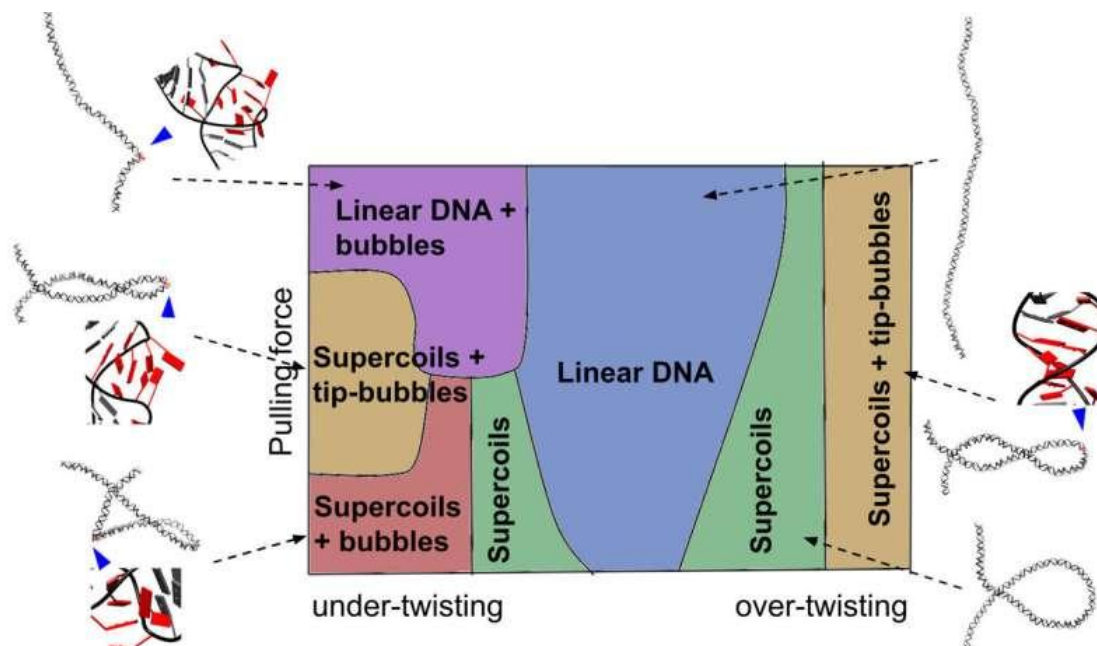
In contrast with relaxed DNA, supercoiled DNA has been difficult to observe closely in experimental settings due to its dynamic nature. In one of their previous studies, the researchers overcame this challenge using a combination of microscopy and atomic resolution simulations.

"As these two methodologies agreed so well on the global shapes found for the DNA, [simulations proved to be an effective boost to microscopy resolution](#)," explained Dr. Noy. "We could see for the first time that undertwisted DNA presents defects on the double helix structure in the form of bubbles (which is when the two DNA strands separate). However, the trick there was the use of tiny DNA circles as a model."

Building on their previous findings, Dr. Noy and her colleagues set out to investigate what happens in linear or longer DNA strands, such as the molecules constituting genomes in living organisms. To do this, they developed novel approaches that could be used to model supercoiled DNA without the need to be circular.

"Our objective was to simulate the main experiments on supercoiling linear DNA where the ends of the molecule are subjected to a controllable amount of torsion and tension," explained Dr. Noy.

"While these experiments have given us a good understanding of how DNA responds to mechanical forces (DNA is also pulled in cells), they can't show us the different structures that DNA can take. Several models tried to paint a picture of it, but none has attempted to characterize DNA at atomic resolution under such conditions."



Simulations generate a phase diagram of the structures that DNA adopts when increasing

the pulling or torque force (in both directions, resulting in under or overtwisted DNA). The structures can include supercoiled loops and bubbles (in red). Credit: Agnes Noy. The researchers performed [molecular dynamics simulations](#) based on classical mechanics equations to determine the motion of individual atoms in DNA. To simulate the desired experimental setup, they also placed restraints on the DNA ends.

"By making sure our simulations reproduced the experimental DNA extension (or end-to-end distances), we mapped the different conditions where DNA presented supercoiled loops or bubbles," said Dr. Noy. "We discovered that DNA forms bubbles more easily than expected, triggered only by changes in its twist and without the need of being pulled, contrary to previous assumptions.

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"This is particularly applicable to AT-rich sequences, as the base pair resulting from adenine (A) and thymine (T) is less stable than the one formed by cytosine (C) and guanine (G). Bubbles form when the two DNA strands are separated and are necessary to read the [genetic information](#)."

Since researchers uncovered the existence of a double helix in DNA, they determined that the molecular elements carrying genetic information (i.e., the nucleobases A, T, C and G) are stored inside this structure and are thus difficult to access. Before this discovery, scientists believed that observed 'bubbles' were formed due to specialized proteins that mechanically destabilize the DNA.

"Our findings mean that the genetic information is easier to read than was previously thought and that sequence codifies which are the most accessible parts," explained Dr. Noy. "This will improve scientists' understanding of how genetic programs unfold, which will help in disease detection and treatment as well as in the synthesis of compounds via synthetic biology."

The recent study by this research team sheds new light on how torsional stress affects the structure of linear and longer DNA strands. In her next studies, Dr. Noy plans to further examine sites in genomes where genetic information is read first, as these generally serve as 'signal points' for the start of a gene.

"These short sequences are known as a gene's 'promoters' and are critical because they control whether the DNA sequence for a specific gene is read and translated into its actual function," added Dr. Noy.

"The formation of bubbles in 'promoters' is carefully regulated, allowing organisms to determine when a feature is presented. I am planning to investigate this regulation so we can better understand which processes control the opening of a DNA bubble in key sites and consequently gene expression."

More information: Atomic description of the reciprocal action between supercoils and melting bubbles on linear DNA. *Physical Review Letters*(2025). DOI: [10.1103/PhysRevLett.134.038403](https://doi.org/10.1103/PhysRevLett.134.038403).

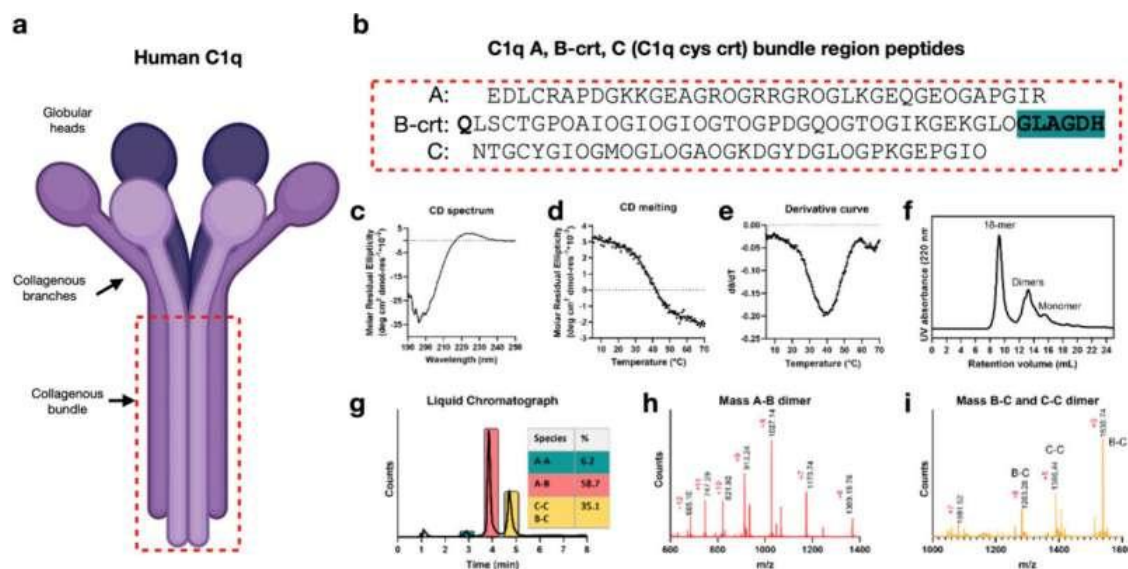
Journal information: [Physical Review Letters](#)

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FEBRUARY 7, 2025

Discovery of unexpected collagen structure shows greater diversity than previously believed

by [Rice University](#)



Characterization of peptide assemblies of A, B-Crt and C. Credit: *ACS Central Science* (2025). DOI: 10.1021/acscentsci.5c00018

Collagen, the body's most abundant protein, has long been viewed as a predictable structural component of tissues. However, a new study led by Rice University's Jeffrey Hartgerink and Tracy Yu, in collaboration with Mark Kreutzberger and Edward Egelman at the University of Virginia (UVA), challenges that notion, revealing an unexpected confirmation in collagen structure that could reshape biomedical research.

The researchers used advanced cryo-[electron microscopy](#) (cryo-EM) to determine the atomic structure of a packed collagen assembly that deviates from the traditionally accepted right-handed superhelical twist. Published Feb. 3 in [ACS Central Science](#), the study suggests collagen's structural diversity may be greater than previously believed.

"This work fundamentally changes how we think about collagen," said Hartgerink, professor of chemistry and bioengineering. "For decades, we have assumed that collagen triple helices always follow a strict structural paradigm. Our findings show that collagen assemblies can adopt a wider range of conformations than previously thought."

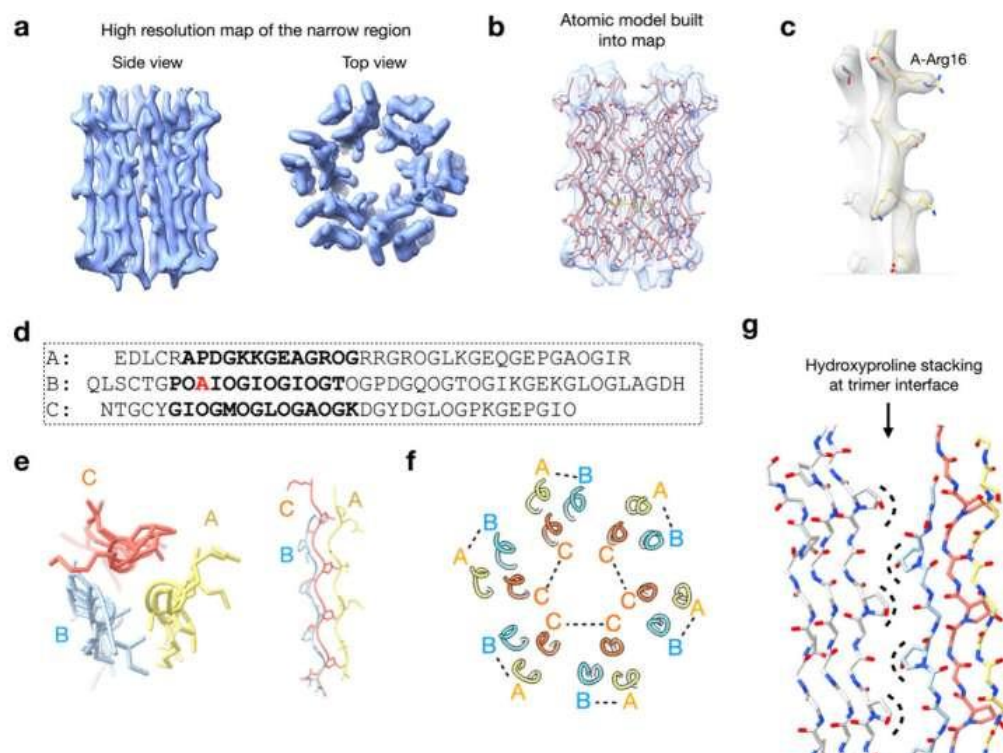
Unveiling a new collagen conformation

To explore collagen assembly at an atomic level, the research team designed a system of self-assembling peptides based on the collagen-like region of C1q, a key immune protein. They then used cryo-EM, a technology that allows scientists to visualize biomolecules in unprecedented detail, to analyze the structure of the assembled peptides. The resulting model revealed a deviation from the canonical right-handed superhelical twist.

This unexpected conformation enables unique molecular interactions, including hydroxyproline stacking between adjacent helices and forming a symmetrical hydrophobic cavity. Such features suggest that collagenous assemblies may be far more structurally diverse than previously believed.

"The absence of the superhelical twist allows for molecular interactions not seen before in collagen," said Yu, a former graduate student of Hartgerink who is now a postdoctoral researcher at the University of Washington.

Kreutzberger, the first author of this study, said that this discovery indeed questions previous beliefs. "It challenges the long-held dogma about collagen structure and opens the door to re-examining its biological roles," Kreutzberger said.



resolution structure of the narrow region of the C1q cys crt stem assembly reveals the amino acid positioning of the three polypeptide chains. Credit: *ACS Central Science* (2025). DOI: 10.1021/acscentsci.5c00018

Significance for medicine and biomaterials

The implications of this discovery could extend beyond fundamental biology. Collagen is not just a structural protein—it plays essential roles in cell signaling, immune function and tissue repair.

By gaining a deeper understanding of collagen's structural variability, researchers may unlock new insights into diseases where collagen assembly is compromised, including Ehlers-Danlos syndrome, fibrosis and certain cancers.

Additionally, this work lays the foundation for innovations in biomaterials and regenerative medicine. By harnessing the unique structural properties of this newly identified collagen conformation, scientists could design novel materials for wound healing, tissue engineering and drug delivery.

Cryo-EM's breakthrough in structural biology

Despite collagen's ubiquity in human biology, studying its higher-order structures at high resolution has been a challenge. Traditional techniques such as X-ray crystallography and fiber diffraction have provided valuable insights but could not capture collagen packing in complex assemblies. Cryo-EM, however, has overcome these limitations, allowing the research team to visualize collagen's intricate architecture in new detail.

"Our research refines our understanding of [collagen](#) and highlights the importance of re-examining other biological structures previously thought to be well understood," said Egelman, study co-corresponding author.

Additional co-authors of the study include Michael Purdy of UVA; Thi Bui and Maria Hancu of the Department of Chemistry at Rice; Tomasz Osinski of the University of Southern California; and Peter Kasson of the Georgia Institute of Technology.

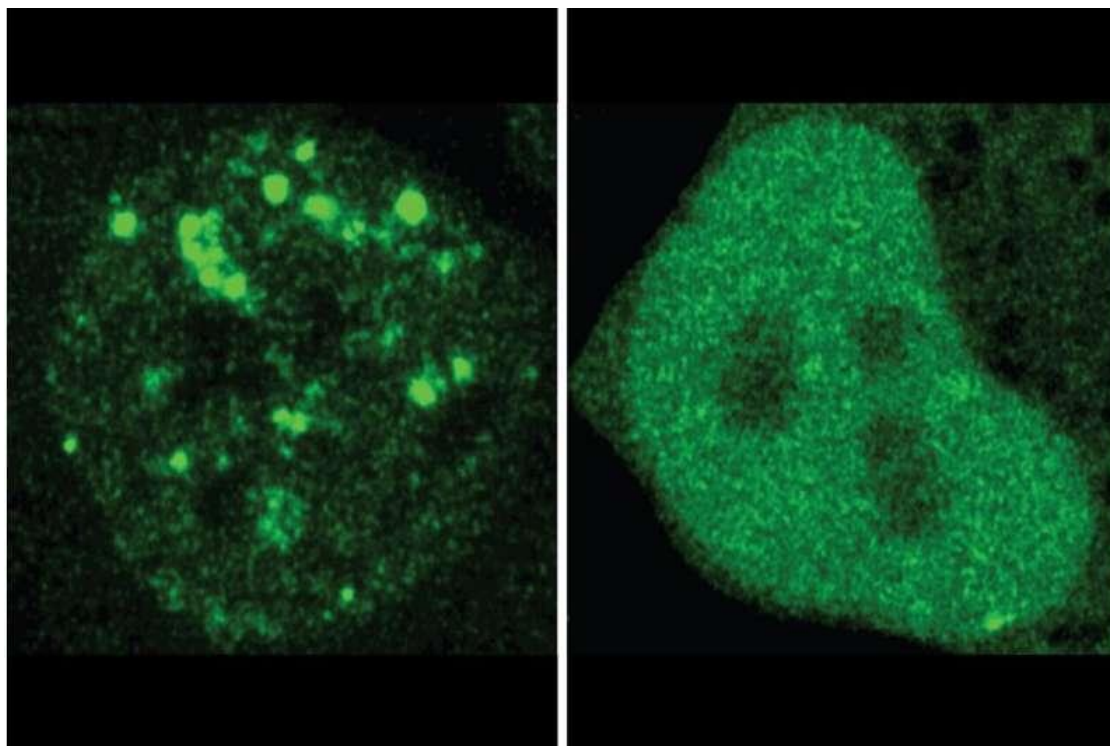
More information: Mark A. B. Kreutzberger et al, A Collagen Triple Helix without the Superhelical Twist, *ACS Central Science* (2025). [DOI: 10.1021/acscentsci.5c00018](https://doi.org/10.1021/acscentsci.5c00018)

Journal information: [ACS Central Science](#)

Provided by [Rice University](#)

FEBRUARY 7, 2025 **New AI model deciphers the code in proteins that tells them where to go**

by Greta Friar, [Whitehead Institute for Biomedical Research](#)



ProtGPS predicts where a protein will localize in a healthy cell (left) and in the instance of a pathogenic mutation (right). Punctate green dots represent localized proteins. Credit: Henry Kilgore and Lena Afeyan/Whitehead Institute

Proteins are the workhorses that keep our cells running, and there are many thousands of types of proteins in our cells, each performing a specialized function. Researchers have long known that the structure of a protein determines what it can do. More recently, researchers are coming to appreciate that a protein's localization is also critical for its function.

Cells are full of compartments that help to organize their many denizens. Along with the well-known organelles that adorn the pages of biology textbooks, these spaces also include a variety of dynamic, membrane-less compartments that concentrate certain molecules together to perform shared functions.

Knowing where a given protein localizes, and who it co-localizes with, can therefore be useful for better understanding that protein and its role in the healthy or diseased cell, but researchers have lacked a systematic way to predict this information.

Meanwhile, [protein structure](#) has been studied for over half a century, culminating in the [artificial intelligence](#) (AI) tool AlphaFold, which can predict protein structure from a protein's amino acid code, the linear string of building blocks within it that folds to create its structure. AlphaFold and models like it have become widely used tools in research.

Proteins also contain regions of amino acids that do not fold into a fixed structure, but are instead important for helping proteins join dynamic compartments in the cell. Whitehead Institute Member Richard Young and colleagues wondered whether the code in those regions could be used to predict protein localization in the same way that other regions are used to predict structure.

Other researchers have discovered some protein sequences that code for protein localization, and some have begun developing [predictive models](#) for protein localization. However, researchers did not know whether a protein's localization to any dynamic compartment could be predicted based on its sequence, nor did they have a comparable tool to AlphaFold for predicting localization.

Now, Young, also a professor of biology at the Massachusetts Institute of Technology (MIT), Young lab postdoc Henry Kilgore, Regina Barzilay, the School of Engineering Distinguished Professor for AI and Health at MIT's Computer Science and Artificial Intelligence Laboratory, and colleagues have built such a model, which they call ProtGPS.

In a [paper](#) published on Feb. 6 in the journal *Science*, with first authors Kilgore and Barzilay lab graduate students Itamar Chinn, Peter Mikhael, and Ilan Mitnikov, the cross-disciplinary team debuts their model.

The researchers show that ProtGPS can predict which of 12 known types of compartments a protein will localize to, as well as whether a disease-associated mutation will change that localization. Additionally, the research team developed a generative algorithm that can design novel proteins to localize to specific compartments.

"My hope is that this is a first step towards a powerful platform that enables people studying proteins to do their research," Young says, "and that it helps us understand how humans develop into the complex organisms that they are, how mutations disrupt those natural processes, and how to generate therapeutic hypotheses and design drugs to treat dysfunction in a cell."

The researchers also validated many of the model's predictions with [experimental tests](#) in cells.

"It really excited me to be able to go from computational design all the way to trying these things in the lab," Barzilay says. "There are a lot of exciting papers in this area of AI, but 99.9% of those never get tested in real systems. Thanks to our collaboration with the Young lab, we were able to test and really learn how well our algorithm is doing."

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Developing the model

The researchers trained and tested ProtGPS on two batches of proteins with known localizations. They found that it could correctly predict where proteins end up with high accuracy. The researchers also tested how well ProtGPS could predict changes in protein localization based on disease-associated mutations within a protein.

Many mutations—changes to the sequence for a gene and its corresponding protein—have been found to contribute to or cause disease based on association studies, but the ways in which the mutations lead to disease symptoms remain unknown.

Figuring out the mechanism for how a mutation contributes to disease is important because then researchers can develop therapies to fix that mechanism, preventing or treating the disease. Young and colleagues suspected that many disease-associated mutations might contribute to disease by changing protein localization. For example, a mutation could make a protein unable to join a compartment containing essential partners.

They tested this hypothesis by feeding ProtGPS more than 200,000 proteins with disease-associated mutations, and then asking it to both predict where those mutated proteins would localize and measure how much its prediction changed for a given protein from the normal to the mutated version. A large shift in the prediction indicates a likely change in localization.

The researchers found many cases in which a disease-associated mutation appeared to change a protein's localization. They tested twenty examples in cells, using fluorescence to compare where in the cell a normal protein and the mutated version of it ended up. The experiments confirmed ProtGPS's predictions.

Altogether, the findings support the researchers' suspicion that mis-localization may be an underappreciated mechanism of disease, and demonstrate the value of ProtGPS as a tool for understanding disease and identifying new therapeutic avenues.

"The cell is such a complicated system with so many components and complex networks of interactions," Mitnikov says. "It's super interesting to think that with this approach, we can perturb the system, see the outcome of that, and so drive discovery of mechanisms in the cell or even develop therapeutics based on that."

The researchers hope that others begin using ProtGPS in the same way that they use predictive structural models like AlphaFold, advancing various projects on protein function, dysfunction, and disease.

Moving beyond prediction to novel generation

The researchers were excited about the possible uses of their prediction model, but they also wanted their model to go beyond predicting localizations of existing proteins, and allow them to design completely new proteins. The goal was for the model to make up entirely new amino acid sequences that, when formed in a cell, would localize to a desired location.

Generating a novel protein that can actually accomplish a function—in this case, the function of localizing to a specific cellular compartment—is incredibly difficult. In order to improve their model's chances of success, the researchers constrained their algorithm to only design proteins like those found in nature.

This is an approach commonly used in drug design, for logical reasons; nature has had billions of years to figure out which protein sequences work well and which do not.

Because of the collaboration with the Young lab, the machine learning team was able to test whether their protein generator worked. The model had good results. In one round, it generated ten proteins intended to localize to the nucleolus. When the researchers tested these proteins in the cell, they found that four of them strongly localized to the nucleolus, and others may have had slight biases towards that location as well.

"The collaboration between our labs has been so generative for all of us," Mikhael says. "We've learned how to speak each other's languages, in our case learned a lot about how cells work, and by having the chance to experimentally test our model, we've been able to figure out what we need to do to actually make the model work, and then make it work better."

Being able to generate [functional proteins](#) in this way could improve researchers' ability to develop therapies. For example, if a drug must interact with a target that localizes within a certain compartment, then researchers could use this model to design a drug to also localize there. This should make the drug more effective and decrease side effects, since the drug will spend more time engaging with its target and less time interacting with other molecules, causing off-target effects.

The machine learning team members are enthused about the prospect of using what they have learned from this collaboration to design novel proteins with other functions beyond localization, which would expand the possibilities for therapeutic design and other applications.

"A lot of papers show they can design a protein that can be expressed in a cell, but not that the protein has a particular function," Chinn says. "We actually had a functional protein design, and a relatively huge success rate compared to other generative models. That's really exciting to us, and something we would like to build on."

All of the researchers involved see ProtGPS as an exciting beginning. They anticipate that their tool will be used to learn more about the roles of localization in protein function and mis-localization in disease. In addition, they are interested in expanding the model's localization predictions to include more types of compartments, testing more therapeutic hypotheses, and designing increasingly functional proteins for therapies or other applications.

"Now that we know that this protein code for [localization](#) exists, and that machine learning models can make sense of that code and even create functional proteins using its logic, that opens up the door for so many potential studies and applications," Kilgore says.

More information: Henry R. Kilgore et al, Protein codes promote selective subcellular compartmentalization, *Science* (2025). DOI: [10.1126/science.adq2634](https://doi.org/10.1126/science.adq2634)

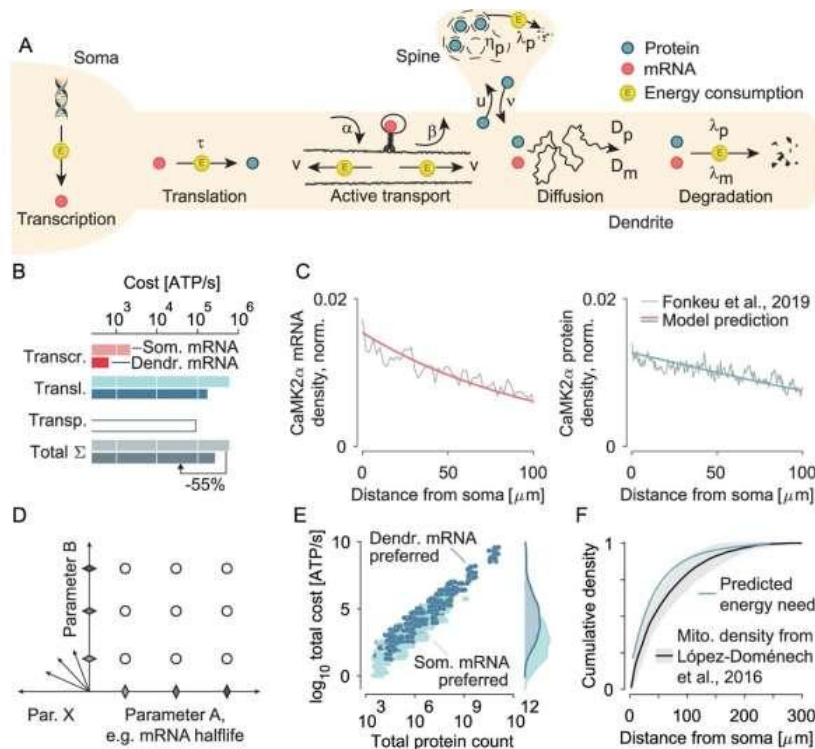
Journal information: [Science](#)

Provided by [Whitehead Institute for Biomedical Research](#)

FEBRUARY 7, 2025

Nerve cells optimize energy by controlling mRNA and protein distribution, study finds

[University Hospital of Bonn](#)



Molecular processes and their individual energy expenditures. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-56640-0

Nerve cells have amazing strategies to save energy and still perform the most important of their tasks. Researchers from the University Hospital Bonn (UKB) and the University of Bonn as well as the University Medical Center Göttingen found that the neuronal energy conservation program determines the location and number of messenger RNA (mRNA) and proteins and differs depending on the length, longevity and other properties of the respective molecule. The work has now been [published](#) in *Nature Communications*.

We have all experienced the need to save energy in recent years. To do this, we all had to come up with strategies to save energy while still meeting our most important needs.

"Our [nerve cells](#) are facing a similar dilemma: They have to supply their synapses, i.e., their contact points with other neurons, but also organize their [protein synthesis](#) in such a way that they don't produce too much or too little proteins.

"At the same time, they have to transport the proteins over long distances to the synapses and also pay attention to their energy budget. How do they manage this?" asked the research team.

Energy-saving measures explain protein distributions

Despite its relatively small size, the brain consumes about 20% of the body's total energy. As with all cells, neuronal functions are subject to strict energy constraints, which are particularly pronounced in the brain due to its high energy requirements. The research team was able to show that the synthesis and degradation of all neuronal molecules represents a

particularly high cellular energy expenditure and therefore requires energy-saving measures.

All cells, including neurons, require proteins to function properly. These are produced through a process known as gene expression, in which the relevant information is copied from a gene into messenger RNA (mRNA). The mature mRNA is then translated into the required protein.

Thanks to advances in biochemistry and microscopy, it is now possible to precisely map the location of individual mRNA copies and the corresponding proteins in cells and quantify the number of thousands of mRNA and protein species. For the first time, this enables researchers to study complex organizational principles that control spatial gene expression patterns and apply them across all types of molecules.

The research team, led by corresponding author Prof. Tatjana Tchumatchenko, research group leader at the Institute for Experimental Epileptology and Cognition Research at the UKB, combined [experimental data](#) from more than 10 large-scale mRNA and proteomics screens involving tens of thousands of molecular species.

"We found that the drive to conserve energy determines mRNA and protein number and location, affecting each molecular species differently depending on the length, lifetime and other properties of the molecule," explains first author Cornelius Bergmann, a Ph.D. student of the University Bonn at the Institute of Experimental Epileptology and Cognition Research at the UKB.

The results show that the energetic costs for synthesis, transport and degradation of molecules, their spatial localization and the total number are limited to energy-efficient solutions. "If certain short-lived proteins were synthesized in the cell body, a large proportion of them would not arrive alive at the synapses due to the long travel time," adds Prof. Tchumatchenko. "This would be a waste of energy on proteins that cannot fulfill their task."

The [model calculations](#) in the present study show that proteins are therefore preferably synthesized in the branched, tapering extensions of a nerve cell, the so-called dendrites, if the energy loss "on the way" from the cell body to the synapses is greater than the energy required to transport the mRNA into the dendrites.

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New perspective on gene expression studies

However, the research team's findings go beyond energy conservation. "Our results shed light on the organizational principles of [gene expression](#) in cells that act across different molecular species and go beyond individual regulatory mechanisms," says co-author Prof. Silvio Rizzoli, Director of the Department of Neuro- and Sensory Physiology at the

University Medical Center Göttingen, spokesperson of the Center for Biostructural Imaging of Neurodegeneration (BIN).

The most surprising result for the research team was that the physical properties of proteins, such as length or lifetime, and not their specific function, have such a strong influence on the energy budget and thus on the site of their synthesis.

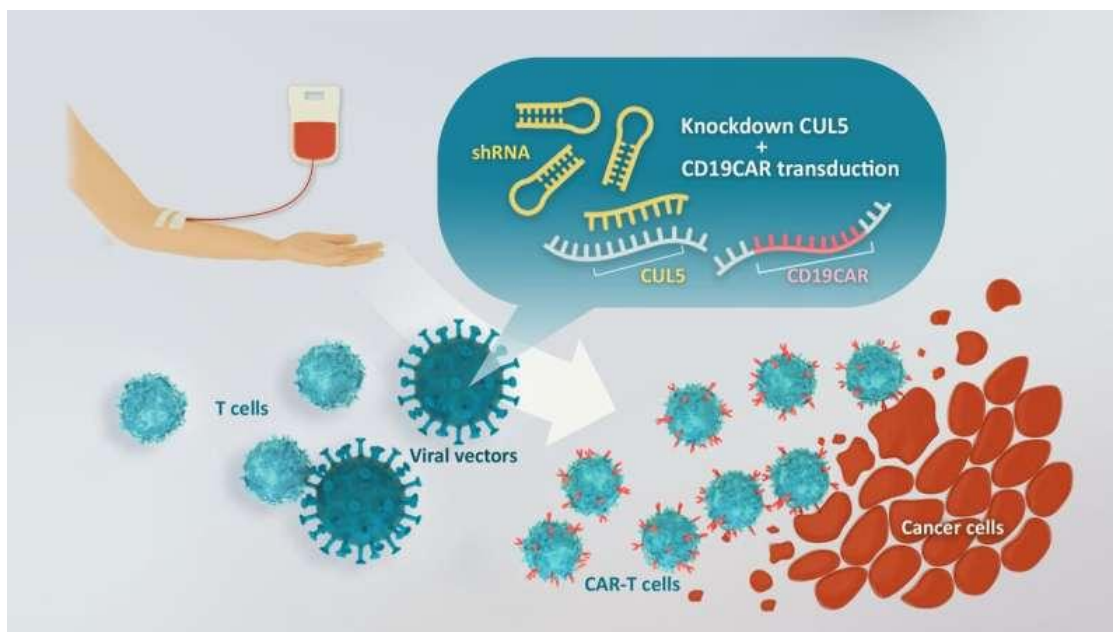
Co-author Kanaan Mousaei, a doctoral student of the University Bonn at the Institute of Experimental Epileptology and Cognition Research at the UKB, emphasizes, "Our model offers a new perspective for correlating dozens of existing data sets from different laboratories."

More information: Cornelius Bergmann et al, How energy determines spatial localisation and copy number of molecules in neurons, *Nature Communications* (2025). [DOI: 10.1038/s41467-025-56640-0](https://doi.org/10.1038/s41467-025-56640-0)

Journal information: [Nature Communications](#)
Provided by [University Hospital of Bonn](#)

FEBRUARY 7, 2025

Gene modification can encourage T cell growth, improving cancer treatment's success rate by [Nagoya University](#)



Knockdown of CUL5 gene enhances CAR-T cells' proliferation and survival compared to conventional CAR-T cells, making them better at fighting cancer. Credit: Reiko Matsushita

Researchers have identified a method to enhance the effectiveness of a promising cancer treatment. They found that modifying a specific gene improves the ability of immune cells to combat cancer for an extended period, potentially reducing the chance of cancer recurring.

The finding that reduced CUL5 gene activity increases CAR-T cell anticancer effects could improve treatment for patients with aggressive cancers such as leukemia, lymphoma, and multiple myeloma. The study was [published](#) in *Nature Communications* by a group led by Yoshitaka Adachi, Seitaro Terakura, and Professor Hitoshi Kiyoi of Nagoya University's Graduate School of Medicine in Japan.

CAR-T cell therapy is an advanced cancer treatment in which the patient's own immune cells (T cells) are genetically modified in a laboratory. A "[chimeric antigen receptor](#)" (CAR) is given to these cells, enabling them to target and eliminate [cancer cells](#). The researchers focused on a CAR that targeted the CD19 protein found in B cells, a type of immune cell that can become cancerous in diseases such as leukemia.

Although clinicians have successfully used this therapy for treatment, many patients experience cancer relapse caused by the hostile environment created by cancerous cells. After repeated encounters with cancer cells, CAR-T cells lose their ability to divide and effectively attack the tumor.

Altering genes to improve efficacy

The research team used a method called CRISPR screening to identify potential genes that could improve CAR-T cell therapy. CRISPR allows scientists to turn off individual genes in cells to see which are important for a specific function.

The gene of interest, CUL5, is involved in the breakdown of certain proteins inside cells. When this gene is inactive, a cell signaling pathway, known as the JAK-STAT signaling pathway, becomes more sustained. This pathway sends signals that encourage T cells to grow and multiply, making them better at fighting cancer.

The researchers discovered that turning off the CUL5 gene improves CAR-T cell growth and longevity, even after repeated exposure to cancer cells. When the team tested their modified CAR-T cells in mice with B-cell lymphoma, the most common cancer in humans, they found that they were much more effective in shrinking tumors and keeping cancer from coming back than regular CAR-T cells.

A new way to create targeted cells

Traditionally, creating these CUL5-deficient cells requires a process called electroporation, which uses electrical pulses to introduce changes into cells. However, this method can damage cells and is not practical for treating large numbers of patients.

The Nagoya University researchers developed a new way to partially reduce CUL5 activity by using a virus to deliver [genetic material](#) to CAR-T cells. "We achieved the CAR-transfection and shCUL5 transduction at once by virus transfection," Terakura said. "As the T lymphocytes were not subjected to electroporation, they remained healthy after transfection."

This discovery points to a way to make cancer treatment more effective. It may become possible to increase the efficacy of CAR-T cell therapy in treating blood cancers such as lymphoma and leukemia. The modified CAR-T cells not only fight tumors better but could also stay active in the body longer, reducing the chances the cancer will come back.

The research team is now investigating whether this same gene-modification approach could help treat other cancers, especially [solid tumors](#) like those found in organs, which have been particularly challenging to treat with current methods.

More information: Yoshitaka Adachi et al, Cullin-5 deficiency promotes chimeric antigen receptor T cell effector functions potentially via the modulation of JAK/STAT signaling pathway, *Nature Communications* (2024). DOI: [10.1038/s41467-024-54794-x](https://doi.org/10.1038/s41467-024-54794-x)

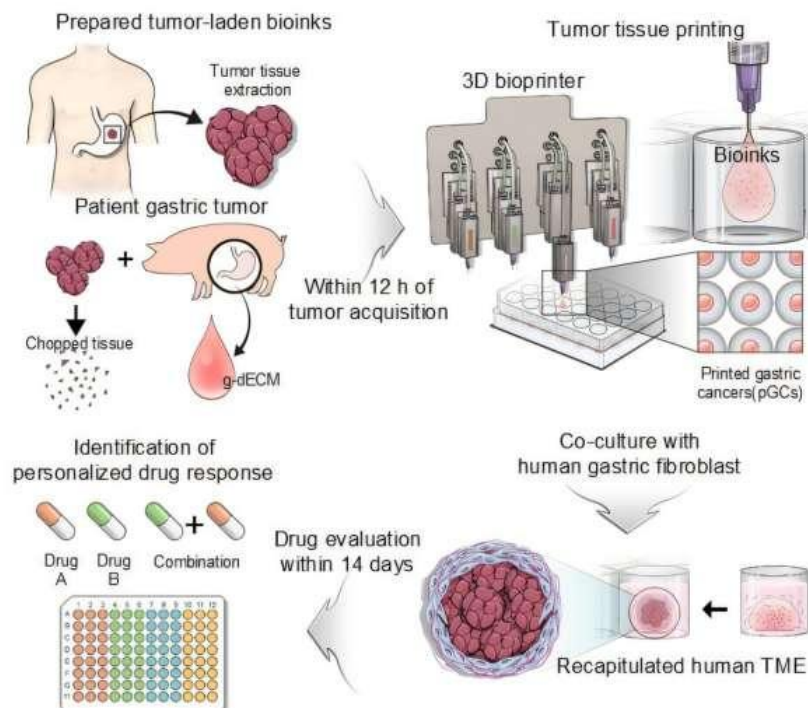
Journal information: [Nature Communications](#)

Provided by [Nagoya University](#)

FEBRUARY 7, 2025

3D bioprinting technology could lead to personalized gastric cancer treatment

by [Pohang University of Science and Technology](#)



Recreating the Tumor Microenvironment with Bioprinting Technology for Personalized Drug Response Identification and Prediction. Credit: POSTECH

A collaborative research team from POSTECH has successfully developed a gastric cancer model using 3D bioprinting technology and patient-derived cancer tissue fragments. This innovative model preserves the characteristics of actual patient tissues and is expected to rapidly evaluate and predict individual patient drug responses. The research has been [published](#) in the journal *Advanced Science*.

Tumor heterogeneity poses a significant challenge in the development and [treatment](#) of cancer therapies, as patient responses to the same [drug](#) varies, and the timing of treatment is a critical factor influencing prognosis. Therefore, technologies that predict the efficacy of anticancer treatments play a vital role in minimizing side effects and enhancing treatment efficiency.

Existing approaches, such as gene panel-based tests and patient-derived xenograft (PDX) models, are limited in their applicability to certain patients, have constraints in predicting drug effects, and require substantial time and costs to establish.

In this study, the research team developed an in vitro gastric cancer model by leveraging 3D bioprinting technology and tissue-specific bioink incorporating patient-derived tissue fragments.

Notably, they encapsulated cancer tissues within a stomach-derived decellularized extracellular matrix (dECM) hydrogel, artificially enabling cell-matrix interactions. By co-culturing these tissues with human gastric fibroblasts, they successfully mimicked cancer cell-stroma interactions, thereby recreating the in vivo tumor microenvironment in vitro.

This model demonstrated the ability to preserve the unique characteristics of gastric tissues from individual patients by replicating both cell-stroma and cell-matrix interactions. It exhibited high specificity in predicting the patient's anticancer drug responses and prognosis. Furthermore, the model's gene profiles related to cancer development, progression, and drug response closely resembled those of patient tissues, surpassing the performance of conventional PDX models.

Additionally, the rapid fabrication method of this model via bioprinting enables drug evaluation within two weeks of tumor [tissue](#) extraction from the patient. This efficient platform is anticipated to significantly contribute to the development of personalized cancer treatments.

Professor Charles Lee from The Jackson Laboratory for Genomic Medicine, who led the study, expressed his expectations for the model, "By reproducing [cancer](#) cell-stroma and cell-matrix interactions, this model enhances the accuracy of drug response predictions and reduces unnecessary drug administration to non-responsive patients."

Professor Jinah Jang of POSTECH emphasized the significance of the research, saying, "This is a critical preclinical platform not only for developing patient-specific treatments but also for validating new anticancer drugs and combination therapies."

More information: Yoo-mi Choi et al, Prediction of Patient Drug Response via 3D Bioprinted Gastric Cancer Model Utilized Patient-Derived Tissue Laden Tissue-Specific Bioink, *Advanced Science* (2025). [DOI: 10.1002/adv.202411769](https://doi.org/10.1002/adv.202411769)

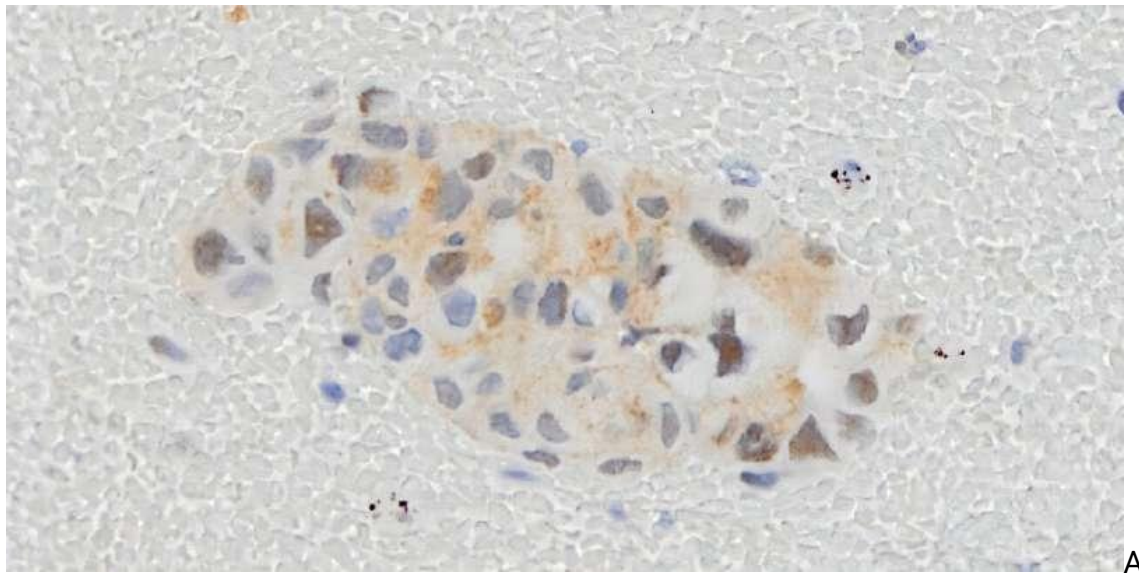
Journal information: [Advanced Science](#)

Provided by [Pohang University of Science and Technology](#)

FEBRUARY 7, 2025

Weakness in lung cancer's defenses found—an enzyme that boosts cancer cell metabolism

[Harvard Medical School](#)



microscope image of lung cancer cells (purple) containing the activated form of a metabolic enzyme called GUK1 (brown) that supports cancer growth. Credit: Haigis lab
Lung cancer is a particularly challenging form of cancer. It often strikes unexpectedly and aggressively with little warning, and it can shapeshift in unpredictable ways to evade treatment.

While researchers have gleaned important insights into the basic biology of [lung cancer](#), some of the disease's molecular maneuvers have remained elusive.

Now, a team led by scientists at Harvard Medical School has made strides in understanding how a genetic flaw in some lung cancers alters cancer cell metabolism to fuel the disease.

Working with mouse models and human cancer cells, the researchers identified a [metabolic enzyme](#) called GUK1 in lung cancers harboring an alteration in the ALK gene. Their experiments showed that GUK1 plays an important role in boosting metabolism in [tumor cells](#) to help them grow.

The findings, [reported](#) Feb. 6 in *Cell*, provide a clearer picture of how metabolism works in lung cancer.

The research could set the stage for developing therapies that target GUK1 to curb cancer growth, the team said.

Lung cancer: A formidable foe

As a thoracic oncologist at Massachusetts General Hospital, co-first author Jaime Schneider regularly treats patients with lung cancer, and sees firsthand how aggressive and persistent the disease can be.

"A huge percentage of patients I see in the clinic do well for some period of time on the currently available therapies, but eventually relapse," said Schneider, who is also an instructor of medicine in [cell biology](#) at HMS.

ADVERTISING

Lung cancer is the leading cause of cancer deaths in the United States and worldwide, and, Schneider noted, cases are increasing among never-smokers and former light smokers for reasons that remain poorly understood.

Schneider's patients—many of whom donated tumor samples for the study—inspired her to learn more about the molecular underpinnings of the disease.

"We need to be thinking outside the box to gain a better understanding of disease biology in lung cancer, and to identify new therapeutic targets," she said.

Schneider joined the lab of senior author Marcia Haigis, a professor of cell biology in the Blavatnik Institute at HMS, who studies how metabolic shifts can accelerate aging and drive disease. While working in the Haigis lab, Schneider connected with co-first author Kiran Kurmi, then a research fellow who has a background in biochemistry and cancer cell signaling.

Cancer cells must change their metabolism in order to continue growing and surviving amid attacks mounted by the immune system and cancer treatments, Haigis explained.

"Our goal was to understand how specific cancer gene aberrations might directly rewire [metabolic pathways](#) to enable [cancer growth](#)," she said.

Haigis deems cancer metabolism an emerging area in cancer research, and one that could inform the design of a new generation of precision cancer therapies targeted directly at the cellular processes that ignite tumor growth.

Metabolic detectives on the case

The researchers set out to study lung cancers caused by an alteration in the ALK gene that leads to the production of an abnormal ALK protein. First, they screened the metabolic

proteins present in these ALK-positive cancers, and identified GUK1 as one of particular interest.

"We were really intrigued by what the interaction between ALK and GUK1 means—and like metabolic detectives, that's what we followed," Haigis said.

Next, they conducted a series of experiments in mice and patient-derived cancer cells to explore GUK1's contribution to metabolic changes in ALK-positive cancer cells.

The scientists determined that GUK1 is an enzyme that helps abnormal ALK proteins make a molecule called GDP, a precursor to the energy-rich molecule GTP that cancer cells need for tasks such as dividing and making proteins. When the researchers disabled GUK1, cancer cell growth slowed considerably, suggesting that ALK-positive cancers become highly dependent on this enzyme as their molecular fuel for mischief.

"GUK1 turned out to be a metabolic liability in this subset of lung cancer that facilitates tumor growth and survival," Schneider said.

The team also found evidence of elevated GUK1 levels in additional subtypes of lung cancer, suggesting that the enzyme may play a role in lung cancers driven by other genetic defects.

"By focusing on the basic biology of lung cancer, we were able to identify a new metabolic mechanism that is important in the disease," Haigis said.

Just the beginning

The researchers note there is a lot more to be uncovered about GUK1 in cancer. They are interested in exploring how many types of cancer are driven by GUK1 in some way. They also want to understand in greater detail how inhibiting GUK1 affects cancer cells. Finally, given that many patients with lung cancer eventually relapse, they want to study whether and how GUK1 helps cancer cells metabolically reprogram themselves to sidestep treatment.

If GUK1 is indeed a key enzyme that gives various cancers the metabolic boost they need to grow quickly and persistently, it could be a compelling target for new cancer therapies.

"We hope that identifying distinct metabolic vulnerabilities like GUK1 will open up new avenues for therapeutic targeting in cancer patients in the future," Schneider said.

More information: Jaime L. Schneider et al, GUK1 activation is a metabolic liability in lung cancer, *Cell* (2025). [DOI: 10.1016/j.cell.2025.01.024](https://doi.org/10.1016/j.cell.2025.01.024)

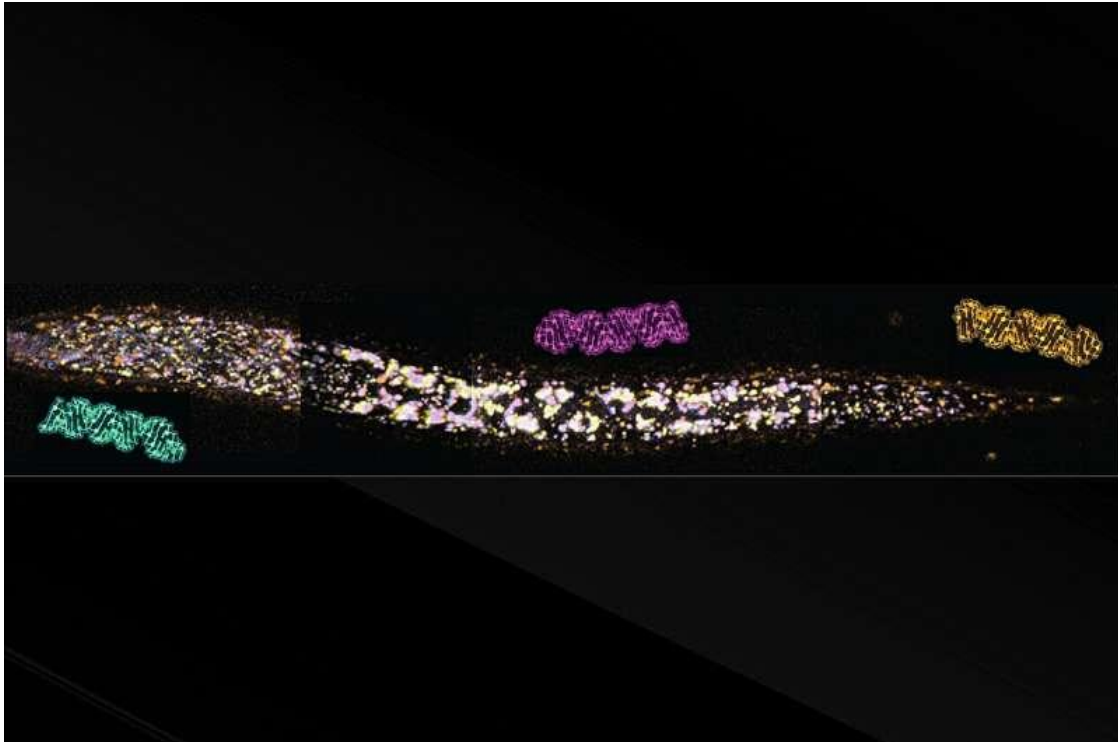
Journal information: [Cell](#)

Provided by [Harvard Medical School](#)

FEBRUARY 5, 2025

Study reveals how RNA travels between cells to control genes across generations

by [University of Maryland](#)



Multiple forms of double-stranded RNA (blue, magenta, orange structures) cross cell membranes with the help of a conserved protein located in novel sites (colored by depth) throughout the roundworm's body. Credit: Antony Jose, University of Maryland Department of Cell Biology and Molecular Genetics

RNA-based medicines are one of the most promising ways to fight human disease, as demonstrated by the recent successes of RNA vaccines and double-stranded RNA (dsRNA) therapies. But while health care providers can now successfully develop drugs that use dsRNA to accurately target and silence disease-causing genes, a major challenge remains: getting these potentially life-saving RNA molecules into cells efficiently.

A [new study](#) published in the journal *eLife* on February 4, 2025, may lead to breakthroughs in RNA-based drug development.

University of Maryland researchers used microscopic roundworms as a model to investigate how dsRNA molecules naturally enter cells and influence many future generations. The

team discovered multiple pathways for dsRNA to enter the worms' cells—a finding that could help improve drug delivery methods in humans.

"Our findings challenge previous assumptions about RNA transport," said the study's senior author Antony Jose, an associate professor of cell biology and molecular genetics at UMD. "We've learned that RNA molecules can carry specific instructions not just between cells but across many generations, which adds a new layer to our current understanding of how inheritance works."

The team found that a protein called SID-1, which acts as a gatekeeper for the transfer of information using dsRNA, also has a role in regulating genes across generations.

When researchers removed the SID-1 protein, they observed that the worms unexpectedly became better at passing changes in [gene expression](#) to their offspring. In fact, these changes persisted for over 100 generations—even after SID-1 was restored to the worms.

"Interestingly, you can find proteins similar to SID-1 in other animals, including humans," Jose noted.

"Understanding SID-1 and its role has significant implications for human medicine. If we can learn how this protein controls RNA transfer between cells, we could potentially develop better targeted treatments for human diseases and perhaps even control the inheritance of certain disease states."

The research team also discovered a gene called *sdg-1* that helps regulate "jumping genes"—DNA sequences that tend to move or copy themselves to different locations on a chromosome.

While jumping genes can introduce new genetic variations that may be beneficial, they are more likely to disrupt existing sequences and cause disease. The researchers found that *sdg-1* is located within a jumping gene but produces proteins that are used to control [jumping genes](#), creating a self-regulating loop that could prevent unwanted movements and changes.

"It's fascinating how these [cellular mechanisms](#) maintain this delicate balance, like a thermostat keeping a house at just the right temperature so it isn't too warm or too cold," Jose explained. "The system needs to be flexible enough to allow some 'jumping' activity while preventing excessive movements that could harm the organism."

Jose believes the team's findings provide valuable insights into how animals regulate their own genes and maintain stable gene expression across generations. Studying these mechanisms could potentially pave the way for innovative future treatments for heritable diseases in humans.

Looking ahead, the team plans to investigate mechanisms related to the transport of different types of dsRNA, where SID-1 is localized and why certain genes are being regulated across generations while others are not.

"We're just scratching the surface," Jose said. "What we discovered is just the beginning of understanding how external RNA can cause heritable changes that last for generations. This work will help scientists better understand how to design and deliver RNA-based medicines to patients more effectively."

More information: Nathan M Shugarts Devanapally et al, Intergenerational transport of double-stranded RNA in *C. elegans* can limit heritable epigenetic changes, *eLife* (2025). DOI: [10.7554/eLife.99149.3](https://doi.org/10.7554/eLife.99149.3)

Journal information: [eLife](#)

Provided by [University of Maryland](#)

Scientists Just Made Bacteria 1000x Bigger – And Discovered Something Incredible

BY BOSTON CHILDREN'S HOSPITAL FEBRUARY 10, 2025



By expanding bacteria 1000x, scientists have unlocked a new way to study their gene expression and behavior. This revolutionary imaging technique reveals how bacteria respond to their environment, adapt to stress, and resist antibiotics—all in real time. (Artist's concept.) Credit: SciTechDaily.com

By combining MERFISH imaging with expansion microscopy, researchers have unlocked a new way to study bacteria at the single-cell level.

This allows them to see how bacteria activate different genes in response to their environment, offering insights into microbial behavior, antibiotic resistance, and infection strategies.

How Bacteria Organize Their Activities

How do bacteria — whether beneficial ones in our bodies or harmful disease-causing strains — coordinate their activities? A recent study has provided new insights by combining advanced genomic-scale microscopy with an innovative technique to track which genes bacteria activate in different conditions and environments. Published recently in the journal *Science*, this breakthrough is set to advance bacterial research significantly.

Jeffrey Moffitt, PhD, and his colleagues at the Program in Cellular and Molecular Medicine (PCMM) at Boston Children's Hospital used MERFISH, a molecular imaging technique Moffitt helped develop, to analyze messenger RNAs (mRNAs) in thousands of individual bacteria at once. This method not only mapped gene expression on a massive scale but also revealed how spatial factors influence which genes bacteria turn on — something never before achieved.



Hundreds of messenger RNAs in a single E. coli cell. Credit: Ari Safatis/Boston Children's Hospital

Overcoming the Challenges of Imaging Bacteria

However, the team first had to overcome a major challenge: bacterial RNAs, or the bacterial transcriptome, are densely packed inside tiny cells, making them difficult to distinguish and image. “It was a complete disaster, we couldn’t see anything,” says Moffitt.

Borrowing a technique developed in the laboratory of Ed Boyden, PhD, at MIT—expansion microscopy—they embedded the samples in a special hydrogel. They anchored the RNAs to this gel and changed the chemical buffer in the gel. This triggered it to swell, expanding the sample 50- to 1000-fold in volume. “All the bacterial RNAs become individually resolvable,” Moffitt says.

Why Measure Bacterial Gene Expression?

Until now, scientists have averaged bacterial behavior across a given bacterial population. The ability to determine what genes individual bacteria are using can give powerful new insights into bacterial interactions, virulence, stress responses, the ability to resist antibiotics, the ability to form biofilms like those in catheters and more.

“We now have the tools to answer fascinating questions about host-microbe and microbe-microbe interactions,” Moffitt says. “We can explore how bacteria might communicate and compete for spatial niches and define the structure of microbial communities. And we can ask how pathogenic bacteria adjust their gene expression as they infect mammalian cells.”

Bacterial-MERFISH can also provide insights into bacteria that are difficult to grow in a culture dish. “Now we don’t have to culture them, we can just go image them in their native environment,” Moffitt says.

Single-Cell Insights into Bacterial Survival Strategies

Several experiments the team performed illustrate the kinds of questions that bacterial-MERFISH can answer. For example, Moffitt and colleagues were able to show that individual *E. coli*, when starved of glucose, try utilizing alternative food sources one after another, altering their gene expression in a specific sequence. Taking a series of genomic snapshots over time enabled the team to piece together this survival strategy.

The team also got insights into how bacteria organize their RNAs within their cells, which may be important in how different aspects of gene expression are regulated. Finally, they showed that intestinal bacteria tap different genes depending on their physical location in the colon.

A New Era in Bacterial Research

“The same bacteria could be doing very different things over a space of tens of microns,” Moffitt says. “They’re seeing different environments and responding differently to them. It was very difficult to address such variation before, but now we can answer the types of questions people have been dreaming about.”

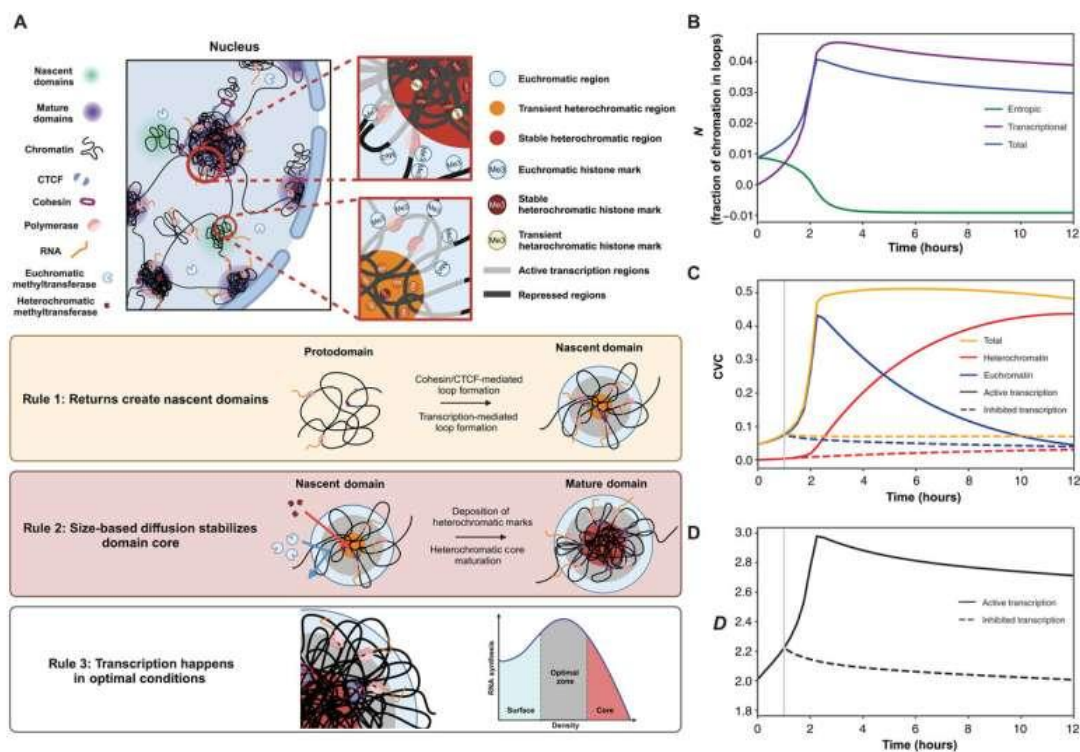
Reference: “Highly multiplexed spatial transcriptomics in bacteria” by Ari Sarfatis, Yuanyou Wang, Nana Twumasi-Ankrah and Jeffrey R. Moffitt, 24 January 2025, *Science*. DOI: [10.1126/science.adr0932](https://doi.org/10.1126/science.adr0932)

The paper’s coauthors were Ari Sarfatis, Yuanyou Wang, PhD, and Nana Twumasi-Ankrah in the Moffitt Lab.

FEBRUARY 10, 2025

Chromatin fiber's genomic 'memory' governs the building blocks of life, study reveals

by Olivia Dimmer, [Northwestern University](https://www.northwestern.edu)



Credit: *Science Advances* (2025). DOI: [10.1126/sciadv.adq6652](https://doi.org/10.1126/sciadv.adq6652)

Northwestern Medicine scientists have discovered new details about how the human genome produces instructions for creating proteins and cells, the building blocks of life, according to a pioneering new study [published](https://doi.org/10.1126/sciadv.adq6652) in *Science Advances*.

While it's understood that genes function as a set of instructions for creating RNA, and thus proteins and cells, the fundamental process by which this occurs has not been well-studied due to technological limitations, said Vadim Backman, Ph.D., the Sachs Family Professor of Biomedical Engineering and Medicine, who was senior author of the study.

"It is still not fully understood how, despite having the same set of genes, cells turn into neurons, bones, skin, heart, or roughly 200 other kinds of cells, and then exhibit stable cellular behavior over a human lifespan which can last for more than a century—or why aging degrades this process," said Backman, who directs the Center for Physical Genomics and Engineering at Northwestern. "This has been a long-standing open question in biology."

Igal Szleifer, Ph.D., professor of Medicine in the Division of Pulmonary and Critical Care, and Luay Almassalha, MD, Ph.D., a fellow in gastroenterology and hepatology, were co-authors of the study.

In the study, investigators utilized nanoscale imaging and sensing technologies along with modeling techniques developed at Northwestern to individually label and observe chromatin fibers: the bundle of DNA and proteins that form chromosomes within the nucleus of cells.

The scientists observed that chromatin self-organizes into "packing domains"—distinct, compact regions of molecular structures that play a crucial role in regulating gene expression.

"In the nucleus of each cell, the genome is folded in such a way as to form thousands of tiny nanoscale 'packing domains,' the three-dimensional structure of which creates 'memories' of transcription and which, amazingly, operates as a powerful geometric computational device—just like the reinforcement learning that powers [neural networks](#) in AI tools like ChatGPT and the behavior of cells in our brains," said Backman, who is also Associate Director for Engineering and Technology at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

The findings show that cells use transcriptional memories to establish predictable, stable behaviors within tissues, Backman said. These genetic memories can degrade over time, resulting in a wide array of diseases associated with aging, including autoimmune disorders, cancer, Alzheimer's and atherosclerosis.

"The discovery of how transcriptional memories are encoded potentially explains how and where to reverse these processes and could lead to entirely new kinds of therapies targeting cancer, enhancing tissue regeneration, and promoting longevity by developing strategies to preserve or even reprogram these transcriptional memories," Backman said.

"Even just focusing on cancers alone, this has significant implications," Almassalha said.

Previously, Backman had found that in every type of cancer, chromatin packing domains are disrupted. Understanding the rules of this geometric system gives investigators insight into why cancers form and how they can rapidly evade treatments.

"Unlike mutations, domains can both be used to store information for decades and be transformed in minutes, so cancer cells have an 'extra gear' that our other cells just can't match," Almassalha said. "We can now design therapies to slow down the calculations in [cancer](#) cells while speeding up the calculations immune cells can do—potentially leveling the playing field."

On the heels of this discovery, Backman and his collaborators will begin work to translate the findings into practical applications for health and disease and explore the development of powerful new computational techniques designed on the principles of geometric genomic calculation.

"The findings could also inspire efforts in [synthetic biology](#), potentially enabling the design of artificial organisms with custom-built transcriptional memories," Backman said.

The Center for Physical Genomics and Engineering will also explore whether similar structures and processes exist in other complex organisms such as plants or fungi and study the evolutionary implications.

"This may provide insights into the evolution of species over millions of years as genome geometries became more complex and computationally powerful," Vadim said.

More information: Luay M. Almassalha et al, Chromatin conformation, gene transcription, and nucleosome remodeling as an emergent system, *Science Advances* (2025). [DOI: 10.1126/sciadv.adq6652](https://doi.org/10.1126/sciadv.adq6652)

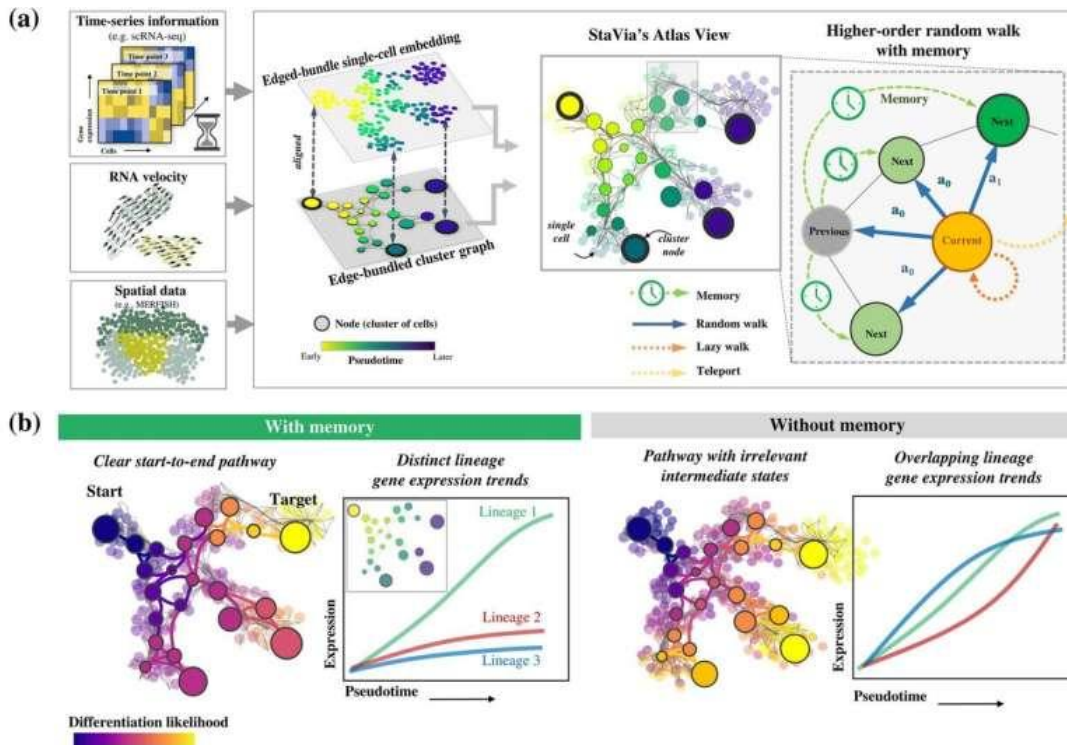
Journal information: [Science Advances](#)

Provided by [Northwestern University](#)

FEBRUARY 10, 2025

Advanced computational tool reveals cellular development processes

by [The University of Hong Kong](#)



The human body is a key subject of research by scientists worldwide. A biomedical engineering research team led by Professor Kevin Tsia, program director of the Biomedical Engineering Program under the Faculty of Engineering of the University of Hong Kong (HKU), has created an all-in-one large-scale computational framework—StaVia—to unlock the vast information hidden in human cells.

Professor Tsia's team collaborated with Professor Joshua Ho and Professor Yuanhua Huang, both from the School of Biomedical Sciences at the Li Ka Shing Faculty of Medicine of HKU (HKUMed). They successfully applied the tool in analyzing the development process of zebrafish embryos—tracking the growth and development from a single cell into a complete organism.

This study, now [published](#) in *Genome Biology*, aids in understanding cellular growth and diseases. Despite the apparent differences between humans and zebrafish, a surprising number of similarities exist. In fact, 70% of human genes can also be found in zebrafish.

"StaVia's findings are significant because they allowed us to explore the entire development of zebrafish embryos, from 10 hours to 10 days fertilization, in detail for the first time. This includes previously overlooked [cell types](#), providing new insights into how different cells form and develop, which could lead to better understanding of growth and development in other organisms, too.

"For example, how does the embryo develop its nervous system (including the brain and spinal cord), the skin, and sensory organs (e.g., eye, ears, and olfactory organ). It's a one-of-a-kind method, allowing us to map out the timeline of development at high resolution," said Professor Kevin Tsia from the Department of Electrical and Electronic Engineering, who is also the Program Director of the Faculty of Engineering's Biomedical Engineering Program.

Significance in developmental biology research

The key developer of StaVia, Dr. Shobana V Stassen, explained, "Another important and unique feature of StaVia is that it represents a new frontier in the field called 'spatiotemporal omics,' from which we can analyze spatial information of physical tissue structure, omics data of cells therein and their time evolution all simultaneously. In StaVia, we could craft an intuitive 'metro-map' for us to analyze the temporal trajectory and spatial habitats of cells in tissues or organs."

Comprising rich information of single cells at high precision, omics data are crucial for probing the properties of cells, and tracking their transformation to gauge the disease progression. The immense value of measuring omics data of cells has been driving a number of global research initiatives (including the U.S., Europe and Asia) to create "cell atlases" of different parts of the human body.

These detailed maps help scientists to study tissues and organs in extraordinary detail—transforming the understanding of how cells develop and function. However, as the data size and diversity of these atlases increase, analyzing them becomes more challenging. The complexity and size make it difficult to clearly track how different cell types form and change over time, and even visualizing this information is also a struggle.

"StaVia synergizes multi-faceted [single-cell](#) omics data, regardless of its complexity, to map the intricate paths the cells take as they develop and change in different biological processes, including embryo development. Our tool works very well with large-scale cell atlases, maintaining all the intricate details embedded in omics data, making it easy and intuitive for scientists to understand complex cell behaviors over time and space," said Professor Tsia.

"It can discover elusive cell lineages and rare cell fates in a variety of biological processes that can hardly be discovered by other methods, providing hints on how diseases evolve."

Advancing fundamental biological discovery

Professor Tsia's colleagues at HKUMed have already adopted StaVia in their cell-related research. "Cells matter because they are the fundamental unit of life. When you are sick, your cells are the source of the problem, and that's how I became interested in studying cells. If you want to know more about something, you should start with the root cause," said Professor Tsia.

Research groups around the world are trying to understand how human health and disease evolve at the cell level. "It may sound simple, seem like information carried in textbooks. But in fact, all along no one has had a clear understanding of the matter," said Professor Tsia.

With vast unknowns about the cell atlases in the human body, StaVia can be applied in basic biological or fundamental research, generating new insights and knowledge for biologists or biomedical scientists. Pertinent discoveries could help address global issues such as aging.

"Brain disease is another hot topic. There is research focusing on how human brain cells and their omics changed over time, say from 50 to 80 years old. The overall goal is to identify the signature and key drivers of aging, and eventually to develop drugs that could treat aging-related brain diseases," said Professor Tsia, whose team is also involved in joint projects on similar topics with universities in the U.S.

He describes StaVia as the third generation of the computational tool he and his team, including doctoral students and post-docs, had developed. "We began jumping into the area of omics back in 2019," he recalled.

Currently, he is continuing collaborations with HKUMed on studying the progress of cancer using StaVia, tracking the evolution of cells from the early stage to the late stage of the disease.

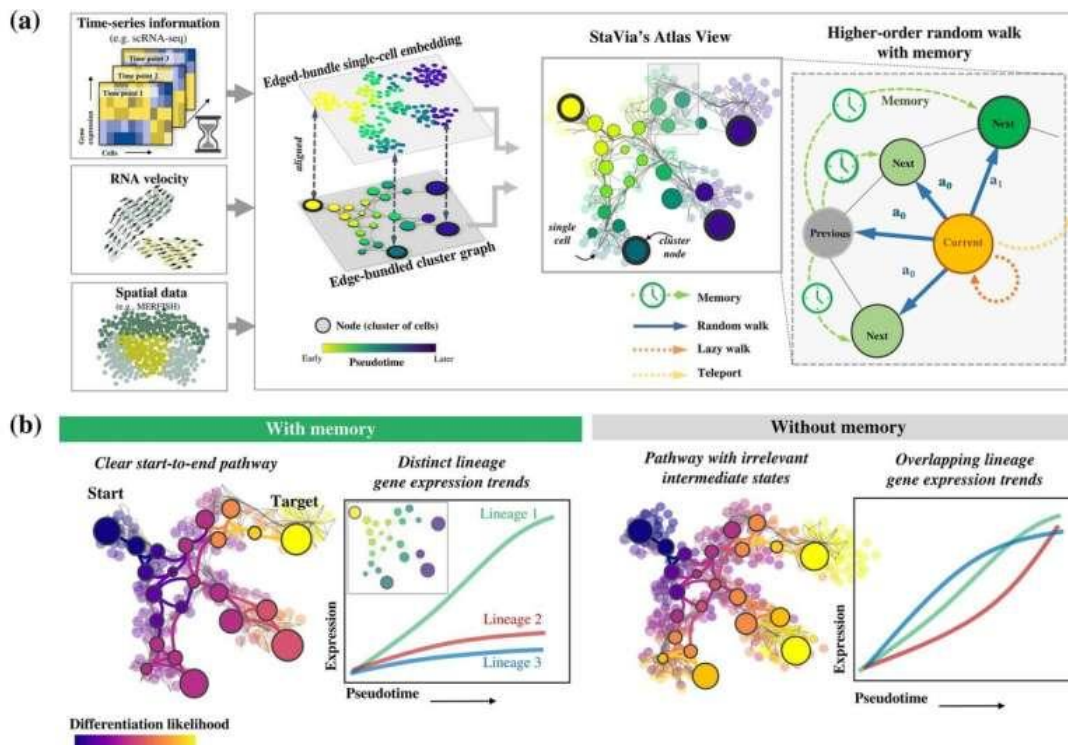
More information: Shobana V. Stassen et al, StaVia: spatially and temporally aware cartography with higher-order random walks for cell atlases, *Genome Biology* (2024). [DOI: 10.1186/s13059-024-03347-y](https://doi.org/10.1186/s13059-024-03347-y)

Journal information: [Genome Biology](#)
Provided by [The University of Hong Kong](#)

FEBRUARY 10, 2025

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Overview

of StaVia. Credit: *Genome Biology* (2024). DOI: 10.1186/s13059-024-03347-y

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Journal information: [Genome Biology](#)

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

FEBRUARY 10, 2025

How genetics, lifestyle promote cognitive health in older adults

by [University of Hawaii at Manoa](#)



Credit: Matthias Zomer from Pexels

For the first time, University of Hawai'i at Mānoa researchers have studied how work, volunteering and leisure activities affect brain health in older adults from diverse backgrounds, while also factoring in a genetic risk factor for Alzheimer's disease. The study, led by the Thompson School of Social Work & Public Health, shows that staying active can help keep the mind sharp with age.

Researchers examined the connection between these activities and [cognitive functioning](#), with a focus on the apolipoprotein E (APOE) $\epsilon 4$ allele—a genetic risk factor for Alzheimer's disease, using data from more than 7,600 participants in the Health and Retirement Study, a nationally representative survey.

The study is led by Yeonjung Jane Lee, assistant professor of social work, and was [published](#) in the *Journal of Alzheimer's Disease Reports*.

Key findings

The study found that working, volunteering and engaging in activities like word games, computer use and socializing improved cognitive health for everyone. However, the benefits

depended on genetics. For those without the APOE ϵ 4 allele, part-time work and high-intensity volunteering were most effective.

"Even if someone has the APOE ϵ 4 allele, modifiable factors like cognitively stimulating activities can promote cognitive health," said Lee. "These findings highlight how integrating such activities into [older adults'](#) lives can support aging well."

Researchers emphasize the importance of offering accessible activities to help reduce the impact of Alzheimer's disease and other dementias, particularly in diverse populations.

More information: Yeonjung Jane Lee et al, The association between activities and cognitive health: Stratified analysis by APOE ϵ 4 status, *Journal of Alzheimer's Disease Reports* (2024). DOI: [10.1177/25424823241290528](https://doi.org/10.1177/25424823241290528)
Provided by [University of Hawaii at Manoa](#)

The Role of Quantum Computing in Studying Animal Genomes

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Quantum computing is an emerging field that harnesses the principles of quantum mechanics to process information. Unlike classical computers, which use bits as the smallest unit of data, quantum computers use qubits, allowing for unprecedented processing power and speed. This power has significant implications for genomics, particularly in the study of animal genomes. By accelerating complex computations involved in genomic sequencing and analysis, quantum computing can transform our understanding of animal biology and evolution.

The Complexity of Animal Genomes

©Strings of different DNA strands, illustrating science and genetics. Image by Google DeepMind via Pexels.

Animal genomes are intricate and vast, consisting of billions of base pairs and thousands of genes. Each genome contains the blueprint for the biological make-up of species, influencing their development, behavior, and adaptation to environments. Traditional computational methods often struggle with the sheer scale and complexity presented by these genomes, making data analysis both time-consuming and resource-intensive. Quantum computing presents a potential solution by dramatically reducing the time required for complex genomic computations.

Quantum Computing: A New Frontier in Genomic Sequencing

©Dropper filling different test tubes. Image by Louis Reed via Unsplash.

Genomic sequencing is critical for decoding the genetic information within animal DNA, and quantum computing can significantly expedite this process. Traditionally, sequencing involves processing large data sets that correlate billions of potential genetic variations. With quantum computing's capability to perform multiple calculations simultaneously, researchers can handle these large datasets more efficiently, leading to faster sequencing times. This opens new possibilities for more comprehensive and timely genomic studies across numerous species.

Enhanced Data Analysis and Pattern Recognition

©Data being analyzed on a screen. Image by Stephen Dawson via Unsplash.

Beyond sequencing, understanding genomes involves analyzing complex patterns and relationships within genetic data. Quantum computing offers advanced pattern recognition and machine learning capabilities, which are beneficial in identifying genetic variations and predicting evolutionary changes. These capabilities enable scientists to uncover hidden biological insights, facilitating a deeper understanding of how genes influence traits and behaviors in animals. This could lead to advancements in areas like conservation biology and veterinary medicine.

Implications for Biodiversity and Conservation

Studying animal genomes is crucial for biodiversity conservation. By gaining insights into genetic diversity within species, researchers can better understand how animals adapt to changing environments and the challenges posed by human activities. Quantum computing can enhance these efforts by providing faster analyses and more accurate predictions about species vulnerability to extinction, informing more effective conservation strategies and policies to protect endangered species.

Challenges and Future Directions

While quantum computing holds great promise, there are still challenges to be addressed before it can be fully integrated into genomics. The technology is still in its early stages, requiring further development in hardware and algorithms to reach its full potential. Moreover, interdisciplinary collaboration is necessary to harness quantum computing effectively in genomics, combining expertise from quantum physicists, computer scientists, and biologists. As these fields converge, we can anticipate groundbreaking advancements in understanding and preserving animal life on Earth.

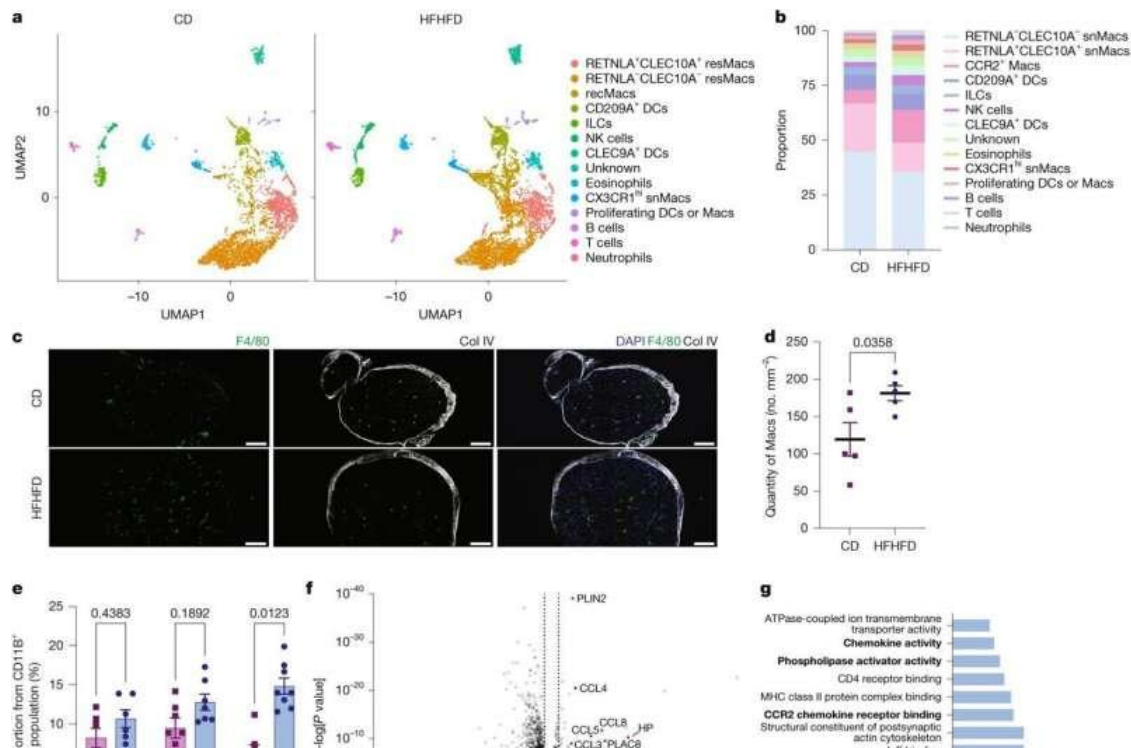
Conclusion

The role of quantum computing in studying animal genomes represents a frontier of scientific research with transformative potential. By speeding up genome sequencing and enhancing data analysis, this technology could revolutionize our understanding of genetics, evolution, and biodiversity. Although still in developmental stages, the future of quantum computing in genomics holds great promise for advancing animal science and addressing global challenges related to conservation and ecological health.

FEBRUARY 12, 2025

Discovery of macrophages' protective role for nerve damage opens new treatment path

by [Children's Hospital Boston](#)



CCR2⁺ macrophages infiltrate sciatic nerves of mice fed HFHFD and resMacs become pro-inflammatory. Credit: *Nature* (2025). DOI: 10.1038/s41586-024-08535-1

An increase in high-fat, high-fructose foods in people's diets has contributed to a dramatic increase in type 2 diabetes. This, in turn, has led to an increase in peripheral neuropathy—nerve damage, typically in the hands and feet—that causes weakness, loss of sensation and, in some, a stabbing, burning, or tingling pain. About half of people with type 2 diabetes are affected, and of these, about half experience severe neuropathic pain.

The damage begins as axons from [sensory neurons](#) begin to retract and disappear from the tissues they innervate. New research from the lab of Clifford Woolf, MB, BCh, Ph.D., director of the F.M. Kirby Neurobiology Center at Boston Children's Hospital, reveals that months before the damage occurs, immune cells flood into [peripheral nerves](#) in an apparent attempt to protect them. This surprising insight, [published](#) in *Nature*, could lead to strategies to prevent peripheral neuropathy or at least minimize and slow the onset of the damage.

Immune cells prevent nerve damage

A team led by Sara Hakim, Ph.D., a graduate student in the lab, created a [mouse model](#) of diabetes induced by a high-fat, high-fructose diet. The model showed that these mice developed all the major features of diabetes within eight to 12 weeks of starting the diet. At about 6 months, axons in the skin began to degenerate, indicating the presence of neuropathy.

"Diabetic neuropathy takes years, or even decades to develop in humans," says Hakim, who is now at Vertex. "By using a mouse model in which symptoms slowly develop over months, we were able to catch the progression of the disease over time, and observe those early protective responses when the body is still trying to fight the disease."

The researchers suspected that peripheral neuropathy is caused by the immune system, so used single-cell sequencing to detect changes in immune cells near sensory neuron axons in peripheral nerves.

One type of immune cell residing in nerves, a pro-inflammatory macrophage, began producing chemokines. These signaling molecules recruited a second population of circulating macrophages, which began infiltrating the nerve 12 weeks after the mice began the diet—as sensory symptoms were starting to appear but before nerve degeneration was seen.

Previously, macrophages were thought to have a pathogenic role in diabetes and were mainly reacting to axon loss. But Hakim, Woolf, and colleagues observed just the opposite.

"To our great surprise, when we blocked infiltration of macrophages into the nerve, neuropathy started getting worse, not better," says Woolf. "The macrophages were protective. They slowed down the onset of neuropathy and reduced its impact."

Potential strategies for peripheral neuropathy

The Woolf Lab is now exploring how the infiltrating macrophages protect against [peripheral neuropathy](#). The next step would be to find a way to induce and sustain this protection and identify biomarkers that would flag those people with diabetes who are at risk.

One potential protective strategy might involve accelerating the recruitment of macrophages into nerves; another might involve mimicking their protective function by harnessing compounds they secrete, such as galectin 3.

"Since we could profile the cells and identify what genes they are expressing, we found a number of signaling molecules known to be protective," says Woolf. "We can now go through that list and check to see which are most active."

The latest work reinforces the idea that pain isn't just a disease of neurons, but results from interactions between the nervous system and the immune system. In a study last year, the Woolf Lab discovered [thousands of molecular interactions between pain-sensing neurons and different types of immune cells](#).

Now, the plot is thickening with this example of immune cells acting to prevent painful [nerve damage](#). "We've now revealed a novel, slower protective effect of the immune system," Woolf says.

More information: Clifford Woolf, Macrophages protect against sensory axon loss in peripheral neuropathy, *Nature* (2025). DOI: [10.1038/s41586-024-08535-1](https://doi.org/10.1038/s41586-024-08535-1). www.nature.com/articles/s41586-024-08535-1

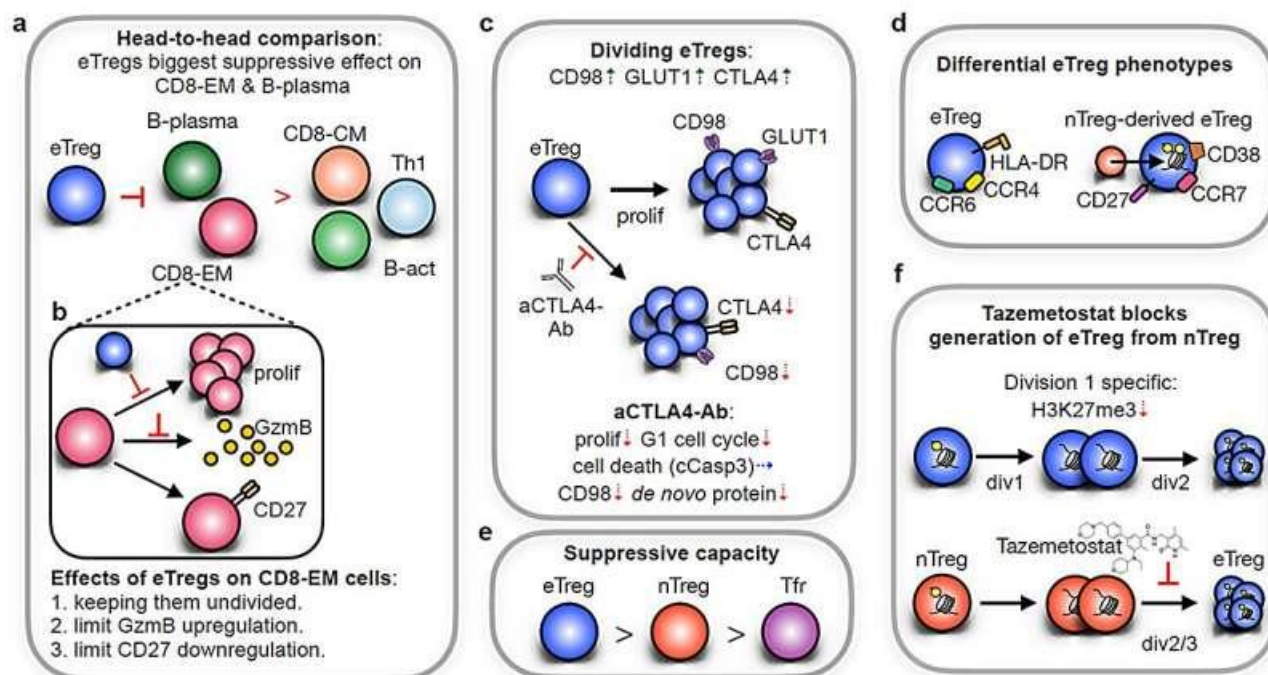
Journal information: [Nature](#)

Provided by [Children's Hospital Boston](#)

FEBRUARY 12, 2025

New immune-probing technique maps regulatory T cell interactions

by [Osaka University](#)



(a) Effector Tregs (eTregs) most strongly affect CD8-EM cells and B-plasma cells. (b) A closer look reveals eTregs control CD8-EM cells by stopping their division and reducing GzmB while maintaining CD27. (c) Dividing eTregs increase CD98, GLUT1, and CTLA4

proteins, and shows how an anti-CTLA4 antibody affects this process. (d) Reveals a potential biomarker by showing two distinct types of eTregs: one expressing HLA-DR and CCR4, and another expressing CD38 and CCR7 - a pattern seen in severe viral infections. (e) Ranks different Treg types by their suppressive ability, with eTregs being strongest. (f) Demonstrates how the drug Tazemetostat blocks naive Tregs from becoming eTregs during early cell division. Credit: 2025 Søndergaard et al., Single cell suppression profiling of human regulatory T cells., *Nature Communications*

Developing effective treatments and understanding how the mechanism of the immune system have always been challenging for scientists. T cells, which are the frontline warriors in the battle against infections, have been a major focus of research.

Regulatory T cells (Tregs) are specialized immune cells that have a challenging task in the body. They must balance the immune system by making it aggressive enough to fight infection and cancer but calm enough not to attack the body's normal cells. Tregs meet this challenge by controlling the actions of other immune cells. However, we don't know exactly how these cells interact during disease and [treatment](#).

In a study recently [published](#) in *Nature Communications*, a research team at Osaka University has developed a new technique that reveals how Tregs exert their control. The new technique, called single-cell suppressive profiling of regulatory T cells (scSPOT), can pinpoint the effects of Tregs on all other [immune cells](#) simultaneously. Previously, researchers could only observe interactions between one or two cell types at a time.

"This new method provides a better understanding of how Tregs function in a complex immune environment in a way that closely resembles what happens in the human body," explains first author of the study Jonas Nørskov Søndergaard. "Using scSPOT, we found that Tregs most strongly affect CD8-EM T cells by suppressing their ability to grow and divide."

CD8-EM T cells are a subset of memory T cells that have a key role in fighting cancer and infections, highlighting how Tregs are closely tied with health and disease. The team also found that Tregs are targets for the cancer drugs ipilimumab and tazemetostat, although the two drugs affect Tregs in different ways. Tregs are indicators of serious viral infection too, since scSPOT identified special types of Tregs like the ones seen in patients with severe COVID-19 [infection](#).

"Our new scSPOT method is a valuable tool that may accelerate the development of treatments for cancer and other diseases," says senior author James Wing. "In particular, the discovery of indicators of severe viral infections may allow [health care professionals](#) to identify high-risk patients earlier, allowing for faster treatment during outbreaks and pandemics."

The team's scSPOT method has already boosted our understanding of the [immune system](#). The insights it provides into the ways existing drugs work could help investigators develop more effective treatment strategies, leading to better outcomes for patients.

More information: Jonas Nørskov Søndergaard et al, Single cell suppression profiling of human regulatory T cells, *Nature Communications* (2025). [DOI: 10.1038/s41467-024-55746-1](https://doi.org/10.1038/s41467-024-55746-1)

Journal information: [Nature Communications](#)

Provided by [Osaka University](#)

Scientists just rewrote our understanding of epigenetics

DNA and RNA epigenetics, once thought to be separate, have now been found to work together to fine-tune gene expression.



Epigenetic modifications made to both DNA and its cousin, RNA, control gene activity. (Image credit: koto_feja/Getty Images)

Scientists have uncovered a new way that cells control their genes — and it may rewrite our understanding of "epigenetics."

[Epigenetics](#) is a form of DNA modification that doesn't affect the DNA sequence itself. Instead, it describes when chemical groups attach to specific genes, thus switching those genes on or off, or else changing the 3D shape of chromosomes.

Now, in a study published Jan. 17 in the journal [Cell](#), scientists have uncovered a whole new method of gene regulation that involves epigenetic tweaks made to both DNA and its molecular cousin [RNA](#), at the same time. Looking forward, the researchers want to unpack how this new type of gene control relates to cancer.

"It is truly exciting to uncover such a new mechanism, further expanding our understanding of gene regulation," [Kathrin Plath](#), director of epigenomics, RNA and gene regulation at UCLA who was not involved in the study, told Live Science in an email.

Related: [Sperm cells carry traces of childhood stress, epigenetic study finds](#)

A new layer of gene regulation

One common type of [epigenetic modification](#) is methylation, which describes the addition of a molecule called a [methyl group](#) to DNA or histones — proteins that DNA wraps around to become more compact and fit into the nucleus. A protein called [DNMT1](#) adds these molecules to DNA, and its activity can turn gene expression up or down depending on where a given gene is methylated.

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In recent years, researchers [have also found that RNA](#) — a molecule that shuttles instructions from DNA out into the cell to make proteins — can also be modified. This is mainly done by a protein complex called [METTL3-METTL14](#). This methylation can destabilize the RNA molecule, reducing the amount of protein made.

Every cell in the body uses both RNA and DNA methylation to regulate gene expression. However, it was previously assumed that these processes operated independently. The new study puts that assumption into question.

In the study, the scientists looked at mouse embryonic stem cells and mapped the locations of DNA and RNA methylation as the cells developed. They found that thousands of genes and their complementary RNA molecules contained both methylation markers.

Through additional experiments, the team found that the METTL3-METTL14 complex that interacts with RNA also recruits and physically binds to DNMT1, the protein that tags DNA. This new, bigger complex can then methylate the same gene at the DNA or RNA level. This enables the cell to further fine-tune its gene regulation during cell differentiation — a process by which a stem cell assumes a specific identity, becoming a heart or lung cell, for example.

Previous studies have shown clear connections between [DNA and histone modifications](#), as well as between [histone and RNA modifications](#).

"So why would a cell not also connect an epigenetic modification of DNA and an epigenetic modification of RNA?" said study co-author [François Fuks](#), director of the ULB Cancer Research Center in Belgium. "[Our study shows] the direct connection between DNA methylation and RNA modification that has not been seen before," he told Live Science. According to Fuks, this study does have some limitations, namely, that it mostly focuses on embryonic stem cell differentiation. DNA and RNA modifications had separately been well characterized in stem cells in past studies, so it made sense for the researchers to start with them. But these same types of DNA and RNA modifications are present in all types of cells.

"Seeing this, it's very unlikely that [this mechanism] will be just in ES cells," Fuks said.

This discovery challenges the established view that these RNA- and DNA-modifying processes are completely separate, and it suggests that it may have broader implications in human biology and disease. To that end, Fuks and his team are trying to determine how this new mechanism relates to cancer.

If the coordination of DNA and RNA epigenetics gets thrown off, you may end up with too much or too little of a protein, Fuk suggested. "Now, a key protein will be expressed at a too high level," he said. "This could be detrimental for a cell and contribute to tumorigenesis," or the formation of tumors.

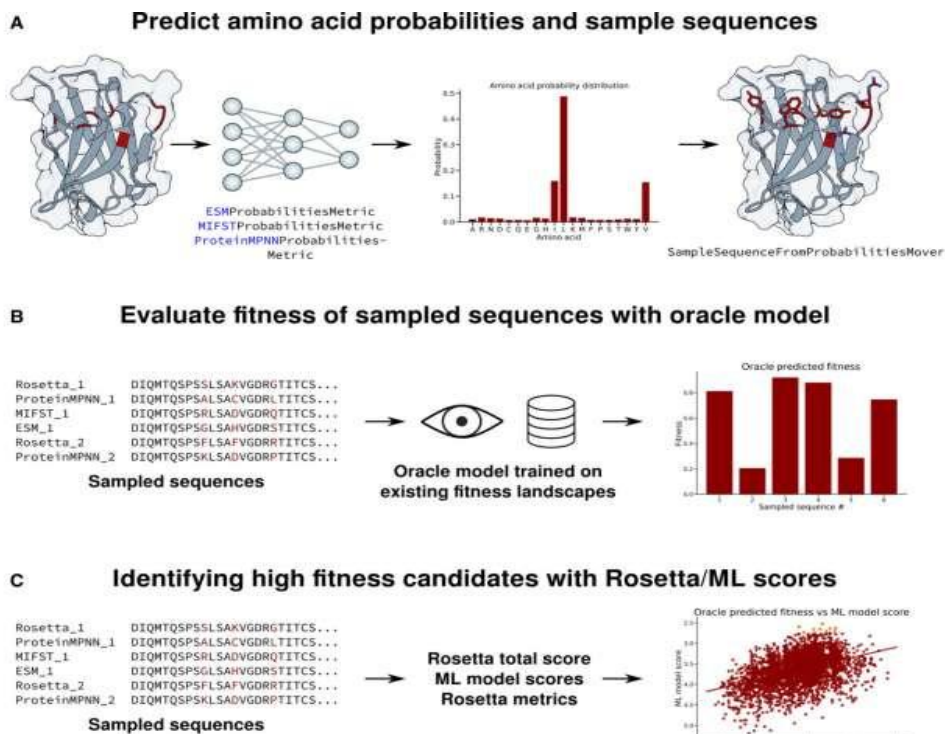
There are already [approved therapies](#) that inhibit the methylation of DNA, and there's an [early-phase clinical trial](#) testing RNA methylation inhibition as a cancer treatment. Fuks and his team are testing the potential of combining these existing therapies to improve patients' outcomes. Preliminary data from their laboratory studies hint this strategy could be useful for patients with leukemia.

At least in petri dishes, "we can revert the cancer progression of leukemic cells by adding these two drugs together," Fuk said. "Eventually, down the line, why couldn't we combine these two drugs to treat patients?"

FEBRUARY 14, 2025

AI and biophysical modeling unite for novel protein design

by [Leipzig University](#)



ML-support framework in Rosetta. Credit: *Science Advances* (2025). DOI: 10.1126/sciadv.adr7338

An interdisciplinary research team from Leipzig University and the Saxon AI center ScaDS.AI has developed a novel approach that integrates artificial intelligence (AI) methods with biophysical modeling. This innovative strategy can be applied to the development of new therapeutics, such as antibodies and vaccines, including those for pandemic preparedness.

The research project, conducted in collaboration with Vanderbilt University in Nashville, US, is the result of extensive preliminary work in computer-aided drug development. [The study](#) has been published in the journal *Science Advances*.

The scientists believe that the current research landscape in the field of computational protein design is akin to a [gold rush](#), with many new methods being published without experimental validation. This often leads to inaccurate assessments of the performance of AI models.

"We urgently need standards for the description and availability of such models," says Professor Clara Schoeder, research group leader at the Institute for Drug Discovery. "Our research makes an important contribution to this goal."

The current findings show that AI methods are particularly good at suggesting sequences that do not disrupt the folding of proteins. However, they struggle when it comes to accurately assessing the effects of individual amino acid changes on folding.

"Our findings make it clear that no AI model or biophysical method is ideally suited to all design problems," explains Humboldt Professor Jens Meiler, one of the project's lead scientists and Director of the Institute for Drug Discovery.

"In the future, we will have to carefully consider which model to use for which purpose. Our work is a first step towards greater comparability between the different methods."

The Rosetta biophysical software suite, which has been used in protein research for many years, provides a framework for integrating different AI methods.

Rosetta is used by more than 100 laboratories worldwide and allows researchers to efficiently combine different approaches, such as large language models (e.g. ESM-2) and the ProteinMPNN model, with biophysical methods. This combination allows researchers to compare and analyze the different behaviors of the design approaches.

"With this development, we can quickly and easily combine AI models with classical methods and use them side by side," explains Professor Meiler.

"This greatly simplifies our work and allows us to take full advantage of all the infrastructure that has been developed in Rosetta over the last 20 years."

This does not mean that the research project is finished. The research groups led by Professor Meiler and Professor Schoeder will continue to refine and experimentally evaluate the developed algorithms, particularly with regard to vaccine design for pandemic preparedness.

"We are investigating which methods reliably suggest amino acid changes that could lead to vaccine candidates," says Professor Clara Schoeder.

Despite the progress made through the use of AI, the so-called scoring problem remains a challenge. This refers to the difficulty of predicting the effect of a single amino acid substitution.

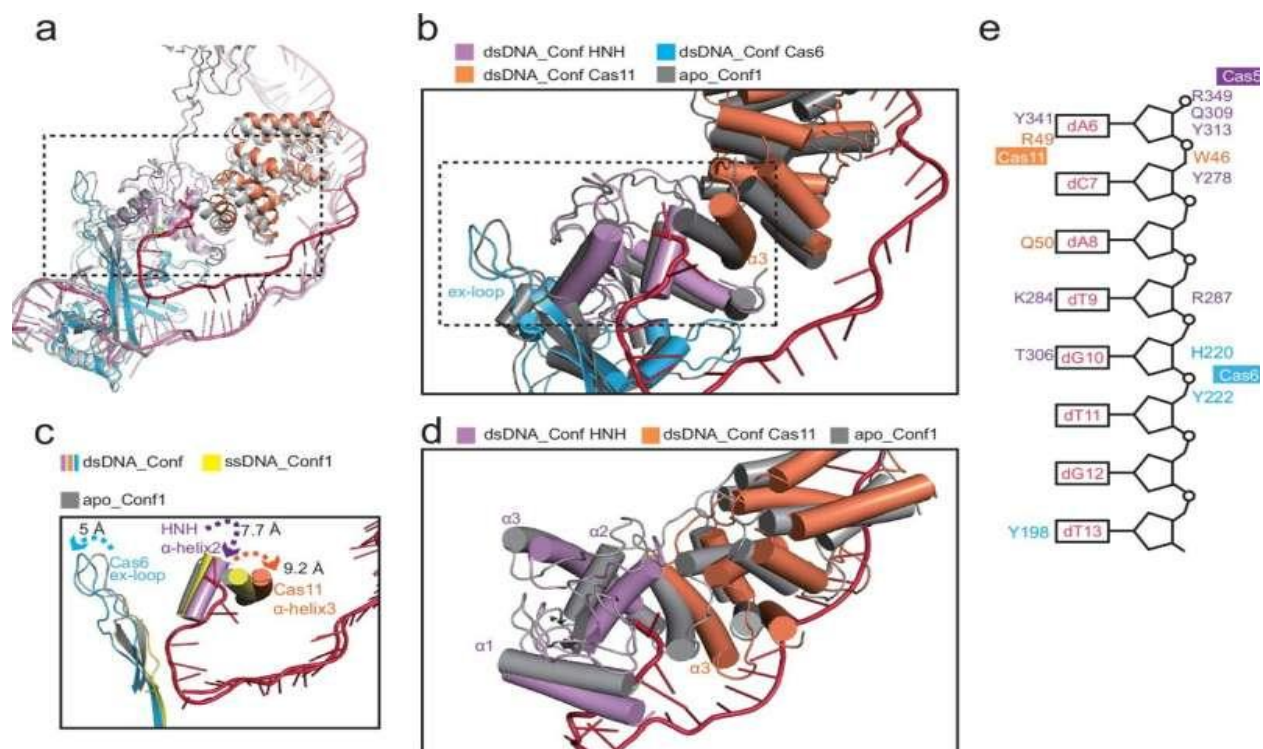
In collaboration with the Center for Scalable Data Analytics and Artificial Intelligence, ScaDS.AI, the research team is optimistic that the combination of AI and biophysical methods will increase the efficiency of protein design.

More information: Moritz Ertelt et al, Self-supervised machine learning methods for protein design improve sampling but not the identification of high-fitness variants, *Science Advances* (2025). [DOI: 10.1126/sciadv.adr7338](https://doi.org/10.1126/sciadv.adr7338)

FEBRUARY 14, 2025

CRISPR system variant shows a novel DNA cleavage mechanism

by [Chinese Academy of Sciences](#)



Dynamics of Cas5-HNH /Cascade complex upon binding target DNA. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-024-55716-7

Researchers have revealed new details about the CRISPR-Cas5-HNH/Cascade complex, a variant of the type I-E CRISPR-Cas system, providing insights into its DNA recognition and cleavage mechanisms.

The study, [published](#) in *Nature Communications*, was conducted by researchers from the Institute of Physics of the Chinese Academy of Sciences.

The CRISPR-Cas5-HNH/Cascade complex, which serves as an immune defense system in [prokaryotes](#), has long been studied for its ability to protect bacteria from invading genetic materials. However, recent research uncovers a novel mechanism in this complex that differs significantly from the well-known type II CRISPR systems like Cas9.

Researchers utilized cryo-[electron microscopy](#) to capture the structures of the Cas5-HNH/Cascade complex in both DNA-bound and unbound states. They revealed striking [conformational changes](#). The complex adopts a more compact structure when bound to double-stranded DNA (dsDNA), with the target DNA strand making a pronounced U-turn and interacting with the HNH nuclease domain.

The target strand is cleaved first, followed by the non-target strand, a departure from the cleavage order seen in other CRISPR systems like Cas12a.

The Cas5-HNH domain itself was found to play a crucial role in the nuclease activity of the Cas5-HNH/Cascade complex. Researchers demonstrated that mutations in key residues of the HNH domain, particularly histidine and aspartate, can completely abolish cleavage activity.

This suggests that the HNH domain is not only essential for target DNA recognition but also for the specific cleavage of DNA, further differentiating the mechanism from other systems.

Moreover, researchers observed that the architecture of the Cas5-HNH/Cascade complex is notably different from canonical type I-E systems. For example, the HNH domain was fused to the C-terminus of Cas5, replacing the need for Cas3, a protein commonly involved in DNA degradation in other systems.

This structural innovation pointed to the complex's ability to cleave DNA independently of the traditional components seen in similar CRISPR systems.

By elucidating the role of the HNH nuclease domain and revealing the structural changes that occur upon DNA binding, this work not only deepens the understanding of CRISPR-Cas5-HNH but also paves the way for refining CRISPR technologies for therapeutic applications.

More information: Yanan Liu et al, Structural basis for RNA-guided DNA degradation by Cas5-HNH/Cascade complex, *Nature Communications* (2025). [DOI: 10.1038/s41467-024-55716-7](https://doi.org/10.1038/s41467-024-55716-7)

Journal information: [Nature Communications](#)

Provided by [Chinese Academy of Sciences](#)

New findings on the power of enzymes could reshape biochemistry

Conformational ensemble of link molecules to energetics via statistical mechanics

I Build ensembles **II Identify molecular changes** **III Map conformations to energy** **IV Calculate catalytic contribution**

Transition state analog bound

Ground state analog bound

Ser195*

Oxyanion hole

Substrate

*Nucleophile

ΔE

Ser195 torsion ($^{\circ}$)

ΔE

Reactant distance ($\text{\AA}$)

$\Delta\Delta G^{\ddagger}$

Solution - Enzyme

Calculated

Measured

Using a series of more than 1,000 X-ray snapshots of the shapeshifting of enzymes in action, researchers at Stanford University have illuminated one of the great mysteries of life—how enzymes are able to speed up life-sustaining biochemical reactions so dramatically. Their findings could impact fields ranging from basic science to drug discovery, and provoke a rethinking of how science is taught in the classroom.

There are lots of ideas and theories that make sense, Herschlag said, but biochemists have not been able to translate those ideas into a specific understanding of the chemical and physical interactions responsible for enzymes' enormous reaction rates. As a result, biochemists don't have a basic understanding and, therefore, have been unable to

predict [enzyme](#) rates or design new enzymes as well as nature does, an ability that would be impactful across industry and medicine.

"Using these detailed ensembles of enzyme states, we've been able to quantify and rigorously explain in chemical detail what features in enzymes provide catalysis and by how much," said the study's first author, Siyuan Du, a doctoral student in Herschlag's lab. Their study [appears](#) in the Feb. 14 issue of the journal *Science*.

"Our new approach—and understanding—starts us down a road to being able to design enzymes that rival those found in nature, though this is just the start, and much more work is needed to achieve that goal," Herschlag added.

Elusive entities

Until 1926, biochemists were perplexed by reactions that were exclusive to living systems, chalking them up to a mysterious "vital force." That year, James Sumner isolated the first known enzyme, urease, in a Nobel Prize-winning study. Biochemists have since spent the last century trying to understand how enzymes make reactions so fast and so specific. That is, they have described how they work in words, not quantitatively, and that has led to debate and contrasting views on how they work.

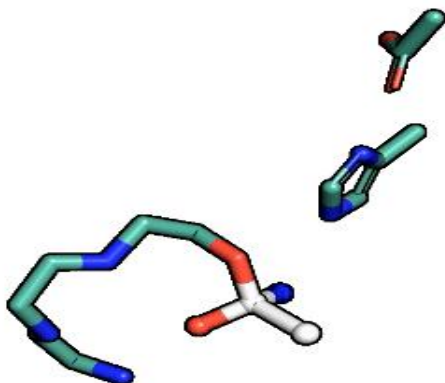
Du and Herschlag built upon a widely held view among biophysicists that enzymes are not a single structure. Instead, they focus on what they term "ensembles," showing how enzymes move between different physical states—or conformational ensembles—during catalysis.

"All existing models use some degree of positioning of the reacting chemicals and groups of chemicals on the enzyme that aid reactions," Herschlag explained. But debate has raged about how much positioning matters, with no way to measure it without this new 'ensemble' approach Herschlag and Du have taken.

"Enzymes are constantly in motion—in an ensemble of states—and the rate of the reaction is determined by the probabilities within the ensemble," Du elaborated.

As their subject, the authors chose a family of enzymes known as the serine proteases, which is the family most biochemistry textbooks use to explain enzymatic processes to budding biochemists.

Exploring these ensembles and comparing reaction states on enzymes to states of uncatalyzed enzymes in pure water, Herschlag and Du broke down enzyme catalysis to the individual energetic contributions at the precise place where enzyme and target molecule meet during a reaction, known as the [active site](#), to understand how they work chemically and physically to speed up reactions.



A close-up showing the serine protease reaction at the active site, place where enzyme and target molecule meet during a reaction. Credit: Siyuan Du

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Potential energy

In one example, Du noted how an enzyme's oxygen atom at the active site encroaches on a carbon atom on the molecule it is "attacking." It is a little like a coiled spring, Du said, but cautioned against a too-literal interpretation, noting that the ways individual atoms and groups of atoms move differ from the smooth motion of a spring.

"There's a little bit of tension forcing these atoms together and, when the reaction happens, all that pent-up energy pushes the reaction forward and it leads to a much faster reaction," she said.

Du then noted that these catalytic strategies appeared across all the serine proteases, as expected, but also in more than 100 other enzymes.

"Nature has evolved these mechanisms independently in multiple enzyme families—this is not an isolated feature, but catalytic mechanisms that have been discovered multiple times by nature through evolution. This means we may be able to copy nature and use this and other features to design and build new enzymes," Du said.

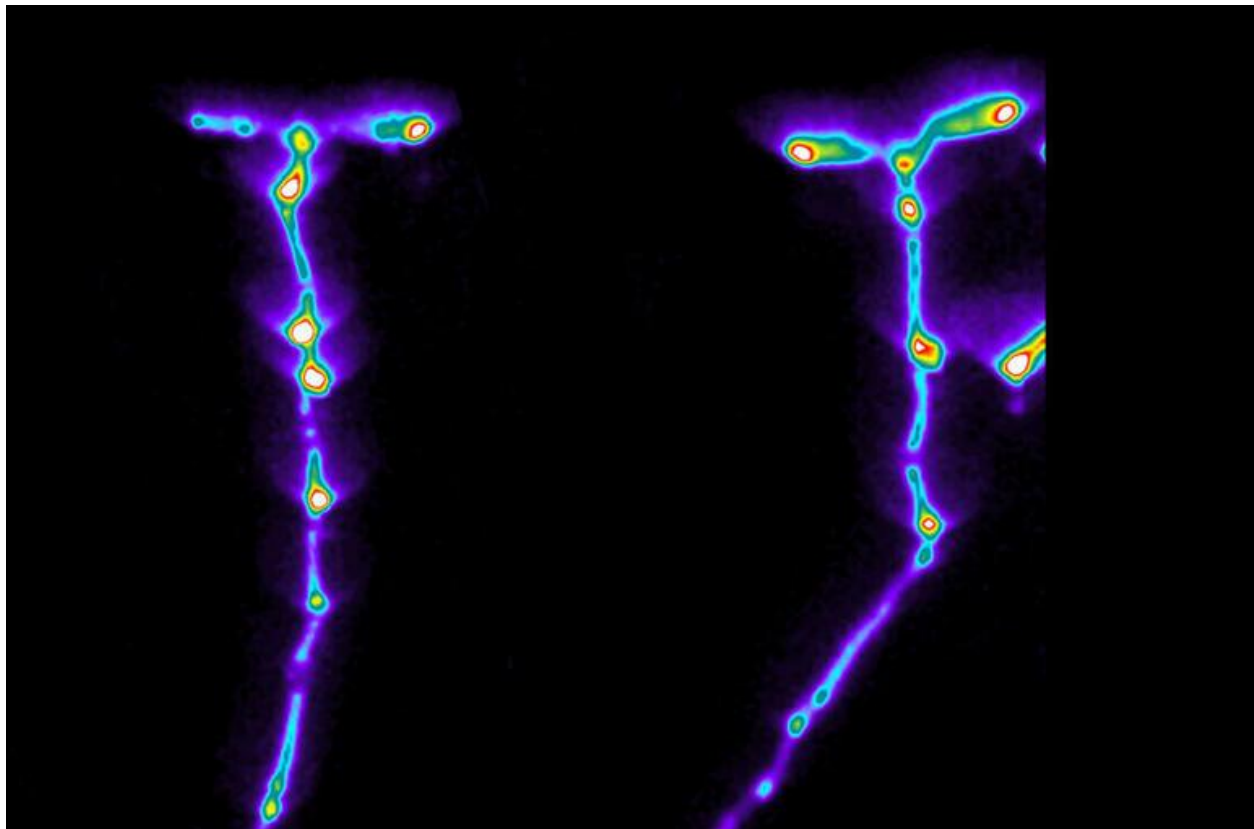
As for what comes next, Herschlag and Du said that the ability to explain the extraordinary abilities of these important biochemicals in simple chemical terms could revolutionize how biochemistry is taught and could speed new science in a number of important fields.

"Bottom line," Herschlag said, "We need to better understand enzymes before we can expect to have real power over them and engineer better ones."

More information: Siyuan Du et al, Conformational ensembles reveal the origins of serine protease catalysis, *Science* (2025). DOI: [10.1126/science.adp5068](https://doi.org/10.1126/science.adp5068)

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

Study finds what gets plant roots to grow strong



To investigate the significance of autophagy, the researchers developed a mutant *Arabidopsis* (thale cress) plant in which its autophagy was disabled which is shown on the right. With an enzyme from fire flies the researchers made it possible to distinguish the normal plant from the plant with its autophagy function disabled. The plant to the right has fewer light areas and thereby fewer potential places to grow new roots with its autophagy function turned off. Credit: Eleazar Rodriguez, Department of Biology, University of Copenhagen. © Provided by Phys.org

A biological mechanism familiar to people who fast helps plant roots grow strong. The discovery by University of Copenhagen scientists provides an answer to a long-unanswered question and a deeper understanding of the "mouths" of plants that can help to develop climate-resilient crops.

Imagine eating with your feet and having half your body underground. Such is the life of most plants, with roots as the mouths through which they eat and drink. Roots also serve to anchor plants and keep them safe in wind and rain. Indeed, roots are critical for a plant's life.

But many things remain unknown about the life of plants. How they grow their roots big and strong has long been a question and there are key pieces missing to the puzzle.

In a new study published recently, researchers from the University of Copenhagen's Department of Biology share their discovery of how plants control root growth.

It turns out that a beneficial clean-up mechanism in plant cells called autophagy plays a key role. The same mechanism exists in humans and is part of a popular health trend.

"Fasting has become popular as it seems to have a range of health-promoting effects in humans, as periods without food cause the body to activate a clean-up processes to dispose of various waste products in cells. In our study, we have proven that the same mechanism, which also exists in the plant kingdom, plays a vital role in the ability of plant roots to grow and absorb water and nutrients for the rest of the plant," explains Assistant Professor Eleazar Rodriguez from the Department of Biology, who led the study.

Roots have a 'heartbeat'

It has long been known that auxin, a plant hormone, controls plant growth, root growth included. Auxin is a fuel for a kind of "heartbeat" that beats in each and every root tip of a plant. Roughly every four to six hours, auxin levels and the heartbeat in a plant's roots reach a maximum that causes new roots to grow.

"The movement of a root is almost like watching a snake slithering forward in search of water and nourishment in the soil. And we can see that the heartbeat is strongest every time the root meanders forth," says Rodriguez.

But how plants control their heartbeat so as to optimize root growth, has remained an unanswered question. This is where the plant's internal clean-up mechanism comes into the picture.

"In our experiments, we disabled the clean-up mechanism to understand its significance. Imagine if every garbage collector in Copenhagen went on strike—it wouldn't be long before trash filled the streets. The same thing happened in the plant cells, as the heartbeats that drive root growth became much weaker and went out of sync," explains Rodriguez.

Doing this allowed the researchers to conclude that the clean-up mechanism helps keep levels of different biochemical components in perfect balance to provide the most efficient root growth.

Can help germinate new climate-resilient crops

According to the researchers, the new knowledge about plant roots may prove important in the fight against climate change. Extended periods of drought and floods are a new normal that place greater demands on food security. As such, the roots of the crops, which must be able to grow even in these harsh conditions.

"Numerous methods to change the genetic characteristics of plants are available today. These can be used to get plants to develop longer roots, faster, and in doing so, become more resistant to droughts or floods. One of the methods enlists the help of bacteria that live in symbiosis with the plant and can cause the plant to change its growth pattern. Several companies in Denmark are working on this right now," explains Ph.D. student Jeppe Ansbøl who co-authored the study.

The new knowledge applies to all flowering plants and perhaps more, according to the researcher. In principle, crops like tomatoes, potatoes, rice, wheat and corn could be altered to grow more and denser roots, because we now know how plants get their roots to grow.

"The more roots the plants have the more water and nutrients they can take, so the plants grow better faster. We're heavily dependent on plants because they feed us, extract CO₂ from the atmosphere and produce the oxygen we breathe. As such, it is extremely important to understand them fully, to which end we have just taken a big step forward," concludes Rodriguez.

Causing the garbage collectors in cells to go on strike

Autophagy means "self-eating" and is a key mechanism when plants develop roots. To investigate the significance of autophagy, the researchers developed a mutant *Arabidopsis* (thale cress) plant in which its autophagy was disabled.

At the same time, they made the ARF7 protein luminescent, which is the protein that controls the auxin responses and which the plant cell's garbage collectors clean up to provide optimal root growth. The plant's garbage collectors collect waste from cells and transport it to a kind of recycling station in the plant called a vacuole.

"When we disrupted the plant's autophagy, there was waste everywhere, and we were able to detect the ARF7 protein among the waste," says Rodriguez.

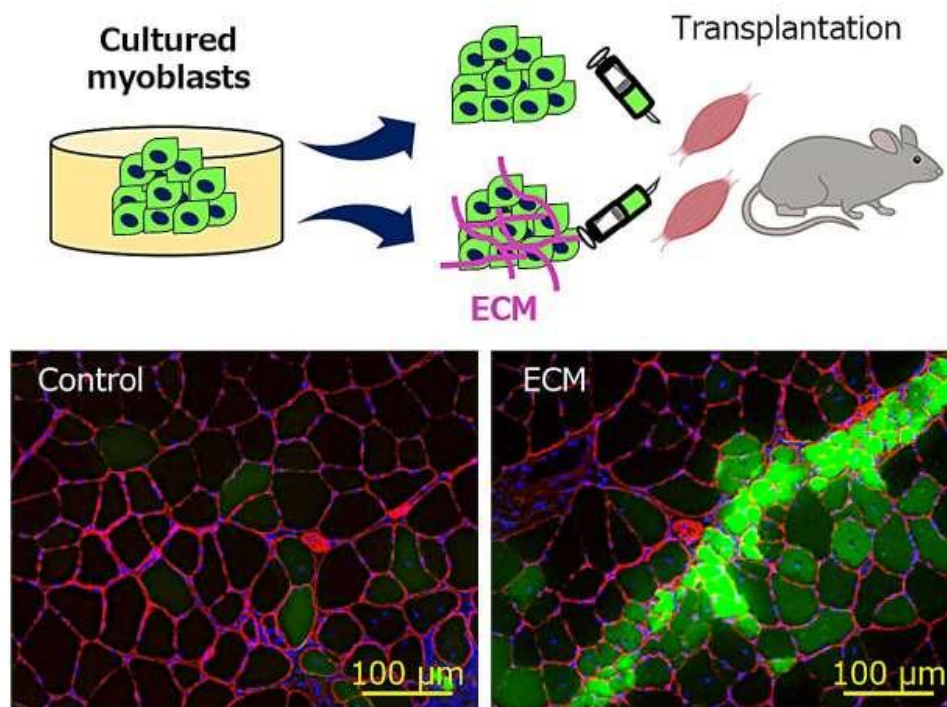
More information: Elise Ebstrup et al, NBR1-mediated selective autophagy of ARF7 modulates root branching, *EMBO Reports* (2024). [DOI: 10.1038/s44319-024-00142-5](https://doi.org/10.1038/s44319-024-00142-5)

Provided by University of Copenhagen

FEBRUARY 17, 2025

Cellular 'scaffold' enables myoblast implants on healthy muscle to advance regenerative medicine

by [Tokyo Metropolitan University](#)



Incorporating cultured myoblasts into healthy tissue. Transplanting myoblasts in a fluid containing ECM helped new cells graft into existing tissue. To confirm engraftment, new cells have been designed to emit a green dye, as seen in the bottom right. Credit: Tokyo Metropolitan University

Researchers from Tokyo Metropolitan University have developed a way to treat age-related muscular atrophy using regenerative medicine. Conventional methods to implant myoblasts, precursors to muscle fiber, require prior scarring for the new cells to graft properly. By adding extracellular matrix (ECM) fluid into the implant, the team successfully grafted myoblasts onto healthy muscle in mice. Their technique opens the way for using implantation to treat unscarred muscle atrophied by aging.

The work is [published](#) in the journal *Frontiers in Cell and Developmental Biology*.

Age-related [muscular atrophy](#) in skeletal muscle can have a devastating impact on people's quality of life, as well as make them more susceptible to a wide range of diseases. Prevention regimens like resistance exercise and the right diet are vital from a [public health perspective](#) but are hardly a complete solution given the scale and immediacy of this societal issue.

That is why researchers have been seeking effective treatments for muscular atrophy. A promising avenue for this work is regenerative medicine, using stem cells to create and augment existing muscle. However, it turns out that this is not so easy. Simply implanting myoblasts, precursors to skeletal muscle, simply does not solve the problem.

For the most part, the new cells do not graft into the existing muscle and simply die out. Interestingly, this is not the case when there is an injury present, or a patient has specific diseases like Duchesne muscular atrophy, where muscle fibers are collapsing faster than they are being repaired.

The common feature is that the muscle is in a "repair mode," when [stem cells](#) in the [skeletal muscle](#) tissue called satellite cells are in an activated state, secreting the right signals to enable cell grafting to occur.

Now, a team led by Associate Professor Yasuro Furuichi from Tokyo Metropolitan University has used this insight to develop a new way of implanting myoblasts. Instead of simply injecting myoblasts by themselves, they added some [extracellular matrix](#) (ECM) to the injection fluid, the "scaffold" that helps keep cells in place in our bodies.

Repair of the ECM is a big part of the process of muscle repair; the team reasoned that the ECM itself may contain some of the right ingredients to trigger the successful grafting of myoblasts into skeletal [muscle fiber](#).

Through experiments on mice, the researchers found that higher amounts of ECM together with myoblasts lead to higher amounts of myoblasts being grafted onto unscarred tissue. This wasn't without its issues; beyond a certain point, fibrils of collagen began to intrude into the new, healthy tissue (fibrosis).

The team was able to solve this by also increasing the concentration of cultured myoblasts in the implant. To date, they have been able to boost the mass of a mouse's tibialis anterior (in the lower leg) by a massive 10%.

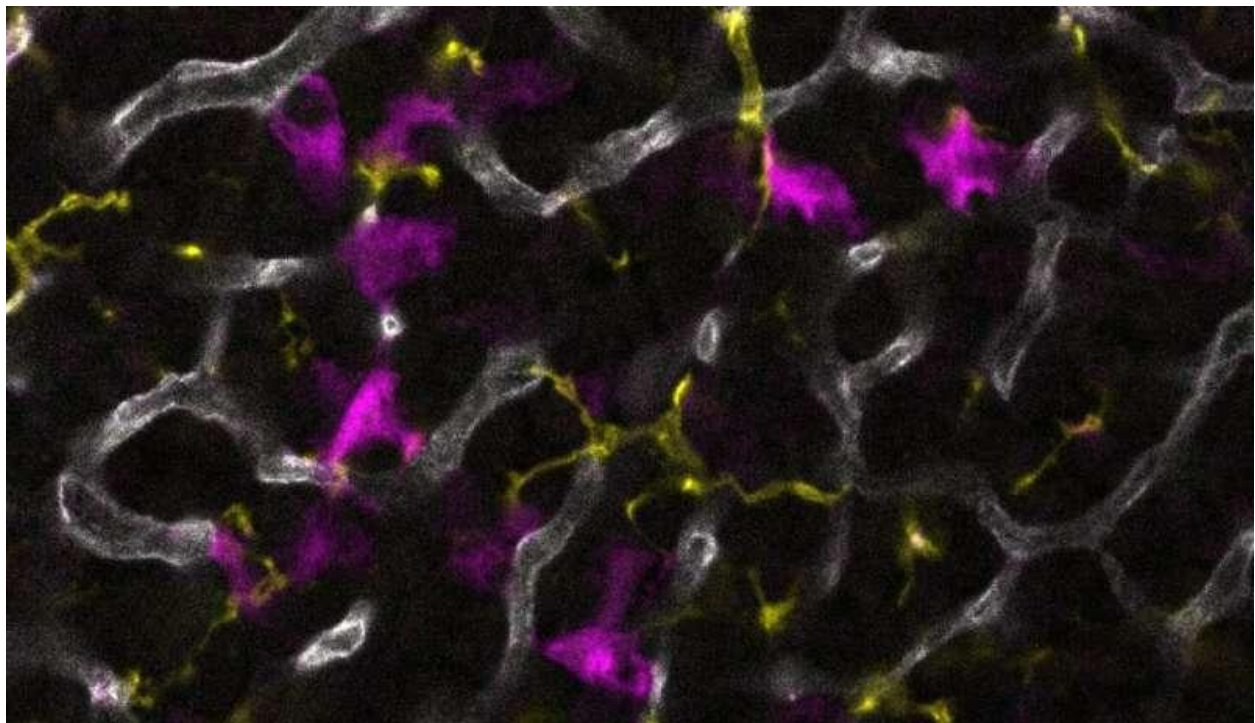
Though they have yet to determine which ingredient of ECM is helping muscle cells incorporate properly, this is a big step forward for using [regenerative medicine](#) to treat a universal public health issue.

More information: Kitora Dohi et al, Achieving myoblast engraftment into intact skeletal muscle via extracellular matrix, *Frontiers in Cell and Developmental Biology* (2025). [DOI: 10.3389/fcell.2024.1502332](https://doi.org/10.3389/fcell.2024.1502332)
Provided by [Tokyo Metropolitan University](#)

FEBRUARY 17, 2025

Immune cells in pituitary gland help balance hormones, researchers discover

by [University of Turku](#)



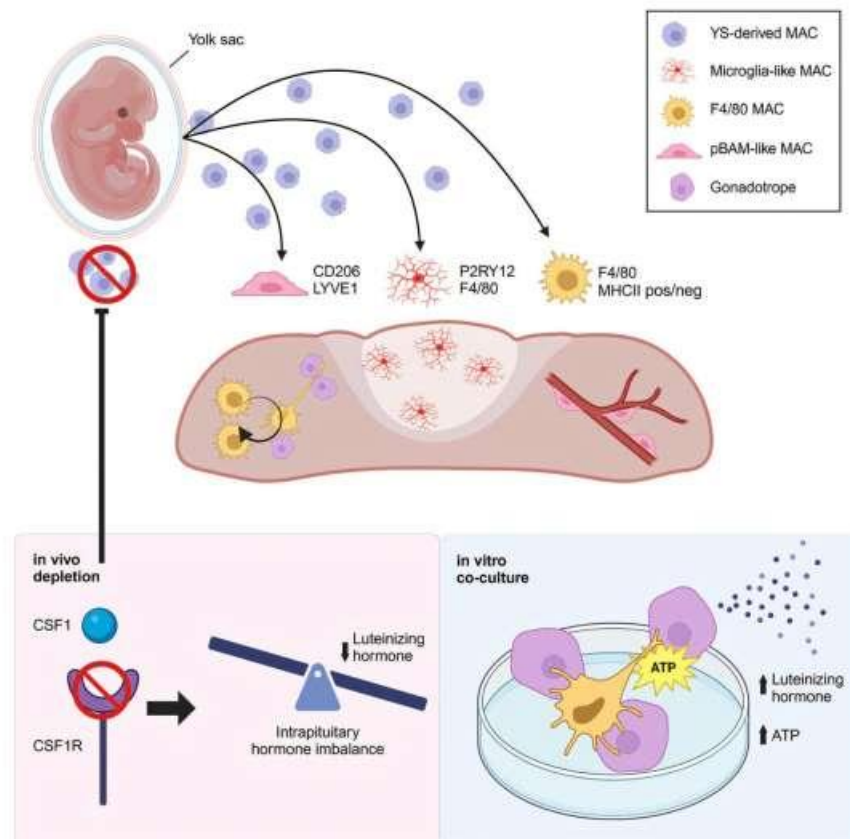
Macrophages, marked in yellow, connect hormone-secreting cells (magenta) and blood vessels (gray) in the mouse pituitary gland. Scale is 10 μm . Credit: Henna Lehtonen
In a new study [published](#) in *Cell Reports*, Finnish researchers show that pituitary macrophages, the immune cells located in the pituitary gland, help regulate hormonal balance. It is possible that in the future, macrophage cells could be used to treat endocrine disorders that can lead, for example, to infertility.

The pituitary gland is a small, pea-sized endocrine gland located at the base of the brain. The hormones it secretes are involved in almost all major body functions, such as growth,

reproduction, water/salt balance, and the regulation of blood pressure and stress. Life is not possible without the hormones produced by the pituitary gland.

"Until now, it has been thought that the pituitary gland receives messages from the rest of the body and increases or decreases [hormone secretion](#) accordingly. In fact, macrophages, the [immune cells](#) located in the pituitary gland, have a local effect on the cells that produce hormones in the pituitary gland," says InFLAMES Flagship Researcher Heli Jokela from Turku Bioscience Center and the University of Turku in Finland.

The removal of macrophages reveals their key role in hormone secretion: When the immune cells are removed, the hormone secretion decreases.



Credit: *Cell Reports* (2025). DOI: 10.1016/j.celrep.2024.115227

Pituitary macrophage cells originate from the fetal period

Macrophages have mostly been thought of as immune defense cells, whose role is to eliminate hostile invaders from tissue. When a virus or another pathogen causes inflammation somewhere in the body, the bone marrow starts to produce monocytes, which turn into the defender cells, i.e., macrophages.

However, not all macrophages originate from the bone marrow and they have more functions than previously thought.

"A particularly novel finding in our study is that all pituitary macrophages originate from the fetal period, rather than from monocytes derived from the bone marrow. They also regenerate themselves to maintain their numbers. The defense cells produced by the [bone marrow](#) do not enter the pituitary gland even when there is a sudden inflammation," explains Doctoral Researcher of the project, Henna Lehtonen.

Leader of the research group, Pia Rantakari, says that, in light of the new discovery about the role of macrophages, it may be possible to use them as a tool to treat human [endocrine disorders](#) in the future.

By regulating the macrophages, it could be possible to increase hormone secretion or reduce it if overproduction is the problem. An example of the latter is PCOS ([polycystic ovary syndrome](#)), the most common female hormone disorder. PCOS is associated with increased morbidity and also infertility. However, Rantakari highlights that the therapeutic use of macrophages in endocrine disorders is not yet feasible and requires a great deal of further research.

"By uncovering the roles of immune cells within the pituitary gland, we have not only advanced our understanding of the physiology of the [pituitary gland](#), but have also gained new insights into how immune cells can affect endocrine health," says Rantakari.

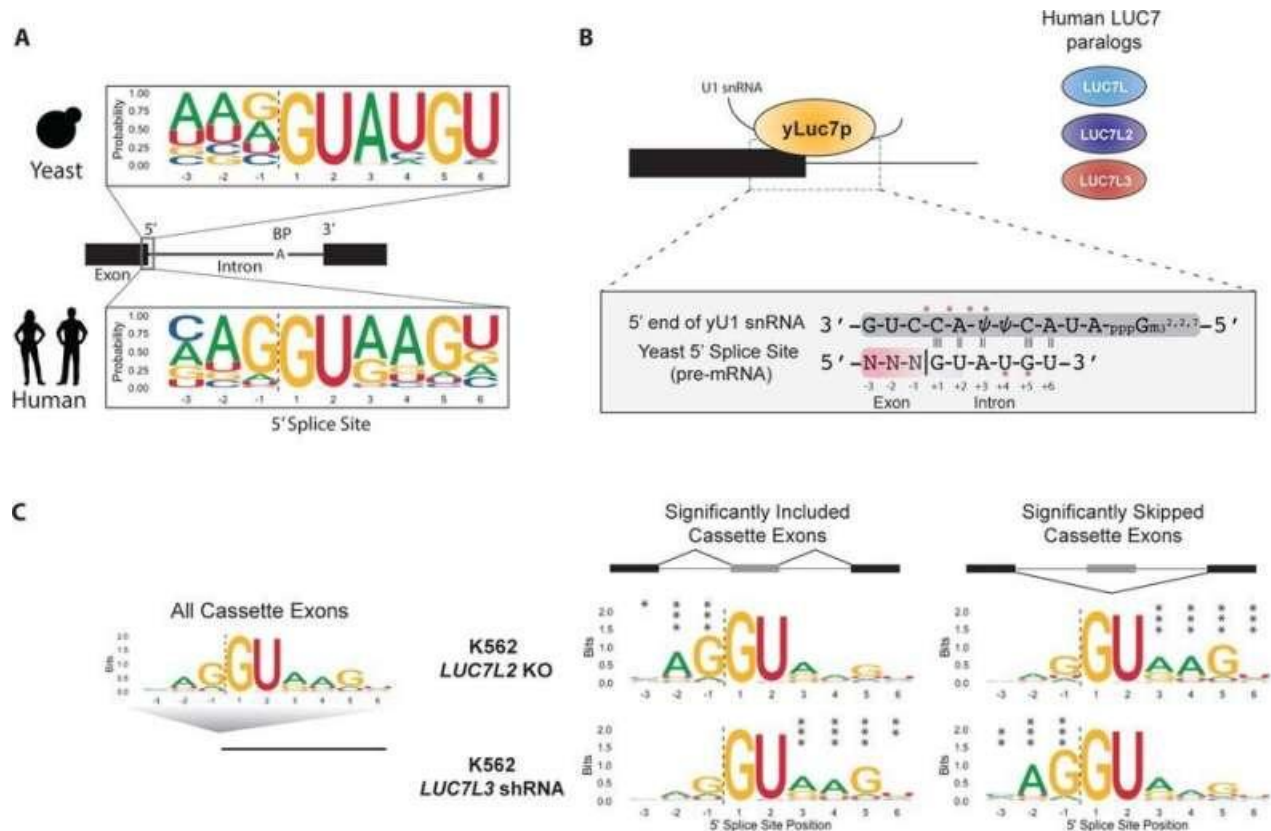
More information: Henna Lehtonen et al, Early precursor-derived pituitary gland tissue-resident macrophages play a pivotal role in modulating hormonal balance, *Cell Reports* (2025). DOI: [10.1016/j.celrep.2024.115227](https://doi.org/10.1016/j.celrep.2024.115227)

Journal information: [Cell Reports](#)

Provided by [University of Turku](#)

Biologists discover a new type of control over RNA splicing

by [Massachusetts Institute of Technology](#)



Human LUC7 proteins impact 5' splice sites with distinct composition. Credit: Connor J. Kenny et al

RNA splicing is a cellular process that is critical for gene expression. After genes are copied from DNA into messenger RNA, portions of the RNA that don't code for proteins, called introns, are cut out and the coding portions are spliced back together.

This process is controlled by a large protein-RNA complex called the spliceosome. MIT biologists have now discovered a new layer of regulation that helps to determine which sites on the messenger RNA molecule the spliceosome will target.

The research team discovered that this type of regulation, which appears to influence the expression of about half of all human genes, is found throughout the animal kingdom, as well as in plants. The findings suggest that the control of RNA splicing, a process that is fundamental to [gene expression](#), is more complex than previously known.

"Splicing in more complex organisms, like humans, is more complicated than it is in some model organisms like yeast, even though it's a very conserved molecular process. There are bells and whistles on the human spliceosome that allow it to process specific introns more efficiently. One of the advantages of a system like this may be that it allows more complex types of gene regulation," says Connor Kenny, an MIT graduate student and the lead author of the study.

Christopher Burge, the Uncas and Helen Whitaker Professor of Biology at MIT, is the senior author of the study, which appears in *Nature Communications*.

Building proteins

RNA splicing, a process discovered in the late 1970s, allows cells to precisely control the content of the mRNA transcripts that carry the instructions for building proteins.

Each mRNA transcript contains coding regions, known as exons, and noncoding regions, known as introns. They also include sites that act as signals for where splicing should occur, allowing the cell to assemble the correct sequence for a desired protein.

This process enables a single gene to produce multiple proteins; over evolutionary timescales, splicing can also change the size and content of genes and proteins, when different exons become included or excluded.

The spliceosome, which forms on introns, is composed of proteins and noncoding RNAs called small nuclear RNAs (snRNAs). In the first step of spliceosome assembly, an snRNA molecule known as U1 snRNA binds to the 5' splice site at the beginning of the intron.

Until now, it had been thought that the binding strength between the 5' splice site and the U1 snRNA was the most important determinant of whether an [intron](#) would be spliced out of the mRNA transcript.

In the new study, the MIT team discovered that a family of proteins called LUC7 also helps to determine whether splicing will occur, but only for a subset of introns—in human cells, up to 50%.

Before this study, it was known that LUC7 proteins associate with U1 snRNA, but the exact function wasn't clear.

There are three different LUC7 proteins in human cells, and Kenny's experiments revealed that two of these proteins interact specifically with one type of 5' splice site, which the researchers called "right-handed." A third human LUC7 protein interacts with a different type, which the researchers call "left-handed."

The researchers found that about half of human introns contain a right- or left-handed site, while the other half do not appear to be controlled by interaction with LUC7 proteins. This type of control appears to add another layer of regulation that helps remove specific introns more efficiently, the researchers say.

"The paper shows that these two different 5' splice site subclasses exist and can be regulated independently of one another," Kenny says.

"Some of these core splicing processes are actually more complex than we previously appreciated, which warrants more careful examination of what we believe to be true about these highly conserved molecular processes."

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'Complex splicing machinery'

Previous work has shown that mutation or deletion of one of the LUC7 proteins that bind to right-handed splice sites is linked to [blood cancers](#), including about 10% of acute myeloid leukemias (AMLs).

In this study, the researchers found that AMLs that lost a copy of the LUC7L2 gene have inefficient splicing of right-handed splice sites. These cancers also developed the same type of altered metabolism seen in earlier work.

"Understanding how the loss of this LUC7 protein in some AMLs alters splicing could help in the design of therapies that exploit these splicing differences to treat AML," Burge says.

"There are also small molecule drugs for other diseases such as spinal muscular atrophy that stabilize the interaction between U1 snRNA and specific 5' splice sites. So the knowledge that particular LUC7 proteins influence these interactions at specific splice sites could aid in improving the specificity of this class of small molecules."

Working with a lab led by Sascha Laubinger, a professor at Martin Luther University Halle-Wittenberg, the researchers found that introns in plants also have right- and left-handed 5' splice sites that are regulated by Luc7 proteins.

The researchers' analysis suggests that this type of splicing arose in a common ancestor of plants, animals, and fungi, but it was lost from fungi soon after they diverged from plants and animals.

"A lot of what we know about how splicing works and what the core components are actually comes from relatively old yeast genetics work," Kenny says. "What we see is that humans and plants tend to have more complex splicing machinery, with additional components that can regulate different introns independently."

The researchers now plan to further analyze the structures formed by the interactions of Luc7 proteins with mRNA and the rest of the spliceosome, which could help them figure out in more detail how different forms of Luc7 bind to different 5' splice sites.

More information: Connor J. Kenny et al, LUC7 proteins define two major classes of 5' splice sites in animals and plants, *Nature Communications* (2025). DOI: [10.1038/s41467-025-56577-4](https://doi.org/10.1038/s41467-025-56577-4)

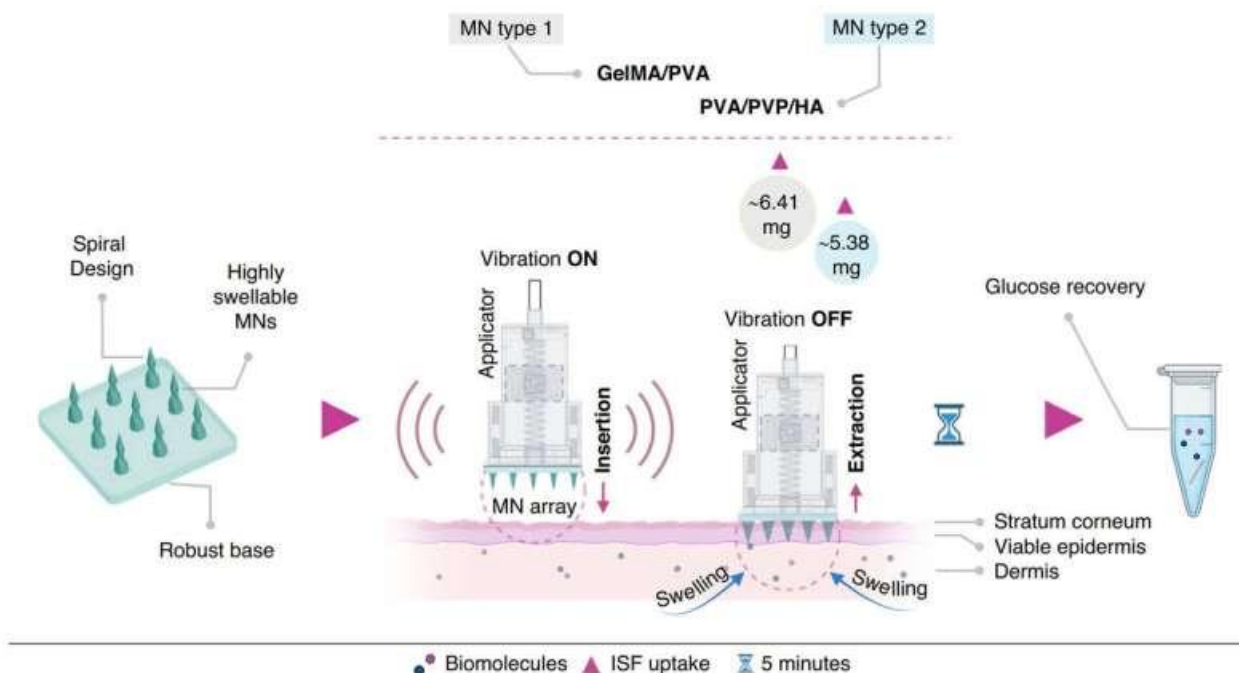
Journal information: [Nature Communications](#)
Provided by [Massachusetts Institute of Technology](#)

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FEBRUARY 20, 2025

Micro-vibration microneedles: Paving the way for rapid and minimally invasive biomarker detection

by Aerospace Information Research Institute, Chinese Academy of Sciences



Schematic illustration of minimally invasive ISF extraction and glucose recovery using highly swellable spiral MNs with the custom-made applicator to generate micro-vibration during the insertion phase. Credit: *Microsystems & Nanoengineering*

Scientists have created a new way to quickly and minimally invasively detect glucose using microneedles. These swellable hydrogel microneedles extract substantial amounts of skin fluid in just five minutes, a less invasive alternative to the finger-prick blood tests.

The [extraction](#) of interstitial fluid (ISF) for diagnostic purposes has long been a challenging process. Traditional methods, such as suction blister and sonophoresis, are not only time-consuming but also often result in significant disruption to the skin's outermost layer, the stratum corneum, causing local trauma.

Microneedles (MNs) have emerged as a promising alternative, offering a less invasive way to access ISF. However, current MN technologies are limited by their low extraction volumes and prolonged extraction times, typically requiring 10–15 minutes to obtain only small amounts of ISF. Given these limitations, there is a critical need for research to develop faster and more efficient ISF extraction methods.

In a [study](#) published in *Microsystems & Nanoengineering*, researchers from the University of Southern Queensland, Australia, present a novel approach to ISF extraction using micro-vibration assisted dual-layer spiral microneedles.

The study details the development and testing of these microneedles, which are designed to rapidly and efficiently extract ISF for biomarker sensing.

The study introduces two innovative types of spiral-shaped, swellable microneedle arrays designed for rapid interstitial fluid (ISF) extraction.

The first array is composed of gelatin methacryloyl (GelMA) and PVA, while the second incorporates a combination of polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), and hyaluronic acid (HA). These microneedles demonstrated impressive swelling ratios of $560 \pm 79.6\%$ and $370 \pm 34.1\%$ in artificial ISF within just 10 minutes, respectively.

A key innovation of this research is the development of a custom-designed Arduino-based applicator that vibrates at frequencies between 50–100 Hz. This micro-vibration technology significantly enhances the skin penetration efficiency of the microneedles, allowing for more effective uptake of ISF.

In ex vivo tests on porcine ear skin, the GelMA/PVA microneedles were able to rapidly uptake 6.41 ± 1.01 mg of ISF in just five minutes, while the PVA/PVP/HA microneedles extracted 5.38 ± 0.77 mg within the same timeframe.

To validate the microneedles' ability to recover glucose as a target biomarker, a mild heating procedure was used, followed by glucose concentration determination using a D-glucose content assay kit. The results showed that the microneedles could efficiently extract ISF and detect glucose, suggesting their potential for rapid and minimally invasive biomarker sensing.

This research not only addresses the limitations of current ISF extraction methods but also opens new avenues for the development of point-of-care diagnostics and real-time health monitoring devices.

According to Dr. Zahra Faraji Rad, the lead researcher, "This study represents a significant advancement in the field of minimally invasive diagnostics. The combination of novel [microneedle](#) design and micro-vibration technology has the potential to simplify the

way we extract and analyze biomarkers, making the process faster, more efficient, and less invasive."

The development of these microneedles has broad implications for point-of-care diagnostics for biomarker detection. They offer a viable alternative to traditional blood sampling, particularly in resource-limited settings or for patients requiring frequent monitoring.

The rapid extraction of ISF and efficient glucose detection capabilities of these microneedles suggest their potential for use in the management of chronic conditions like diabetes, where frequent finger pricks are typically required to draw blood for glucose detection.

More information: Khaled Mohammed Saifullah et al, Micro-vibration assisted dual-layer spiral microneedles to rapidly extract dermal interstitial fluid for minimally invasive detection of glucose, *Microsystems & Nanoengineering* (2025). DOI: [10.1038/s41378-024-00850-x](https://doi.org/10.1038/s41378-024-00850-x)

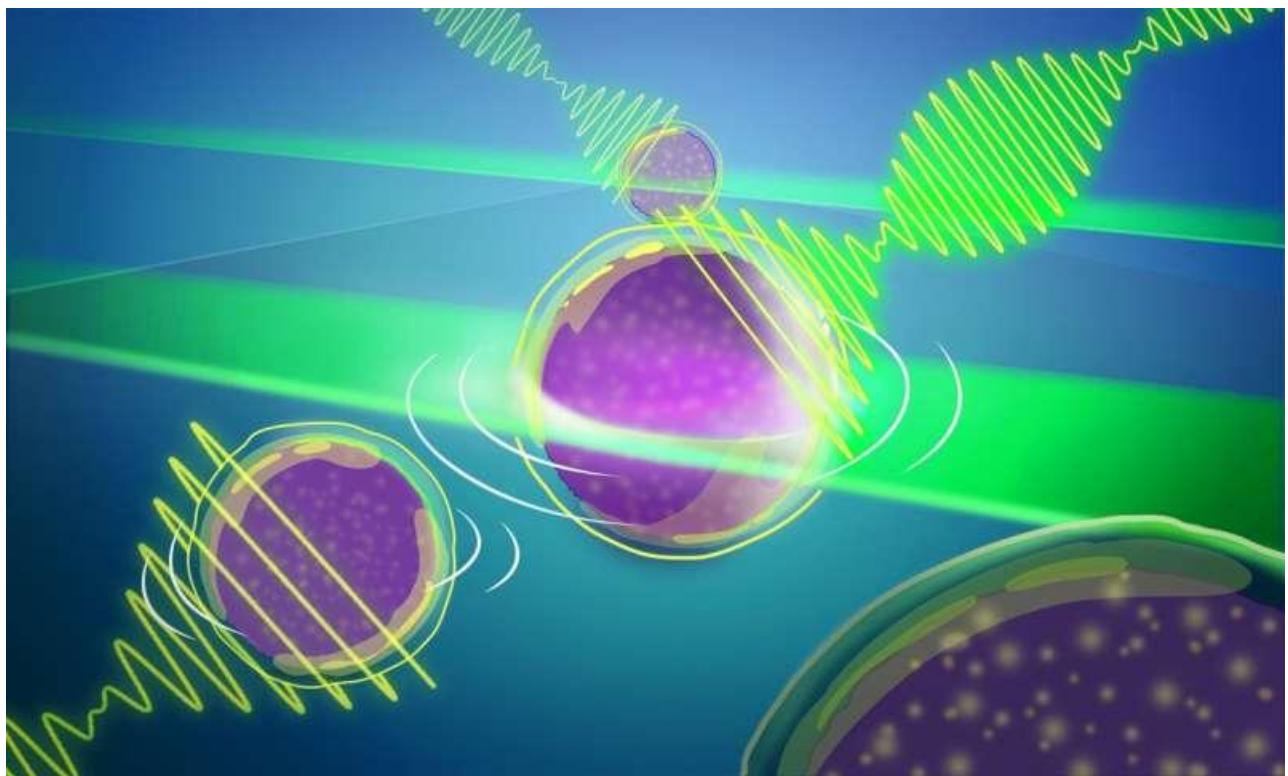
Journal information: [Microsystems and Nanoengineering](#)

Provided by Aerospace Information Research Institute, Chinese Academy of Sciences

FEBRUARY 20, 2025

Pushing the limits of 'custom-made' microscopy: 3-D imaging of light-sensitive samples now 1,000 times faster

by [European Molecular Biology Laboratory](#)



An artist's representation of the new Brillouin microscopy approach that allows entire light-sheets to interact with 3D biological samples. The scattered light reveals a unique optical interference signal that can be recorded with a custom-developed spectrometer, tremendously speeding up image acquisition. Credit: Daniela Velasco/EMBL

EMBL tech developers have made an important leap forward with a novel methodology that adds an important microscopy capability to life scientists' toolbox. The advance represents a 1,000-fold improvement in speed and throughput in Brillouin microscopy and provides a way to view light-sensitive organisms more efficiently.

"We were on a quest to speed up [image acquisition](#)," said Carlo Bevilacqua, optical engineer in EMBL's Prevedel team and lead author on a paper [published](#) about this [technological development](#) in *Nature Photonics*.

"Over the years, we have progressed from being able to see just a pixel at a time to a line of 100 pixels, to now a full plane that offers a view of approximately 10,000 pixels."

The technology is based on a [phenomenon first predicted](#) in 1922 by French physicist Léon Brillouin. He showed that when light is shone on a material, it interacts with naturally occurring thermal vibrations within, exchanging energy and thereby slightly shifting the frequency (or color) of the light. Measuring the spectrum (colors) of the [scattered light](#) reveals information about a material's physical characteristics.

Using Brillouin scattering for microscopy purposes came much later—in the early 2000s—when other technological advancements enabled scientists to measure tiny frequency shifts with high precision and sufficient throughput. This allowed them to compute [mechanical properties](#) of living [biological samples](#).

However, at that point, scientists were only able to view one pixel at a time. The process was therefore quite time-consuming, and it severely limited how the microscopy method could be used in biology.

In 2022, Bevilacqua and others in the Prevedel group were able to first expand the field of view to a line, and now with this latest development, to a full 2D field of view, which also helps speed up 3D imaging.

"Just as the development of light-sheet microscopy here at EMBL marked a revolution in [light microscopy](#) because it allowed for faster, high-resolution, and minimally phototoxic imaging of biological samples, so too does this advance in the area of mechanical or Brillouin imaging," said Robert Prevedel, Group Leader and senior author on the paper.

"We hope this new technology—with minimal light intensity—opens one more 'window' for life scientists' exploration."

More information: Bevilacqua, C. et al. Full-field Brillouin microscopy based on an imaging Fourier transform spectrometer, *Nature Photonics* (2025). [DOI: 10.1038/s41566-025-01619-y](https://doi.org/10.1038/s41566-025-01619-y)

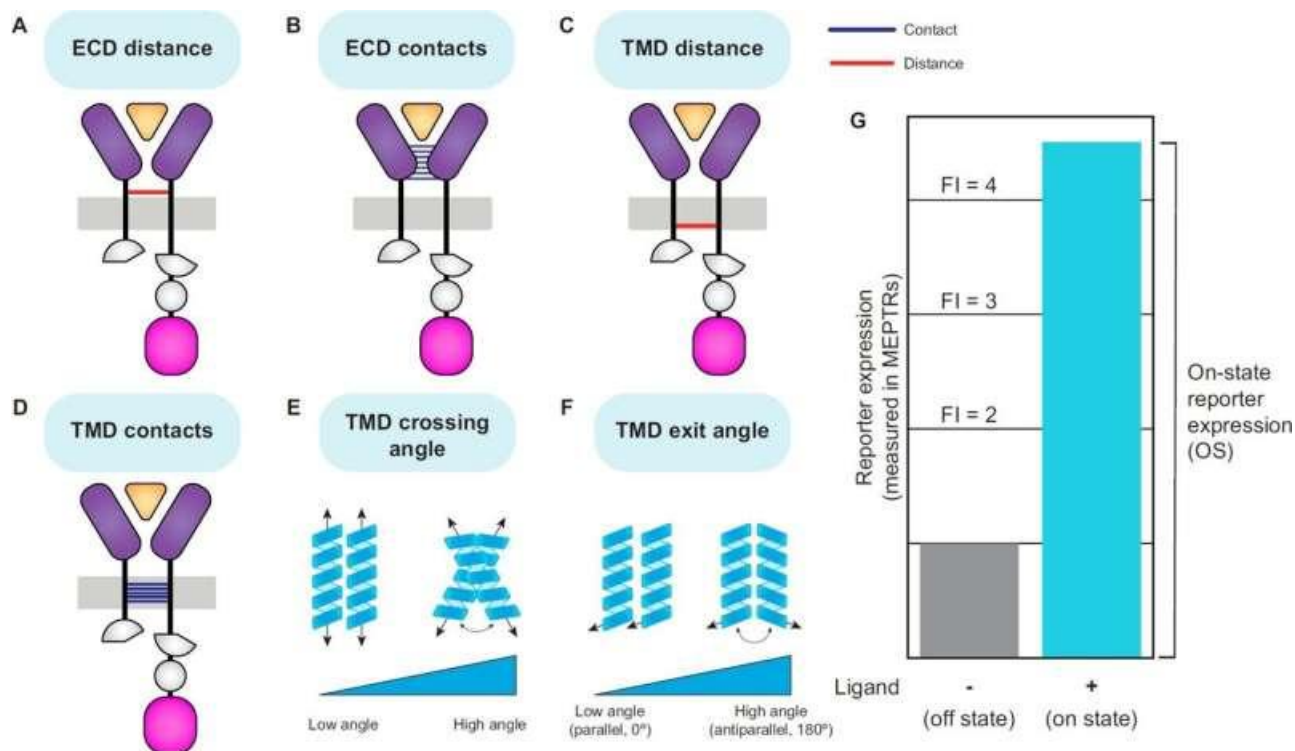
Journal information: [Nature Photonics](#)

Provided by [European Molecular Biology Laboratory](#)

FEBRUARY 20, 2025

Unraveling structure and function relationships in synthetic cell receptors

by Justin Jackson , Phys.org



Definition of structural features and performance metrics. Credit: *GEN Biotechnology* (2025). DOI: 10.1089/genbio.2024.0057

Northwestern University researchers have identified structural features in engineered cell receptors that correlate with variations in receptor function.

Computational protein structure prediction tools were used to analyze a library of synthetic receptors, revealing that specific structural attributes such as ectodomain (ECD) distance and [transmembrane domain](#) (TMD) interactions are associated with receptor performance.

Engineered cell therapies rely on synthetic receptors to transduce external signals into intracellular responses. The precise relationship between receptor structure and function remains poorly understood. Advances in protein structure prediction tools, such as AlphaFold and ColabFold, have enabled the modeling of complex proteins, including single-pass transmembrane receptors.

In the study, "Exploring Structure-Function Relationships in Engineered Receptor Performance Using Computational Structure Prediction," [published](#) in *GEN Biotechnology*, researchers integrated predicted protein conformations with experimental performance

metrics across four engineered receptor families, examining whether certain molecular features correlated with functional output.

Researchers analyzed a library of engineered receptors derived from natural cytokine receptors, focusing on Modular Extracellular Sensor Architecture (MESA) receptors. MESA receptors use ligand-induced dimerization to activate a split Tobacco Etch Virus Protease (TEVp), which releases a transcription factor to drive gene expression.

ColabFold was used to generate structural models of receptor ECDs in complex with their ligands, while PREDDIMER was employed to model TMD interactions.

Structural features were quantified, including ECD distance, ECD contacts, TMD distance, TMD contacts, TMD crossing angle, and TMD exit angle. Receptor performance was assessed based on on-state reporter expression (OS) and fold induction (FI) in experimental data.

Substantial variation in receptor performance was explained by structural features. Shorter ECD and TMD distances correlated with higher OS, while greater ECD and TMD contacts were also associated with improved performance. TMD exit angle had a significant relationship with receptor function in certain receptor families, particularly in [tumor necrosis factor](#) (TNF) MESA.

Structural models explain less variation in performance for heterotetrameric receptors, such as interleukin-10 (IL-10) MESA and transforming growth factor beta (TGFb) MESA. This suggests that additional factors, such as higher-order receptor complex formation, may contribute more to the performance of these receptors.

To complement structural analyses, the researchers evaluated categorical variables representing domain choices within receptor chains. One-hot encoding of receptor components revealed that VEGF MESA receptors containing a CD28 TMD in the C-terminal chain and a VEGFR1 ECD exhibited higher OS. The reduced categorical model explained 57% of OS variation, closely aligning with the structural model's performance.

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A combined model integrating both structural and categorical features demonstrated superior predictive power, explaining 79% of OS variation. This improvement indicates that while structural and categorical models share some information, they capture distinct determinants of receptor performance.

The findings present actionable hypotheses for synthetic receptor engineering. For instance, modifying receptor linkers to enhance ECD contacts or selecting TMD pairs that favor closer C-terminal proximities could improve [receptor function](#).

A notable challenge in this work was modeling the entire single-pass transmembrane receptor, including the natural ectodomain (ECD), the transmembrane domain (TMD), and the split TEVp intracellular domains (NTEVp or CTEVp) using ColabFold.

Specifically, the tool struggled with aligning the shorter TEVp regions within long receptor sequences. During the multiple sequence alignment (MSA) search step, the sizable ECD and native TMD often dominated the alignment results, causing ColabFold to drop or poorly cover the TEVp segments.

As a result, the predicted structures sometimes failed to show a properly folded NTEVp or CTEVp, yielding low-confidence scores (pLDDT) in those intracellular portions.

Shorter ectodomains (e.g., IL-10 receptors) were more likely to retain coverage for the TEVp domains, allowing a few full-length models to converge on structures where the NTEVp and CTEVp were reconstituted.

Because of these alignment issues, the study opted for a modular approach, modeling ECD–ligand complexes separately with ColabFold and then using PREDDIMER to capture TMD–TMD interactions.

While this strategy prevented direct visualization of how NTEVp and CTEVp might orient themselves under membrane constraints, it ensured higher confidence in the predicted extracellular and transmembrane regions. The trade-off is that intermolecular effects were not fully captured.

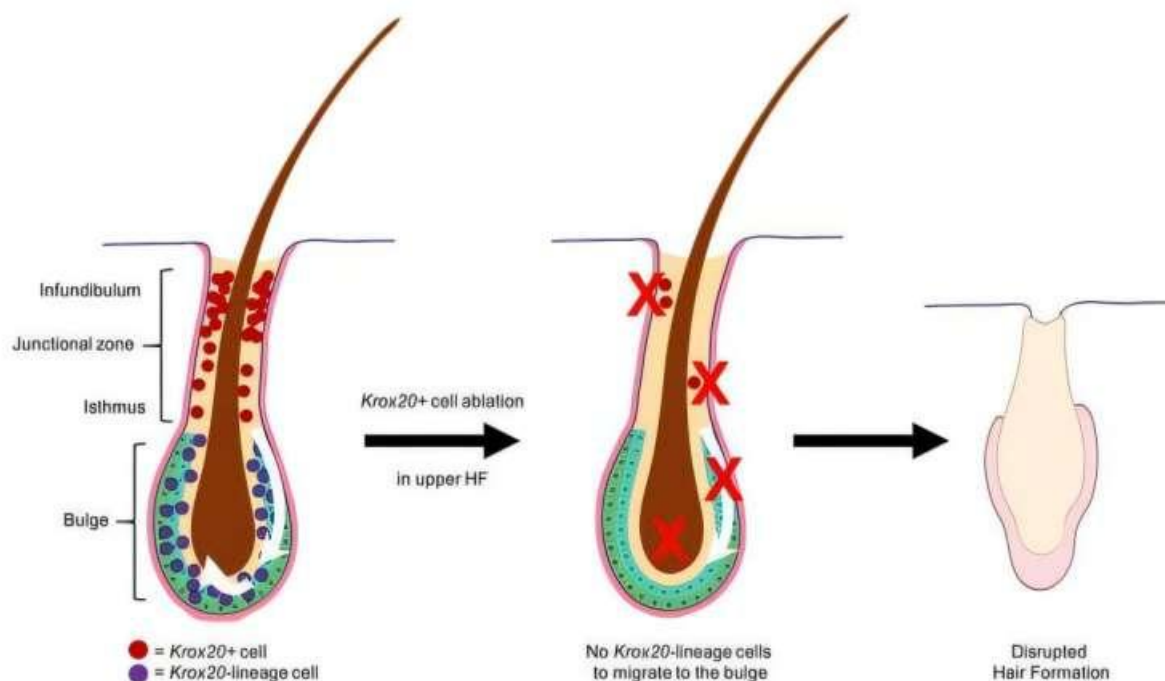
More information: William K. Corcoran et al, Exploring Structure—Function Relationships in Engineered Receptor Performance Using Computational Structure Prediction, *GEN Biotechnology* (2025). [DOI: 10.1089/genbio.2024.0057](https://doi.org/10.1089/genbio.2024.0057)

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FEBRUARY 20, 2025

Epithelial stem cell ancestors for hair follicle formation

by Josh Barney, [University of Virginia](#)



Credit: *Journal of Clinical Investigation* (2024). DOI: 10.1172/JCI180160

What if the secret to curing baldness has been hiding in your hair all along? University of Virginia School of Medicine researchers have discovered a little-known group of stem cells in hair follicles that could bring back lost locks, challenging some long-held beliefs.

UVA's Dr. Lu Q. Le and his team have identified a previously overlooked stem cell population in the upper and middle sections of the hair [follicle](#) that plays a crucial role in [hair growth](#). When these cells are depleted, hair growth stops, suggesting that replenishing or activating these stem cells could restore hair growth. The research is [published](#) in the *Journal of Clinical Investigation*.

Le's team found these malleable stem cells in the upper and middle regions of the hair follicle serve as early ancestors of our hair, upending the long-accepted belief that hair growth begins with stem cells in an area near the bulbous base of the follicle, technically known as "the bulge."

"These findings add new foundational knowledge to hair follicle biology, showing, for the first time, that the bulge cells actually arise from this novel stem cell population," said Le, chair of the Department of Dermatology at the UVA School of Medicine and UVA Health. "It

is our hope that these stem cells could one day provide a novel therapy for treating [hair loss](#) in people."



University of Virginia researchers say a group of stem cells in the upper and middle sections of the hair follicle could help restore hair growth. Credit: John DiJulio, University Communications

Understanding hair growth—and loss

Each of the millions of hairs on our bodies grows from an individual follicle, like a tulip grows from a bulb. Le's research casts new light on follicle formation, showing that the bulge above the follicle's base develops from stem cells located closer to the skin's surface.

Researchers found that stem cells—cells that can turn into other types of cells—continue to play an essential role in hair growth after the follicle forms. Located along the hair shaft beneath the skin's surface, the stem cells move downward to nourish and resupply the bulge at the follicle's base. Le and his collaborators believe these cells serve as the building blocks for hair formation.

In their lab tests, researchers found depleting these stem cells at certain times halted hair growth, highlighting their essential role in hair formation and their potential link to hair loss.

Based on their findings, Le and his team believe keeping the stem cells active to ensure the follicle has adequate supply for hair growth could, with further research, offer a new way to combat hair loss.

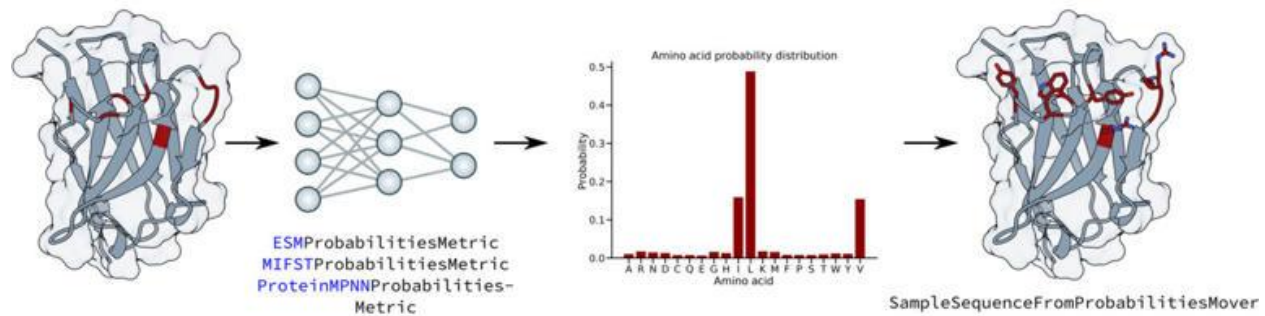
"We plan to fully investigate the potential of these stem cells in human hair follicles," Le said. "Importantly, we found that in the human bald scalp, although the hair shafts are gone, this population of novel hair [stem cells](#) is still present in the upper hair follicle. This means that if we could reactivate these cells to migrate down and repopulate the bulge, they could potentially regrow hair on a bald scalp."

More information: Elnaz Ghotbi et al, Transcription factor KROX20 marks epithelial stem cell ancestors for hair follicle formation, *Journal of Clinical Investigation* (2024). [DOI: 10.1172/JCI180160](#)

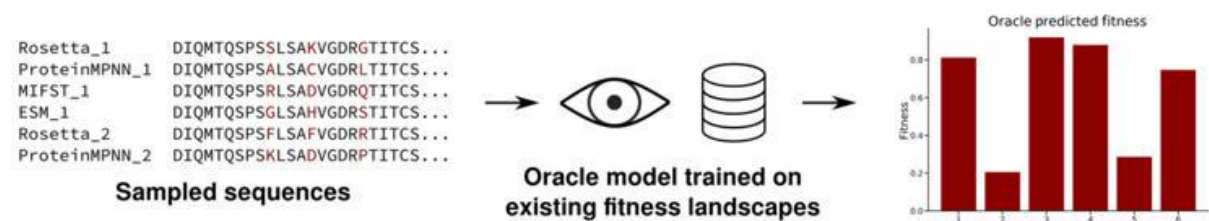
Journal information: [Journal of Clinical Investigation](#)
 Provided by [University of Virginia](#)

AI and biophysical modeling unite for novel protein design

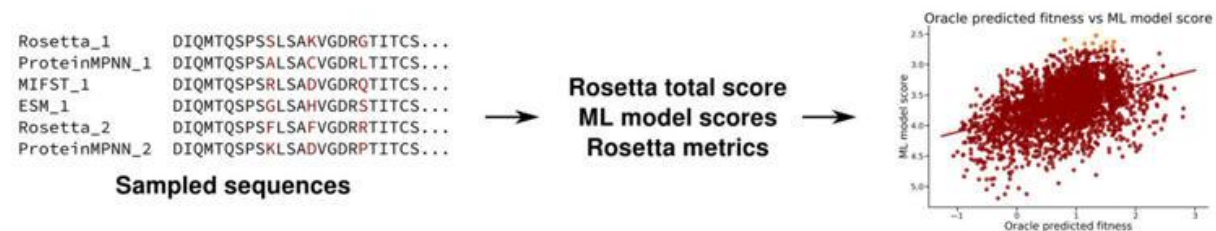
A Predict amino acid probabilities and sample sequences



B Evaluate fitness of sampled sequences with oracle model



c Identifying high fitness candidates with Rosetta/ML scores



An interdisciplinary research team from Leipzig University and the Saxon AI center ScaDS.AI has developed a novel approach that integrates artificial intelligence (AI) methods with biophysical modeling. This innovative strategy can be applied to the development of new therapeutics, such as antibodies and vaccines, including those for pandemic preparedness.

The research project, conducted in collaboration with Vanderbilt University in Nashville, US, is the result of extensive preliminary work in computer-aided drug development. [The study](#) has been published in the journal *Science Advances*.

The scientists believe that the current research landscape in the field of computational protein design is akin to a gold rush, with many new methods being published without experimental validation. This often leads to inaccurate assessments of the performance of AI models.

"We urgently need standards for the description and availability of such models," says Professor Clara Schoeder, research group leader at the Institute for Drug Discovery. "Our research makes an important contribution to this goal."

The current findings show that AI methods are particularly good at suggesting sequences that do not disrupt the folding of proteins. However, they struggle when it comes to accurately assessing the effects of individual amino acid changes on folding.

"Our findings make it clear that no AI model or biophysical method is ideally suited to all design problems," explains Humboldt Professor Jens Meiler, one of the project's lead scientists and Director of the Institute for Drug Discovery.

"In the future, we will have to carefully consider which model to use for which purpose. Our work is a first step towards greater comparability between the different methods."

The Rosetta biophysical software suite, which has been used in protein research for many years, provides a framework for integrating different AI methods.

Rosetta is used by more than 100 laboratories worldwide and allows researchers to efficiently combine different approaches, such as large language models (e.g. ESM-2) and the ProteinMPNN model, with biophysical methods. This

combination allows researchers to compare and analyze the different behaviors of the design approaches.

"With this development, we can quickly and easily combine AI models with classical methods and use them side by side," explains Professor Meiler.

"This greatly simplifies our work and allows us to take full advantage of all the infrastructure that has been developed in Rosetta over the last 20 years."

This does not mean that the research project is finished. The research groups led by Professor Meiler and Professor Schoeder will continue to refine and experimentally evaluate the developed algorithms, particularly with regard to vaccine design for pandemic preparedness.

"We are investigating which methods reliably suggest amino acid changes that could lead to vaccine candidates," says Professor Clara Schoeder.

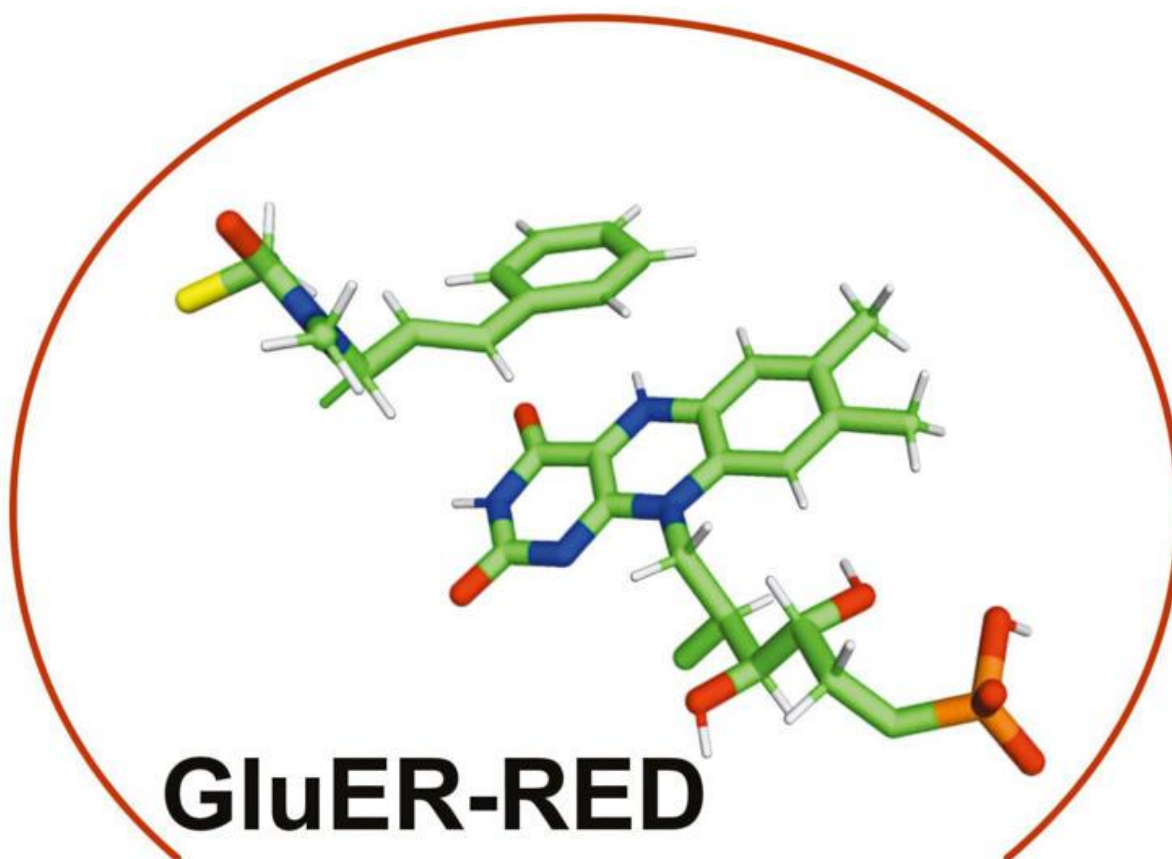
Despite the progress made through the use of AI, the so-called scoring problem remains a challenge. This refers to the difficulty of predicting the effect of a single amino acid substitution.

In collaboration with the Center for Scalable Data Analytics and Artificial Intelligence, ScaDS.AI, the research team is optimistic that the combination of AI and biophysical methods will increase the efficiency of protein design.

More information: Moritz Ertelt et al, Self-supervised machine learning methods for protein design improve sampling but not the identification of high-fitness variants, *Science Advances* (2025). [DOI: 10.1126/sciadv.adr7338](https://doi.org/10.1126/sciadv.adr7338)

Provided by Leipzig University

Computational chemistry promises to upset traditional methods of chemical synthesis



Charge Transfer Complex Engineering

Graphical abstract. Credit: Chem (2024). DOI: 10.1016/j.chempr.2024.09.017

The process of discovering and designing new chemicals has always been arduous—Sijia Dong wants to change that. As an assistant professor in the department of chemistry and chemical biology, with affiliations in physics and

chemical engineering, Dong uses "physics-based simulations, AI and quantum computing" to accelerate chemical discovery.

When we think of chemistry, we may think of liquids in test tubes and under microscopes, but chemicals, too, are composed of subatomic particles like electrons and protons, a fact that Dong and her research team take advantage of in their study of enzymes—proteins that help one chemical transform into another.

Photochemistry, Dong says, is the study of how chemicals change in response to photons—light. With recent research, [published](#) in *Chem*, Dong and her collaborators use photochemistry to enable novel enzymatic synthesis through a physical process called charge transfer.

This allows them to engineer unique, light-driven "photoenzymes for large-scale, energy-efficient chemical synthesis," she says.

"These charge transfers actually happen on electronic excited states," Dong says, meaning that the electrons of the molecule are at higher energy levels. Incorporating these "excited states into the enzyme design strategy" is "something that hasn't been explored much before."

"We found through computational studies that by engineering the protein we can actually modulate or control the electronic structure of these charge transfer complexes," and thus control the reaction.

When it comes to light-driven chemistry, pharmaceutical companies, she continues, are always interested in new synthesis methods "because it could potentially become an energy-efficient and low-cost way to make drugs."

Dong's ongoing work "focuses on developing a computational framework for the mechanistic studies, prediction and design of photoenzymes," she says.

This computational framework, she says, "will provide a new approach to catalyst design and could potentially revolutionize chemical discovery," she wrote in a follow-up.

"There are things that you can't measure experimentally—or cannot be cheaply done experimentally," she says, including the mechanism behind many reactions and the "high-throughput screening of" mutations in a protein.

Current engineering methods often rely on what's known as directed evolution, where scientists "are randomly mutating the protein and then seeing what happens," Dong says, picking the mutations that are closest to their goal for a particular chemical, and then repeating this iterative process.

Dong sees an alternative, to do "inverse design with machine learning." Instead of starting with one protein and haphazardly directing its evolution—through scattershot, random mutations—"if we know what kind of functionality we want," Dong says, they can leverage "both machine learning and first-principles simulations to basically predict what protein sequence can achieve that" functionality.

Artificial intelligence and new simulation methods will also help researchers "predict what properties enzymes might have given certain mutations," as opposed to running through the entire costly evolution process.

The directed evolution of enzymes, while it was revolutionary in its own time, "can be very costly," Dong says, and "you are not guaranteed to find what you want to find."

With Dong's physics-based framework, "you are more likely to find a protein variant you want, [in a] shorter amount of time with less money."

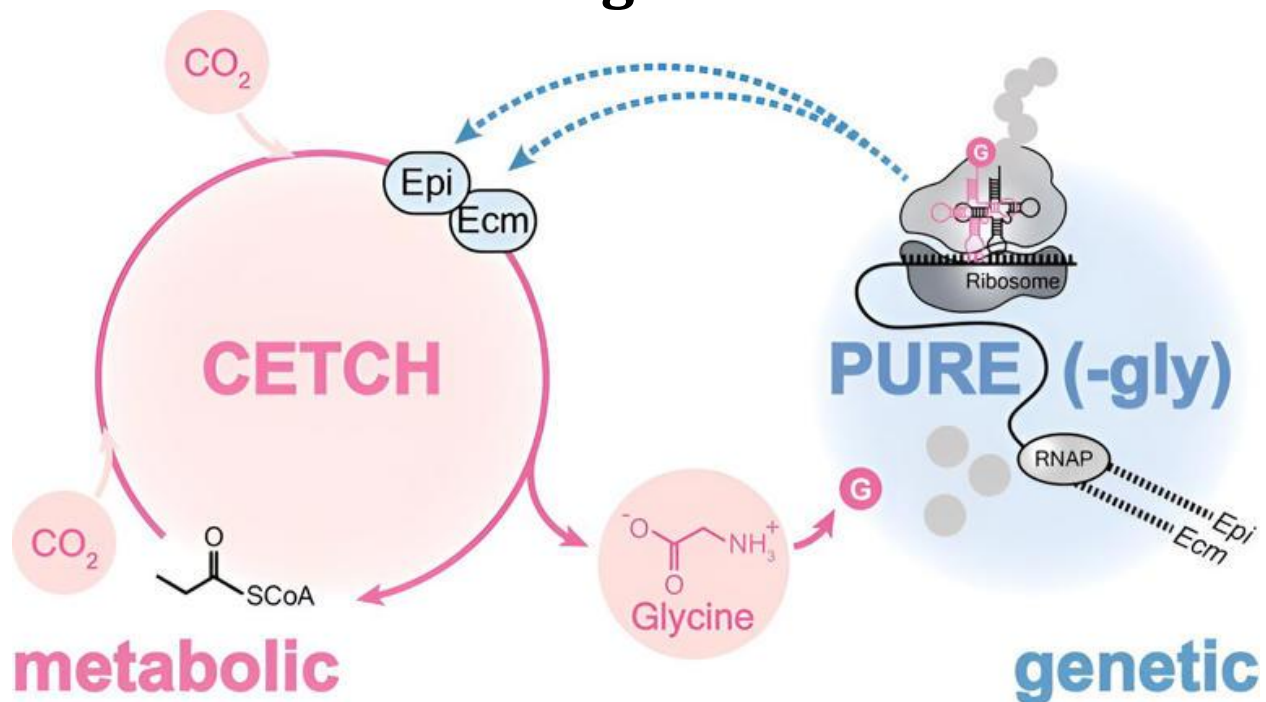
The 2024 Nobel Prize in Chemistry was partly awarded to a pioneer in the field of computational protein design. "We are on an emerging front of the field," Dong wrote, "developing a computational framework for designing proteins that can enable light-driven chemistry."

More information: Jose M. Carceller et al, Engineering a photoenzyme to use red light, *Chem* (2024). DOI: [10.1016/j.chempr.2024.09.017](https://doi.org/10.1016/j.chempr.2024.09.017)

This story is republished courtesy of Northeastern Global News news.northeastern.edu.

Provided by Northeastern University

Team develops the first cell-free system in which genetic information and metabolism work together



Cell-free system composed of interdependent metabolic (Cetch cycle, pink) and genetic (Pure, blue) levels that recursively interact with one another. Pure produces the missing enzymes for CO_2 fixation (i.e. Epi and Ecm) by transcription and translation (TX-TL) of Epi and Ecm genes; Cetch utilizes such enzymes for synthesizing glycine from CO_2 , thus sustaining protein production. Enzyme abbreviations Epi, Ecm, and RNAP stand for methylmalonyl-/ethylmalonyl-CoA epimerase, ethylmalonyl-CoA mutase, and RNA polymerase respectively. Credit: MPI f. Terrestrial Microbiology/ Giaveri© Provided by Phys.org

The capacity of all living systems to develop, organize and sustain themselves is based upon a cyclical process in which genes and metabolism interact in parallel. While genes encode the components of metabolism, metabolism provides the energy and building blocks to maintain and process genetic information.

In synthetic biology, researchers explore the principles of life by reconstructing its systems from the bottom-up, starting with the minimum number of parts required. In recent years, this approach has made it possible to develop complex metabolic networks and cell-free genetic systems outside the cell environment—in vitro—for example, in microfluidic chambers.

What these approaches have in common is that all the biocatalysts that function in these systems are added from the outside, and the whole process only continues as long as it is supplied with a continuous stream of new building blocks, information and energy.

By interlinking the metabolic and genetic levels, researchers want to create self-sustaining synthetic biological systems that can generate their own building blocks and drive processes in a reciprocal manner—just like in living cells. A team led by Tobias Erb from the Max Planck Institute for Terrestrial Microbiology in Marburg, Germany, has now made a significant step towards this goal.

The team has developed the first cell-free system in which a genetic and a metabolic network keep each other running. The system produces metabolic enzymes itself and works both in the test tube and in artificial cell-mimics. It is based on the synthetic CETCH cycle, a metabolic network that uses CO₂ as a raw material to produce organic molecules.

The work is [published](#) in the journal *Science*.

The trick: Interdependence

"We coupled the CETCH cycle with an existing genetic system called Pure, a synthetic transcription and translation machine that works with a mixture of ribosomes, DNA, RNAs, and proteins, outside living cells. We engineered the two levels to work together like an engine. Once started, it keeps going because the two networks feed on each other," explains Simone Giaveri, EMBO fellow and first author of the paper.

To make this work, the researchers made the components dependent on each other. They programmed Pure to produce two of the CETCH enzymes. However, this Pure variant lacks the essential amino acid glycine, which is needed to build proteins. CETCH was modified to produce glycine directly from CO₂. As Pure obtains the glycine from CETCH, the cycle is closed.

To prove that their approach worked, the researchers first added glycine to Pure, which contained the information for the production of a fluorescent protein. Its glow indicated the sought-after activity of the genetic network. The next step was to introduce the synthetic CETCH cycle. Once the synthetic pathway was

introduced, the coupled system became capable of producing the glycine itself—and in turn two proteins of the CETCH, as well as the fluorescent protein.

Of the more than 50 proteins in the system, the system produces only two by itself. Yet that is all that is needed to drive the synthetic cycle.

"Without the genetic component and the mutual feedback, the cycle would only run for less than one hour. The fact that there is self-regeneration means that it will last at least twelve hours before the system stops for various reasons, for example, because components fail, or byproducts accumulate too much," explains Giaveri. "You have to start it with a minimal amount of glycine and it will keep going."

Most of the elements of the synthetic metabolism are still provided from outside.

"We're still a long way from a system that can regenerate all its own components," says Erb. This would involve encoding complete metabolic networks, coding self-repair programs to extend the lifespan of in vitro systems, as well as integrating biochemical recycling cycles.

"So far, we have only managed to produce one building block, and we are still a long way from being able to produce all the building blocks from CO₂. However, we have developed a basic operating system that will benefit from future developments in this fast-moving field of research. Looking even further into the future, you can imagine that in the future we will be able to run such a system on light or even sustainable electricity."

A basic operating system for future sustainable systems

The orchestration of more than 50 proteins, energy sources, genetic information and building blocks is the result of an enormous number of experiments in which Giaveri tested and optimized combinations in parallel. Each element in Giaveri's highly complex system is precisely designed for its purpose.

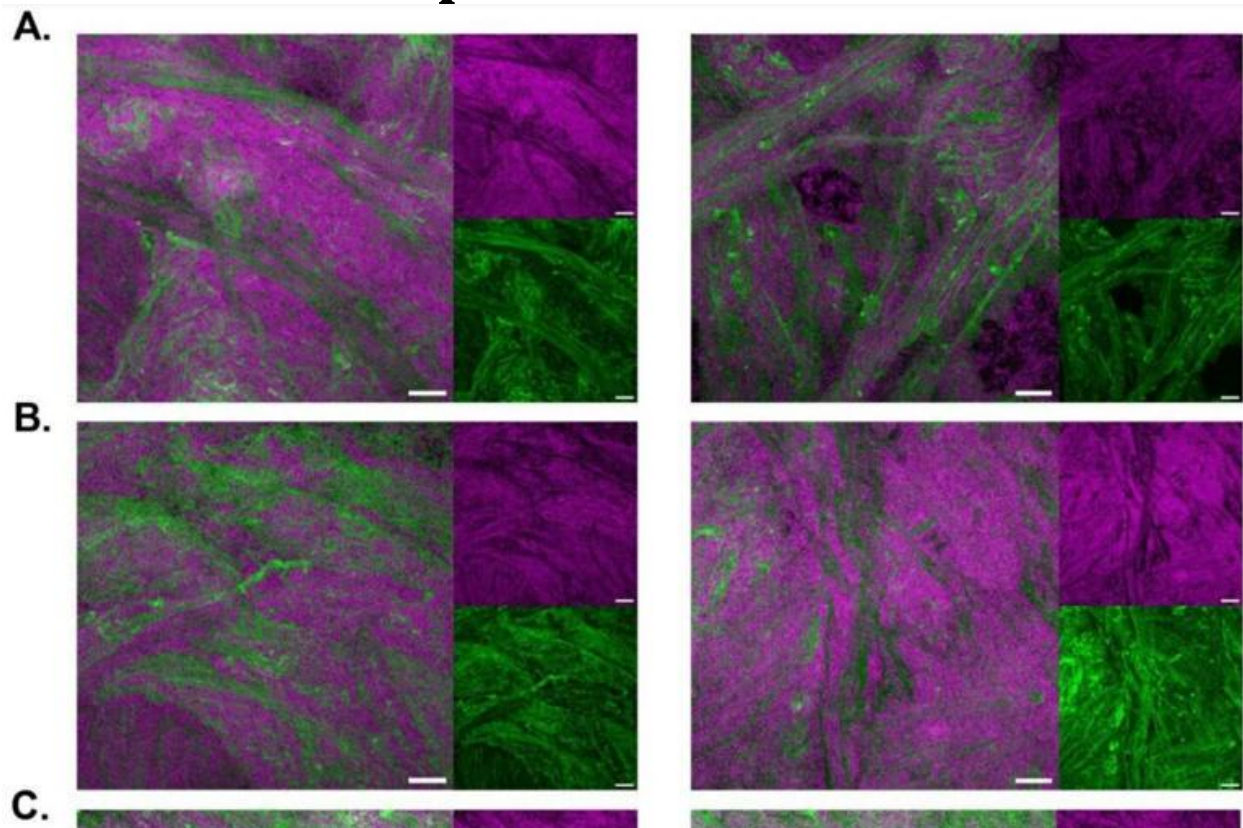
"You can use our system as an operating unit, as a basic engine for in vitro systems," says Erb. "And because it is based on CO₂, this would become possible

in a fully sustainable way, because this raw material is available in practically unlimited quantities."

More information: Simone Giaveri et al, Integrated translation and metabolism in a partially self-synthesizing biochemical network, *Science* (2024). [DOI: 10.1126/science.adn3856](https://doi.org/10.1126/science.adn3856)

Provided by Max Planck Society

Customized living materials: Genetic tweaks enable precise control



Different fields of view of the BUD variants using confocal microscopy. Credit: ACS Synthetic Biology (2024). DOI: 10.1021/acssynbio.4c00336

Rice University researchers have revealed novel sequence-structure-property relationships for customizing engineered living materials (ELMs), enabling more precise control over their structure and how they respond to deformation forces like stretching or compression.

The study, published in a special issue of [ACS Synthetic Biology](#), focuses on altering protein matrices, which are the networks of proteins that provide structure to ELMs. By introducing small genetic changes, the team discovered they could make a substantial difference in how these materials behaved. These findings could open doors for advancements in tissue engineering, drug delivery and even 3D printing of living devices.

"We are engineering cells to create customizable materials with unique properties," said Caroline Ajo-Franklin, professor of biosciences and the study's corresponding author. "While synthetic biology has given us tools to tweak these properties, the connection between genetic sequence, material structure and behavior has been largely unexplored until now."

Using synthetic biology techniques, the team worked with a bacterium called *Caulobacter crescentus*. Previous members of the lab engineered the bacteria to produce a protein called BUD (short for "bottom-up de novo"), which helps cells stick together and form a supportive matrix. This allowed the bacteria to grow into centimeter-sized structures, which the group calls BUD-ELMs.

Adopting this engineering approach, the researchers varied the length of specific protein segments called elastin-like polypeptides (ELPs) and created new materials. The team characterized the original midlength BUD-ELM and two new variants and discovered each exhibited different properties.

The first material, termed BUD₄₀, had the shortest ELPs and formed thicker fibers that resulted in a stiffer bulk material. The second type, BUD₆₀, had midlength ELPs and created a combination of globules and fibers, producing the strongest material under deformation oscillation stress. Lastly, BUD₈₀, which had the longest ELPs, generated thinner fibers, resulting in a less stiff material that breaks easily under deformation stress.

Advanced imaging and mechanical tests showed that these differences weren't just cosmetic—they also affected how the materials handled stress and flowed under pressure. BUD₆₀, for example, could withstand more force and adapt better to changes in its environment, making it ideal for applications like 3D printing or drug delivery.

All three materials had two things in common: They exhibited shear-thinning behavior and held a lot of water—about 93% of their weight—which makes them well suited for biomedical uses such as scaffolds to support cell growth in tissue engineering or systems for delivering medications in a controlled way.

"This study is one of the first to focus on building living materials from the ground up with tailored mechanical properties rather than just adding biological functions," said Esther Jimenez, a graduate student in biosciences and first author of the study. "By making small tweaks to protein sequences, we've gained valuable insights into how to design materials with specific mechanical properties."

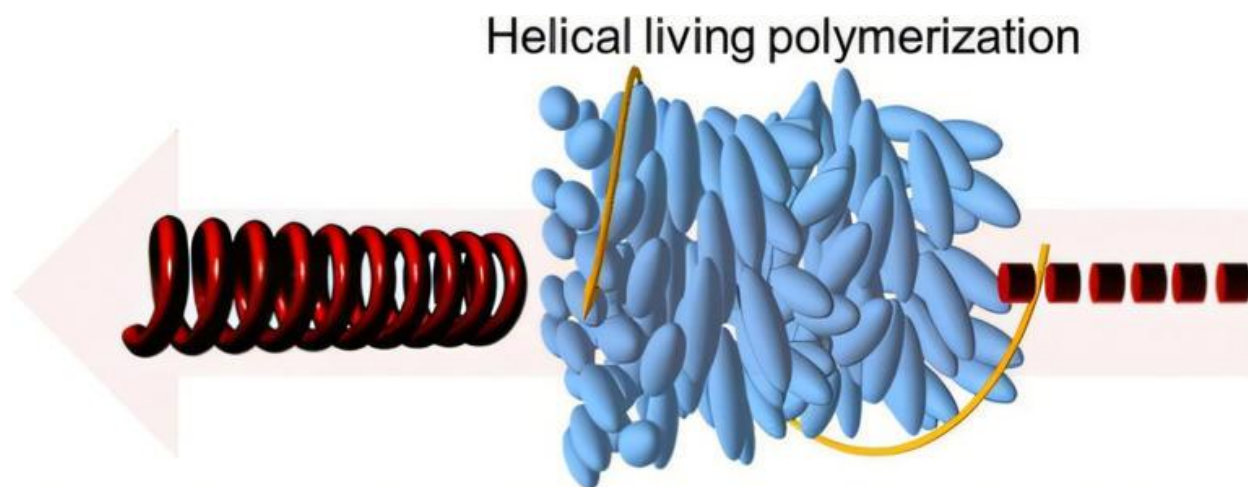
The potential uses extend beyond the biomedical field; these self-assembling materials could be adapted for environmental cleanup or renewable energy applications like building biodegradable structures or harnessing natural processes to generate energy.

"This work emphasizes the importance of understanding sequence-structure-property relationships," said senior Carlson Nguyen, a biosciences major and second author of the study. "By identifying how specific genetic modifications affect material properties, we're building a foundation for designing next-generation living materials."

More information: Esther M. Jimenez et al, Genetically Modifying the Protein Matrix of Macroscopic Living Materials to Control Their Structure and Rheological Properties, *ACS Synthetic Biology* (2024). [DOI: 10.1021/acssynbio.4c00336](https://doi.org/10.1021/acssynbio.4c00336)

Provided by Rice University

Biomimetic polymerization: Liquid crystals enable chiral polymer synthesis



Graphical abstract. Credit: *Macromolecules* (2025). DOI: 10.1021/acs.macromol.4c01017

By using optically active liquid crystals as reaction sites, researchers at University of Tsukuba have successfully achieved the living polymerization of polymers with aligned helical structures. In this process, optically inactive monomers adopt the chiral (mirror-image) structure in liquid crystals as they grow, resulting in optically active polymers.

The paper is [published](#) in the journal *Macromolecules*. This advance represents a pioneering achievement in both asymmetric chemistry and polymer chemistry.

Polyisocyanides are polymers distinguished by their helical structures, where the helix's winding direction (right- or left-handed) can be controlled through catalysts designed for synthesizing chiral molecules. This feature allows the exhibiting of optical properties such as circular dichroism and optical rotation in polyisocyanides, making them stable, optically active polymers.

In their study, the research team synthesized optically active conducting polymers from non-optically active monomers through physical rather than chemical methods using a liquid crystal reaction field as an external environment.

For the first time, they achieved asymmetric (chiral) living polymerization of optically active polyisocyanides using liquid crystals with chiral (mirror-image isomer) structures as a solvent.

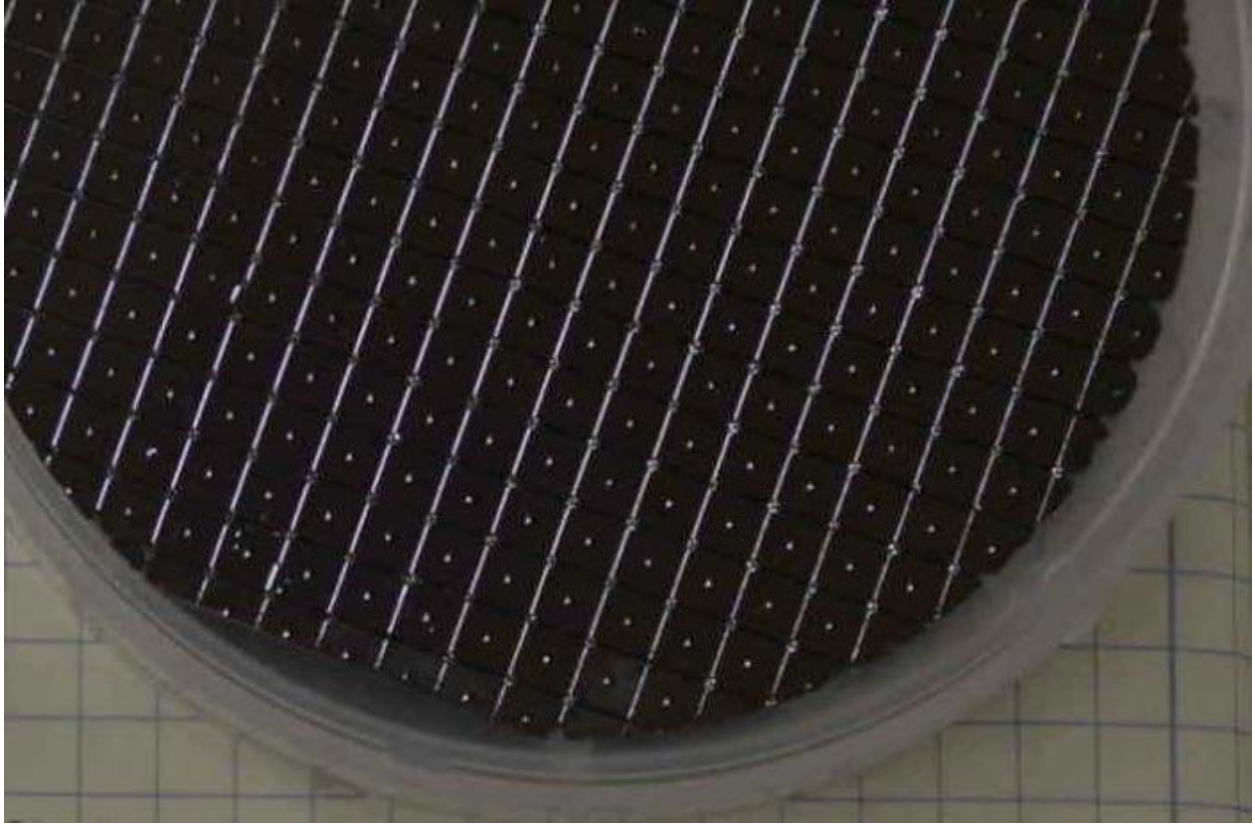
Circular dichroism measurements of the resulting polyisocyanides confirmed their optical activity, which can be attributed to their helical structures. Additionally, the liquid crystal used in the reaction exhibited properties of the twisted-bend nematic phase—a recently discovered phase that has been attracting considerable attention in liquid crystal research.

The identification of a twisted-bend nematic liquid crystal within a polymer is a notable finding in liquid crystal science.

This reaction is analogous to the enzymatic growth of amino acids with chiral structures *in vivo*, which leads to the synthesis of proteins with helical structures. As such, it holds promise as a biomimetic technology—a field that mimics and leverages the functional principles of living organisms.

More information: Hiromasa Goto et al, Asymmetric Synthesis of Chiral Polyisocyanides from Achiral Monomers with Living Polymerization in a Liquid Crystal Reaction Field, *Macromolecules* (2025). DOI: [10.1021/acs.macromol.4c01017](https://doi.org/10.1021/acs.macromol.4c01017)

Revolutionary nanopore sensor can detect diseases from a single molecule



Nanopore chip technology is reshaping diagnostics with faster, more accurate tests and advancing protein research, promising personalized medicine breakthroughs. (CREDIT: Goeppert)© The Brighter Side of News

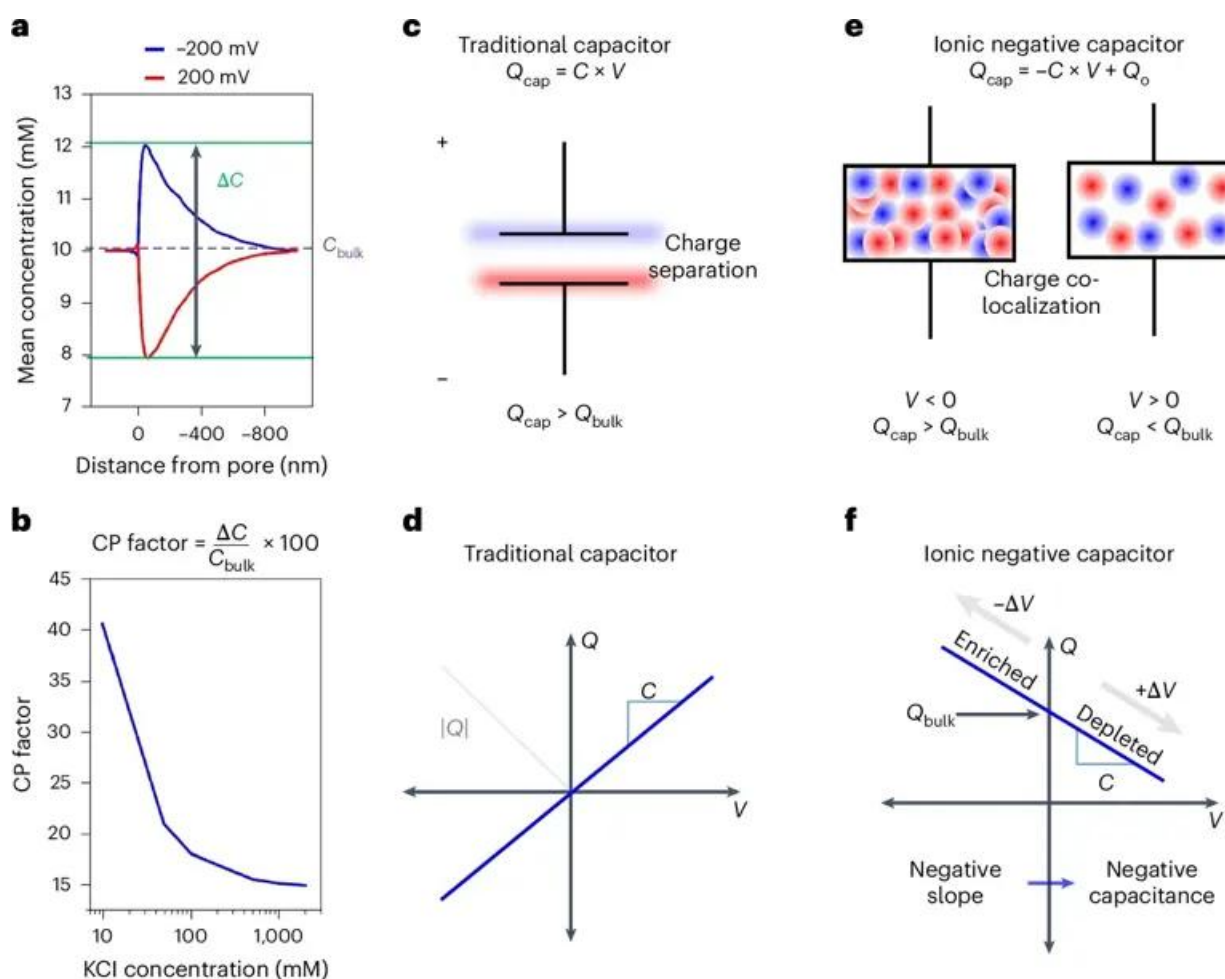
The study of ionic dynamics in nanopores has uncovered a groundbreaking phenomenon that could transform diagnostics and [protein research](#). This advancement, led by a team of researchers, sheds light on how ions behave under different voltage polarities and provides a foundation for developing more precise diagnostic tools.

Nanopores, tiny openings just nanometers wide, offer unique properties that distinguish them from traditional sensing systems. When molecules pass through these pores, they influence ionic currents, creating detectable signals.

The latest research, published in the journal, [Nature Nanotechnology](#), demonstrates that nanopores can exhibit both positive and negative capacitance, depending on voltage polarity.

Negative capacitance, a transient reduction in current, occurs during voltage switches to a negative state, while positive capacitance emerges under opposite conditions. These discoveries highlight the intricate interplay of ionic flux and charge storage within nanopores.

Experiments using conical nanopores filled with potassium chloride (KCl) solution revealed key insights into ionic behavior. Researchers applied voltage pulses ranging from -500 millivolts to $+500$ millivolts and observed distinct changes in ionic currents.



CP and charge storage model. (CREDIT: Nature Nanotechnology)© The Brighter Side of News

Under a negative voltage step, the ionic current gradually increased until equilibrium was reached, signifying an enriched state. Conversely, a positive voltage step caused ionic concentration to deplete, reducing current flow.

This phenomenon is attributed to concentration polarization (CP), where ion concentrations near the pore are either enriched or depleted based on the [applied voltage](#). The enriched state—associated with negative capacitance—occurs as ions accumulate within the tapered region of the nanopore. Conversely, a depleted state corresponds to positive capacitance, marked by a traditional current spike.

Advanced simulations using COMSOL Multiphysics validated these findings, highlighting the time-dependent redistribution of voltage across the pore's resistive elements.

These simulations demonstrated the complex relationship between ionic flux, capacitance, and voltage polarity. They also emphasized the importance of a Warburg-like circuit element, which accounts for the slow decay of ionic diffusion within the nanopore.

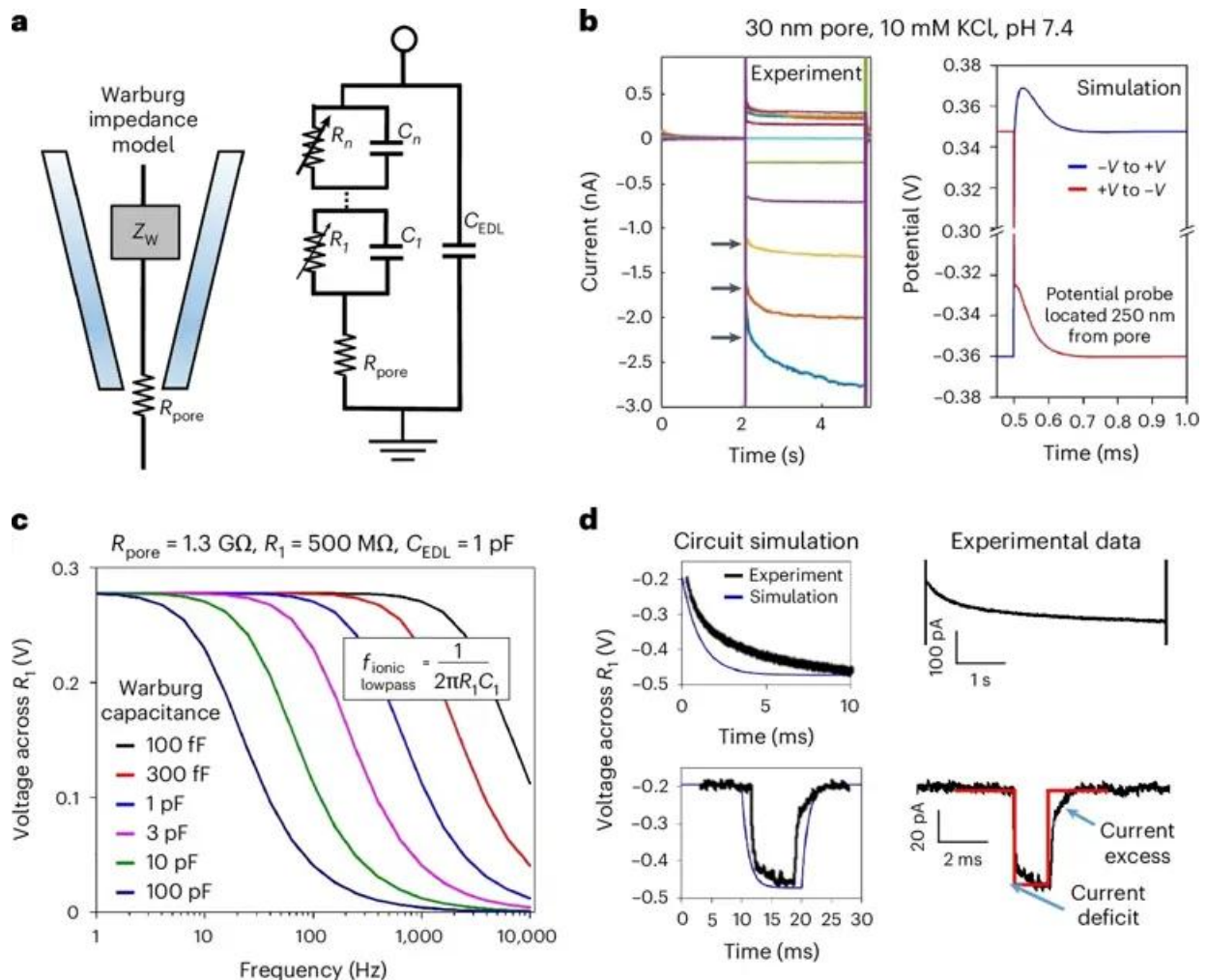
Notably, the experiments and simulations showed that the equilibration time—the time required for ionic concentrations to stabilize—varies depending on the voltage applied. Negative voltage steps were associated with longer equilibration times, while positive steps reached steady states more quickly.

These results underscore the nuanced interplay of electrical and ionic dynamics in nanopores, which are key to their diagnostic potential.

Building on these discoveries, researchers have developed a nanopore-based tool that could revolutionize diagnostics. Current diagnostic methods often require large quantities of biological samples to detect diseases, but this technology is sensitive enough to analyze individual molecules.

Kevin Freedman, assistant professor of bioengineering at [UC Riverside](#), explains, “Right now, you need millions of molecules to detect diseases. We’re showing that it’s possible to get useful data from just a single molecule.”

The device relies on nanopores to detect changes in ionic currents as molecules pass through. By accounting for both positive and negative capacitance, it achieves unparalleled sensitivity.



Warburg impedance model and its effects on nanopore current measurements. (CREDIT: Nature Nanotechnology)© The Brighter Side of News

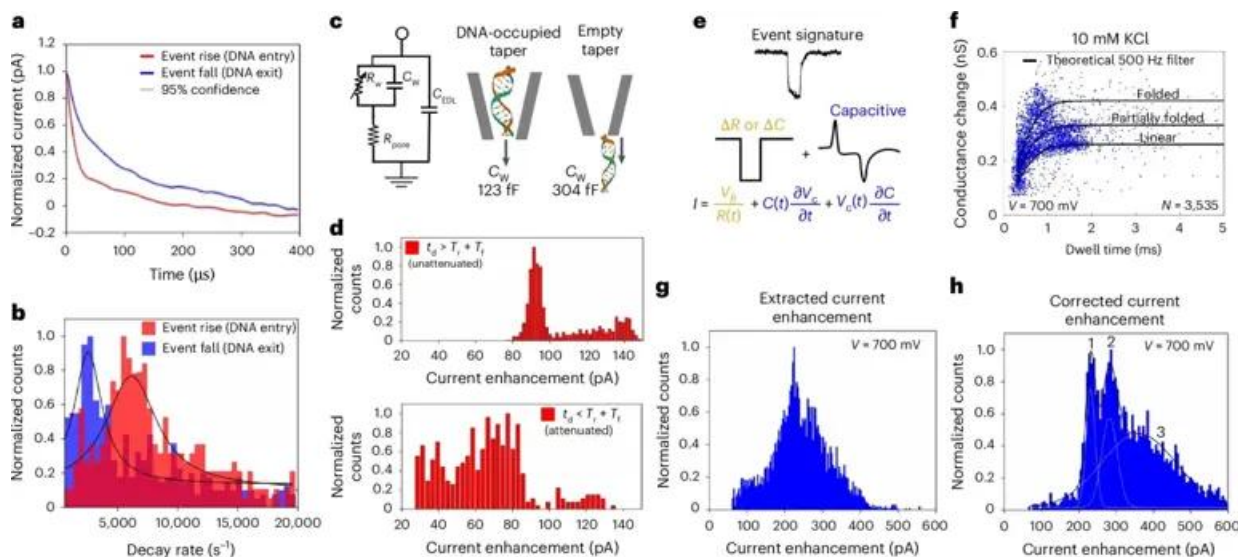
Unlike traditional sensors that require external filters—which risk losing critical information—the nanopore itself acts as a filter, preserving valuable molecular signals. This breakthrough significantly enhances the accuracy and reliability of diagnostic tests.

Freedman's team envisions portable diagnostic devices small enough to fit in a [USB drive](#). These devices could detect infections within 24 to 48 hours, a significant improvement over existing tests, which often take days to yield results. Such rapid detection could be invaluable in containing fast-spreading diseases. "Nanopores offer a way to catch infections sooner—before symptoms appear and before the disease spreads," Freedman notes.

This technology also promises to improve the study of proteins, which play critical roles in cellular processes. Subtle differences in protein structures, often undetectable with current tools, can now be analyzed. Such precision could pave the way for personalized treatments, tailored to individual patients' needs.

The nanopore device moves scientists closer to achieving single-molecule protein sequencing, a long-sought goal in biology. While DNA sequencing deciphers [genetic instructions](#), protein sequencing reveals how those instructions are expressed and modified in real time. This deeper understanding could revolutionize disease detection and treatment.

Freedman's research, supported by a grant from the National Human Genome Research Institute, focuses on refining nanopore technology for [single-protein sequencing](#). He believes these advances signal a shift in molecular diagnostics and biological research. "This tool moves us one step closer to personalized medicine," Freedman states.



Ionic filter characterization and correction. (CREDIT: Nature Nanotechnology)© The Brighter Side of News

Protein sequencing offers unique advantages over DNA sequencing. While DNA provides a static blueprint of genetic information, proteins reveal dynamic changes in cellular processes. These changes can indicate early signs of diseases or subtle responses to treatment. By detecting these variations, nanopore technology opens the door to more effective therapies and preventative care.

In addition to medical applications, this research enhances our understanding of fundamental biological processes. Proteins drive nearly every function within

cells, from metabolism to [immune responses](#). The ability to analyze proteins at the single-molecule level provides unprecedented insights into these processes, enabling breakthroughs across multiple fields of science.

As nanopore devices become more affordable and accessible, they are likely to become standard features in both research and healthcare settings. Freedman anticipates their integration into everyday diagnostic kits for home or clinical use. "I'm confident that nanopores will become part of everyday life," he says. "This discovery could change how we'll use them moving forward."

The development of nanopore technology reflects a broader trend toward miniaturization and precision in scientific tools. By combining advanced circuit modeling with innovative experimental techniques, researchers are creating devices that are not only smaller but also more capable. These devices promise to make cutting-edge diagnostics accessible to a wider audience, including resource-limited settings.

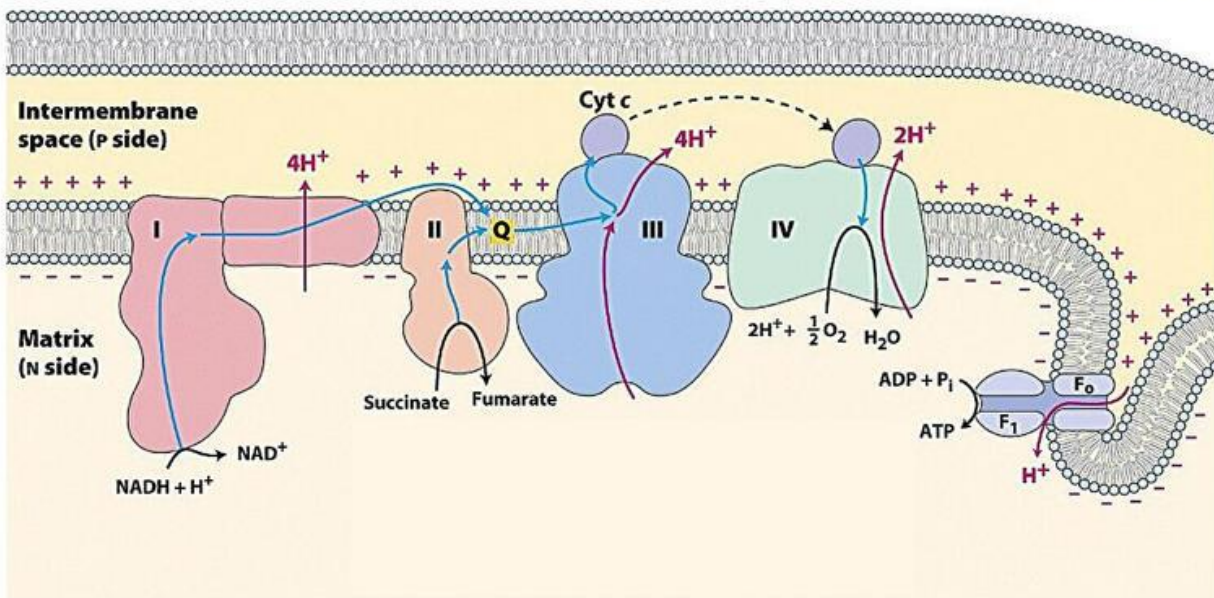
Looking ahead, the potential applications of nanopore technology are vast. Beyond diagnostics and protein research, nanopores could play a role in environmental monitoring, and detecting pollutants or pathogens in water supplies. They may also contribute to advancements in [synthetic biology](#), enabling the creation of engineered proteins with specific functions.

By bridging the gap between theoretical models and practical applications, this research underscores the transformative potential of nanopores. From accelerating [disease diagnosis](#) to advancing protein research, nanopore technology is set to redefine the future of science and medicine.

Creating a simplified form of life: Scientists build modules for a synthetic cell

Producing ATP in mitochondria

>100 proteins

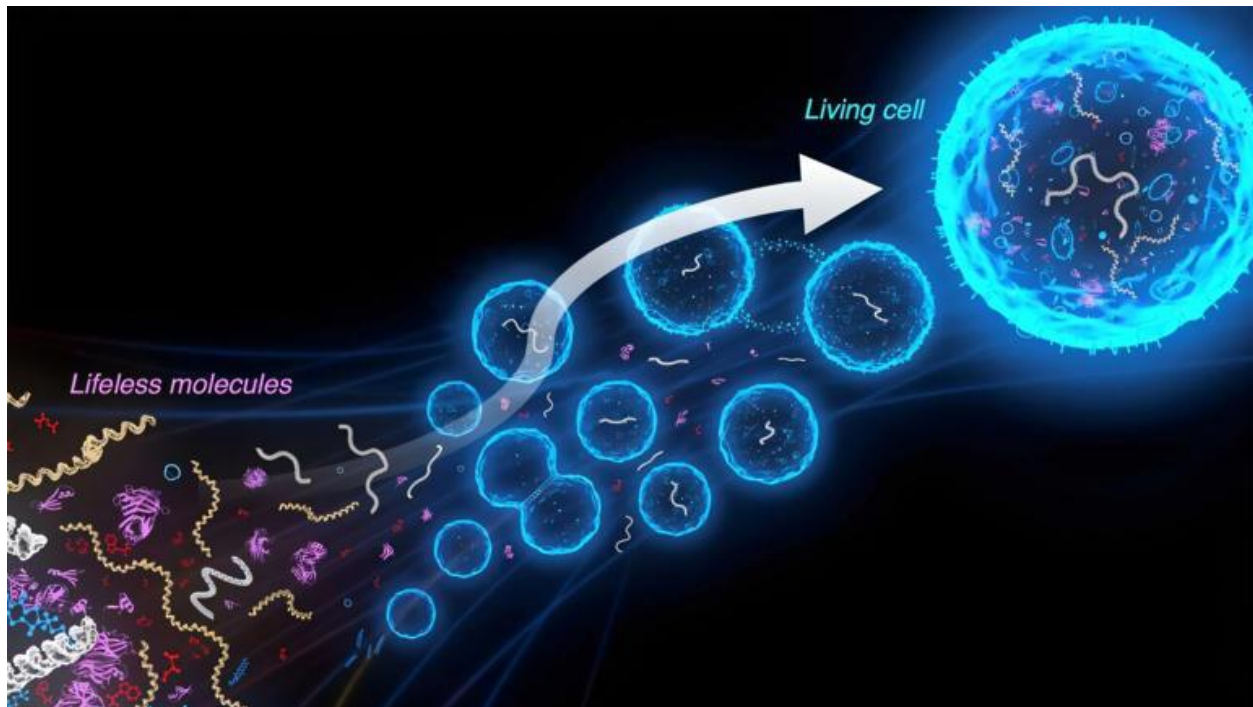


Producing ATP in functional analogs of mitochondria and enabling cross-feeding

5 proteins

The production of ATP in a mitochondrion, requiring > 100 proteins, and the synthetic vesicles producing ATP, with only 5 proteins. Credit: University of Groningen, Poolman lab

It is one of the most fundamental questions in science: how can lifeless molecules come together to form a living cell? Bert Poolman, Professor of Biochemistry at the University of Groningen, has been working on this problem for over 20 years. He aims to understand life by trying to reconstruct it; he is building simplified artificial versions of biological systems that can be used as components for a synthetic cell.



A simplified synthetic equivalent of a cell would be like a blueprint for life. Credit: EVOLF project

Poolman has published two papers in [Nature Nanotechnology](#) and [Nature Communications](#). In the first paper, he describes a system for energy conversion and cross-feeding of products of this reaction between synthetic cells, while he describes a system for concentrating and converting nutrients in cells in the second paper.

Six Dutch research institutes are collaborating in the consortium [BaSyc](#) (Building a Synthetic Cell) to build the elements needed for a synthetic cell. Poolman's group has been working on energy conversion.

The real-life equivalents he aims to replicate are mitochondria, the 'energy factories' of the cell. These use the molecule ADP to produce ATP, which is the standard 'fuel' that cells require to function. When ATP is converted back into ADP, the energy is released and used to drive other processes.

Artificial energy factories

"Instead of the hundreds of components of mitochondria, our system for energy conversion uses just five," says Poolman. "We set out to simplify it as much as

possible." This may sound odd, as evolution has done a great job of producing functional systems.

"However, evolution is a one-way street, it builds on existing components and this often makes the outcome very complex," explains Poolman. An artificial replica, on the other hand, can be designed with a specific outcome in mind.

The five components were placed inside vesicles, tiny cell-like sacs, that can absorb ADP as well as the amino acid arginine from the surrounding fluid. The arginine is 'burned' (deaminated) and thus provides the energy to produce ATP, which is secreted from the vesicle.

"Of course, the simplification comes at a price: we can only use arginine as the energy source, while cells use all kinds of different molecules, such as amino acids, fats, and sugars."

Next, the Poolman group designed a second vesicle that is able to absorb the secreted ATP and use it to drive an energy-consuming reaction. The energy is provided by turning ATP back into ADP, which is then secreted and can be absorbed by the first vesicle, closing the loop.

Such a cycle of ATP production and use is the foundation of metabolism in every living cell and drives the 'machinery' for energy-consuming reactions such as growth, cell division, protein synthesis, DNA replication, and more.

An artificial pumping system

The second module that Poolman created was a bit different: a vesicle in which a chemical process causes the interior to build up a negative charge and, in doing so, form an electrical potential, similar to that of an electronic circuit. The electrical potential is used to couple charge movement to the accumulation of nutrients inside the vesicle, which is carried out by transporters.

These proteins in the membrane of the vesicle work a bit like a water wheel: positively charged protons 'flow' through it from outside the vesicle to the negatively charged interior. This flow drives the transporter, which in this case imports a sugar molecule, lactose. Again, this is a very common process in living

cells, requiring many components that Poolman and his team mimicked with just two components.

When he submitted a paper describing this system, a reviewer asked if he couldn't do something with the lactose that is being transported, as cells use nutrients like this to produce useful building blocks. Poolman took up the challenge and added three more enzymes to the system, which oxidized the sugar and enabled the production of the coenzyme NADH.

"This helper molecule plays an essential role in the proper functioning of all cells," explains Poolman. "And by adding NADH production, we have shown that it is feasible to expand the system."

But what about the synthetic cell?

Having a simplified synthetic equivalent of two key features of life is fascinating, but many more steps need to be integrated to form an autonomously growing and dividing synthetic cell. "The next step we want to take is adding our metabolic energy producing systems to a synthetic cell division system created by colleagues," says Poolman.

The BaSyc program is entering its final years; funding for a new program has recently been secured.

This [EVOLF](#) project is set to run for another 10 years and aims to find out how many more lifeless modules can come together and create living cells.

"Ultimately, this would give us a blueprint for life, something that is currently lacking in biology," concludes Poolman. "This may eventually have all kinds of applications, but will also help us to better understand what life is."

More information: Laura Heinen et al, Synthetic syntrophy for adenine nucleotide cross-feeding between metabolically active nanoreactors, *Nature Nanotechnology* (2024). [DOI: 10.1038/s41565-024-01811-1](https://doi.org/10.1038/s41565-024-01811-1)

Miyer F. Patiño-Ruiz et al, Chemiosmotic nutrient transport in synthetic cells powered by electrogenic antiport coupled to decarboxylation, *Nature Communications* (2024). [DOI: 10.1038/s41467-024-52085-z](https://doi.org/10.1038/s41467-024-52085-z)

FEBRUARY 24, 2025

New carbon–phosphorus stapled Au compound with cancer-fighting properties

by [University of Kentucky](#)



Samuel Awuah, Ph.D., right, works with teaching assistant Justin Holmes in the lab. Credit: Jeremy Blackburn | UK Research Communications

University of Kentucky researchers have developed a new class of gold-based compounds that show promise in fighting various types of cancer.

The study, led by UK Markey Cancer Center researcher Samuel Awuah, Ph.D., and [published](#) in *Dalton Transactions*, showed that the compounds could kill [cancer cells](#) by disrupting their [energy production](#).

The new compounds work by targeting and shutting down mitochondria, which generate energy for cells. In lab tests, they were effective against several types of cancer cells, including those from breast, ovarian and lung tumors.

The research shows how gold-based compounds can be used in a new way to fight cancer, and potentially other diseases, says Awuah, an associate professor in the UK College of Arts & Sciences Department of Chemistry.

"By creating compounds that remain stable in the body and specifically target cancer cells' energy source, this opens the doors for the development of new and more effective treatments," Awuah said.

The study builds upon recent research that shows auranofin—a gold-based drug approved by the FDA in 1985 for treating [rheumatoid arthritis](#)—has potential as a cancer therapy.

The research team designed the new compound to be more stable in the body than auranofin through a chemical process they refer to as "stapling." This method joins gold molecules to other chemical structures in ways that help them resist breaking down inside cells.

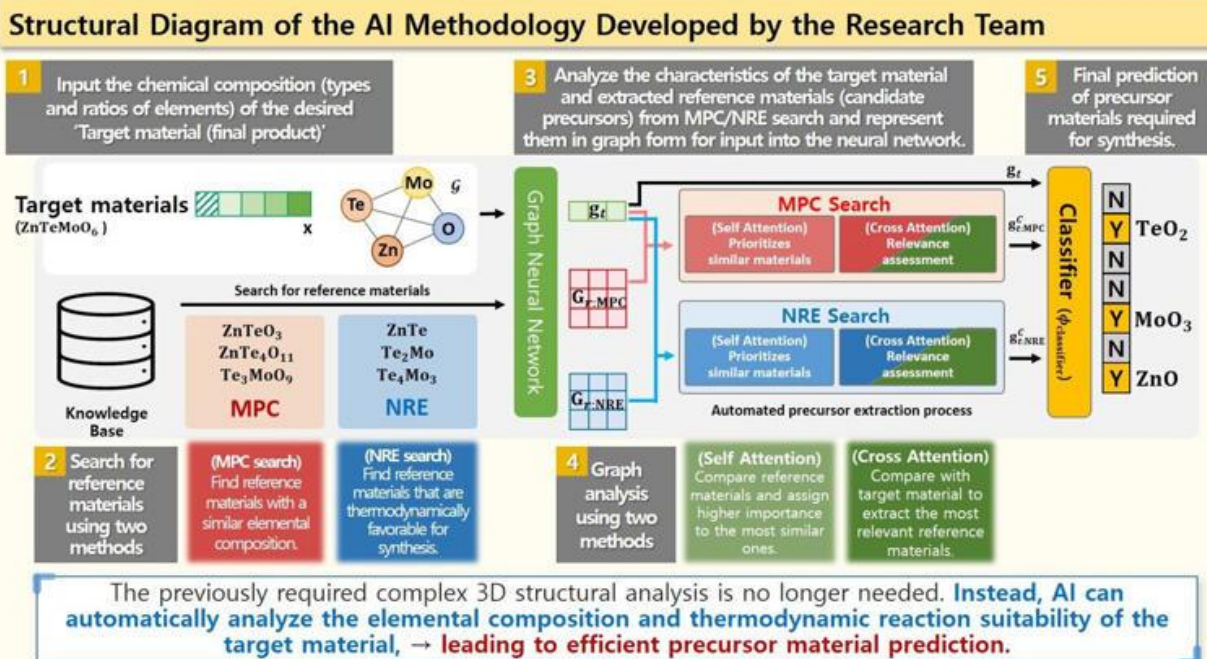
The increased stability means the [compounds](#) could maintain their cancer-fighting properties longer in the body, making them better-suited as a [cancer therapy](#).

More information: Sean T. Gilpatrick et al, Carbon–phosphorus stapled Au(i) anticancer agents via bisphosphine induced reductive elimination, *Dalton Transactions* (2024). DOI: [10.1039/D4DT01929F](https://doi.org/10.1039/D4DT01929F)

Journal information: [Dalton Transactions](#)

Provided by [University of Kentucky](#)

AI predicts the precursor materials needed for material synthesis



Structural Diagram of the AI Methodology Developed by the Research Team. Credit: Korea Research Institute of Chemical Technology(KRICT)

Researchers in Korea have developed a technology that automatically identifies the necessary precursor materials to synthesize specific target materials.

A joint research team led by Senior Researcher Gyoung S. Na from the Korea Research Institute of Chemical Technology (KRICT) and Professor Chanyoung Park from the Korea Advanced Institute of Science and Technology (KAIST) has developed an AI-based retrosynthesis methodology that predicts the required precursor materials solely based on the chemical formula of the target material without expensive material descriptors and chemical analysis.

Precursor materials refer to all essential materials required in the synthesis process of the desired target material.

In recent years, materials discovery has become a crucial task across various industries, including batteries and semiconductors. Traditionally, finding the right intermediate materials for synthesis has required costly and repetitive

experiments. However, there is a growing demand for utilizing AI to identify these materials efficiently.

Existing AI-based technologies for predicting material synthesis processes have primarily focused on organic materials, such as drug compounds, whereas research on inorganic materials has been relatively insufficient. This is because inorganic compounds, such as metals, possess complex structures and diverse elemental compositions, making it challenging to determine synthesis pathways.

The research team developed an innovative AI technology that can learn the inverse process of predicting the necessary precursor materials of the target material using only its chemical formula.

Previously, KRICT developed and transferred the "ChemAI" platform in 2022, which allows users to predict synthesis information without advanced programming skills and expensive hardware infrastructures.

This newly developed technology overcomes the challenges posed by the complex 3D structures of inorganic materials, such as atomic arrangements and bonding information. Instead, the AI analyzes the types and ratios of elements present in the target material and calculates the thermodynamic formation energy differences to identify precursors that facilitate easier synthesis reactions.

To improve the accuracy of precursor material predictions, the team employed a deep neural network specialized in chemical data. The AI model was trained on approximately 20,000 published research papers detailing material synthesis processes and precursor materials.

The AI model was tested on around 2,800 synthesis experiments that were not provided in the training dataset. The evaluation results showed that it successfully predicted the necessary precursor materials in over 80% of cases within just 0.01 seconds by utilizing GPU acceleration.

Looking ahead, the research team plans to expand the training dataset through research projects of KRICT to achieve 90% prediction accuracy. By 2026, they aim to establish a web-based public service for AI-based materials discovery. Future research will focus on fully-automated materials discovery that predicts both precursor materials and synthesis pathways based solely on the target material's chemical formula.

The research team emphasized the novelty of their approach, stating, "Unlike conventional precursor prediction AI models that are limited to specific material types, our AI can predict precursor materials universally, regardless of the applications of the target materials."

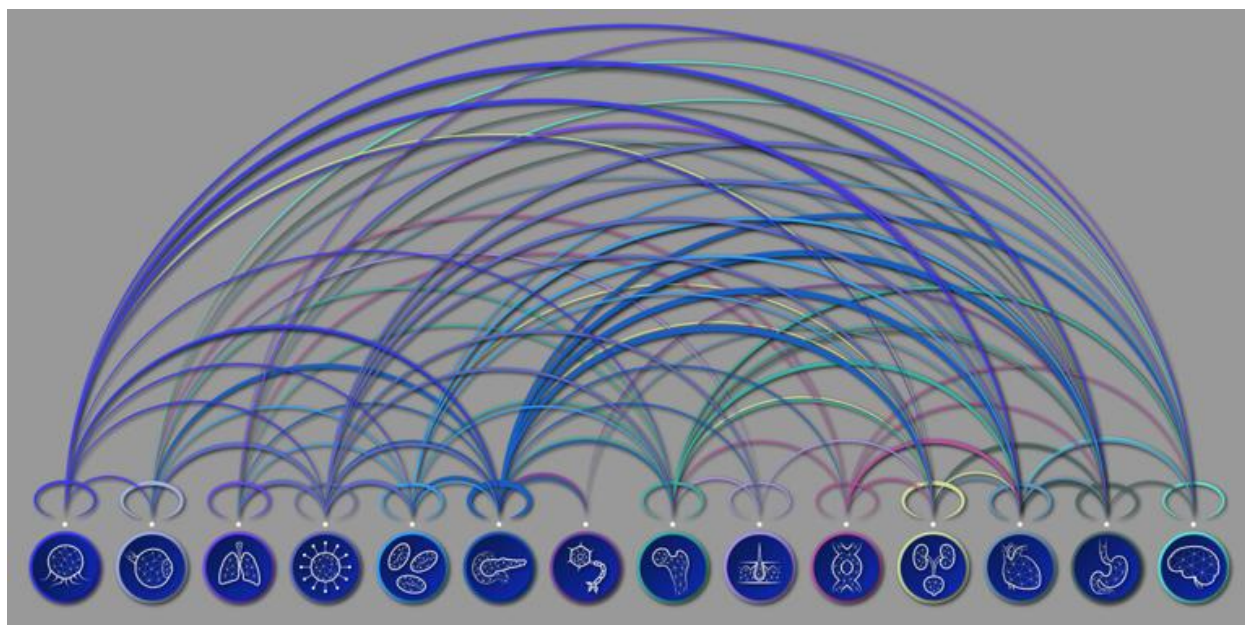
KRICT President Young-Kuk Lee added, "This research is expected to enhance the efficiency of new material development across various industries."

The work is [published](#) on the *arXiv* preprint server.

More information: Heewoong Noh et al, Retrieval-Retro: Retrieval-based Inorganic Retrosynthesis with Expert Knowledge, *arXiv* (2024). [DOI: 10.48550/arxiv.2410.21341](https://doi.org/10.48550/arxiv.2410.21341)

Provided by National Research Council of Science and Technology

AI tool maps hidden links between diseases



By uncovering hidden links between diseases, the AI-powered tool created by KAUST researchers reveals how treating one illness could help prevent another. Credit: 2025 KAUST

An AI-powered tool from KAUST researchers is helping scientists trace hidden connections between diseases, revealing insights into how one illness might lead to another and, by extension, how treating one illness could help prevent another.

The work is [published](#) in the journal *Bioinformatics*.

By systematically combing through medical literature and real-world patient data, this tool maps cause-and-effect relationships, creating a framework that could guide targeted therapeutic strategies and uncover the potential for drug repurposing.

Think of it as the ultimate disease relationship detective. Using natural language processing, the tool scans vast quantities of biomedical research to pinpoint causal connections—like how high blood pressure can set the stage for heart failure.

"Instead of treating diseases as unrelated outcomes, our approach facilitates the identification of shared risk factors among causally linked diseases," says Sumyyah Toonsi, a graduate student in the Bio-Ontology Research Group.

"This deepens our understanding of human diseases and enhances the performance of risk-prediction tools for personalized medicine."

The tool's power lies in its ability to go beyond mere association. Traditional methods might highlight which diseases commonly co-occur, but the KAUST tool—developed by Toonsi and her team under the guidance of computer scientist Robert Hoehndorf—identifies which diseases can trigger others.

For example, type 2 diabetes leads to high blood sugar, causing small blood vessel disease, ultimately resulting in a diabetic eye condition. Mapping these relationships suggests that treating one "upstream" condition may help prevent or lessen downstream complications.

To achieve these insights, the tool integrates scientific literature with data from the UK Biobank, a large-scale health database of about half a million Britons. This dual approach validates disease connections by checking that diseases follow a logical sequence, with causes preceding outcomes. This process strengthens the evidence of causation while highlighting new connections that might otherwise be overlooked.

Among its discoveries, the tool unearthed surprising links. As Toonsi explains, "We found endocrine, metabolic and nutritional diseases to be leading drivers of

diseases in other categories," including cardiovascular, nervous system and inflammatory diseases of the gut and eye.

"This is interesting because many metabolic diseases can be managed with lifestyle changes, opening opportunities for broad disease prevention," she says.

A standout feature is the tool's ability to improve polygenic risk scores (PRS)—calculations that assess a person's genetic susceptibility to disease. Standard PRS models don't account for how one genetic variant might affect multiple diseases, but by adding causal disease relationships, the KAUST tool produces an enhanced PRS that improves prediction accuracy, especially for complex diseases.

This helps disentangle pleiotropic effects, where a single gene variant can impact multiple conditions. By factoring in these causal links, the tool offers a more holistic view of genetic risk.

Now freely available to the research community, this tool represents a major advancement for scientists exploring disease connections. Its potential applications range from refining prevention strategies to suggesting new uses for existing drugs. As researchers further investigate disease pathways, this tool could serve as a key resource in the quest to decode the interconnected landscape of human health.

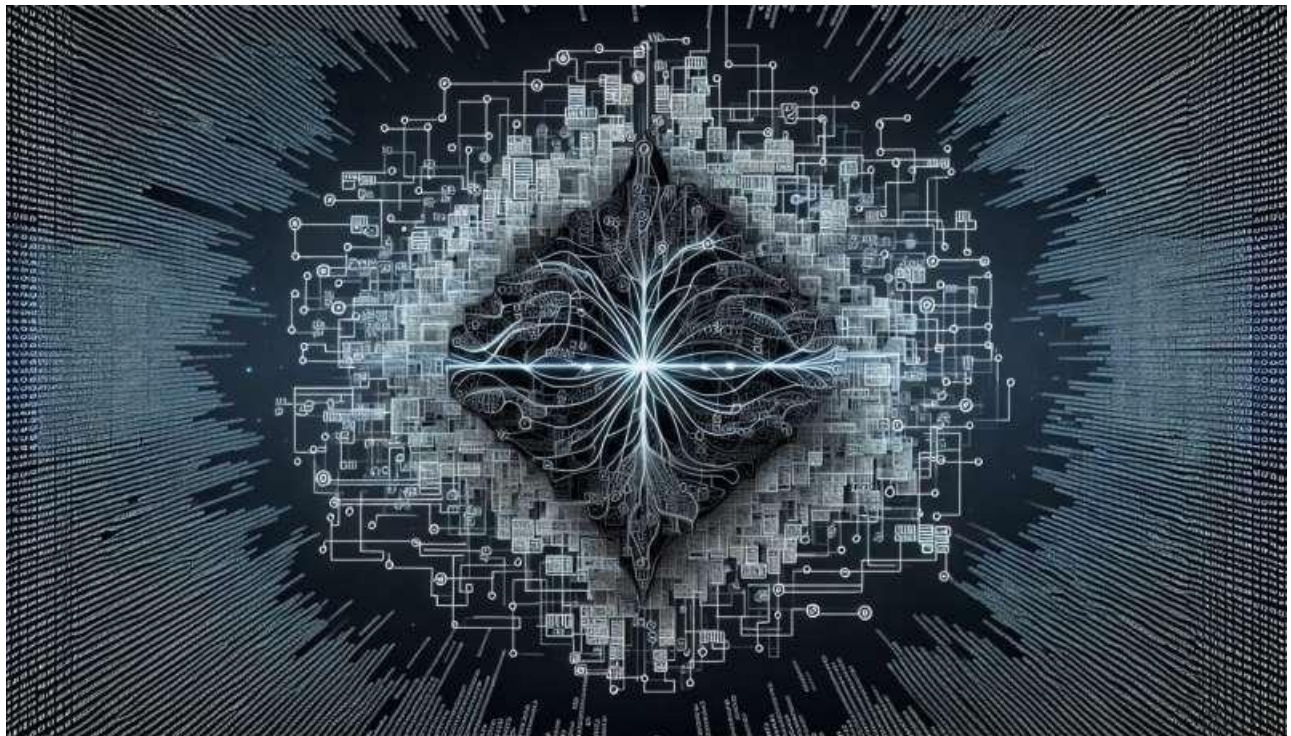
More information: Sumyyah Toonsi et al, Causal relationships between diseases mined from the literature improve the use of polygenic risk scores, *Bioinformatics* (2024). [DOI: 10.1093/bioinformatics/btae639](https://doi.org/10.1093/bioinformatics/btae639)

Provided by King Abdullah University of Science and Technology

FEBRUARY 26, 2025

Unveiling the 'functionome': Online resource describes functions of more than 20,000 human genes

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



Credit: AI-generated image

A new resource from the Gene Ontology Consortium, a comprehensive encyclopedia of the known functions of all protein-coding human genes, has been completed and released on a new website. For the first time, researchers from the Keck School of Medicine of USC, the Swiss Institute of Bioinformatics and other institutions used large-scale evolutionary modeling to integrate data on human genes with genetic data collected from other organisms.

This has culminated in a [searchable public resource](#) that lists the known functions of more than 20,000 genes using the most accurate and complete evidence available. A paper describing the resource was [published](#) in *Nature*.

The Gene Ontology, a knowledge base that has been continually expanded and improved for more than 25 years, has become a mainstay of the biomedical research process. Already, it

is used in more than 30,000 publications each year to aid with [data analysis](#) and interpretation.

Biomedical researchers who conduct "omics" experiments—large-scale studies of DNA, RNA, proteins and other [biological molecules](#)—generate data that can identify hundreds of genes of interest. For example, a researcher might learn which genes are turned "on" or "off" in [cancerous cells](#) compared to healthy ones.

Reviewing thousands of published papers on the known functions of each gene is not feasible, so many scientists turn instead to the Gene Ontology.

"Our knowledge base allows scientists to go from just a list of genes to an understanding of their biological functions, including what might be useful for treatment," said Paul D. Thomas, Ph.D., a principal investigator of the Gene Ontology Consortium and director of the division of bioinformatics and a professor of population and public health sciences at the Keck School of Medicine.

Now, this latest milestone provides a new resource within the knowledge base that uses evolutionary modeling to make the tool even more powerful.

The approach allows the researchers to combine experimental data collected from human genes with that obtained from related genes in model organisms, such as mice and zebrafish. It provides a more complete picture of human gene function, including filling in gaps in scientific knowledge where direct evidence from human studies is not available.

"We'd previously amassed a huge knowledge base that has become an authoritative reference on human gene functions," said Thomas, who is also lead author of the new publication.

"And now, by adding information about when each function arose in evolution, we're now providing an even more complete, accurate, and concise description of the functions encoded by human genes."

An evolutionary view

The new resource was compiled by a team of more than 150 biologists around the world, including at the Keck School of Medicine of USC.

Since 1998, the group has meticulously reviewed over 175,000 scientific publications on gene function, searching for data on gene functions in well-studied organisms and every gene in the human genome—primarily the more than 20,000 [protein-coding genes](#) that control key biological processes.

After reviewing the literature, they categorized each gene according to the biological functions it performs, either on its own or in combination with other genes. They selected

from a catalog they developed of more than 40,000 functions that span cell division, cell signaling, immune response, molecular transport and many more.

Understanding the precise functions performed by groups of genes can help researchers understand what goes wrong in cancer and other diseases and design targeted approaches to treatment.

The new resource of gene function descriptions, called the "[PAN-GO functionome](#)," will essentially be used in the same way by the scientific community—to analyze omics data among other applications—but it will yield more accurate results, Thomas said.

That's because the recent work has brought together all the information in the knowledge base using large-scale evolutionary models (which track the evolutionary history of thousands of genes and related proteins), creating a more complete and accurate picture of gene function.

In many cases, experimental data from human genes is not available, but scientists have studied related genes in mice, rats, zebrafish, fruit flies, yeast or E. coli. By understanding when and how specific functions (such as energy processing or [cell signaling](#)) evolved, researchers can use data obtained from other organisms to gain an understanding of gene function in humans.

"This helps us infer the functional characteristics of human genes, even when there is no direct evidence from an experiment on the human gene itself," Thomas said.

Going forward, the Gene Ontology Consortium is requesting that researchers use the PAN-GO functionome in their analyses. The information is structured in a machine-readable format that allows scientists to use computational tools, such as artificial intelligence, to quickly search and use the data.

The consortium is also issuing a call to action: Researchers can now submit suggestions for updating the knowledge base on specific genes through the project's website. Crowdsourcing knowledge of gene functions and categorizing them in a structured way ensures that the shared resource continues to improve over time and that its insights are easy to apply.

Though it is the most comprehensive resource available on gene functions, the PAN-GO functionome is not yet complete. It contains data on 82% of protein-coding genes, but no [experimental data](#) exists for the other 18%—roughly 3,600 genes, the biological functions of which remain unknown.

"We now have a real picture of where we are missing information, and that's where future research in this area may want to focus," Thomas said.

More information: Paul Thomas, A compendium of human gene functions derived from evolutionary modelling, *Nature* (2025). DOI: [10.1038/s41586-025-08592-0](https://doi.org/10.1038/s41586-025-08592-0). www.nature.com/articles/s41586-025-08592-0

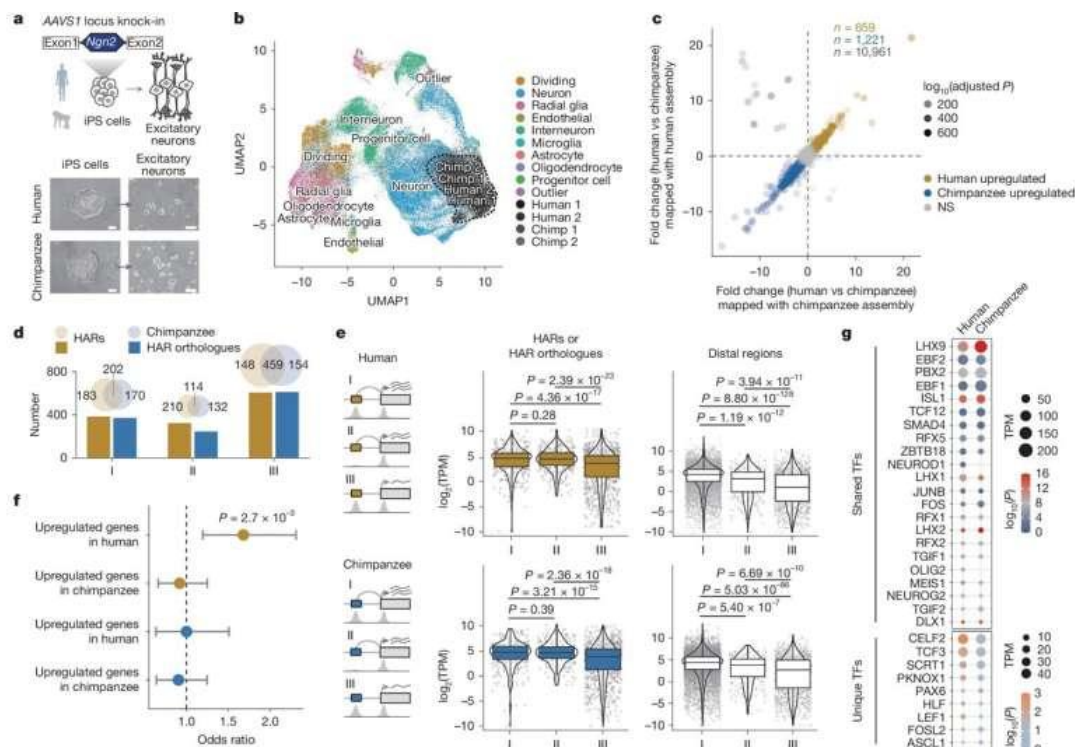
Journal information: *Nature*

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

FEBRUARY 26, 2025

Human chromosomes evolved at hyperspeed to give us better brains, but there's a catch

by [University of California, San Francisco](#)



HARs exhibit enhancer function in excitatory neurons. Credit: *Nature* (2025). DOI: [10.1038/s41586-025-08622-x](https://doi.org/10.1038/s41586-025-08622-x)

How did humans evolve brains capable of complex language, civilization, and more? The answer could lie in exceptional DNA. Scientists at UC San Francisco have found that parts of our chromosomes have evolved at breakneck speeds to give us an edge in brain development compared to apes. But it might also put us at risk for uniquely human brain disorders.

The study [appears](#) in *Nature*.

The research focused on parts of chromosomes known as human accelerated regions (HARs), which have evolved most rapidly since humans split from chimpanzees on the evolutionary tree—changing 10 times faster than the expected rate of evolution in mammals.

The scientists, led by Yin Shen, Ph.D., professor in the UCSF Weill Institute for Neurosciences and the UCSF Institute for Human Genetics, studied the effects of HARs in [artificial neurons](#) derived from human and chimpanzee cell lines.

The human and chimpanzee genomes are 99% similar. HARs make up a big portion of the 1% difference, which can lead to dramatically different outcomes in human and chimp neurons in petri dishes. The human neurons grew multiple neurites, wiry projections that help the nerve cells send and receive signals. But the chimp neurons only grew single neurites. When human HARs were engineered into artificial chimp neurons, the chimp neurons grew many more of these wires.

"More neurites during development could mean more complexity in our [neural networks](#)," Shen said. "These networks facilitate the transmission of signals in the nervous system and support our higher cognitive functions. But disruptions in their development may contribute to neurodevelopmental disorders like autism."

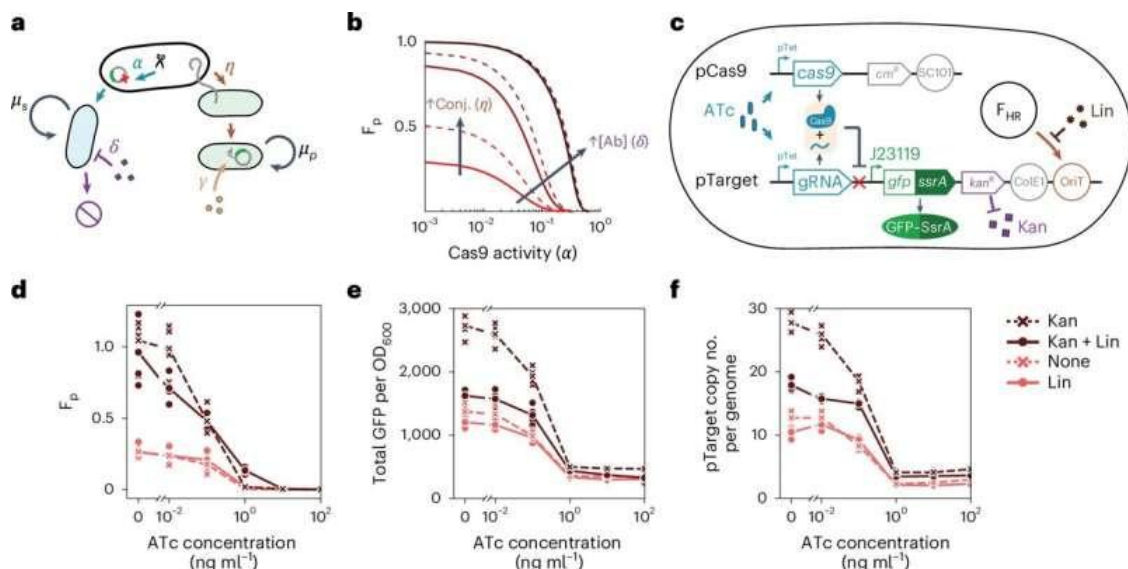
More information: Xiekui Cui et al, Comparative characterization of human accelerated regions in neurons, *Nature* (2025). [DOI: 10.1038/s41586-025-08622-x](https://doi.org/10.1038/s41586-025-08622-x)

Journal information: [Nature](#)

Provided by [University of California, San Francisco](#)

A new approach to controlling gene expression in microbial populations

by Alissa Kocer, [Duke University](#)



ADEPT tunes plasmid abundance and population-level gene expression. Credit: *Nature Chemical Biology* (2025). DOI: 10.1038/s41589-024-01817-9

The ability to control gene expression across a wide range is crucial for many fields, including bioengineering, disease detection, and environmental monitoring. Research led by Lingchong You, Ph.D., professor of biomedical engineering and molecular genetics and microbiology, developed a system to better regulate gene expression that could be applied to biosensors, toxin production, and metabolic pathway regulation.

Inspired by the immune system, Prof. You and team's ADEPT system (Amplification of Dynamic gene Expression by Programmable gene Transfer) amplifies or suppresses specific cell populations in response to environmental cues. Their study is [published](#) in *Nature Chemical Biology*.

The system works by regulating the behavior of plasmids, which are small, circular DNA molecules. Plasmids are used in molecular biology to build gene circuits because they are easy to modify and can boost gene expression. However, plasmid copy numbers can fluctuate, causing inconsistent gene expression within bacterial populations.

By balancing CRISPR-Cas-mediated cutting and gene transfer, ADEPT dynamically controls both the plasmid copy number within [individual cells](#) and the fraction of plasmid-carrying cells in a population, thereby tuning collective gene expression with an amplified dynamic range.

ADEPT can control gene expression in microbial communities by regulating plasmid behavior, such as their transfer, loss, and influence on cell function. Unlike traditional methods that operate at the single-cell level, ADEPT enables gene expression control across entire populations, allowing for much greater flexibility and scalability.

"Stable gene circuits enhance the reliability of biosensors, bioproduction processes, and therapeutic applications," You said. "ADEPT achieves this by lowering plasmid loss rates and reducing the metabolic burden on host cells."

ADEPT has already demonstrated its effectiveness in regulating gene expression and has been tested on a tetrathionate (TTR) biosensor, a [diagnostic tool](#) relevant to inflammatory bowel disease. This highlights ADEPT's potential for tuning [gene expression](#) in real-world applications.

As research progresses, ADEPT could be expanded to engineer complex [microbial communities](#), providing a powerful tool for [synthetic biology](#), environmental monitoring, and biomedicine.

"The flexibility of ADEPT opens up many possibilities," You said.

More information: Hye-In Son et al, Population-level amplification of gene regulation by programmable gene transfer, *Nature Chemical Biology* (2025). [DOI: 10.1038/s41589-024-01817-9](https://doi.org/10.1038/s41589-024-01817-9)

Journal information: [Nature Chemical Biology](#)
Provided by [Duke University](#)

FEBRUARY 27, 2025

An ancient RNA-guided system could simplify delivery of gene editing therapies

by Jennifer Michalowski, McGovern Institute for Brain Research



The Tas protein uses an RNA guide to recognize a specific target DNA sequence. Credit: Max Wilkinson

A vast search of natural diversity has led scientists at MIT's McGovern Institute and the Broad Institute of MIT and Harvard to uncover ancient systems with the potential to expand the genome-editing toolbox. These systems, which the researchers call TIGR (Tandem Interspaced Guide RNA) systems, use RNA to guide them to specific sites on DNA.

TIGR systems can be reprogrammed to target any DNA sequence of interest, and they have distinct functional modules that can act on the targeted DNA. In addition to its modularity, TIGR is very compact compared to other RNA-guided systems, like CRISPR, which is a major advantage for delivering it in a therapeutic context.

These findings [appear](#) in the journal *Science*.

"This is a very versatile RNA-guided system with a lot of diverse functionalities," says Feng Zhang, the James and Patricia Poitras Professor of Neuroscience at MIT who led the

research. The TIGR-associated (Tas) proteins that Zhang's team found share a characteristic RNA-binding component that interacts with an RNA guide that directs it to a specific site in the genome. Some cut the DNA at that site, using an adjacent DNA-cutting segment of the [protein](#). That modularity could facilitate tool development, allowing researchers to swap useful new features into natural Tas proteins.

"Nature is pretty incredible," remarks Zhang, who is also an investigator at the McGovern Institute and the Howard Hughes Medical Institute, a core member of the Broad Institute, a professor of brain and cognitive sciences and [biological engineering](#) at MIT, and co-director of the K. Lisa Yang and Hock E. Tan Center for Molecular Therapeutics at MIT.

"It's got a tremendous amount of diversity, and we have been exploring that natural diversity to find new biological mechanisms and harnessing them for different applications to manipulate biological processes," he says.

Previously, Zhang's team had adapted bacterial CRISPR systems into gene-editing tools that have transformed modern biology. His team has also found a variety of programmable proteins, both from CRISPR systems and beyond.

In their new work, to find novel programmable systems, the team began by zeroing in on a structural feature of the CRISPR Cas9 protein that binds to the enzyme's RNA guide. That is a key feature that has made Cas9 such a powerful tool.

"Being RNA-guided makes it relatively easy to reprogram, because we know how RNA binds to other DNA or other RNA," Zhang explains. His team searched hundreds of millions of biological proteins with known or predicted structures, looking for any that shared a similar domain. To find more distantly related proteins, they used an iterative process: from Cas9, they identified a protein called IS110, which had previously been shown by others to bind RNA. They then zeroed in on the structural features of IS110 that enable RNA binding and repeated their search.

At this point, the search had turned up so many distantly related proteins that the team turned to artificial intelligence to make sense of the list.

"When you are doing iterative, deep mining, the resulting hits can be so diverse that they are difficult to analyze using standard phylogenetic methods, which rely on conserved sequences," explains Guilhem Faure, a computational biologist in Zhang's lab.

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With a protein large language model, the team was able to cluster the proteins they had found into groups according to their likely evolutionary relationships. One group set apart from the rest, and its members were particularly intriguing because they were encoded by genes with regularly spaced repetitive sequences reminiscent of an essential component of CRISPR systems. These were the TIGR-Tas systems.

Zhang's team discovered over 20,000 different Tas proteins, mostly occurring in bacteria-infecting viruses. Sequences within each gene's repetitive region—its TIGR arrays—encode an RNA guide that interacts with the RNA-binding part of the protein. In some, the RNA-binding region is adjacent to a DNA-cutting part of the protein. Others appear to bind to other proteins, which suggests they might help direct those proteins to DNA targets.

Zhang and his team experimented with dozens of Tas proteins, demonstrating that some can be programmed to make targeted cuts to DNA in human cells. As they think about developing TIGR-Tas systems into programmable tools, the researchers are encouraged by features that could make those tools particularly flexible and precise.

They note that CRISPR systems can only be directed to segments of DNA that are flanked by short motifs known as PAMs (protospacer adjacent motifs). TIGR Tas proteins, in contrast, have no such requirement.

"This means theoretically, any site in the genome should be targetable," says scientific advisor Rhiannon Macrae.

The team's experiments also show that TIGR systems have what Faure calls a "dual-guide system," interacting with both strands of the DNA double helix to home in on their target sequences, which should ensure they act only where they are directed by their RNA guide. What's more, Tas proteins are compact—a quarter of the size of Cas9 on average—making them easier to deliver, which could overcome a major obstacle to therapeutic deployment of gene editing tools.

Excited by their discovery, Zhang's team is now investigating the natural role of TIGR systems in viruses as well as how they can be adapted for research or therapeutics. They have determined the molecular structure of one of the Tas proteins they found to work in human cells, and will use that information to guide their efforts to make it more efficient. Additionally, they note connections between TIGR-Tas systems and certain RNA-processing proteins in human cells.

"I think there's more there to study in terms of what some of those relationships may be, and it may help us better understand how these systems are used in humans," Zhang says.

More information: Guilhem Faure et al, TIGR-Tas: A family of modular RNA-guided DNA-targeting systems in prokaryotes and their viruses, *Science* (2025). [DOI: 10.1126/science.adv9789](https://doi.org/10.1126/science.adv9789)

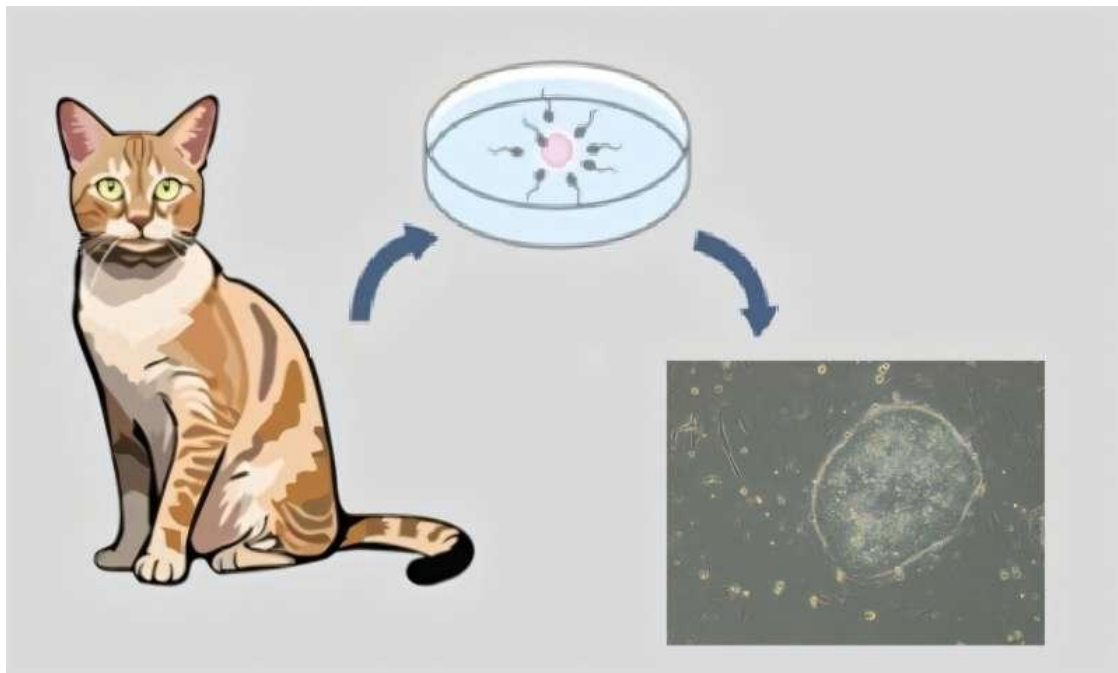
Journal information: [Science](#)

Provided by McGovern Institute for Brain Research

FEBRUARY 27, 2025

Pioneering feline embryonic stem cells could transform veterinary regenerative medicine

by [Osaka Metropolitan University](#)



New advancements in veterinary regenerative medicine plausible with these pluripotent cells.
Credit: Osaka Metropolitan University

As different as they may seem, humans and cats have similar ailments, but in terms of health care, veterinary regenerative medicine is not as advanced. A possible solution rests in embryonic stem cells, which can differentiate into various types of cells and be transplanted to restore internal damage. Further, they are characterized by their near-natural state, similar to induced pluripotent stem (iPS) cells.

Recent research has successfully generated feline iPS cells, but not embryonic stem cells, so research on these [cell lines](#) is essential to improve the quality of iPS cells.

Osaka Metropolitan University Professor Shingo Hatoya led a Graduate School of Veterinary Science team in pioneering the generation of feline embryonic stem cells using lab-grown blastocysts. The team performed in vitro fertilization of sperm and oocytes taken from discarded [reproductive organs](#) during feline sterilization surgeries.

The research is [published](#) in the journal *Regenerative Therapy*.

Through the isolation of inner cell mass from blastocyst stage embryos and culturing them, the researchers succeeded in generating high-quality feline [embryonic stem cells](#). These can be maintained in an undifferentiated state and can differentiate into the three germ layers: endoderm, ectoderm, and mesoderm.

"Embryonic stem cells are pluripotent cells, so we believe that comparative studies with iPS cells will further promote veterinary regenerative medicine research," stated Professor Hatoya.

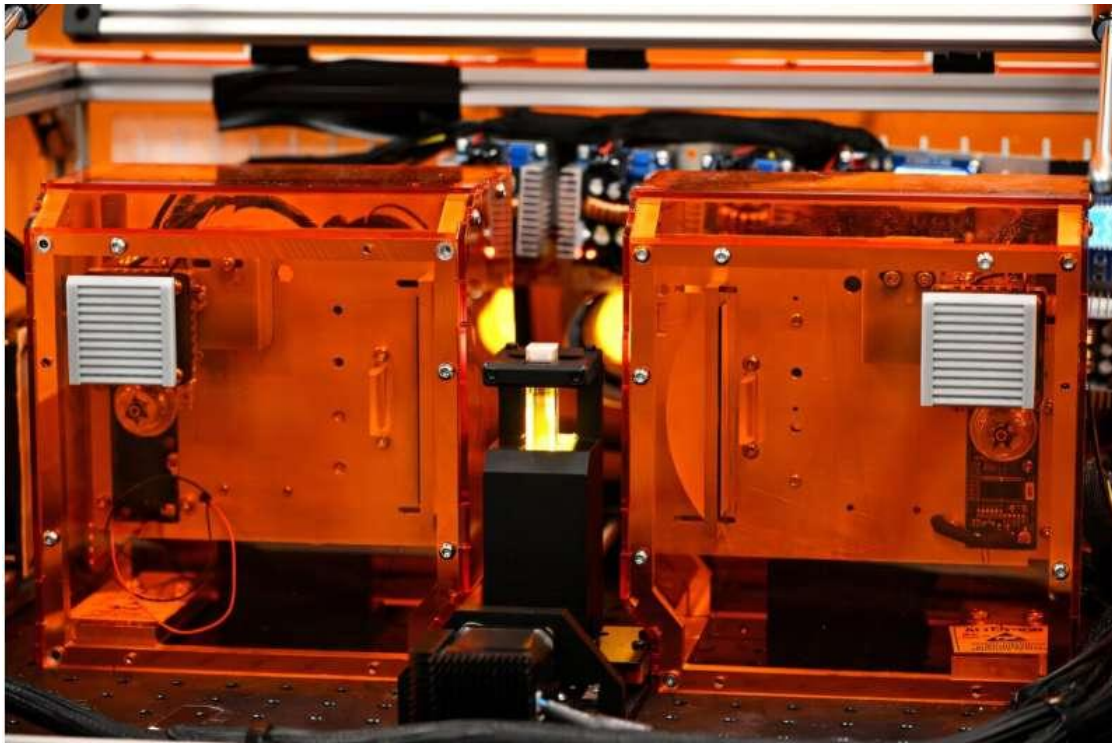
"The successful establishment of feline ES cells in this study can advance veterinary regenerative medicine by enabling [comparative studies](#) with feline iPS cells. Moreover, the potential to derive sperm and oocytes from feline ES cells could contribute to the conservation of endangered wild cat species."

More information: Takumi Yoshida et al, Establishment of feline embryonic stem cells from the inner cell mass of blastocysts produced in vitro, *Regenerative Therapy* (2024). [DOI: 10.1016/j.reth.2024.11.010](#)
Provided by [Osaka Metropolitan University](#)

FEBRUARY 27, 2025

Xolography-based method enables 3D printing of living tissues with light

by Marjolein Pijnappels, [Eindhoven University of Technology](#)



The first 3D printer to print living tissue with light, Xolography printer, a custom version of the Xube, xolo GmbH, Berlin. Credit: Bart van Overbeeke

Xolography is a novel light printing technique that has been explored for dental products and in-space manufacturing. At Eindhoven University of Technology (TU/e), this technique has now been adapted to 3D print living cells. This research can pave the way for 3D-printed kidneys and muscle tissue. The team pioneered the Xolography-based method to produce tiny structures with features as small as 20 μm —approximately the size of a human cell.

These results are [published](#) in *Advanced Materials*.

Is Xolography the technique that will enable a future of 3D-printed hearts and kidneys?

"Unfortunately, this is still entirely speculative for now, I'm afraid," cautions researcher Miguel Dias Castilho. "For now, we still view technology as a hacker space."

This pioneering spirit is perfectly reflected in the printer, an early tissue printing prototype, whose sheer orange acrylic casing reveals an inside of wires, projectors, copper coils, and tiny digital displays.

While it may seem speculative for now, the detailed and lightning-fast printing of living tissue in a suitcase-sized, orange 3D printer is completely real.

"Our research is a necessary first step for the future of tissue engineering. Right now, it can print more physiologically relevant 3D environments for cell culture, and in the long term, it could help make 3D-printed organs a reality," says Dias Castilho.

Tissue printing with light

At the heart of the machine sits a tiny cuvette containing a fluid that transforms into a solid as if by magic. But instead of waving a magic wand, Lena Stoecker, who is a Ph.D. of Dias Castilho's brand-new Biomaterials Engineering and Biofabrication group, projects beams of light onto liquids to conjure up viable cell-laden geometries.

Stoecker has successfully adapted a novel 3D printing technique called Xolography to print biomaterials. While demonstrating the printer by putting a cuvette with a liquid inside, Stoecker explains what drew her to 3D printing tissues: "I first encountered 3D printing as a student assistant during my studies of mechanical engineering and business administration. We employed 3D printing mainly for prototyping and tooling for small series production, and I was fascinated by the technology's possibility to realize (almost) any idea."

Biomedical challenges

It is no surprise that Stoecker gravitated towards tissue engineering, as it is by nature a multidisciplinary field combining the expertise of molecular biologists, engineers and designers.

The biggest trifold challenge facing tissue engineers everywhere is to create viable 3D tissues that closely resemble the natural environment of cells, to create them fast, and to do it precisely. This is the holy grail.

"There was a big hype around 3D printing for [biomedical engineering](#), but technologies failed to meet the high expectations," Stoecker explains. "My dream for Xolography would be to develop into a technology that is actually able to create tissue and organ models to study disease and develop cures."

A technique from the field of design

Xolography is a groundbreaking fusion of engineering, physics and chemistry, where light is used to 3D print liquid polymers. It harnesses the power of intersecting light beams of distinct wavelengths within a light-reactive fluid. As light rays converge, they turn the fluid into a detailed, solid 3D object the size of a gummi bear in under a minute.

The technology was developed by German chemist Stefan Hecht and physicist Martin Regehly, who further adapted it for diverse applications in their spin-off business Xolo. Four years ago, Hecht mused about Xolography potentially being used for generating complex biological structures.

Dias Castilho explains, "Four years ago, Xolo was looking to advance its technology into biomedical applications, while my team was searching for a disruptive technology that could potentially offer high resolution, fast manufacturing speeds, and scalability—so it's a perfect marriage."

Today, the TU/e-researchers at the Biomaterials Engineering and Biofabrication group made printing tissue with light a reality. Hecht and Regehly follow the findings of the research group with interest, as they are the first scientists to use this technology to print living materials in the world.

That did not happen overnight, as the researchers had to overcome some additional challenges to adapt Xolography to [printing](#) living tissue.

"The materials used must be biocompatible, for one. Besides the hydrogels we were developing for the process, we found that the photoinitiator system itself was not very cell-friendly and had to be replaced. In close collaboration with the company, we developed and optimized the material formulations to ensure they are safe for biomedical applications," says Dias Castilho.

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Printing scaffolds to grow cells in the lab

Stoecker printed hydrogel scaffolds that can be used as temporary support structures to grow cells in the lab. She says, "To successfully grow tissue, we aim for the hydrogel scaffolds to contain features that mimic the natural environment of, for example, bone marrow cells."

"We were able to print detailed scaffolds with pores in the range of 100 μm to 1 mm, which could ensure nutrient supply throughout the scaffold during cell culture. Tiny raised elements could be printed down to only 20 μm , in the size range of a human cell."

Tuning 3D material properties with light

Printing on a small scale alone is not enough to mimic natural tissue and exert precise control over the cell's behavior.

"Natural tissues show a variety of properties. For example, they are stiffer in one place and more flexible in another. Existing techniques print objects that are more homogenous," says

Stoecker. "We succeeded in creating materials where we control the properties completely in 3D, so we can create stiffer and flexible regions where we desire them."

By varying the projected light intensity, the researchers could tightly control tissue properties.

Artificial muscles

Dias Castilho says, "It has been very hard to replicate materials that can change their shape—and change it back again, which is essential to creating tissues that function like organic tissue:"

The team managed to implement thermally responsive hydrogels to allow the creation of 4D printed structures, where the fourth dimension is time.

"These materials can change shape or properties over time in response to temperature changes, enabling more complex and functional tissue constructs," says Dias Castilho, "such as artificial muscles that can flex and extend in response to subtle temperature changes.

"We have now demonstrated that this technology could unlock exciting possibilities in health care by producing more realistic and functional tissue models and implants."

The results are considered a hallmark publication.

"We believe this is a foundational paper," says Dias Castilho. "I believe insights in the paper will help to advance light-based high-resolution fabrication of cell-laden hydrogels with programmable mechanical properties and shape. In the next phase, in vitro models and bioprint solutions for tissue repair will be improved."

Stoecker adds, "I am well aware that our research still has to go a long way to reach the clinic, but I like the idea that maybe one day, the techniques we develop in the lab will contribute to improving the health and thereby the life of somebody."

More information: Lena Stoecker et al, Xolography for Biomedical Applications: Dual-Color Light-Sheet Printing of Hydrogels With Local Control Over Shape and Stiffness, *Advanced Materials* (2025). DOI: [10.1002/adma.202410292](https://doi.org/10.1002/adma.202410292)

Journal information: [Advanced Materials](#)

Provided by [Eindhoven University of Technology](#)

A Generative, Foundational AI Model for Genetics

This might completely change how genomic instability is handled.

Feb 24, 2025

The Arc Institute, a nonprofit research organization, has published a manuscript on its creation of **Evo 2, an AI foundation model that is capable of both understanding and building full genomes of organisms.**

A new step in understanding biology

The authors of this paper, a group of professionals largely from the Arc Institute and well-known universities in California, begin by discussing Evo 2's unprecedented size. Unlike the original Evo, which was only trained on organisms that lack nuclei (prokaryotes), this model was trained on organisms with nuclei (eukaryotes) as well, a classification that includes everything from amoebae to human beings, and a total of 9.3 trillion base pairs were included in its training set.

The researchers created two variants, one with 7 billion parameters (7B) and another with 40 billion parameters (40B), and both models use a context window of a million single base pairs. This model is open source, including both the training and inference code along with its parameters and the training data originating from OpenGenome2.

This paper goes into detail describing how the model was trained. Like the commonly known large language models (LLMs), this model was fundamentally trained to predict the next "token"; instead of predicting the next word in the English language, however, Evo 2 was built to predict the next DNA base pair. This model was built on StripedHyena2, a convolutional, multi-hybrid system that directs it to think in different, layered ways (stripes) about the training information it's receiving.

Predicting the effects of mutations

The researchers found that Evo 2 was able to predict whether or not a genetic mutation would impact essential function, which had never been accomplished before in eukaryotes. Evo 2 had learned to predict the likelihood of mutations as they related to

start and stop codons; this, the researchers claimed, meant that it had an understanding of such “fundamental genetic features” despite solely being trained on base pairs and not taught what they meant.

Furthermore, by testing its predictions against known effects in RNA sequences, the researchers determined that the model was able to accurately ascertain whether any given mutation would affect the essential function of the sequence, and it was even able to grasp that effects in noncoding regions would have significant consequences. The 40B model was found to be substantially better than the 7B model at this.

This held true even for sequences derived from human beings. Mutations in the BRCA1 gene often lead to breast cancer, and 40B Evo2 was able to predict whether or not any given mutation in this gene would be dangerous or not, especially when it was specifically supervised to do so, even beating out specialized models made for the purpose. This, the researchers note, is in spite of the model being trained on only one reference human genome within its expansive dataset; its predictions are fundamentally derived from how organisms work, not humans in particular.

Grasping genetics from the ground up

The researchers took a close look at Evo2’s thought process. They realized that it was accurately able to identify features associated with CRISPR-related phage sequences within *E.coli* bacteria. Rather than memorizing the bacterial phages themselves, the model identified the CRISPR spacers instead. Similarly, the model was able to identify frameshift mutations and premature stop codons. It was able to identify exons and introns that it learned from the human genome and notice them in the woolly mammoth genome, which it had never been trained on.

As this is a generative AI, the researchers set it to the task of generating genomes. The genomes it created were found to have many natural features, including reasonable chromatin accessibility, although the authors judged its performance based on other algorithms and did not actually create any physical structures based on Evo2’s outputs. They posit that their model can, with further training related to sequences and their associated functions, be used to generate effective genetic structures.

To prevent this open-source model from being used for bioterrorism, the researchers intentionally excluded infectious diseases from its training set, and they red-teamed their model to ensure that it was no better than random chance in generating or understanding the effects of infectious diseases. However, they did note that they cannot prevent malefactors from training the model with such diseases.

This model may have significant benefits for diagnosing and treating both **mitochondrial dysfunction** and **genomic instability**, such as by identifying and better understanding the age-related mutations that give some cells or mitochondria a reproductive advantage over others at the expense of the overall organism. It may even be possible for future research to use this model to test individual people for mutated cells or even to create individually targeted gene therapies. It is still a foundational model, however, and nothing based on Evo2 has been put to such tasks.

This manuscript was published on the Arc Institute's website and not in a peer-reviewed publication. However, the depth and detail of this paper's explanations, along with its authorship of researchers from reputable institutions, lend weight to its claims being correct. As this is an open-source tool for the research community, it will swiftly become clear whether or not it can be used to advance oncology, develop treatments for genetic diseases, or directly impact aging at the genetic level.

The Underexplored Applications of Longevity Biotechnology

This field has very broad potential.

Feb 24, 2025

No other human endeavor today holds more promise than understanding and targeting aging. The molecular mechanisms that drive aging impact overall vigor, environmental stress resistance, reproductive health, and broad disease risk, and they fundamentally change what life means by radically changing our relationship to death. Intriguingly, aging mechanisms are highly evolutionarily conserved, so much so that the same subcellular changes that drive aging in single-celled organisms and small animals also drive aging in larger mammals, including companion pets and humans. Truly, from applications to beneficiaries, the potential of targeting aging to transform life is vast.

Seeking to realize the promise of longevity technologies (defined here as any intervention that extends healthy organismal lifespan), longevity biotechnology (LongBio) has continued to mature over the last 10 years.

LongBio's focus has largely centered on its biopharmaceutical applications. Indeed, many people have even ventured to assert that biopharmaceutical applications define longevity biotechnology itself [1]. Biopharma LongBio has understandably led the charge, as the need for new disease treatments is great, and geroscience theory makes a compelling case that aging targets overlap with myriad disease states.

However, longevity biotech applications are not limited to treating disease; they hold the key to a radical transformation in industries far beyond healthcare.

The foundational science behind longevity is simple: maintaining and extending the healthy function of biological systems. Yet, outside of applications into current medical practice, the potential of longevity biotech remains vastly underexplored. From conservation biology to space travel, the ability to preserve, optimize, and extend the vitality of living organisms is an untapped goldmine.

Expanding the scope of longevity biotechnology

Dietary supplements and consumer products

Products marketed as “anti-aging” existed well before LongBio. The major challenge with consumer-ready LongBio products is the same with any other product: does it work as claimed? With no regulatory body that assesses non-clinical product claims and the morass around treating longevity/aging as an FDA-approved indication, quality assurance across consumer LongBio products is left to the manufacturer. Interestingly, the dominance of biopharma LongBio and the lack of clarity around aging as an indication have set the stage for consumer LongBio groups becoming best positioned to truly move our understanding of longevity technologies forward.

To find something, the most obvious strategy is to directly look for it. This is true for longevity technologies. However, the target-based reductionism prevalent in biopharma drug development has created a situation where, instead of directly measuring extended lifespan (the gold standard analysis for a longevity technology), longevity technologies are called such based on whether they modify a known “Hallmark of Aging” [2].

At its most extreme, biopharma LongBio is fundamentally misaligned to assessing whether an intervention extends healthy lifespan. For biopharma LongBio, disease indications are the focus, not longevity. Consumer LongBio products, on the other hand, are focused on directly extending healthy lifespan. This creates a major opportunity for these groups to validate longevity technologies by directly measuring healthy lifespan.

A major unmet need in this space is an unbiased, third-party system to evaluate longevity claims made by consumer LongBio products. Elevating standards of quality and supporting companies’ scientific efforts by choosing their products will create alignment and lead to better longevity technologies being developed faster.

Biomarkers and precision longevity

Along with effective longevity technologies, biomarkers that predict successful extended healthy lifespan are the biggest unmet need in LongBio. Today’s biomarkers, most prominently the numerous “clocks” in the consumer marketplace, have questionable use beyond serving as entertainment products.

Advancements in longevity biomarkers can refine personalized medicine by predicting disease risk, optimizing interventions, and even guiding lifestyle choices based on real-time biological data. In a commercial sense, longevity-focused biomarker technology could create a new wave of diagnostics, health optimization services, and AI-driven longevity coaching.

Reproductive health

The connection between reproductive health and longevity is becoming clearer, opening doors for new fertility-enhancing treatments that also promote long-term vitality. Longevity biotech could support extended reproductive windows, healthier pregnancies, and delayed reproductive aging, creating opportunities in both clinical and consumer health markets.

Veterinary and pet longevity

Veterinary medicine is already seeing interest in longevity applications for pets, but why stop there? A broader application of these technologies could enhance the health and lifespan of pets outside of veterinary care. The pet care industry alone, valued at over \$200 billion globally, is primed for disruption through longevity-driven innovations.

Longevity in unexplored commercial frontiers

Conservation biology & remediation

Longevity technologies could revolutionize conservation efforts by extending the lifespans and/or reproductive viability of endangered and threatened species. A longer-lived, healthier wildlife population could improve biodiversity conservation, making longevity biotech a potential tool in ecosystem restoration.

Completely overlooked as of now is how improved healthy lifespan and stress resistance could improve the function of organisms that perform bioremediation and carbon fixing. Longevity technologies may also provide benefit in the context of environmental mitigation, which seeks to offset environmental and ecological damage produced during real estate and other development. Combined, remediation, environmental mitigation, and carbon markets have a combined market size of over \$1 trillion.

Agriculture & food security

Healthier, longer-living crops and livestock could transform agriculture, reducing losses due to disease and environmental stress while increasing yield stability. Longevity technologies could enhance plant resilience, while longevity-focused veterinary applications could improve livestock productivity, addressing both economic and ethical concerns in food production.

Military performance & readiness

Servicemember readiness, retention, and performance are all priorities for leaders across the Department of Defense. Longevity biotech offers unprecedented potential for improving soldier performance, recovery, and retention. Enhancing cellular resilience, injury recovery, and cognitive longevity could create a new era of soldier optimization: one where extended healthspans mean fewer medical discharges and greater operational readiness. The military has always been a driver of cutting-edge biotech, and LongBio should be no exception.

Space medicine & interstellar longevity

Human space travel is limited by biological aging, radiation exposure, and long-term health deterioration. Longevity biotechnologies could mitigate these risks by promoting cellular repair, bolstering immune resilience, and extending astronaut viability for deep-space missions. As commercial space travel expands, so too will the demand for longevity-focused space medicine solutions.

Industrial & environmental applications

Any system reliant on biological organisms—whether it be wastewater treatment using microbial life or bio-based manufacturing—stands to benefit from longevity advancements. Healthier, longer-lived microbes, plants, and engineered biological systems could drive new efficiencies in bioindustrial processes.

The next commercial revolution

The potential of longevity biotechnology extends far beyond personal health and wellness; it is a foundational tool for any industry that relies on the health of living systems. The next wave of biotech-driven commercialization will not just be about treating disease

but about optimizing the very biology of life itself. As we expand our understanding of aging and cellular health, we will uncover new markets, drive unprecedented innovation, and reshape industries that have yet to recognize the longevity revolution knocking at their door.

The question isn't whether longevity biotechnology will expand into new industries—it's how quickly we'll seize the opportunity.

Literature

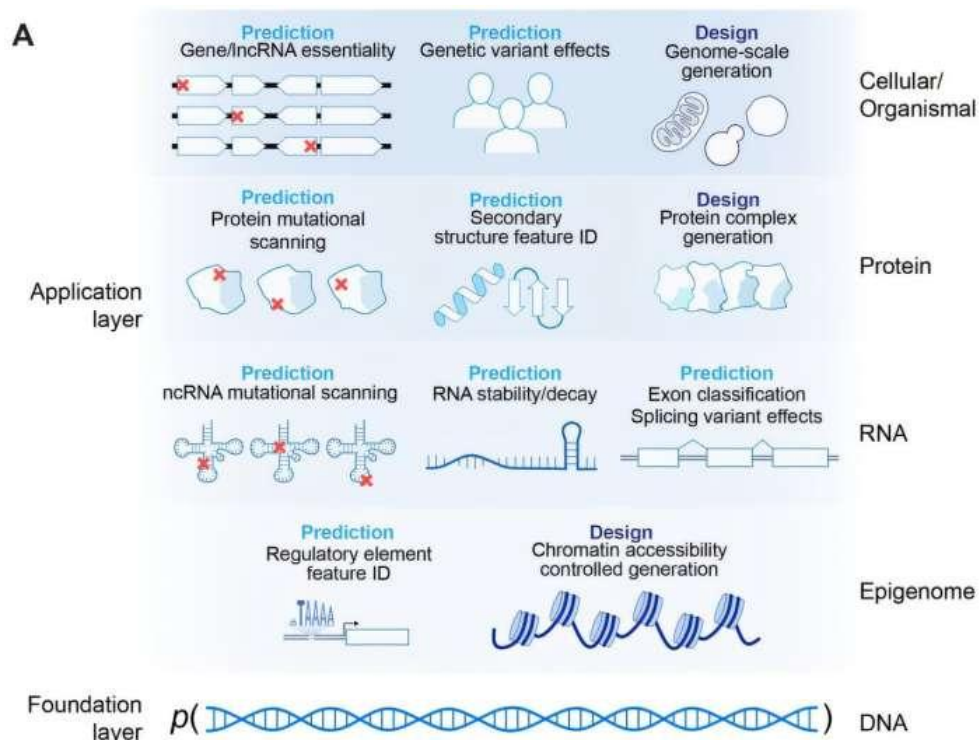
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MARCH 3, 2025

Introducing Evo 2, a predictive and generative genomic AI for all domains of life

by Justin Jackson , Phys.org



Evo 2 models DNA sequence and enables applications across the central dogma, spanning molecular and cellular scales. Credit: *bioRxiv* (2025). DOI: 10.1101/2025.02.18.638918
Researchers at the Arc Institute, Stanford University, and NVIDIA have developed Evo 2, an advanced AI model capable of predicting genetic variations and generating genomic sequences across all domains of life.

Testing shows that Evo 2 accurately predicts the functional effects of mutations across prokaryotic and eukaryotic genomes. It also successfully annotated the woolly mammoth genome from raw [genomic sequences](#) without a direct training reference, showing an ability to generalize function from the sequence alone.

Current genomic models struggle with predicting functional impacts of mutations across diverse biological systems, particularly for eukaryotic genomes. Machine learning approaches have demonstrated some success in modeling [protein sequences](#) and prokaryotic genomes. The complexity of eukaryotic DNA, with its long-range interactions and regulatory elements, presents more of a challenge.

Evo 2 was developed to address these limitations by incorporating a large-scale training dataset spanning bacteria, archaea, eukaryotes, and bacteriophages, with a focus on broad genomic patterns across species rather than being trained for a single specific function.

In the study, "Genome Modeling and Design Across All Domains of Life with Evo 2," [published](#) as a *bioRxiv* preprint, the team details how a model trained on 9.3 trillion DNA base pairs enables genome-scale predictions and design.

Evo 2 trained on 9.3 trillion nucleotides (A, T, C, or G), making it one of the largest biological models ever developed. The model can analyze and generate up to 1 million nucleotides at a time, allowing it to capture long-range patterns and relationships within DNA sequences.

During training, Evo 2 learned by predicting the next base pair in a sequence, similar to how language models predict the next word in a sentence. This approach enables Evo 2 to identify complex genomic structures and accurately model the functional impact of genetic variations across all domains of life.

The training dataset, OpenGenome2, was carefully curated to exclude genomic sequences from viruses that infect eukaryotic hosts to mitigate potential misuse.

A two-phase training strategy was used, beginning with a pretraining phase that prioritized functional genetic elements and a midtraining phase that extended context length to capture broader genomic patterns.

Evo 2 employs StripedHyena 2, a novel architecture combining input-dependent convolution operators with attention mechanisms, optimized to efficiently handle long DNA sequences at scale. The model was trained using 1,024 GPUs at the 40-billion-parameter level, achieving higher efficiency compared to traditional transformer models.

Results showed that Evo 2 accurately predicts the functional effects of mutations across prokaryotic and eukaryotic genomes without the need for task-specific fine-tuning. The model demonstrated sensitivity to mutations in start codons, splice sites, and conserved genomic regions, with performance aligning with known biological constraints.

Specialized models such as AlphaMissense and GPN-MSA performed slightly better for coding single-nucleotide variants, whereas Evo 2 demonstrated superior accuracy for indels and noncoding variants. Embedding-based classifiers trained on Evo 2 representations achieved state-of-the-art performance in classifying BRCA1 breast cancer variants.

Interpretability analysis revealed that Evo 2 autonomously learns key biological structures, including transcription factor binding sites, exon-intron boundaries, and protein structural motifs.

Sparse autoencoder techniques identified latent features corresponding to mobile genetic elements, prophages, and CRISPR-associated sequences. Evo 2's ability to generalize was demonstrated by successfully annotating the woolly mammoth genome, a species not present in its training data.

Genome-scale sequence generation was also tested, with Evo 2 successfully creating complete mitochondrial genomes, bacterial genomes, and yeast chromosome-scale sequences. Generated sequences exhibited realistic structural and evolutionary properties, including accurate synteny patterns, protein-coding regions, and regulatory elements.

When prompted with mitochondrial genome sequences, Evo 2 produced DNA with the correct number of coding genes, tRNAs, and rRNAs.

Beyond sequence generation, Evo 2 was applied in an inference-time controlled design task to engineer DNA sequences with programmable chromatin accessibility. Integrating chromatin accessibility models such as Enformer and Borzoi, Evo 2 generated sequences with specific regulatory features, including the ability to encode Morse code messages within epigenetic structures.

Evo 2 represents a significant advancement in genomic AI, combining predictive accuracy with generative capabilities at [genome](#)-wide scales. By making Evo 2's training code, model parameters, and the OpenGenome2 dataset openly available, researchers hope to accelerate genomic research.

Future applications of Evo 2 may include large-scale population genetics studies, synthetic biology, and advanced epigenomic design.

More information: Garyk Brixi et al, Genome modeling and design across all domains of life with Evo 2, *bioRxiv* (2025). DOI: [10.1101/2025.02.18.638918](https://doi.org/10.1101/2025.02.18.638918)

Journal information: [bioRxiv](#)

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How to trick the body's metabolism: Mouse study reveals new path for weight-loss and diabetes treatments

by [University of Southern Denmark](#)

Many people who have tried to lose weight by cutting calories are familiar with this frustrating reality: At some point, the body stops shedding pounds. It senses the reduced calorie intake and responds by slowing down metabolism, causing it to burn fewer calories than before the diet.

This happens because the body perceives a potential starvation threat and adapts by conserving energy while still carrying out essential functions. It may seem incredibly unfair that the body doesn't recognize the goal of weight loss and instead works against it by holding on to calories.

Now, a new study from the University of Southern Denmark has identified a possible way to maintain calorie burning even when consuming fewer calories. The work [appears](#) in *Cell Metabolism*.

This discovery could be particularly important for patients using weight-loss or diabetes medicines like Wegovy and Ozempic. Many people taking these medications find that their weight loss plateaus after losing about 20–25% of their body weight.

According to Kim Ravnskjaer, a Principal Investigator and associate professor at the Department of Biochemistry and Molecular Biology, University of Southern Denmark, this stall is likely due to the body's natural response.

"It usually goes well at first, but as people lose some of the weight they aim to shed, their progress stalls because the body's metabolism adapts," he said.

If it were possible to control this metabolic adaptation, it could be a game-changer for anyone trying to lose weight. A medication that could counteract this effect might extend the benefits of treatments like Wegovy, which often stop working after a certain point.

This is where the new study by Ravnskjaer and colleagues comes into play.

"If we could develop a medication that helps maintain fat or sugar burning at its original high level alongside weight-loss treatments, people could continue losing weight beyond the usual plateau," he explains.

However, he stresses that the team's findings are currently based on mouse models, meaning [human trials](#) are still a long way off, and potential treatments even further down the line.

"It is a long way from insights in mouse experiments to bringing a drug to the market—but this is obviously the potential in our research," says Ravnskjaer.

The researchers' discovery was unexpected when they were investigating the function of a gene called Plvap in certain [liver cells](#) in mice. The team knew from previous studies that humans born without this gene have problems with their lipid metabolism, a connection the research team set out to investigate.

It turned out that the Plvap gene enables the body's metabolic shift from burning sugar to fat when fasting. And when Plvap is turned off—as the researchers did in their [laboratory mice](#)—the liver does not recognize that the body is fasting and continues burning sugar.

In other words, the research team has found an entirely new way in which the liver's metabolism is regulated, which may have medical applications.

"If we can control the liver's burning of sugar and fat, we might also increase the effectiveness of weight-loss and diabetes medications," says Ravnskjaer.

Beyond the intriguing ability of Plvap knockout to "trick" the liver into thinking it is not fasting, the researchers made several other important observations in their study:

1. The signal that triggers metabolic changes during fasting comes from the liver's stellate cells rather than hepatocytes, the liver's most abundant cells responsible for carrying out metabolic processes. This suggests that stellate cells play a previously unknown role in controlling liver metabolism by directing other cell types, introducing a new mode of cell-to-cell communication.
2. Although fat was redirected to the muscles instead of the liver, the mice showed no negative effects. In fact, they experienced improved insulin sensitivity and lower blood sugar levels.

Ravnskjaer finds this particularly exciting. "It's well known that elevated blood sugar may lead to chronic complications for people with type 2 diabetes. Understanding Plvap could help diabetics better regulate their blood sugar in the future," he says.

This discovery could have far-reaching implications—not just for obesity treatments, but also for improving our understanding of how fat and sugar are processed in metabolic diseases. In the long run, it may open new avenues for treating conditions like type 2 diabetes and steatotic liver disease.

How the study was done

The research team discovered that the Plvap gene, which plays a role in lipid metabolism in mammals, is expressed in the stellate cells in the liver of mice. This was surprising because stellate cells have not previously been associated with [lipid metabolism](#).

To investigate this further, the researchers turned off the Plvap gene in the stellate cells and observed the mice. At first, they were disappointed—the mice appeared completely normal. But when they fasted the mice, everything changed.

The mice's livers were unable to burn fat and produce ketones, which typically happens in all healthy mammals during fasting.

The metabolic programs responsible for this process simply didn't activate. Although fat was released from adipose tissue into the bloodstream, the liver did not absorb it as expected. Instead, the fatty acids were redirected to the skeletal muscles.

Interestingly, a liver without the Plvap gene "does not recognize" that the body is fasting. As a result, it continues to burn [sugar](#) in a process that appears beneficial for overall metabolism.

More information: Hepatic stellate cells regulate liver fatty acid utilization via plasmalemma vesicle2 associated protein, *Cell Metabolism* (2025). DOI:

[10.1016/j.cmet.2025.01.022](https://doi.org/10.1016/j.cmet.2025.01.022). [www.cell.com/cell-metabolism/f ...](https://www.cell.com/cell-metabolism/f...) 1550-4131(25)00022-1

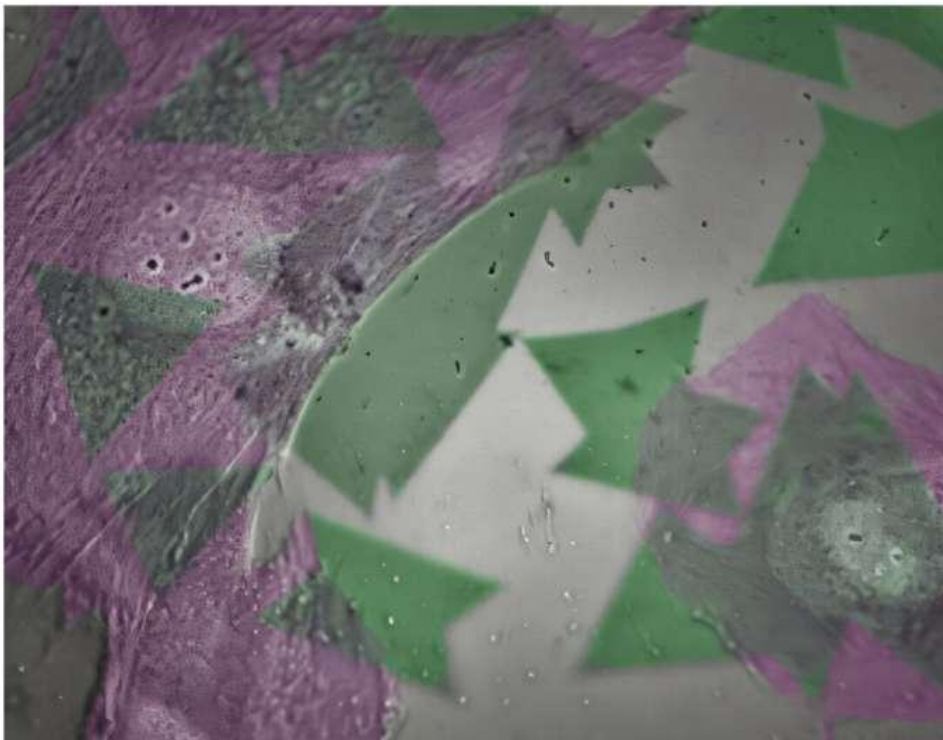
Journal information: [Cell Metabolism](#)

Provided by [University of Southern Denmark](#)

MARCH 3, 2025

Quantum properties in atom-thick semiconductors offer new way to detect electrical signals in cells

by Liezel Labios, [University of California - San Diego](#)



Top: Colored SEM image of heart muscle cells (green) cultured on top of monolayer semiconductor crystals (purple). Bottom: Optical recording traces of the cellular action potentials. Credit: Cubukcu lab

For decades, scientists have relied on electrodes and dyes to track the electrical activity of living cells. Now, engineers at the University of California San Diego have discovered that quantum materials just a single atom thick can do the job—using only light.

A new study in *Nature Photonics*, shows that these ultra-thin semiconductors, which trap electrons in two dimensions, can be used to sense the biological electrical activity of living cells with high speed and resolution.

Scientists have continually been seeking better ways to track the electrical activity of the body's most excitable cells, such as neurons, heart muscle fibers and pancreatic cells. These tiny electrical pulses orchestrate everything from thought to movement to metabolism, but capturing them in real time and at large scales has remained a challenge.

Traditional electrophysiology, which relies on invasive microelectrodes, offers precise recordings but is limited in scalability. Implanting electrodes across large regions of tissue can cause significant damage, and even the most advanced probes are limited to recording just a few hundred channels at once.

Optical techniques like calcium imaging, while capable of monitoring large populations of cells, offer only an indirect glimpse into electrical activity. Instead of recording the actual voltage shifts that drive cellular communication, they capture secondary changes that can introduce significant discrepancies.

UC San Diego engineers have demonstrated a new approach that could bridge this gap: a high-speed, all-optical method for recording voltage changes using atom-thick semiconductors. The key lies in how these materials' electrons interact with light: When exposed to an electric field, they switch between two states—excitons (electron-hole pairs that are electrically neutral) and trions (charged excitons).

Fluorescence wide-field microscope video of the MoS₂ PL recorded at 100 frames per second and played back at 50 frames per second. The two bright spots are the locations of the porated cells. The MoS₂ PL has become brighter after exposure to the high intensity laser used to porate the cells. The blinking of the PL at these two spots are due to the intracellular action potential of the cardiomyocytes. Credit: *Nature Photonics* (2025). DOI: 10.1038/s41566-025-01637-w

The researchers found that the conversion from excitons to trions in atom-thick semiconductors can be harnessed to detect the electrical signals of heart muscle cells—without the need for tethered electrodes or voltage-sensitive dyes, which can interfere with cellular function.

In other words, the quantum properties of the material itself can be used as a sensor.

"We believe that the voltage sensitivity of excitons in monolayer semiconductors has the potential to enable high spatiotemporal investigation of the brain's circuitry," said study senior author Ertugrul Cubukcu, a professor in the Aiso Yufeng Li Family Department of Chemical and Nano Engineering, as well as the Department of Electrical and Computer Engineering, at the UC San Diego Jacobs School of Engineering.

Cubukcu and his team studied the quantum properties of monolayer molybdenum sulfide. In addition to its biocompatibility, they found that this semiconductor material possesses a particular advantage: It naturally forms sulfur vacancies during its production, which creates a high density of trions. This built-in defect makes it exceptionally responsive to changes in nearby electric fields, including the ones generated by living cells, which in turn allow spontaneous exciton-to-trion conversion.

By tracking changes in the material's photoluminescence, the researchers could map the electrical activity of heart muscle cells in real time, at speeds unmatched by any other imaging technology to date, they noted.

This technology has a variety of potential applications. It could enable researchers to map network dysfunctions across large areas of excitable tissue, from the surface down to

deeper layers. It could provide insights into the mechanisms underlying neurological and cardiac disorders, offering a clearer picture of how diseases disrupt the body's electrical circuits. It may also refine therapeutic strategies that rely on electrical neuromodulation, such as [deep brain stimulation](#) for Parkinson's disease or cardiac pacing for arrhythmias.

Furthermore, this work could lead to the discovery of new [quantum materials](#) that can offer a non-invasive, high-speed method to probe electrical activity in living systems.

More information: Yundong Ren et al, Trionic all-optical biological voltage sensing via quantum statistics, *Nature Photonics* (2025). DOI: [10.1038/s41566-025-01637-w](https://doi.org/10.1038/s41566-025-01637-w)

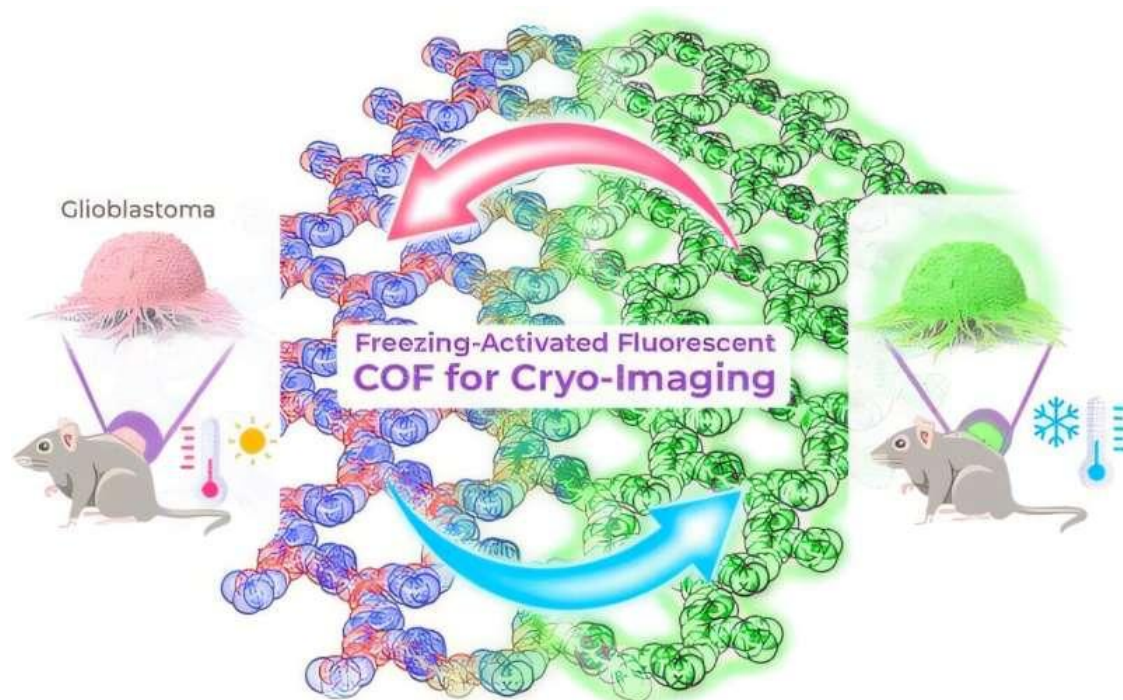
Journal information: [Nature Photonics](#)

Provided by [University of California - San Diego](#)

MARCH 3, 2025

Nanoscale material illuminates cancer cells in freezing conditions for precise cryosurgery

by [New York University](#)



Credit: *Journal of the American Chemical Society* (2025). DOI: [10.1021/jacs.4c13848](https://doi.org/10.1021/jacs.4c13848)

Researchers at NYU Abu Dhabi (NYUAD) have developed an innovative tool that enhances surgeons' ability to detect and remove cancer cells during cryosurgery, a procedure that uses extreme cold to destroy tumors. This breakthrough technology involves a specialized nanoscale material that illuminates cancer cells under freezing conditions, making them easier to distinguish from healthy tissue and improving surgical precision.

Detailed in the [study](#) "Freezing-Activated Covalent Organic Frameworks for Precise Fluorescence Cryo-Imaging of Cancer Tissue" in the *Journal of the American Chemical Society*, the Trabolsi research group at NYUAD designed a unique nanoscale covalent organic framework (nTG-DFP-COF) that responds to [extreme cold](#) by increasing its fluorescence. This makes it possible to clearly differentiate between cancerous and healthy tissues during surgery.

The material, prepared by Gobinda Das, Ph.D., a researcher in the Trabolsi Research Group at NYUAD, is engineered to be biocompatible and low in toxicity, ensuring it interacts safely within the body. Importantly, it maintains its fluorescent properties even in the presence of ice crystals inside cells, allowing [real-time](#) monitoring during cryosurgery.

This advancement not only improves the accuracy and safety of cryosurgical procedures—helping surgeons preserve more [healthy tissue](#) while removing cancer cells—but also combines diagnostic and treatment functions into one platform. This could reduce the need for repeat surgeries and speed up patient recovery.

Fluorescence imaging, a non-invasive technique that uses light-sensitive dyes to highlight tumors, has gained traction for its ability to provide real-time insights during surgery. However, its use in cryosurgery has remained largely unexplored until now.

"We believe this is a transformative tool that could revolutionize cancer surgery," said Farah Benyettou, Ph.D., a research scientist in the Trabolsi Research Group at NYU Abu Dhabi. "By making [tumor removal](#) more precise, this technology has the potential to reduce additional surgeries and accelerate patient recovery. It's a major step forward in treating aggressive, hard-to-target cancers."

"This breakthrough bridges the gap between imaging and therapy, providing surgeons with a real-time tool to visualize and remove cancer with unprecedented precision," said Ali Trabolsi, Professor of Chemistry and principal investigator of the Trabolsi Research Group at NYU Abu Dhabi. "By integrating [fluorescence imaging](#) with cryosurgery, we are pushing the boundaries of cancer treatment and offering new hope for patients with difficult-to-treat tumors."

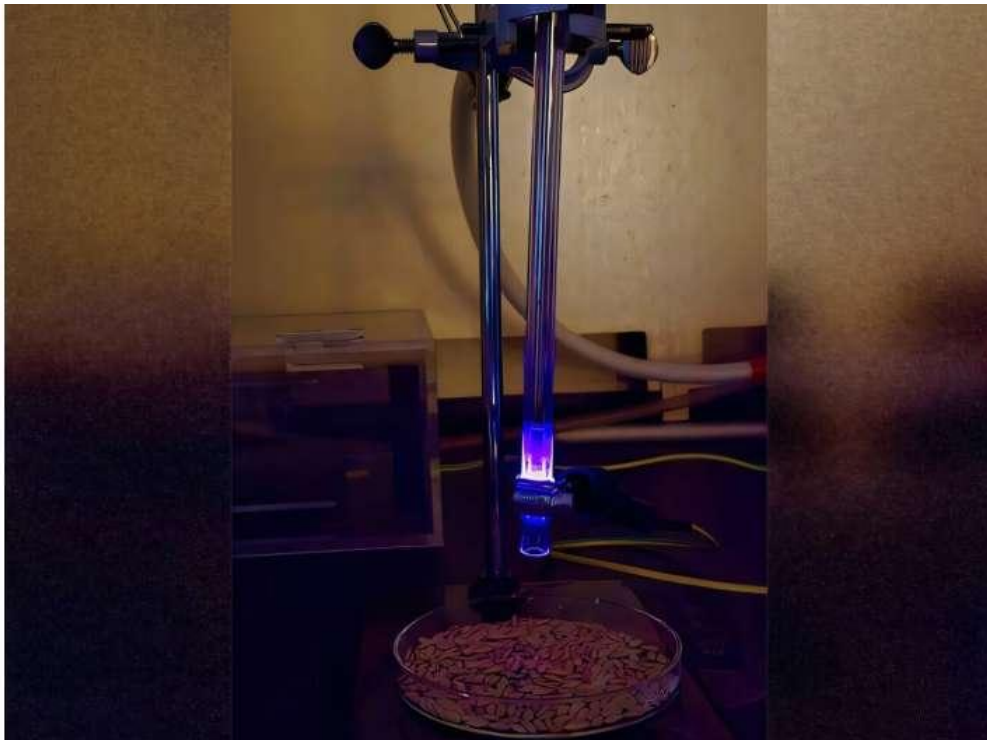
More information: Farah Benyettou et al, Freezing-Activated Covalent Organic Frameworks for Precise Fluorescence Cryo-Imaging of Cancer Tissue, *Journal of the American Chemical Society* (2025). DOI: [10.1021/jacs.4c13848](https://doi.org/10.1021/jacs.4c13848)

Journal information: [Journal of the American Chemical Society](#)
Provided by [New York University](#)

MARCH 3, 2025

Cold-plasma-treated seeds show potential to protect plants and reduce pesticide use

by [University of Arkansas](#)



Cold plasma is applied to rice seeds to investigate its effects on plant growth and defense against the fall armyworm. Credit: Rupesh Kariyat

The same substance that paints the sky with the Northern Lights also appears to enhance plant growth and insect defense, according to a new study.

Food science and entomology researchers from the Arkansas Agricultural Experiment Station teamed up to harness plasma and measure its effects on rice seed. The project began after Mahfuzur Rahman, assistant professor of food science, acquired a machine that produces cold plasma.

Known as the fourth state of matter, plasma is an electrically charged gas that has fluid-like behavior. Rahman points to the Northern Lights as the most familiar example of cold plasma, which means it is considered low temperature compared to the much higher temperatures of plasma in stars. Other examples of cold plasma like that generated in Rahman's lab include fluorescent lights and neon signs.

Rupesh Kariyat, associate professor of crop entomology, became interested in investigating cold plasma's effects from an insect perspective—an area he said had not been studied adequately.

"I thought it would be a good idea that we expose our seeds to cold plasma and then grow those seeds out into plants and ask the question of whether the plants are doing better," Kariyat said.

"If this works, then we can come up with a method to expand at a scale where we can add cold plasma to complement existing seed treatments to boost their growth and defense against insect herbivores," Kariyat said, noting the potential to reduce insecticide use.

One of Kariyat's graduate students, Deepak Dilip, led the project in collaboration with Nikitha Modupalli, a postdoctoral fellow in [food science](#) and member of Rahman's lab. Their study, "Atmospheric cold plasma alters plant traits and negatively affects the growth and development of fall armyworm in rice," was [published](#) in *Scientific Reports* in January.

Dilip served as the lead author, with Modupalli, Rahman and Kariyat serving as co-authors. Both Rahman and Kariyat are researchers with the Arkansas Agricultural Experiment Station, the research arm of the U of A System Division of Agriculture.

Tracking seed germination and plant growth

The study specifically investigated rice plant defense against fall armyworm. Seeds were treated with cold plasma and then irrigated with cold plasma-activated water, which is water that has been treated with cold plasma and has some antimicrobial properties. The plasma interacts with [water molecules](#) to generate highly reactive molecules containing oxygen and nitrogen, which effectively kill bacteria.

The results revealed that rice seeds treated with cold plasma could negatively impact fall armyworms' growth and development.

Researchers also observed signs of improved [plant growth](#) such as more leaf growth. They also saw a faster germination rate in cold plasma-treated plants, though this was not statistically significant. It has been found that cold plasma can increase germination by eroding a seed's surface.

Additionally, though germination rates were quicker, control plants eventually caught up with treated ones in terms of growth, making final germination counts similar between untreated and cold plasma-treated seeds. Researchers point out that this suggests cold plasma applications, though they can benefit initial plant growth, would not be as beneficial in later stages of the plant's growth cycle.

As for the study's impacts on the future, Kariyat and Rahman hope to apply cold plasma to the field of organic food production.

Rahman explained that the U.S. Department of Agriculture is evaluating [cold plasma](#) as an organic technology, potentially paving the way to alternatives for pesticides.

"In the future, if we can optimize this technology for organic production, it will create a very new avenue for organic food growth," Rahman said.

More information: Deepak Dilip et al, Atmospheric cold plasma alters plant traits and negatively affects the growth and development of fall armyworm in rice, *Scientific Reports* (2025). DOI: [10.1038/s41598-025-87560-0](https://doi.org/10.1038/s41598-025-87560-0)

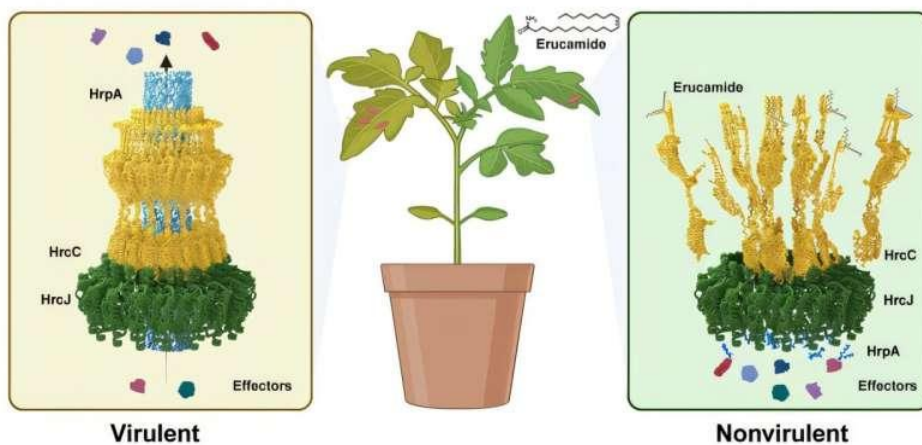
Journal information: [Scientific Reports](#)

Provided by [University of Arkansas](#)

MARCH 3, 2025

Widespread plant metabolite shows potential for combating bacterial diseases in crops

by Zhang Nannan, [Chinese Academy of Sciences](#)



Model for the erucamide-mediated disruption of T3SS injectisome assembly in the bacterial pathogen. Credit: IGDB

Bacterial pathogens, such as those causing rice bacterial blight, tomato bacterial wilt, and kiwifruit bacterial canker, pose significant threats to global agriculture. However, effective pesticides to control these diseases are scarce, with copper-based bactericides and antibiotics offering limited efficacy and posing environmental risks.

Chinese scientists have recently made a breakthrough in this area, however, by showing that a widespread plant defense metabolite may help combat bacterial diseases in crops. The metabolite, erucamide, inhibits the virulence of pathogenic bacteria by specifically targeting the Type III Secretion (T3SS) injectisome assembly—a needle-like molecular machine used by Gram-negative bacteria to inject effector proteins directly into host cells.

The research was led by Prof. Zhou Jianmin's team at the Institute of Genetics and Developmental Biology of the Chinese Academy of Sciences, in collaboration with Prof. Lei Xiaoguang's group at Peking University. The study was [published](#) in *Science* on February 28.

The researchers determined that erucamide, an ancient and broad-spectrum plant defense metabolite, inhibits T3SS activity in various bacterial pathogens. Genetic analysis demonstrated that plants with elevated erucamide levels exhibit enhanced resistance to bacterial pathogens, whereas those with reduced levels show decreased resistance. These results indicate that erucamide plays a crucial role in plant immunity against bacteria.

Through a combination of advanced techniques—including [electron microscopy](#), biochemical assays, protein structure prediction, molecular docking, and [molecular dynamics simulations](#)—the researchers demonstrated that erucamide binds to HrcC, a conserved component of T3SS. This interaction disrupts the assembly of the T3SS injectisome, a structure used by bacteria to inject toxins into host cells.

Remarkably, the binding pocket for erucamide in HrcC is highly conserved across diverse bacterial species, suggesting that this mechanism could have broad-spectrum applicability.

Additionally, the researchers showed that exogenous application of erucamide could protect crops from bacterial diseases, highlighting its potential as a biopesticide for sustainable agriculture.

This study provides important insights into plant immunity and paves the way for developing new, environmentally friendly antibacterial agents, as well as molecular breeding strategies for bacterial disease-resistant crops.

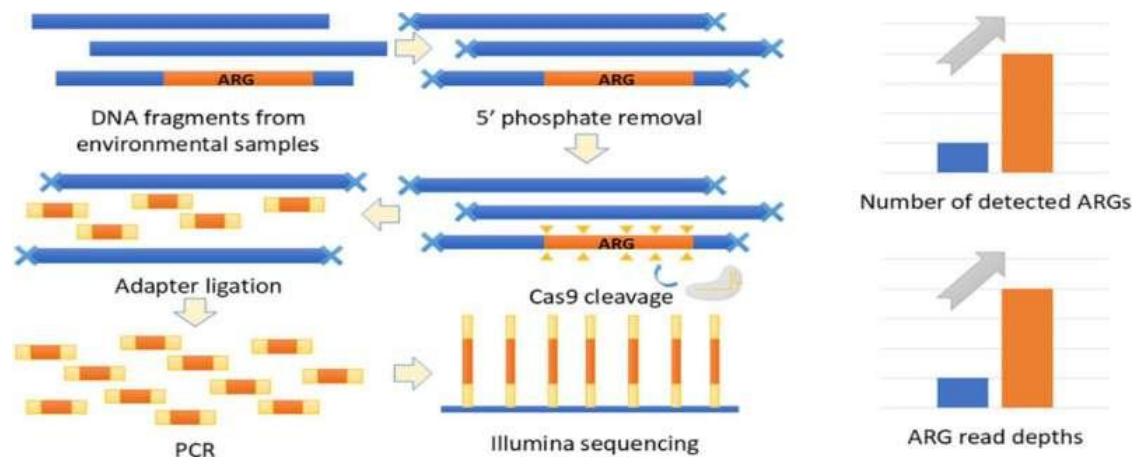
More information: Pei Miao et al, A widespread plant defense compound disarms bacterial type III injectisome assembly, *Science* (2025). DOI: [10.1126/science.ads0377](https://doi.org/10.1126/science.ads0377)

Journal information: [Science](#)

Provided by [Chinese Academy of Sciences](#)

CRISPR-based method enhances detection of antibiotic resistance in wastewater

by Katie Brady, [University of Illinois at Urbana-Champaign](#)



Credit: *Water Research* (2024). DOI: 10.1016/j.watres.2024.123056

Antibiotic resistance is a global concern that threatens our ability to prevent and treat bacterial infections in humans and animals. To better monitor the emergence and spread of resistance, researchers at the Carl R. Woese Institute for Genomic Biology have developed a CRISPR-enriched metagenomics method for the enhanced surveillance of antibiotic resistance genes (ARGs) in wastewater.

The research is [published](#) in the journal *Water Research*.

While antibiotics are powerful modern tools for combating infections, bacteria change and adapt over time in response to antibiotic exposure, therefore decreasing effectiveness. Widespread overuse and misuse of antibiotics in the health care and food industries further accelerate this problem.

Beyond direct exposure to antibiotics, resistance is also passed between different bacteria through the transfer of small pieces of bacterial DNA called [antibiotic resistance](#) genes. There are over 5,000 identified ARGs, and these genes can be found in [clinical samples](#), as well as bodies of water, originating from hospitals, farms, and sewage systems.

"ARGs can reduce the life-saving power of drugs used to treat bacterial infections," said Helen Nguyen (IGOH), a professor of civil and environmental engineering at the University of Illinois Urbana-Champaign. "Wastewater detection of ARGs with clinical significance allows public health authorities and physicians to anticipate what is circulating in communities."

Wastewater contains numerous different ARGs mixed together with genetic material from various sources, including humans, viruses, and bacteria. Because ARGs only make up a tiny percentage of the total DNA content, uncovering them in wastewater samples requires sensitive detection methods. The most common technique is quantitative polymerase chain reaction (qPCR). This method uses RNA guides called primers to identify the specific DNA sequences of known ARGs, which are then amplified for detection.

"qPCR is a sensitive method that many people in public health are well-trained to do, but it requires primary design and validation, which is very time-consuming," said Yuqing Mao, a doctoral student in civil and [environmental engineering](#) who was the first author of the paper. "Since qPCR is used to pull out targeted gene sequences, all the other genetic material in the sample remains completely unknown."

The second method, metagenomics, is not as sensitive as qPCR, but captures a more complete story of the genetic information contained in a sample. Metagenomics involves breaking all the sample DNA into millions of smaller fragments which are simultaneously sequenced using next generation sequencing technologies. Computational algorithms piece together the full DNA sequences for comparison against databases to determine their identities.

"ARGs make up less than 1%—probably even closer to 0.1%—of DNA in the sample. Using standard metagenomics methods, 99.9% of the DNA detected is not associated with ARGs," Mao said.

To enrich the amount of ARG-associated fragments in the samples, Mao, Nguyen, and their collaborator, Joanna Shisler, who is affiliated with the Department of Microbiology at Illinois, leveraged the CRISPR-Cas9 system—a highly effective tool for gene editing.

The DNA is fragmented in random locations when using standard metagenomics methods, but the incorporation of CRISPR-Cas9 allows for targeted fragmentation within ARGs. By designing a pool of 6,010 different guide RNAs that could specifically bind to DNA at different sites found in ARGs, the Cas9 protein could be directed to cut at these locations.

"Our new CRISPR method increases the abundance of ARG fragments in the sample, which increases their chances of being read and detected. CRISPR also has better potential for multiplexed assays than something like PCR because the molecular interaction is simple and straightforward for CRISPR," Mao said.

Their new method lowered the detection limit of ARGs by an order of magnitude, from 10^{-4} to 10^{-5} , compared to standard metagenomics, and found 1,189 more ARGs and 61 more ARG families that are low in abundance in wastewater samples.

As a sixth-year graduate student, Mao built this project from the ground up—overcoming scientific obstacles and learning many new techniques along the way. She said, "The first time I got the sequencing results, I never expected how much more sensitive it would be compared to the regular method—it detected many more ARGs than we thought it would. After finishing the project, I feel like I have grown up."

But while this work is wrapped up, Mao and Nguyen are already pursuing multiple new directions, including expanding the applications of their CRISPR-Cas9 metagenomic method to a broader range of environmental samples and using their results to guide the design of new qPCR primers.

More information: Yuqing Mao et al, Enhanced detection for antibiotic resistance genes in wastewater samples using a CRISPR-enriched metagenomic method, *Water Research* (2024). DOI: [10.1016/j.watres.2024.123056](https://doi.org/10.1016/j.watres.2024.123056)

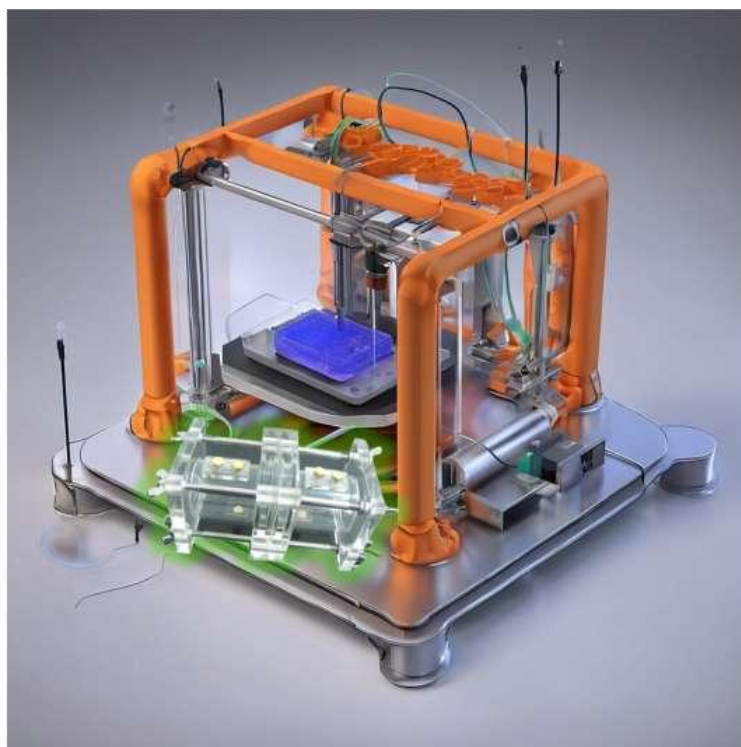
Journal information: [Water Research](#)

Provided by [University of Illinois at Urbana-Champaign](#)

MARCH 3, 2025

3D printing in microbial electrochemistry: A way to power a cleaner environment

by Higher Education Press



Graphical abstract. Credit: Mingyi Xu , Miriam Fernandez-Avila Cobo , Danfei Zeng , Yifeng Zhang

Microbial electrochemical systems (MES) are gaining significant attention for their potential to tackle pressing environmental challenges. By harnessing microorganisms to transfer electrons, MES can simultaneously degrade pollutants and generate electricity, presenting a promising solution for sustainable wastewater treatment and energy production.

However, the traditional methods of constructing MES components often limit their design flexibility, impeding performance optimization. To address these constraints and improve MES efficiency, innovative approaches are necessary—approaches that can precisely tailor the structure and function of reactor components.

Recently, researchers from the Department of Environmental and Resource Engineering at the Technical University of Denmark published an extensive [review](#) in the journal *Frontiers of Environmental Science & Engineering*. The study delves into how 3D printing is revolutionizing MES, with a focus on reactor design, [electrode](#) fabrication, and bioprinting applications. The review provides a thorough analysis of the potential for 3D printing to significantly enhance MES through greater design flexibility and precision.

The review highlights several innovations made possible by 3D printing. One of the most significant advancements is the ability to rapidly prototype and customize reactor designs. This flexibility enables researchers to optimize fluid dynamics and [mass transfer](#) within reactors, resulting in improved system performance.

Moreover, the precision of 3D printing allows for the fabrication of electrodes with tailored geometries and materials—key factors in enhancing electron transfer and biocompatibility. For example, 3D-printed electrodes can be designed with specific surface properties and porosity to maximize microbial adhesion and facilitate efficient electron exchange.

Additionally, the integration of bioprinting techniques enables the construction of stable biofilms on electrodes. By meticulously controlling the architecture and composition of these biofilms, researchers can optimize interactions between microbes and electrodes, further boosting MES efficiency. These breakthroughs address existing design limitations and unlock new possibilities for sustainable applications in wastewater treatment and bioenergy production.

Dr. Yifeng Zhang, the study's senior author, said, "The integration of 3D [printing technology](#) into MES represents a major breakthrough. It provides the precision and flexibility needed to optimize [reactor](#) designs and electrode structures, which are critical for enhancing system performance.

"This innovation not only accelerates the development of sustainable environmental technologies but also opens up new avenues for addressing global challenges in energy and waste management. The potential applications are vast, and we are excited to see how this technology will continue to evolve and impact the field."

The application of 3D printing in MES promises far-reaching implications for multiple sectors, including environmental management and renewable energy. In wastewater treatment, optimized MES reactors could lead to more efficient pollutant degradation, mitigating the environmental impact of industrial and municipal waste.

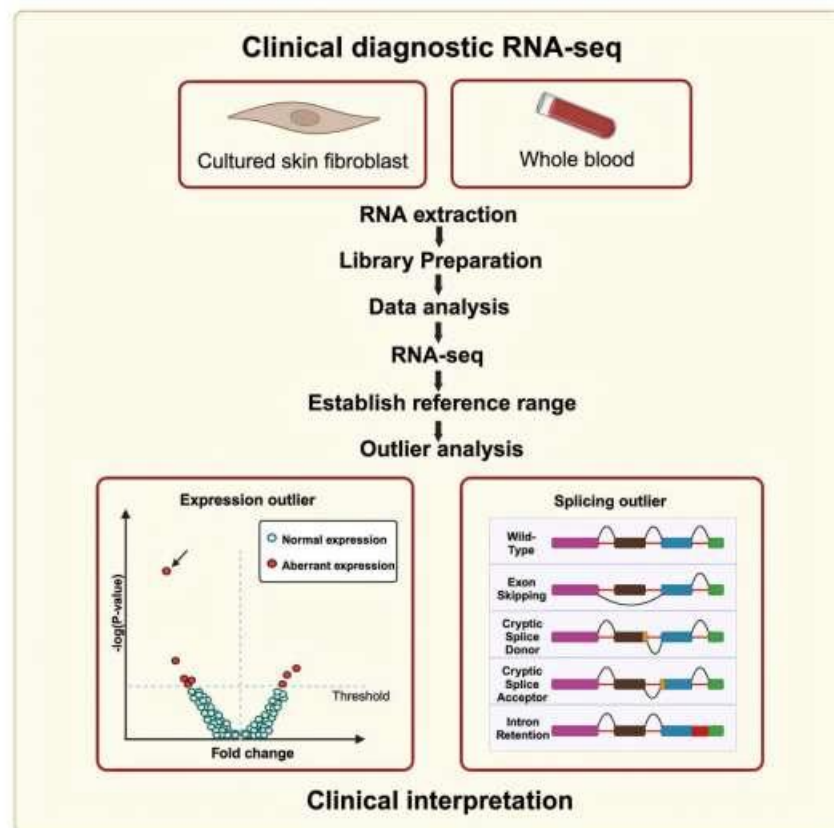
For energy generation, advanced electrode designs could boost the power output of microbial fuel cells, positioning them as a viable alternative for sustainable [energy production](#). Moreover, the scalability and customization of 3D printing allow for tailored MES solutions across a wide range of applications, from small-scale settings to large industrial operations. This technology holds the potential to contribute to a more sustainable future by enhancing resource utilization and reducing carbon footprints.

More information: Mingyi Xu et al, Leveraging 3D printing in microbial electrochemistry research: current progress and future opportunities, *Frontiers of Environmental Science & Engineering* (2024). DOI: [10.1007/s11783-025-1921-y](https://doi.org/10.1007/s11783-025-1921-y)
Provided by Higher Education Press

MARCH 4, 2025

First clinical RNA sequencing test promises enhanced genetic diagnostics

by Molly Chiu, [Baylor College of Medicine](#)



Credit: *The American Journal of Human Genetics* (2025). DOI: 10.1016/j.ajhg.2025.02.006
RNA sequencing has emerged as a powerful supplement to DNA sequencing for Mendelian disease diagnosis, but clinical translation of diagnostic RNA-seq has not been widely achieved. Researchers at Baylor College of Medicine's Medical Genetics and Multiomics Laboratory have published the clinical validation of the first RNA sequencing test for diagnostic whole-transcriptome analysis for genetic disorders.

The findings, which [appear](#) in *The American Journal of Human Genetics*, establish a comprehensive transcriptome sequencing pipeline for clinical use, expanding the role of RNA sequencing beyond targeted analysis.

"This validation represents the first attempt to unleash the full transcriptome potential of RNA sequencing for [clinical diagnostics](#)," said corresponding author Dr. Pengfei Liu,

associate professor of molecular and [human genetics](#) and director of the Medical Genetics and Multiomics Laboratory (MGML) at Baylor. "While RNA sequencing has been used in clinical testing, it has been restricted to targeted gene analysis. In fact, when we applied for accreditation from the CAP (College of American Pathologists), we worked with them to create the first whole-transcriptome sequencing activity as a reportable assay."

The RNA-seq test uses samples from fibroblasts or blood and analyzes for outliers in [gene expression](#) and splicing patterns. Researchers validated the test using 130 samples, including 40 samples with a positive molecular diagnosis and 90 negative samples from apparently healthy people for control. They developed benchmarks for expression and splicing using RNA-seq data from a lymphoblastoid sample in the publicly available Genome in a Bottle Consortium. The team established reference ranges for each gene based on control data.

To assess clinical performance, the team evaluated the test using samples with previously identified diagnostic findings from the Undiagnosed Diseases Network (UDN). The study confirmed the assay's ability to detect diagnostic RNA findings through both transcriptome-driven and DNA-driven analysis modes, demonstrating its potential to enhance molecular diagnosis.

This test is the first launched by the MGML and is now being offered for clinical RNA sequencing in the UDN.

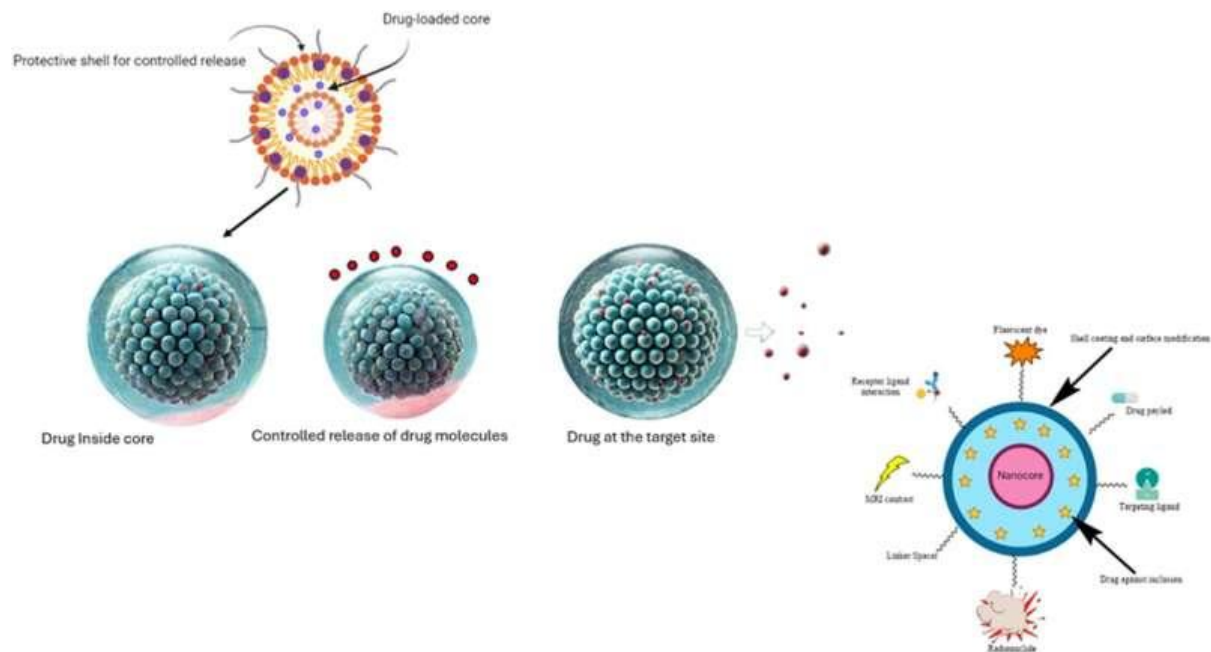
More information: Sen Zhao et al, Clinical validation of RNA sequencing for Mendelian disorder diagnostics, *The American Journal of Human Genetics* (2025). DOI: [10.1016/j.ajhg.2025.02.006](https://doi.org/10.1016/j.ajhg.2025.02.006)

Journal information: [American Journal of Human Genetics](#)
Provided by [Baylor College of Medicine](#)

MARCH 5, 2025

Innovations in core-shell nanoparticles advance drug delivery and precision medicine

by [Mary Ann Liebert, Inc](#)



Core-shell NP mechanism for drug delivery. NP, nanoparticle. Credit: *OMICS: A Journal of Integrative Biology* (2025). DOI: 10.1089/omi.2024.0182

A review in *OMICS: A Journal of Integrative Biology* [explores](#) how core-shell nanoparticles could revolutionize drug delivery systems and play a key role in advancing personalized and precision medicine.

Suren A. Ramadhan, from Knowledge University in Erbil, Iraq, and Diyar S. Ali, from Knowledge University and Salahaddin University-Erbil, describe the benefits of core-shell nanoparticles, which provide effective drug encapsulation, shielding the drug from degradation and allowing for controlled release.

"By enabling targeted drug release, this controlled mechanism can help improve treatment outcomes and reduce side effects," stated the authors.

Various materials, including polymers, lipids, and inorganic substances, can be used to create these nanoparticles, and these materials can be tailored for better drug loading, compatibility with the host organism, and specific chemical properties to suit different therapeutic needs.

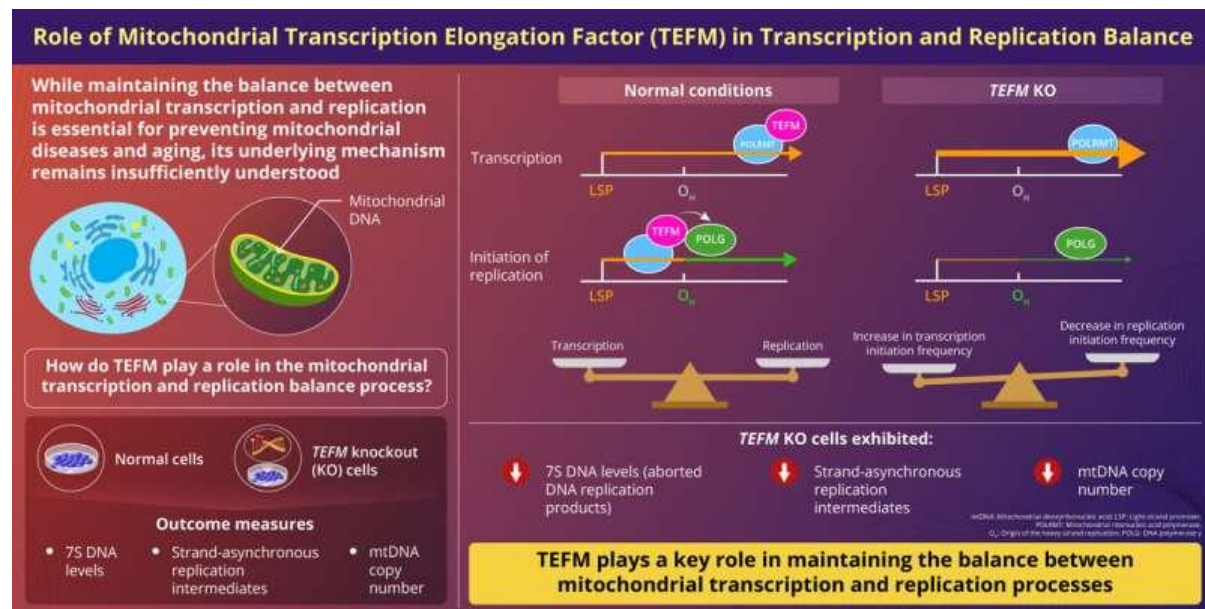
"This innovation analysis highlights the emerging convergence of nanotechnology with precision/[personalized medicine](#) by unpacking the advances in drug delivery being enabled by core-shell nanoparticles," says Vural Özdemir, MD, MSc, Ph.D., DABCP, MA, Editor-in-Chief of *OMICS*.

More information: Suren A. Ramadhan et al, Innovations in Core–Shell Nanoparticles: Advancing Drug Delivery Solutions and Precision Medicine, *OMICS: A Journal of Integrative Biology* (2025). DOI: [10.1089/omi.2024.0182](https://doi.org/10.1089/omi.2024.0182)
 Provided by [Mary Ann Liebert, Inc](#)

MARCH 5, 2025

Mitochondria research reveals mechanism that maintains balance between transcription and replication processes

by Juntendo University



Mitochondrial transcription elongation factor maintains the balance between transcription and replication of mitochondrial DNA offering insights into potential treatments for

mitochondrial disease and aging. Credit: Dr. Takehiro Yasukawa / Juntendo University, Japan

Mitochondrial deoxyribonucleic acid (mtDNA) is essential for cellular energy production and overall cell function. Abnormalities in mtDNA are linked to various diseases and are also implicated in aging.

Understanding the process of replication and transcription of mtDNA is crucial for improving our knowledge of human health, disease, and aging. However, the mechanisms that regulate the balance between transcription and replication of mtDNA remain unclear.

To unveil the mechanisms, a team of researchers led by Takehiro Yasukawa, an Associate Professor from the Department of Molecular Pathogenesis, Graduate School of Medicine, Juntendo University, Japan, along with Dongchon Kang, an Emeritus Professor of Kyushu University, Japan, and Shigeru Matsuda, an Assistant Professor from Tohoku University, Japan, investigated the role of mitochondrial transcription elongation factor (TEFM) by utilizing genome editing techniques in cultured human cells.

Their study is published in the journal *Communications Biology*.

"While mtDNA is much smaller than nuclear DNA, it plays a crucial role in life forms through energy production. During my graduate studies, I investigated mitochondrial transfer ribonucleic acids (RNAs) with disease-related mutations, which further intrigued me to explore the mechanism of mtDNA replication and maintenance in real depth," says Dr. Yasukawa.

Using cultured human cells with genome-edited TEFM knockout, the team studied the effects of deletion of TEFM on mtDNA replication. By knocking out TEFM, they observed a notable reduction in mtDNA copy number, alongside a decrease in 7S DNA levels and strand-asynchronous replication intermediates.

These findings suggest that TEFM is crucial for the proper regulation of mtDNA replication, particularly at the origin of replication of the heavy strand.

In addition, the deletion of TEFM resulted in an increase in transcription initiation from the light-strand promoter, as suggested by higher levels of mitochondrial tRNA^{Pro}, but replication intermediates were still significantly reduced.

This suggests that the absence of TEFM disrupts the proper balance between the replication and transcription processes, which has consequences on mtDNA maintenance and expression. Another significant finding of this study was the interaction between TEFM and the DNA polymerase γ (POLG), an essential enzyme involved in mtDNA replication.

Despite the significant progress made in understanding the role of TEFM in mtDNA replication, further research is needed to fully unravel the detailed mechanisms behind its action. Future studies are required to identify the exact locations of TEFM and POLG interaction on mtDNA and how they influence the entire replication process.

"Our study addresses one of the fundamental questions of gene expression regulation in mitochondria. In addition, it deepens our understanding of the role of TEFM in maintaining the balance between [transcription](#) and [replication](#) of mtDNA, potentially paving the way for the development of treatment strategies for diseases that result from abnormalities in mtDNA," concludes Dr. Yasukawa.

More information: Shigeru Matsuda et al, TEFM facilitates transition from RNA synthesis to DNA synthesis at H-strand replication origin of mtDNA, *Communications Biology* (2025). DOI: [10.1038/s42003-025-07645-4](https://doi.org/10.1038/s42003-025-07645-4)

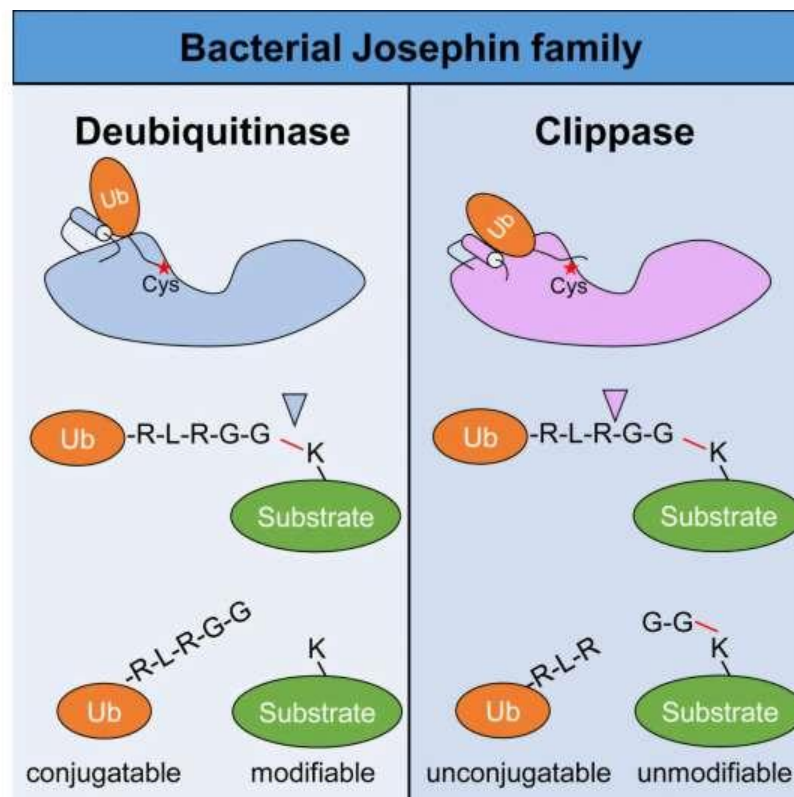
Journal information: [Communications Biology](#)

Provided by Juntendo University

MARCH 5, 2025

Enzyme trick allows bacteria to embed themselves permanently in host cells

by Gabriele Meseg-Rutzen, [University of Cologne](#)



Credit: *Molecular Cell* (2025). DOI: [10.1016/j.molcel.2025.02.002](https://doi.org/10.1016/j.molcel.2025.02.002)

Working in collaboration with colleagues at the University of Leiden in the Netherlands, scientists at the University of Cologne's Institute for Genetics have discovered a strategy in bacteria by which they embed themselves permanently in host cells.

The researchers have established that specific intracellular types of living bacteria possess special enzymes which allow them to permanently remove what is referred to as [ubiquitin](#) marking. This marking represents a key stage in defense against bacteria. In this process, bacteria are labeled as foreign bodies within cells, thereby signaling their destruction by the cellular recycling system.

The study, titled "A family of bacterial Josephin-like deubiquitinases with an irreversible cleavage mode," conducted by the Cologne research team led by Professor Kay Hofmann, has been [published](#) in the journal *Molecular Cell*.

These [bacterial enzymes](#), referred to as ubiquitin clippases, split the ubiquitin molecule into two parts in such a way that the released fragment is too short to be used again. At the same time, a small fragment remains on the bacterial substrate and thus blocks renewed ubiquitination. This trick allows the bacteria to make themselves at home in the [host cell](#) and avoid falling prey to the immune system.

Working together with the University of Cologne structural biologists led by Professor Ulrich Baumann, the team was able to identify the molecular structures of several bacterial clippases along with a closely related deubiquitinase without clippase properties. The direct comparison of these structures reveals how, in the course of evolution, the cleavage position has been shifted, thus causing the change in activity.

This discovery not only provides insights into the evolutionary arms race but also has practical applications for research into the human ubiquitin system. Thus, the treatment of cell or [tissue samples](#) with clippases allows us to identify which proteins were originally modified with ubiquitin.

More information: Thomas Hermanns et al, A family of bacterial Josephin-like deubiquitinases with an irreversible cleavage mode, *Molecular Cell* (2025). DOI: [10.1016/j.molcel.2025.02.002](https://doi.org/10.1016/j.molcel.2025.02.002)

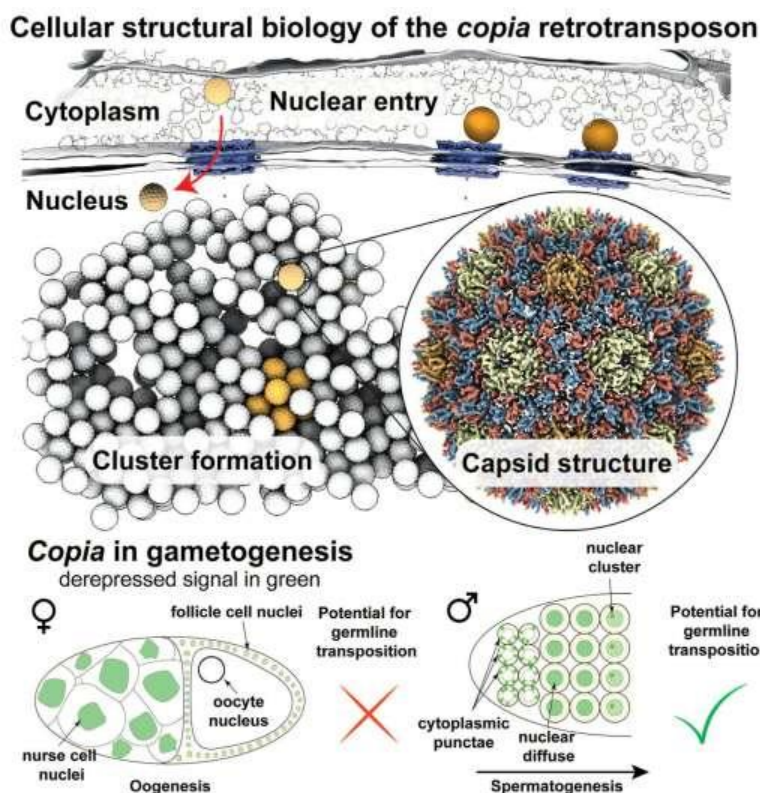
Journal information: [Molecular Cell](#)

Provided by [University of Cologne](#)

MARCH 5, 2025

'Jumping gene' caught in the act: Advanced imaging provides new insights into retrotransposons

by Manel Llado, Institut für Molekulare Biotechnologie der Österreichischen Akademie der Wissenschaften GmbH



Credit: *Cell* (2025). DOI: 10.1016/j.cell.2025.02.003

An arms race is unfolding in our cells: Transposons, also known as jumping genes or mobile genetic elements as they can replicate and reinsert themselves in the genome, threaten the cell's genome integrity by triggering DNA rearrangements and causing mutations. Host cells, in turn, protect their genome using intricate defense mechanisms that stop transposons from jumping.

Now, for the first time, a retrotransposon has been caught in action inside a cell: Refining cryo-Electron Tomography (cryo-ET) techniques, scientists imaged the retrotransposon *copia* in the egg chambers of the fruitfly *Drosophila melanogaster* at sub-nanometer resolution. The paper is [published](#) in the journal *Cell*.

Among the international team of scientists achieving this detailed visualization are three scientists with Vienna BioCenter ties: Sven Klumpe, currently in the laboratory of Jürgen

Plitzko at the Max Planck Institute of Biochemistry in Martinsried, will join IMBA and IMP to build a group as a Joint Fellow; Julius Brennecke, a Senior Group Leader at IMBA, the Institute of Molecular Biotechnology of the Austrian Academy of Sciences; and Kirsten Senti, staff scientist in the Brennecke group. Also involved in this collaboration is the group of Martin Beck at the Max Planck Institute of Biophysics in Frankfurt.

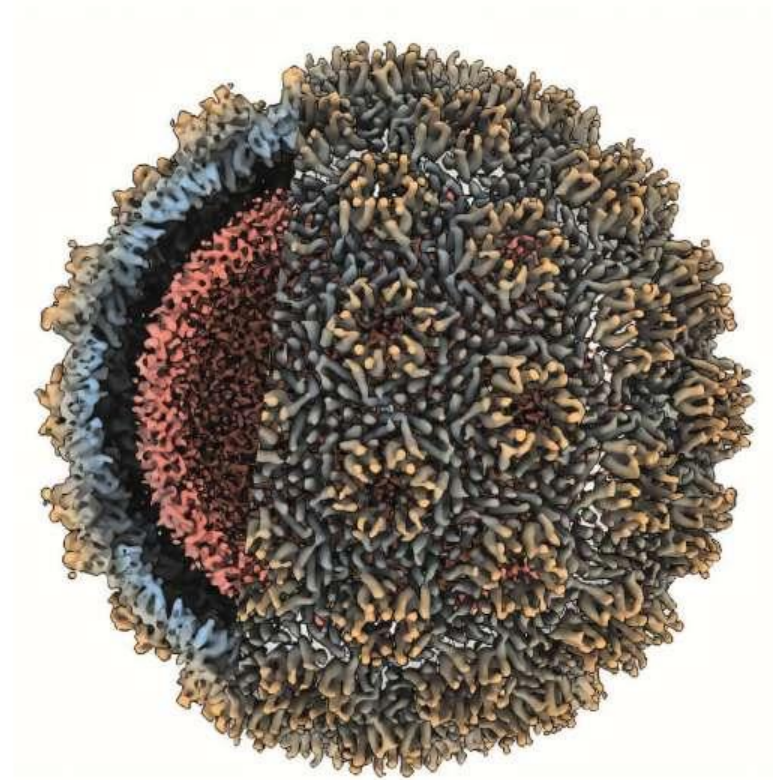
Cryo-Electron Tomography is an imaging technique used to visualize cellular landscapes in three dimensions at molecular resolution. In cryo-ET, a series of 2D images is captured from various angles of the sample, and then combined to form a detailed 3D reconstruction. Cryo-ET has given researchers unprecedented insights into the ultrastructure of cells.

So far, however, cryo-ET has mostly been used to image unicellular organisms, as cryo-ET samples must be rapidly frozen in a process known as "vitrification" to prevent ice crystal formation. Multicellular tissues, which require high-pressure freezing for vitrification, are typically too thick to be prepared for cryo-ET imaging using standard methods.

Capsid resembles retroviral capsids

In the new study, the researchers employed cryo-lift-out, a technique that allows researchers to prepare complex tissues for cryo-ET by combining focused ion beams and advanced micromanipulation techniques at cryogenic temperatures. Working with egg chambers of *Drosophila melanogaster* and cells isolated from them, the researchers resolved the structure of the retrotransposon copia's capsid to 7.7 Å resolution—the first structure of a retrotransposon at sub-nanometer resolution in its native cellular environment.

Employing recent advances in AI-based structure prediction, the team generated an integrative model of capsid assembly using AlphaFold 2, allowing the researchers to subsequently design structure-guided experiments. Through this, they were able to show that the copia retrotransposon adopts a capsid fold similar to the mature capsid of HIV-1, confirming previous observations of transposable element structures from purified samples.



Capsid structure of the copia retrotransposon. Credit: Sven Klumpe

Insights into the retroviral lifecycle

Klumpe and colleagues also provided snapshots of copia's replication cycle within intact egg chambers. Similar to retroviruses, retrotransposons are transcribed from the genome, the transcript is exported and translated in the cytoplasm, where virus-like particles form. Finally, their RNA genome is reverse transcribed. However, a major problem in retrotransposon research revolves around the question of how a retrotransposon gets back into the nucleus, where a new copy of the retrotransposon integrates into the host genome.

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Looking at copia capsids inside the cell, the researchers discovered that viral particles in the cytoplasm are within reach of nuclear pores, which connect the cytoplasm and the nucleus. Similar to the evolutionarily related HIV-1, copia likely enters the nucleus as intact particles by traveling through nuclear pores.

Here, the nuclear pore complex appears to act like a molecular sieve: only viral particles of a certain size are observed in, and therefore enter, the nucleus. Furthermore, [genetic manipulation](#), which disturbed the active transport through nuclear pores, led to the copia particles being retained in the cytoplasm.

Although many retrotransposons are found in the *Drosophila* genome, copia is by far the most frequently expressed one. Previous research has shown that copia predominantly targets the male germ line. In the new study, the researchers also explored how *Drosophila*'s transposon repression system, the PIWI-piRNA pathway, silences copia.

In the fruitfly testes, anti-sense piRNAs targeting copia turned out to be highly abundant. Looking at fruitflies in which the piRNA pathway is inactive and transposons are therefore freely expressed, the scientists found copia in female flies in a seemingly dead end, namely the abundant germ line nuclei that will not become the oocyte's genetic material and, thus, are destined to undergo programmed cell death.

In male flies, however, copia retrotransposons move from the cytoplasm to the gamete nucleus during spermatogenesis, indicating that nuclear entry could be an essential part of its replication cycle tailored to the element's niche—the male testes.

"Transposons were long overlooked as junk DNA but have a broad impact on their host's biology and evolution. Our study demonstrates the power of cryo-ET for studying the cellular structural biology of transposons and obtaining detailed insights into the cell biological mechanisms underlying their replication cycles," Klumpe says.

More information: In-cell structure and snapshots of copia retrotransposons in intact tissue by cryo-electron tomography, *Cell* (2025). DOI:

[10.1016/j.cell.2025.02.003](https://doi.org/10.1016/j.cell.2025.02.003). [www.cell.com/cell/fulltext/S0092-8674\(25\)00159-X](https://www.cell.com/cell/fulltext/S0092-8674(25)00159-X)

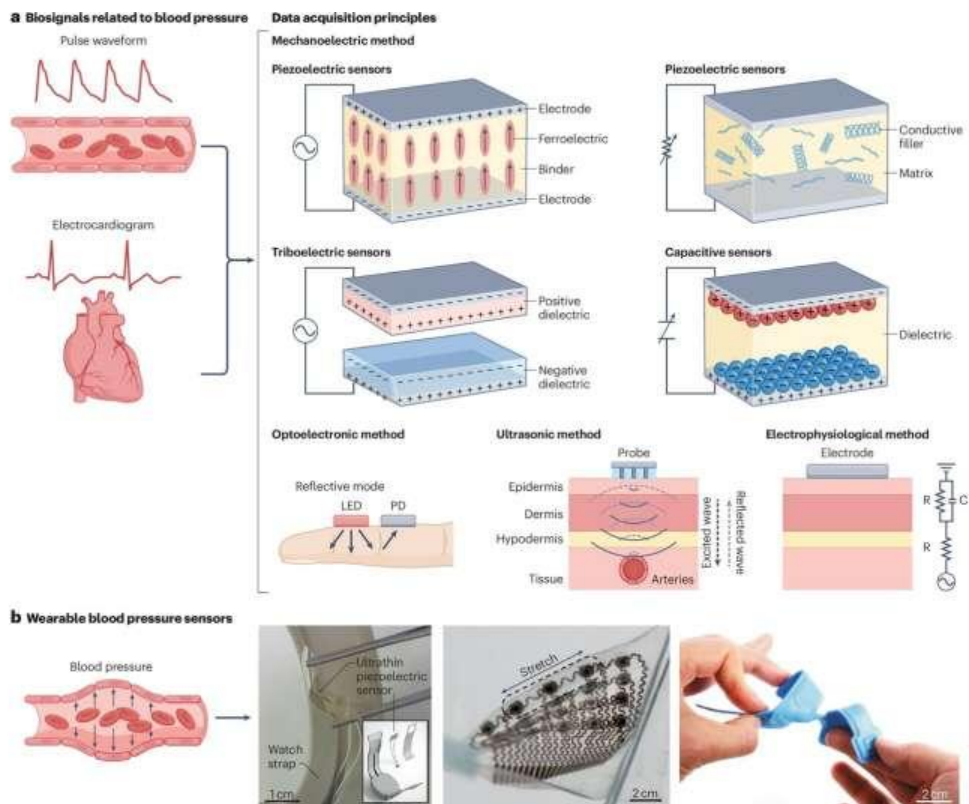
Journal information: *Cell*

Provided by Institut für Molekulare Biotechnologie der Österreichischen Akademie der Wissenschaften GmbH

MARCH 5, 2025

AI-driven wearable blood pressure sensors promise continuous health monitoring

by The Korea Advanced Institute of Science and Technology (KAIST)



Wearable BP sensors for cardiovascular health care. Credit: *Nature Reviews Cardiology* (2025). DOI: 10.1038/s41569-025-01127-0

A KAIST research team led by Professor Keon Jae Lee has proposed an innovative theoretical framework and research strategies for AI-based wearable blood pressure sensors, paving the way for continuous and non-invasive cardiovascular monitoring.

Hypertension is a leading chronic disease affecting more than 1 billion people worldwide and is a major risk factor for severe cardiovascular conditions such as [myocardial infarction](#), stroke, and [heart failure](#). Traditional blood pressure measurement relies on intermittent, cuff-based methods, which fail to capture real-time fluctuations and present challenges in continuous patient monitoring.

Wearable blood pressure sensors offer a non-invasive solution for continuous blood pressure monitoring, enabling real-time tracking and personalized cardiovascular health management. However, current technologies lack the accuracy and reliability required for [medical applications](#), limiting their practical use. To address these challenges,

advancements in high-sensitivity sensor technology and AI signal processing algorithms are essential.

Building on their [previous study](#) in *Advanced Materials*, which validated the clinical feasibility of flexible piezoelectric blood pressure sensors, Professor Lee's team conducted an in-depth review of the latest advancements in cuffless wearable sensors, focusing on key technical and clinical challenges. Their review highlights clinical aspects of clinical implementation, real-time data transmission, signal quality degradation, and AI algorithm accuracy.

The review, titled "Wearable blood pressure sensors for cardiovascular monitoring and machine learning algorithms for blood pressure estimation," was [published](#) in the February 18 issue of *Nature Reviews Cardiology*.

Professor Keon Jae Lee said, "This paper systematically demonstrates the feasibility of medical-grade wearable blood pressure sensors, overcoming what was previously considered an insurmountable challenge. We propose theoretical strategies to address technical barriers, opening new possibilities for future innovations in this field. With continued advancements, we expect these sensors to gain trust and be commercialized soon, significantly improving quality of life."

More information: Seongwook Min et al, Wearable blood pressure sensors for cardiovascular monitoring and machine learning algorithms for blood pressure estimation, *Nature Reviews Cardiology* (2025). DOI: [10.1038/s41569-025-01127-0](https://doi.org/10.1038/s41569-025-01127-0)

Journal information: [Advanced Materials](#)

Provided by [The Korea Advanced Institute of Science and Technology \(KAIST\)](#)

MARCH 7, 2025

A federated future to support genomic medicine

by Vicky Hatch, [European Molecular Biology Laboratory](#)



FEGA nodes. Credit: Karen Arnott/EMBL-EBI

The [Federated European Genome-phenome Archive \(FEGA\)](#) is transforming how sensitive human genomic data is shared and accessed. Building on the longstanding [European Genome-phenome Archive \(EGA\)](#)—a database for human genetic, phenotypic, and clinical data—FEGA enables researchers to securely discover and analyze human genomic data while ensuring compliance with national and international data protection regulations.

By decentralizing data storage across national nodes, FEGA ensures data remains secure within its country of origin while also being accessible to researchers worldwide.

[FEGA's paper](#) has been published in *Nature Genetics*.

From centralization to federation

In the last two decades, as the volume of human genomic datasets grew larger and [legal requirements](#) to access the data were tightened, it became clear that a single repository like the EGA could no longer meet the global community's needs. The EGA team proposed adopting a federated model, in line with local legal and ethical frameworks, while also allowing access to these data globally.

What is a federated model?

A federated model is a distributed network in which multiple entities operate under a common framework. Each node or entity retains control over its own data and processes, while agreed-upon standards and protocols allow them to collaborate and share data globally. This approach enables secure and coordinated data sharing across different countries, ensuring that local legal and ethical requirements are met.

EMBL-EBI and the Center for Genomic Regulation (CRG) in Spain have co-managed the EGA since 2008. Together, they helped shape the federated data-sharing model now used by FEAGA.

Two major projects also helped make FEAGA's federated model possible. The [ELIXIR-EXCELERATE](#) initiative—a program supporting international data sharing—helped lay the early groundwork with proof-of-concept studies. [ELIXIR-CONVERGE](#)— a project to standardize data management across Europe—has accelerated the development of the first national FEAGA nodes.

"In the early days of setting up FEAGA, we were grappling with the limitations of a centralized system. It felt like we were facing enormous challenges," said Mallory Freeberg, Human Genomics Team Leader at EMBL-EBI.

"Through collaboration, we overcame those obstacles to build the foundations of FEAGA. I'm immensely proud to have been part of this endeavor. It's an exciting time for this network, and there is so much more to achieve as we continue pushing the boundaries."

By 2020, the foundation for FEAGA's federated model was set, leading to the official launch of the resource in September 2022. The first collaboration agreements were signed by nodes in Sweden, Norway, Finland, Germany, and Spain.

Impact through global collaboration

"Global health challenges like pandemics and [rare diseases](#) do not respect national borders," said Arcadi Navarro, ICREA Research Professor at the Universitat Pompeu Fabra and Director of the EGA team at the Center for Genomic Regulation.

"By expanding beyond Europe and adding the Canadian node, we consolidate the Federated EGA as the world's most comprehensive, secure, and diverse resource for genomic and health data to tackle these urgent questions."

The [first datasets were submitted to FEGA](#) by late 2023, proving the federated model in practice. These data have since continued to grow, with FEGA now holding nearly 40 datasets.

The network has also expanded with nodes in Portugal and Poland joining in 2023, and Canada in December 2024. Discussions are also ongoing with many other collaborators, including a Swiss node who are currently 'Observers' of FEGA.

"This milestone partnership provides Canadian researchers with a swift, [secure connection](#) to global collaborators, fostering scientific and clinical innovation while continuing to uphold our commitment to privacy and compliance," said Steven Jones, lead for the CGA node and Co-Director of Canada's Michael Smith Center for Genome Sciences at BC Cancer.

FEGA aims to support global research in disease diagnosis and personalized treatment. The following are a few examples.

- FEGA data from the [Swedish Childhood Tumor Biobank](#) will help drive pediatric cancer studies.
- [Circulating small RNA sequencing data](#) have been made available from the node in Norway; these can be used to identify biomarkers for endometrial cancer.
- The [first dataset shared from Poland](#) is being used by researchers at the University of Vilnius to investigate the genetic basis of overgrowth syndrome, a rare genetic disorder that causes excessive growth in children.

A federated future

Looking ahead, FEGA will also continue to refine its metadata standards, including those developed as part of the Global Alliance for Genomics and Health (GA4GH), to increase data discoverability and interoperability. This will support future integration of multi-omics datasets, as well as clinical health records for a more complete picture of disease biology.

Efforts to support more data submissions are also underway, including the development of training materials and the establishment of FEGA node-specific help desks to assist local users. Federated analytics are also in the works, which will enable secure, multi-node analyses without the need to download sensitive data.

As FEGA evolves, it sets a high standard for global human genomics data sharing. By integrating multi-omics and [clinical data](#), FEGA will support research towards improved personalized medicine and help inform public health strategies to ultimately improve patient outcomes.

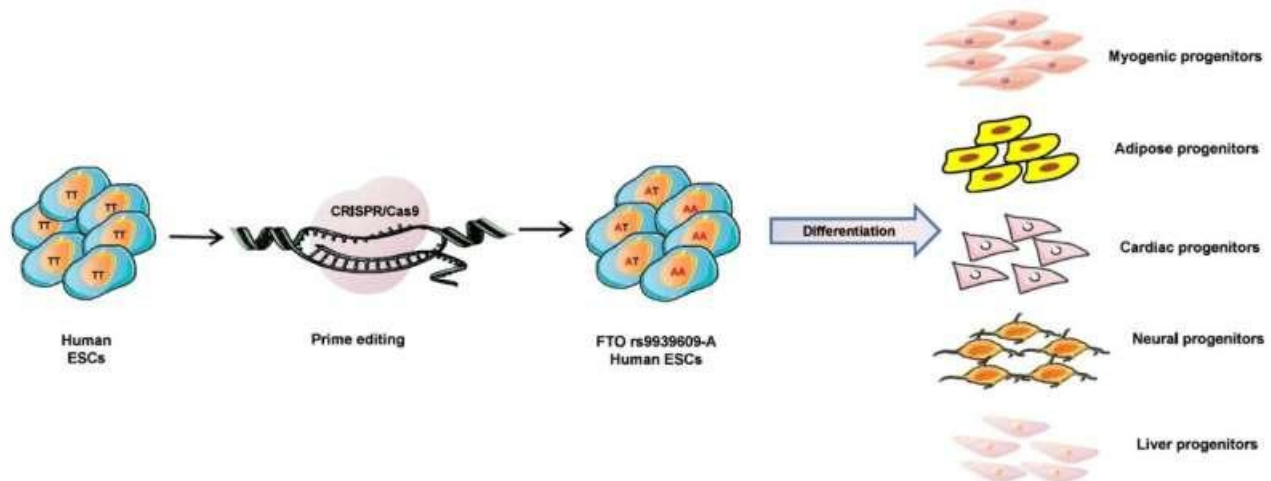
More information: Teresa D'Altri et al, The Federated European Genome–Phenome Archive as a global network for sharing human genomics data, *Nature Genetics* (2025). DOI: [10.1038/s41588-025-02101-9](https://doi.org/10.1038/s41588-025-02101-9)

Journal information: [Nature Genetics](#)

MARCH 7, 2025

Genome-edited stem cells reveal new hope for obesity treatment without muscle loss

by Beijing Institute of Stem Cells and Regeneration



A schematic diagram illustrating our workflow utilizing CRISPR/Cas9-based prime editing of hESCs to study the effects of a specific FTO SNP on cellular differentiation. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-024-53820-2

In a study [published](#) in *Nature Communications*, researchers at the Beijing Institute of Stem Cells and Regeneration (BISCRM) and the Institute of Zoology (IOZ) have cracked the code of the notorious FTO gene, reconciling its dual role in obesity and muscle growth. The revelation could improve obesity and diabetes treatments, potentially offering an alternative to popular GLP-1 receptor agonists that may cause undesirable muscle wasting.

"We've solved a long-standing puzzle in obesity genetics," declares Dr. Ng Shyh-Chang, the study's lead author. "We now understand how a single genetic variant can be Jekyll and Hyde—accelerating muscle growth in youth but also accelerating aging-related decay later in life."

The study zeroes in on the FTO gene variant rs9939609-A, a common genetic quirk linked to increased obesity risk in ~45% of Europeans, ~24% of Africans, ~30% of East Asians, and ~35% of South Asians. This A variant, the researchers discovered, sets off a cellular chain reaction involving H19 and IGF2 genes to accelerate development, initially boosting muscle growth but eventually exhausting the stem cells, leading to premature aging.

In a startling twist, the team found that stem cells carrying this variant rapidly turned into skeletal muscles, but also rapidly developed [insulin resistance](#) when exposed to high-fat conditions. This suggests that [skeletal muscle](#) could be the first domino to fall in the FTO variant's influence on accelerated development and aging.

"This study rewrites our understanding of how type 2 diabetes develops," Dr. Ng Shyh-Chang explains.

"We've known that reduced glucose clearance and high insulin levels appear decades before diagnosis of type 2 diabetes. Now using CRISPR genome editing, we have a new human tissue avatar that explains how it all starts in the muscles for humans with rs9939609-A."

This paradigm-shifting research not only deepens our grasp of obesity genetics but also provides a platform to screen for better CRISPR-based drugs or small molecules for the millions grappling with overweight issues and muscle wasting from current treatments.

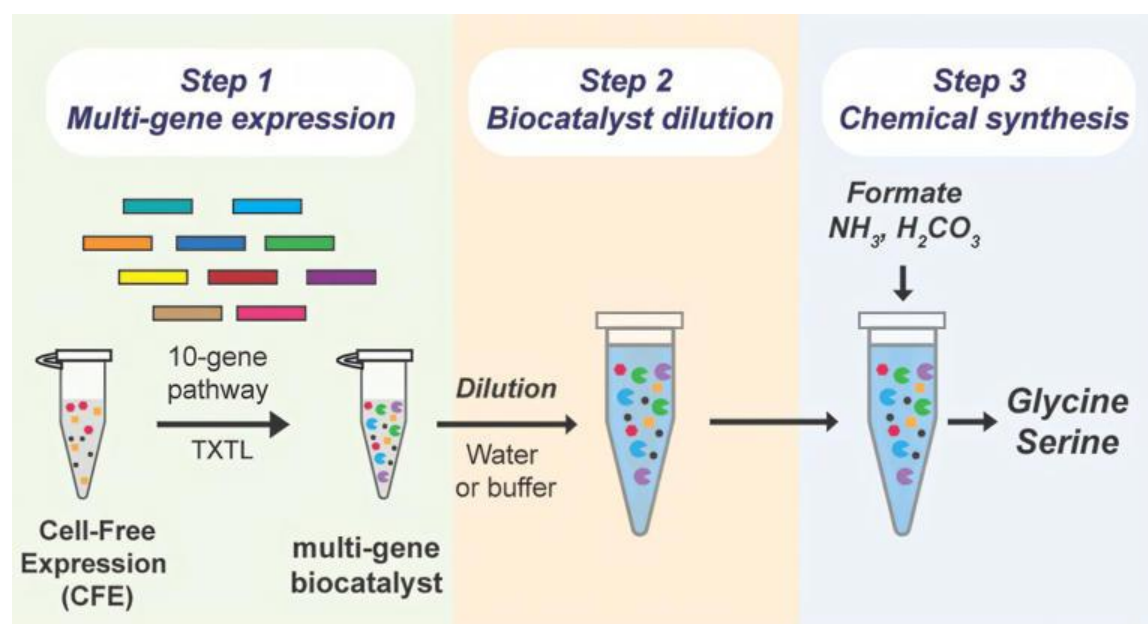
As the race for better [obesity](#) therapies intensifies, this breakthrough could be the key to unlocking new therapeutic strategies that finely control FTO to trim fat while boosting [muscle growth](#).

More information: Lu Guang et al, An obesogenic FTO allele causes accelerated development, growth and insulin resistance in human skeletal muscle cells, *Nature Communications* (2025). DOI: [10.1038/s41467-024-53820-2](https://doi.org/10.1038/s41467-024-53820-2)

Journal information: [Nature Communications](#)

Provided by Beijing Institute of Stem Cells and Regeneration

A new carbon-negative method to produce essential amino acids



Credit: ACS Synthetic Biology (2024). DOI: 10.1021/acssynbio.4c00359

Amino acids are essential for nearly every process in the human body. Often referred to as "the building blocks of life," they are also critical for commercial use in products ranging from pharmaceuticals and dietary supplements, to cosmetics, animal feed, and industrial chemicals.

Costly chemicals

There are two key challenges to synthesizing amino acids on a large scale: the cost of materials, and the speed at which the system can generate amino acids.

While many living systems like cyanobacteria can synthesize amino acids from CO_2 , the rate at which they do it is too slow to be harnessed for industrial applications, and these systems can only synthesize a limited number of chemicals.

2 into critical amino acids, like glycine and serine."

The team was particularly interested in what could be accomplished by a "cell-free" system that leveraged some process of a cellular system—but didn't actually involve living cells, Peralta-Yahya says, adding that systems using living cells need to use part of their CO₂ to fuel their own metabolic processes, including cell growth, and have not yet produced sufficient quantities of amino acids.

"Part of what makes a cell-free system so efficient," Westenberg explains, "is that it can use cellular enzymes without needing the cells themselves. By generating the enzymes and combining them in the lab, the system can directly convert carbon dioxide into the desired chemicals.

"Because there are no cells involved, it doesn't need to use the carbon to support cell growth—which vastly increases the amount of amino acids the system can produce."

A novel solution

While scientists have used cell-free systems before, one of the necessary chemicals, the cell lysate biocatalyst, is extremely costly. For a cell-free system to be economically viable at scale, the team needed to limit the amount of cell lysate the system needed.

After creating the 10 enzymes necessary for the reaction, the team attempted to dilute the biocatalyst using a technique called "volumetric expansion."

"We found that the biocatalyst we used was active even after being diluted 200-fold," Peralta-Yahya explains. "This allows us to use significantly less of this high-cost material—while simultaneously increasing feedstock loading and amino acid output."

It's a novel application of a cell-free system, and one with the potential to transform both how amino acids are produced, and the industry's impact on our changing climate.

"This research provides a pathway for making this method cost-effective and scalable," Peralta-Yahya says. "This system might one day be used to make chemicals ranging from aromatics and terpenes, to alcohols and polymers, and all in a way that not only reduces our carbon footprint, but improves it."

"Part of what makes a cell-free system so efficient," Westenberg says, "is that it can use cellular enzymes without needing the cells themselves. By generating the enzymes and combining them in the lab, the system can directly convert carbon dioxide into the desired chemicals."

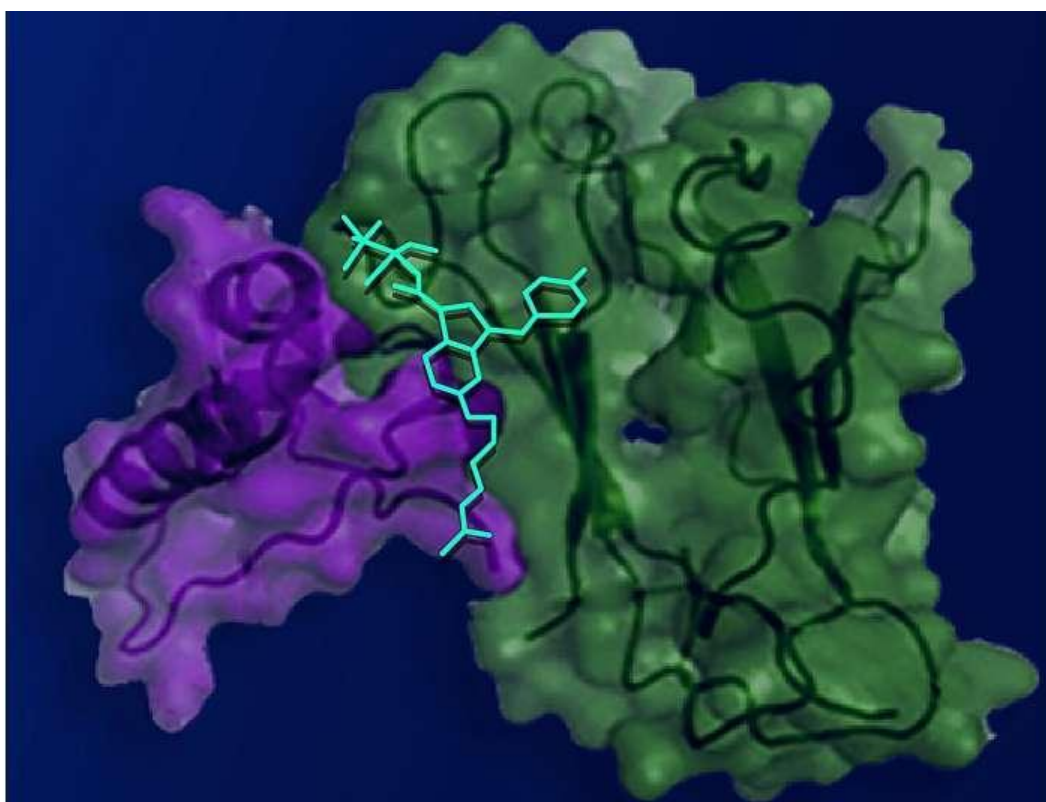
More information: Shaafique Chowdhury et al, Carbon Negative Synthesis of Amino Acids Using a Cell-Free-Based Biocatalyst, *ACS Synthetic Biology* (2024). DOI: [10.1021/acssynbio.4c00359](https://doi.org/10.1021/acssynbio.4c00359)

Provided by Georgia Institute of Technology

MARCH 5, 2025

Compound mimics cannabis for pain relief without the side effects: Mouse study points to effective opioid alternative

by [Washington University in St. Louis](#)



Researchers at WashU Medicine and Stanford University developed a compound that relieves pain in mice but doesn't affect the brain, thereby avoiding mind-altering side effects and abuse potential. The custom-designed molecule, derived from cannabis, may provide an alternative to opioids for treating chronic pain. The compound is illustrated here in cyan, nestled within a protein (green and purple) involved in sensing pain. Credit: Tasnia Tarana

Treatment for chronic pain still relies heavily on opioids. While effective, they are highly addictive and potentially deadly if misused.

In the quest to develop a safe, effective alternative to opioids, researchers at Washington University School of Medicine in St. Louis and Stanford University have developed a compound that mimics a natural molecule found in the [cannabis plant](#), harnessing its pain-relieving properties without causing addiction or mind-altering side effects in mice.

While more studies are needed, the compound shows promise as a nonaddictive pain reliever that could help the estimated 50 million people in the U.S. who suffer from chronic pain. The study is [published](#) in *Nature*.

"There is an urgent need to develop nonaddictive treatments for chronic pain, and that's been a major focus of my lab for the past 15 years," said the study's senior author Susruta Majumdar, Ph.D., a professor of anesthesiology at WashU Medicine.

"The custom-designed compound we created attaches to pain-reducing receptors in the body but, by design, it can't reach the brain. This means the compound avoids psychoactive side effects such as mood changes and isn't addictive because it doesn't act on the brain's reward center."

Opioids dull the sensation of pain in the brain and hijack the brain's reward system, triggering the release of dopamine and feelings of pleasure, which make the drugs so addictive. Despite widespread public health warnings and media attention focused on the dangers of opioid addiction, numerous overdose deaths still occur.

In 2022, some 82,000 deaths in the U.S. were linked to opioids. That's why scientists are working so hard to develop alternative treatments for pain.

"For millennia, people have turned to marijuana as a treatment for pain," explained co-corresponding author Robert W. Gereau, Ph.D., the Dr. Seymour and Rose T. Brown Professor of Anesthesiology and director of the WashU Medicine Pain Center.

"Clinical trials have also evaluated whether cannabis provides long-term pain relief. But inevitably, the psychoactive side effects of cannabis have been problematic, preventing cannabis from being considered as a viable treatment option for pain. However, we were able to overcome that issue."

The mind-altering properties of marijuana stem from natural molecules found in the cannabis plant, referred to as cannabinoid molecules. They bind to a receptor, called [cannabinoid receptor](#) one (CB1), on the surface of brain cells and on pain-sensing nerve cells throughout the body.

Working with collaborators at Stanford University, co-first author Vipin Rangari, Ph.D., a WashU Medicine postdoctoral research associate in Majumdar's laboratory, designed a cannabinoid molecule with a positive charge, preventing it from crossing the blood-brain barrier into the brain while allowing the molecule to engage CB1 receptors elsewhere in the body.

By modifying the molecule such that it only binds to pain-sensing nerve cells outside of the brain, the researchers achieved pain relief without mind-altering side effects.

They tested the modified synthetic cannabinoid compound in mouse models of nerve-injury pain and migraine headaches, measuring hypersensitivity to touch as a proxy for pain.

Applying a normally non-painful stimulus allows researchers to indirectly assess pain in mice. In both mouse models, injections of the modified compound eliminated touch hypersensitivity.

For many pain relievers, particularly opioids, tolerance to the medications over time can limit their long-term effectiveness and require higher doses of medication to achieve the same level of pain relief.

In this study, the modified compound offered prolonged pain relief—the animals showed no signs of developing tolerance despite twice-daily treatments with the compound over the course of nine days. This is a promising sign that the molecule could be used as a nonaddictive drug for relief of [chronic pain](#), which requires continued treatment over time.

Eliminating the compound's tolerance resulted from the bespoke design of the compound. The Stanford collaborators performed sophisticated computational modeling that revealed a hidden pocket on the CB1 receptor that could serve as an additional binding site.

The hidden pocket, confirmed by structural models, leads to reduced cellular activity related to developing tolerance compared to the conventional binding site, but it had been considered inaccessible to cannabinoids. The researchers found that the pocket opens for short periods of time, allowing the modified cannabinoid compound to bind, thus minimizing tolerance.

Designing molecules that relieve pain with minimal side effects is challenging to accomplish, said Majumdar. The researchers plan to further develop the compound into an oral drug that could be evaluated in [clinical trials](#).

More information: Susruta Majumdar, A cryptic pocket in CB1 drives peripheral and functional selectivity, *Nature* (2025). DOI: [10.1038/s41586-025-08618-7](https://doi.org/10.1038/s41586-025-08618-7). www.nature.com/articles/s41586-025-08618-7

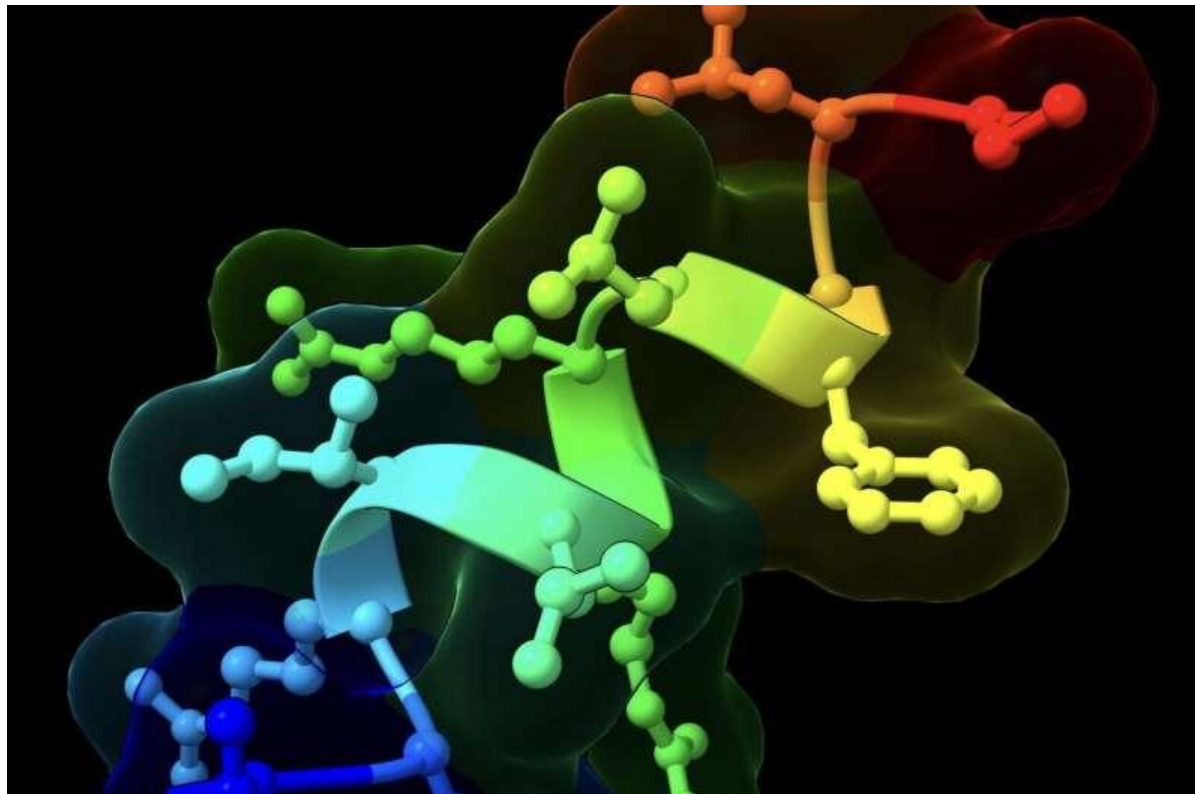
Journal information: [Nature](#)

Provided by [Washington University in St. Louis](#)

MARCH 6, 2025

Naturally occurring molecule rivals Ozempic in weight loss, sidesteps side effects

by Krista Conger, [Stanford University Medical Center](#)



The 12-amino-acid BRP peptide (spheres are atoms and sticks are bonds) suppresses appetite and reduces weight gain in mice and pigs without causing nausea or food aversion. Credit: Katrin Svensson/Stanford Medicine

A naturally occurring molecule identified by Stanford Medicine researchers appears similar to semaglutide—also known as Ozempic—in suppressing appetite and reducing body weight. Notably, testing in animals also showed that it worked without some of the drug's side effects, such as nausea, constipation and significant loss of muscle mass.

The newly discovered molecule, BRP, acts through a separate but similar metabolic pathway and activates different neurons in the brain—seemingly offering a more targeted approach to body weight reduction.

"The receptors targeted by semaglutide are found in the brain but also in the gut, pancreas and other tissues," said assistant professor of pathology Katrin Svensson, Ph.D.

"That's why Ozempic has widespread effects, including slowing the movement of food through the digestive tract and lowering blood sugar levels. In contrast, BRP appears to act specifically in the hypothalamus, which controls appetite and metabolism."

Svensson has co-founded a company to launch clinical trials of the molecule in humans in the near future.

Svensson is the senior author of the [research](#), which was published in *Nature*. Senior research scientist Laetitia Coassolo, Ph.D., is the lead author of the study.

The study would not have been possible without the use of [artificial intelligence](#) to weed through dozens of proteins in a class called prohormones.

Prohormones are biologically inert molecules that become active when they are cleaved by other proteins into smaller pieces called peptides; some of these peptides then function as hormones to regulate complex biological outcomes, including [energy metabolism](#), in the brain and other organs.

Each prohormone can be divided in a variety of ways to create a plethora of functional peptide progeny. But with traditional methods of protein isolation, it's difficult to pick peptide hormones (which are relatively rare) out of the biological soup of the much more numerous natural byproducts of protein degradation and processing.

The researchers focused on the prohormone convertase 1/3 (also known as PCSK1/3), which separates prohormones at specific amino acid sequences and is known to be involved in human obesity.

One of the peptide products is glucagon-like peptide 1, or GLP-1, which regulates appetite and blood sugar levels; semaglutide works by mimicking the effect of GLP-1 in the body. The team turned to artificial intelligence to help them identify other peptides involved in energy metabolism.

Peptide Predictor

Instead of manually isolating proteins and peptides from tissues and using techniques like [mass spectrometry](#) to identify hundreds of thousands of peptides, the researchers designed a computer algorithm they named "Peptide Predictor" to identify typical prohormone convertase cleavage sites in all 20,000 human protein-coding genes.

They then focused on genes that encode proteins that are secreted outside the cell—a key characteristic of hormones—and that have four or more possible cleavage sites. Doing so narrowed down the search to 373 prohormones, a manageable number to screen for their biological effects.

"The algorithm was absolutely key to our findings," Svensson said.

Peptide Predictor predicted that prohormone convertase 1/3 would generate 2,683 unique peptides from the 373 proteins. Coassolo and Svensson focused on sequences likely to be biologically active in the brain. They screened 100 peptides, including GLP-1, for their ability to activate lab-grown neuronal cells.

As expected, the GLP-1 peptide had a robust effect on the [neuronal cells](#), increasing their activity threefold over control cells. But a small peptide made up of just 12 amino acids bumped up the cells' activity 10-fold over controls. The researchers named this peptide BRP based on its parent prohormone, BPM/retinoic acid inducible neural specific 2, or BRINP2 (BRINP2-related-peptide).

When the researchers tested the effect of BRP on lean mice and minipigs (which more closely mirror human metabolism and eating patterns than mice do), they found that an intramuscular injection of BRP prior to feeding reduced food intake over the next hour by up to 50% in both animal models.

Obese mice treated with daily injections of BRP for 14 days lost an average of 3 grams—due almost entirely to fat loss—while control animals gained about 3 grams over the same period. The mice also demonstrated improved glucose and insulin tolerance.

Behavioral studies of the mice and pigs found no differences in the treated animals' movements, water intake, anxiety-like behavior or fecal production. And further studies of physiological and brain activity showed that BRP activates metabolic and neuronal pathways separate from those activated by GLP-1 or semaglutide.

The researchers hope to identify the cell-surface receptors that bind BRP and to further dissect the pathways of its action. They are also investigating how to help the peptide's effects last longer in the body to allow a more convenient dosing schedule if the peptide proves to be effective in regulating human body weight.

"The lack of effective drugs to treat obesity in humans has been a problem for decades," Svensson said. "Nothing we've tested before has compared to semaglutide's ability to decrease appetite and body weight. We are very eager to learn if it is safe and effective in humans."

Researchers from the University of California, Berkeley; the University of Minnesota; and the University of British Columbia contributed to the work.

Svensson and Coassolo are inventors on patents regarding BRP [peptides](#) for metabolic disorders. Svensson is a co-founder of Merrifield Therapeutics.

More information: Laetitia Coassolo et al, Prohormone cleavage prediction uncovers a non-incretin anti-obesity peptide, *Nature* (2025). DOI: [10.1038/s41586-025-08683-y](https://doi.org/10.1038/s41586-025-08683-y)

Journal information: [Nature](#)

Provided by [Stanford University Medical Center](#)

MARCH 10, 2025

Exploring the Greenland shark's secret to extreme longevity

by Justin Jackson , Phys.org

Greenland sharks are thought to have lifespans that can reach 400 years. University of Tokyo-led researchers have now sequenced the first chromosome-level genome of the Greenland shark (*Somniosus microcephalus*), revealing genetic adaptations linked to its extraordinary lifespan, immune function, and deep-sea survival.

Greenland sharks inhabit the North Atlantic and Arctic Oceans, reaching lengths of over six meters and weights exceeding 1,400 kilograms. A growth rate of approximately one centimeter per year suggests an extended lifespan, confirmed by radiocarbon dating of the eye lens, which estimated one individual to be about 400 years old.

Existing genomic studies on other long-lived species, including elephants and rockfish, have identified specific gene variations associated with extended lifespans. Yet, no genomic research had been conducted on the Greenland shark before this study.

Large genome sizes, technical challenges in sequencing, and limited conservation data have hindered a full understanding of Greenland shark biology. Research efforts have been constrained by difficulties in obtaining high-quality genomic material. A comprehensive genome sequence could provide insight into the species' exceptional longevity, [cancer resistance](#), and environmental adaptations.

In the study titled "The Greenland Shark Genome: Insights into Deep-Sea Ecology and Lifespan Extremes," [published](#) as a preprint on *bioRxiv*, researchers conducted whole-genome sequencing to investigate genetic factors linked to longevity and deep-sea adaptation.

A female Greenland shark was captured in Kongsfjorden, Svalbard Archipelago, as part of an ongoing biotelemetry study. Tissue samples (fin clips and blood) were taken before the shark was released back into the wild.

High-fidelity long-read genome sequencing was performed on the samples, yielding approximately 34.5x coverage of the genome. A chromosome-scale genome assembly was constructed using Hi-C sequencing data, resulting in a 5.9-gigabase genome with an N50 scaffold length of 233 megabases. A total of 37,125 [protein-coding genes](#) were annotated, achieving a completeness score of 86.5%.

Comparative analyses identified 549 expanded and 1,461 contracted [gene families](#). Among the expanded families, genes involved in NF-κB signaling, DNA repair, and immune function

showed significant increases. The TNF, TLR, and LRRFIP gene families, all of which regulate NF- κ B signaling, exhibited a higher copy number compared to shorter-lived shark species. NF- κ B plays a crucial role in cellular protection, inflammatory response, and apoptosis, suggesting a genetic foundation for prolonged lifespan and disease resistance.

Several genes known to influence cancer suppression, including FOXF2, FSCN1, and MAD2L1BP, showed signs of positive selection. FOXF2 regulates the tumor immune microenvironment, while FSCN1 influences cell migration and tumor progression. MAD2L1BP is involved in chromosome stability and DNA repair, key processes in cancer resistance.

Greenland sharks live at extreme depths with minimal light exposure. A rhodopsin gene (RHO) variant in this species displayed amino acid substitutions consistent with a spectral shift toward blue light, a characteristic adaptation to deep-sea environments. Comparisons with other chondrichthyan species confirmed similarities with known deep-sea dwellers, indicating [genetic adaptations](#) for dim-light vision.

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Field observations of the captured shark showed that Greenland sharks responded to submersible lights underwater and to nearby movements while on deck, challenging previous assumptions about their poor vision due to corneal parasites.

Researchers analyzed [population genetics](#) between Greenland sharks and their closest relatives, Pacific sleeper sharks (*Somniosus pacificus*). Genomic data suggested a long-term decline in effective population size for Greenland sharks, whereas Pacific sleeper sharks experienced a historical bottleneck followed by signs of population recovery.

Divergence estimates revealed two genetic separation signals: an earlier divergence around 10 million years ago and a more recent genetic isolation event approximately 3 million years ago. Additionally, analysis of runs of homozygosity suggests that Greenland sharks may have undergone recent inbreeding, while Pacific sleeper sharks exhibit evidence of past inbreeding followed by population expansion.

Runs of homozygosity analysis suggested higher inbreeding in Greenland sharks compared to Pacific sleeper sharks, while heterozygosity analysis indicated a long-term effective population size approximately 1.5 times greater in Greenland sharks than their relatives.

Sequencing data revealed multiple genetic mechanisms potentially linked to longevity, cancer resistance, and immune regulation. Expansions in NF- κ B-related genes, along with positively selected cancer-related genes, suggest evolutionary adaptations that contribute to its extended lifespan and disease resilience. A spectral tuning adaptation in rhodopsin indicates a visual system optimized for deep-sea conditions.

Greenland sharks reach maturity at approximately 150 years, making them extremely vulnerable to overfishing and environmental changes. The study provides a foundational

genomic resource for understanding population dynamics, evolutionary history, and potential conservation strategies for this long-lived species.

The findings also indicate a strong association between specific gene families and longevity, immune response, and cancer resistance, providing a foundation for future human aging studies.

More information: Kaqiao Yang et al, The Greenland shark genome: insights into deep-sea ecology and lifespan extremes, *bioRxiv* (2025). DOI: [10.1101/2025.02.19.638963](https://doi.org/10.1101/2025.02.19.638963)

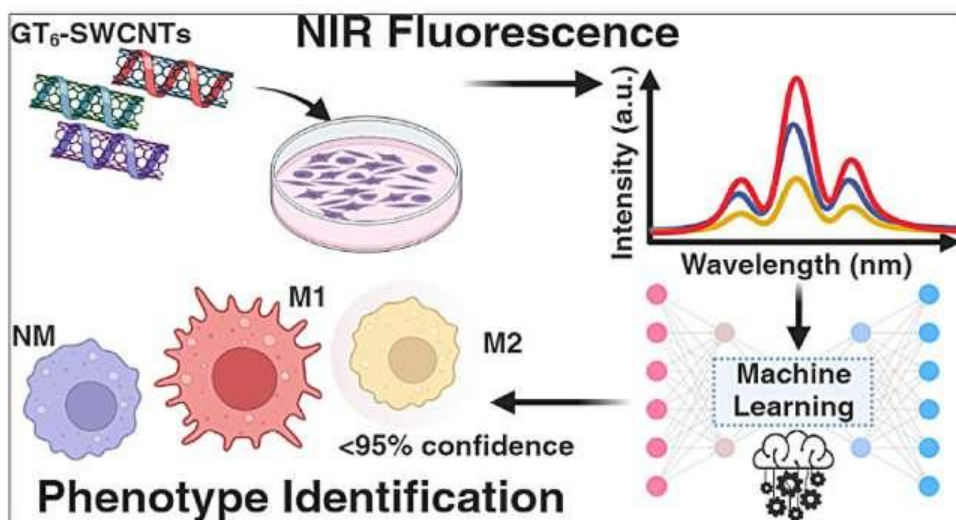
Journal information: [bioRxiv](#)

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MARCH 10, 2025

Carbon nanotubes and machine learning: A new way to spot subtle immune cell differences

by Nicholas Phillips, [University of Rhode Island](#)



Graphical abstract. Credit: *ACS Nano* (2024). DOI: [10.1021/acsnano.4c03387](https://doi.org/10.1021/acsnano.4c03387)

Early diagnosis is crucial in disease prevention and treatment. Many diseases can be identified not just through physical signs and symptoms but also through changes at the cellular and molecular levels.

When it comes to a majority of chronic conditions, early detection, particularly at the cellular level, gives patients a better chance for successful treatment. Detection of early changes at the cellular level can also dramatically improve cancer outcomes.

It's against this backdrop that a University of Rhode Island professor and a former Ph.D. graduate student looked at understanding the smallest changes between two similar cells.

Daniel Roxbury, an associate professor of chemical engineering at the University of Rhode Island, and recently graduated doctoral researcher Acer Nadeem recently [published](#) a proof-of-concept paper in *ACS Nano* demonstrating how the use of carbon nanotubes could be combined with machine learning to detect subtle differences between closely related immune cells.

The cells they worked with were macrophages of the M1 and M2 variety, that help fight infection as well as sterilize and heal wounds. Expanding on this research could eventually aid in the early detection of diseases like cancer.

Carbon nanotubes are aptly named. They're composed of a single sheet of carbon atoms and are so small that thousands of them can fit inside a living cell. You can fit about 150,000 of them across the width of a human hair. A unique thing about them are their fluorescent properties, which allow them to emit a distinct optical signature when exposed to infrared light.

"When added to cells, we can use the light given off by nanotubes to detect minute differences between closely related cells," said Roxbury.

These nanotubes emit a variety of infrared light. Broadly speaking, by looking at variations in the [infrared light](#) emitted from the nanotubes, they can detect diverse cellular changes, including pH levels, protein concentrations, and ion variations. This can be particularly important because research shows that high pH levels are linked to an increased likelihood of a tumor.

Nanotubes are commonly used in applications like [composite materials](#) and [carbon fiber](#), but Roxbury and Nadeem are using them in a novel way at URI—to distinguish between healthy and unhealthy cells.

Nadeem was tasked with developing new sensors using carbon nanotubes to detect proteins in the blood that would help identify cancer.

"Inside the cell are a million different proteins, lipids, and sugars," said Nadeem. "So, starting this project, we didn't know if we were actually going to see anything reflected back from the nanotubes because all these different proteins and ions aren't in a very high concentration inside a cell."

For Nadeem, it was a welcome challenge. Researching and studying methods to detect some of the most common diseases early on was critical for him. Part of Nadeem's motivation was the fact that he has a family history of Alzheimer's disease and was eager to develop better methods for early detection.

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"I wanted to figure out a way to diagnose these diseases—neurodegenerative diseases as well as cancer—in their very early stages," said Nadeem.

Roxbury and Nadeem used an in vitro experiment that involved placing live cells into a culture dish, adding carbon nanotubes, and then using a specialized microscope with an infrared camera to observe the emitted light from each cell.

The camera generated millions of data points. Each data point reflected cellular activity. Healthy cells emitted one type of light, while potentially unhealthy or changing cells emitted different light patterns.

"Analyzing the data was what took the most time," said Nadeem. "That's where integrating machine learning came into this project because we got around 4 million-plus data points."

Integrating machine learning allowed the researchers to distill those millions of data points into a comprehensive understanding of what was happening at the cellular level, such as high or low acidity.

"As a direct continuation of Aceer's work, we are currently working to discern cancer versus non-cancer," said Roxbury. "We've demonstrated immune cell discrimination. We are now looking at breast cancer cells and tissue versus healthy breast tissue and trying to uncover the difference there."

While it will be some time before experiments will be able to be translated to animals, the potential industry uses are vast. Nanotubes could potentially be used inside the human body to help in the early detection of not only cancer, but Alzheimer's and other diseases, making it less expensive and leading to a quicker diagnosis.

"All of these different diseases have their own distinct biomarkers with them, even at the very early stage," said Nadeem. "So, there is immense potential to use this as an early diagnostic tool for many diseases."

More information: Aceer Nadeem et al, Machine Learning-Assisted Near-Infrared Spectral Fingerprinting for Macrophage Phenotyping, *ACS Nano* (2024). DOI: [10.1021/acsnano.4c03387](https://doi.org/10.1021/acsnano.4c03387)

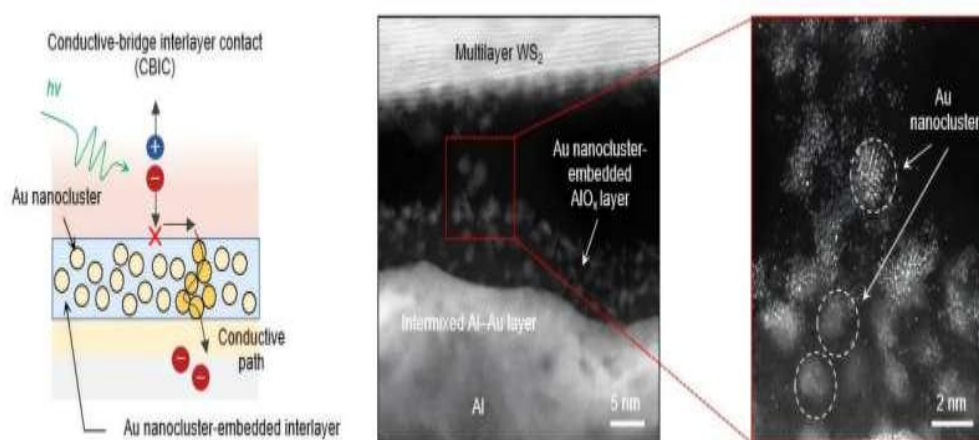
Journal information: [ACS Nano](#)

Provided by [University of Rhode Island](#)

MARCH 10, 2025

2D semiconductor sensor: Gold nanoparticles boost optical signal efficiency

by [National Research Council of Science and Technology](#)



The new electrode (CBIC) developed by the researchers can effectively reduce the resistance of the electrode by forming gold nanoparticles inside. Transmission electron microscopy confirms that gold nanoparticles are indeed formed inside the electrode. Credit: Korea Institute of Science and Technology

Next-generation imaging technology is rapidly expanding beyond smartphones into intelligent devices, robotics, extended reality (XR) devices, health care, CCTV, and various other industries. At the core of these technological advances are highly efficient, ultra-compact image sensors that convert light signals into electrical signals. Image sensors capture and process visual information from objects and environments, enabling precise reconstruction of their shape, size, and spatial position.

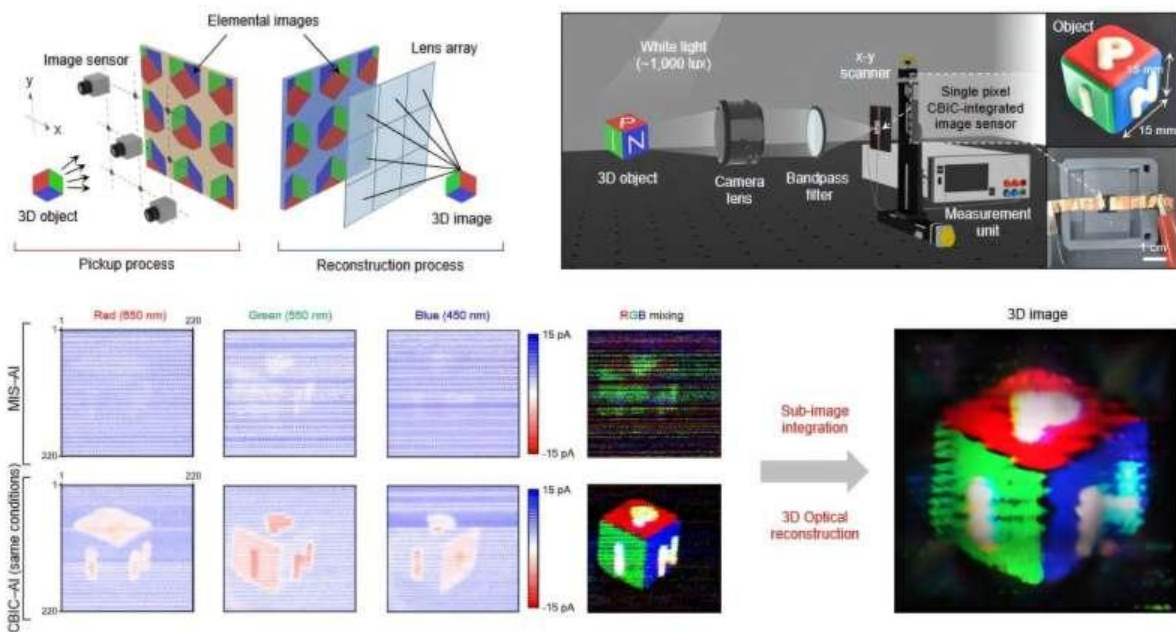
Currently, commercial image sensors are primarily based on silicon semiconductors. However, research into next-generation image sensors utilizing two-dimensional (2D) semiconductor nanomaterials—potential replacements for silicon—is actively underway. These nanomaterials, composed of atomically thin layers just a few nanometers thick, offer exceptional optical properties and miniaturization potential, making them highly suitable for high-performance image sensors.

However, maximizing their performance requires low-resistance electrodes capable of efficiently processing optical signals. Conventional 2D semiconductor-based sensors face challenges in achieving low resistance electrodes, resulting in poor optical signal processing efficiency, which has been a major obstacle to commercialization.

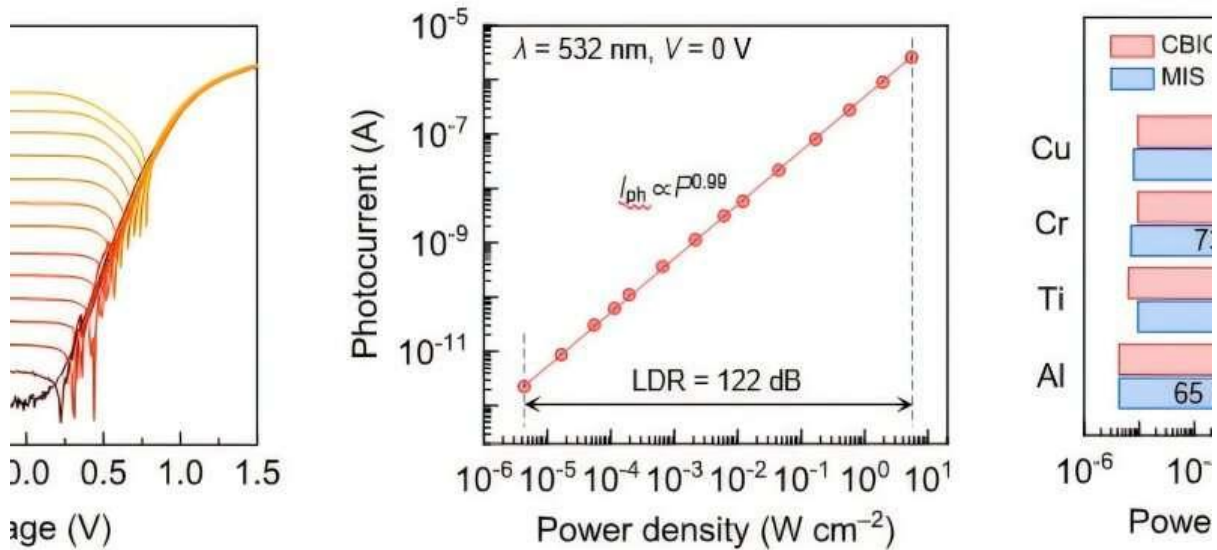
Do Kyung Hwang (Post-Silicon Semiconductor Institute, KIST; KU-KIST Graduate School, KIST School) and Dr. Min-Chul Park (Post-Silicon Semiconductor Institute, KIST; Korea University, and Yonsei University), along with their joint research team at KIST, have successfully developed an innovative electrode material called Conductive-Bridge Interlayer Contact (CBIC), enabling the realization of a 2D semiconductor-based image sensor with high optical signal efficiency.

The paper is [published](#) in the journal *Nature Electronics*.

By incorporating gold nanoparticles within the electrode, the team significantly reduced its resistance, leading to a substantial improvement in the performance of the 2D semiconductor image sensor. Furthermore, they effectively addressed the issue of Fermi level pinning, a common challenge in conventional electrode materials, thereby further enhancing the sensor's optical signal efficiency.



Using the developed electrodes, we demonstrated integral imaging based 3D imaging and display using a lens array to verify its performance. Credit: Korea Institute of Science and Technology



- We evaluated the performance of the 2D semiconductor photodetector utilizing CBIC electrodes and found that the linear dynamic range characteristics were significantly improved compared to conventional MIS electrodes. Credit: Korea Institute of Science and Technology
- Using the developed electrodes, we demonstrated integral imaging based 3D imaging and display using a lens array to verify its performance. Credit: Korea Institute of Science and Technology
- We evaluated the performance of the 2D semiconductor photodetector utilizing CBIC electrodes and found that the linear dynamic range characteristics were significantly improved compared to conventional MIS electrodes. Credit: Korea Institute of Science and Technology

In particular, the team applied this technology to successfully implement integral imaging based 3D imaging and glasses-free display technology, inspired by the compound eye structure of the dragonfly. Using integral imaging technology, they achieved the acquisition and reproduction of RGB full-color 3D images, enabling the recording and reconstruction of 3D object shapes.

In the future, these high-performance [image sensors](#) are expected to be widely used in various advanced industries, including XR devices, artificial intelligence (AI), and autonomous driving systems.

"By overcoming the technical limitations caused by electrode issues in existing 2D [semiconductor devices](#), this research is expected to significantly accelerate the industrialization of next-generation imaging system technologies, which offer advantages in light absorption and miniaturization," said Dr. Do Kyung Hwang.

He further emphasized the scalability of the research, stating, "The developed [electrode](#) material is easy to fabricate and scalable to large areas, making it widely applicable to various semiconductor-based optoelectronic devices."

Dr. Min-Chul Park added, "2D semiconductor-based optoelectronic devices that overcome the challenge of Fermi level pinning will have a significant impact across industries that demand ultra-compact, ultra-high-resolution, and high-performance visual sensors in the future."

More information: Jisu Jang et al, Conductive-bridge interlayer contacts for two-dimensional optoelectronic devices, *Nature Electronics* (2025). DOI: [10.1038/s41928-025-01339-9](https://doi.org/10.1038/s41928-025-01339-9)

Journal information: [Nature Electronics](#)

Provided by [National Research Council of Science and Technology](#)

MARCH 12, 2025

Cells 'speed date' to find their neighbors when forming tissues

by [Cell Press](#)



The heart (cyan) forms from two distant regions of the embryo (far left). These regions migrate to the embryo midline, where they fuse into a tube to make the first heart structure (far right). Precise alignment and pairing of these cells are crucial for proper heart development. Credit: Thamarailingam Athilingam and Kate McDole

In developing hearts, cells shuffle around, bumping into each other to find their place, and the stakes are high: pairing with the wrong cell could mean the difference between a beating heart and one that falters.

A study published in the *Biophysical Journal* demonstrates how heart cells go about this "matchmaking" process. The researchers model the intricate movements of these cells and predict how genetic variations could disrupt the heart development process in [fruit flies](#).

In both humans and fruit flies, the heart's tissues arise from two distinct regions of the embryo, which are initially far apart. As development progresses, these cells journey toward each other, ultimately merging into a tube-like shape that will become the heart. For the heart to develop correctly, these cells must align and pair up precisely.

"As the cells come together, they jiggle and adjust, and somehow always end up pairing with a heart cell of the same type," says the lead author, Timothy Saunders of the University of Warwick. This observation inspired the team to explore how cells match up in the first place and how they know when they've found the right fit.

Developing heart cells have tentacle-like protrusions called filopodia, which probe and grab onto potential partners. Saunders' previous work found that proteins create waves that pull mismatched cells apart, giving them another chance to find the right match.

"It's basically like cells are speed dating," says Saunders. "They have just a few moments to determine if they're a good match, with molecular 'friends' ready to pull them apart if they're not compatible."

The researchers found that heart cells seek stability where they remain closest to stillness—like a rolling ball that eventually comes to a stop, known as energy equilibrium in physics.

In developing [heart cells](#), this principle applies when cells find a balance between connection forces and their ability to adjust to strain—also known as adhesive energy and elasticity. Based on this observation, the team developed a model that shows how cells can self-organize.

Next, the team tested their model on fruit fly hearts with mutations and misalignments. By calculating the adhesive energy between different cell types and assessing tissue elasticity, the model predicted how cells would match and rearrange.

"Although rare, sometimes the heart tube ends up with one cell on one side when it should have two, or two cells when there should be four," says Saunders. "We could input these imperfections into the model and run it." The model produced outcomes that closely mirrored what was observed in real embryos.

The team notes that their model not only enhances our understanding of how cells match and align during heart development but also has broader applications. Similar cell-matching processes are crucial in neuronal connections, wound repair, and facial development, where hiccups can lead to conditions like cleft lip.

"Essentially, we're putting numbers to [biological processes](#) to explain what we observe," Saunders adds.

More information: Interfacial energy constraints are sufficient to align cells over large distances, *Biophysical Journal* (2025). DOI: [10.1016/j.bpj.2025.02.011](https://doi.org/10.1016/j.bpj.2025.02.011)

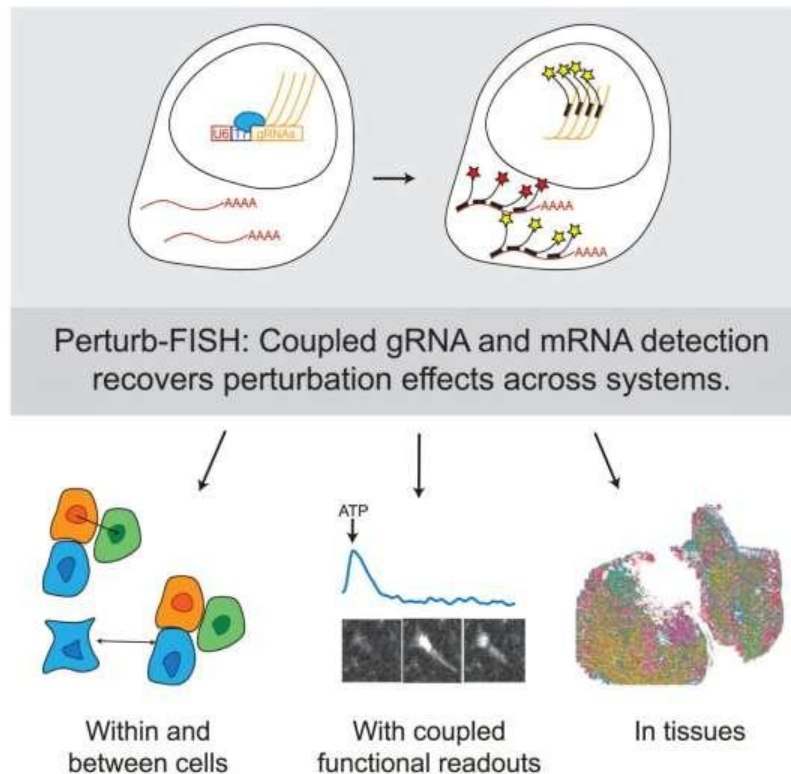
Journal information: *Biophysical Journal*

Provided by [Cell Press](#)

MARCH 12, 2025

New technology puts a spatial lens on CRISPR screening

by Leah Eisenstadt, [Broad Institute of MIT and Harvard](#)



Credit: *Cell* (2025). DOI: [10.1016/j.cell.2025.02.012](https://doi.org/10.1016/j.cell.2025.02.012)

Recently, scientists have been able to explore gene circuitry in individual cells using methods that suppress particular genes and measure the impact on the expression of other genes. These methods, however, fail to capture spatial information such as the effects from, or on, neighboring cells, which can provide important clues to a cell or gene's role in health and disease.

Now, a technology developed in the Spatial Technology Platform at the Broad Institute of MIT and Harvard builds on these methods with cutting-edge spatial advances. Their method, known as Perturb-FISH, combines imaging-based spatial transcriptomic measurements with large-scale detection of CRISPR guide RNAs.

The researchers demonstrated Perturb-seq's ability to uncover new cellular and functional insights, including the effects of autism-related genes on cellular activity and the interactions between human tumor and [immune cells](#) in an animal model. Further refinements to Perturb-FISH could make it even more widely accessible and enable a range of new biological investigations. The technology and demonstrations of its utility are [published](#) in *Cell*.

"With Perturb-FISH, we've developed a powerful new way to examine the roles of genes and [genetic circuits](#) in tissue development, homeostasis, and dysfunction," said co-senior author Sami Farhi, director of the Spatial Technology Platform at the Broad Institute.

"Our team is dedicated to devising spatial tools for the benefit of the scientific community, and we hope this new method is just the first of many more that we'll build and share." Farhi led the work along with co-senior author Brian Cleary, a former Broad Fellow and Merkin Institute Fellow who is now an assistant professor at Boston University.

Gone FISH-ing

Previously, researchers had combined single-cell RNA sequencing with CRISPR screening to examine gene networks within cells using tools such as Perturb-seq, but the cells' spatial context wasn't captured. Another method known as optical pooled screening measures the effects of gene-editing perturbations on cell fitness or other phenotypes, but doesn't capture gene transcriptional states.

Scientists in the Spatial Technology Platform aimed to develop a comprehensive method that could measure at once which genes are altered in a cell, which genetic perturbation caused the changes, and the location of those affected cells in relation to other cells.

Key developments that made Perturb-FISH possible were [computational methods](#) developed by Cleary and a new way of amplifying the signal from single molecules (either CRISPR guide RNAs or gene transcripts) so they can be detected over background levels of fluorescence.

Traditional amplification methods don't work with molecules as small as guide RNAs, so first author and former postdoctoral researcher Loïc Binan devised an innovative strategy to generate many local copies of each guide RNA at its original site. By combining that with a fluorescence-based spatial transcriptomic method called MERFISH, Perturb-FISH can reveal both the identity of each perturbation and the cell's transcriptome in their spatial context.

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The researchers demonstrated Perturb-FISH's ability to measure the effects of 35 genes that help regulate immune cell response to stimulation, finding that their results aligned with similar data generated using Perturb-seq. They also showed how it can shed light on

intercellular networks, finding that cell density can alter the effects of gene perturbations and that non-perturbed cells can be impacted by perturbations in neighboring cells.

To illustrate Perturb-FISH's potential for investigating functional effects of even subtle genetic adjustments, the researchers used CRISPR inhibition to turn down genes associated with autism in human brain cells known as astrocytes and observed changes in calcium activity and gene expression.

In addition, the research team tested the method in a more complex system, using a xenograft model developed in the Broad Cancer Program. After perturbing genes related to the NF- κ B pathway in human tumor cells, they used Perturb-FISH to measure the genetic interactions between tumor cells and responding immune cells in the animal model.

"We were excited to see that we could observe effects in a more complicated system with multiple cell types interacting with each other and still pick up interesting biology," said Farhi.

Members of the platform are now working to make Perturb-FISH more robust and more accessible, for example, by modifying the method so that only a single imaging instrument is required to run the method. They also want to increase the number of genes they can examine in each experiment, which is currently limited to 500.

"Because we developed this in the Spatial Technology Platform, it allows us to take what would typically just be an academic project and keep working on it and refining it to the point that it can be more broadly used," said Farhi.

Along with related methods recently launched by other research groups, Perturb-FISH represents a step forward in the spatial technology field that will give users more experimental opportunities and choices. "We're happy to see others pursuing these technologies, which bring exciting possibilities for scientists wanting to launch spatial investigations," said Farhi. "The more methods we all have, the more likely people are to use them, which is our ultimate goal."

More information: Loïc Binan et al, Simultaneous CRISPR screening and spatial transcriptomics reveal intracellular, intercellular, and functional transcriptional circuits, *Cell* (2025). DOI: [10.1016/j.cell.2025.02.012](https://doi.org/10.1016/j.cell.2025.02.012)

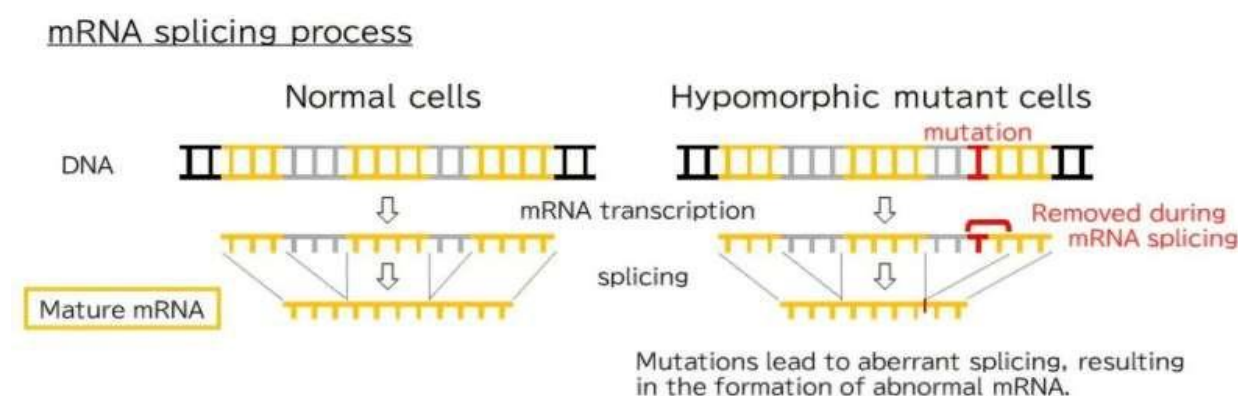
Journal information: *Cell*

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

MARCH 12, 2025

Genome editing technique enables partial inhibition of gene function in crops

by [Kumamoto University](#)



CRISPR-Cas9-mediated mutation at mRNA splicing site. Credit: *Journal of Plant Research* (2024). DOI: 10.1007/s10265-024-01597-2

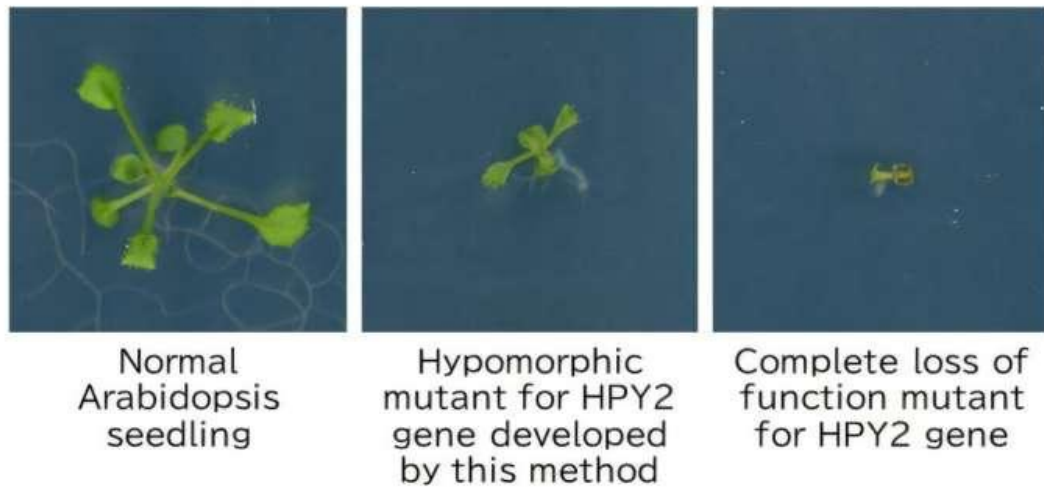
Researchers at Kumamoto University have successfully executed a practical trial of a new genome-editing technique that allows for the partial inhibition of essential gene function without causing lethality. This innovative approach, which leverages CRISPR-Cas9 technology, opens new doors for genetic research and agricultural advancements by enabling the study and modification of genes that were previously difficult to analyze.

Genes that are crucial for survival often pose a challenge for researchers, as completely disabling them can be fatal to the organism. Traditional gene knockout methods, including CRISPR-Cas9, typically result in complete loss of function, making it difficult to investigate these vital genetic components.

To address this limitation, the research team led by Associate Professor Takashi Ishida, Faculty of Advanced Science and Technology, Kumamoto University, conceived a method to introduce hypomorphic mutations, which reduce—but do not entirely eliminate—gene function.

Using the model plant *Arabidopsis thaliana*, the team successfully applied their method to the HPY2 gene, which is essential for [cell division](#) and plant growth. While complete loss of

this gene results in seedling lethality, the newly engineered hypomorphic mutants exhibited delayed growth but remained viable, paving the way for researchers to analyze gene function in greater detail in future studies.



Phenotypes of wild type, hpy2 hypomorphic mutant and hpy2 null mutant. Credit: *Journal of Plant Research* (2024). DOI: 10.1007/s10265-024-01597-2

Applications for agriculture and beyond

This breakthrough, [published](#) in the *Journal of Plant Research*, has significant implications beyond basic [genetic research](#). By fine-tuning gene activity instead of completely disabling genes, this technique could be used to enhance desirable traits in crops without causing harmful side effects. For example, modifying genes responsible for stress resistance in plants could lead to crops that are more resilient to climate change while maintaining their growth and yield.

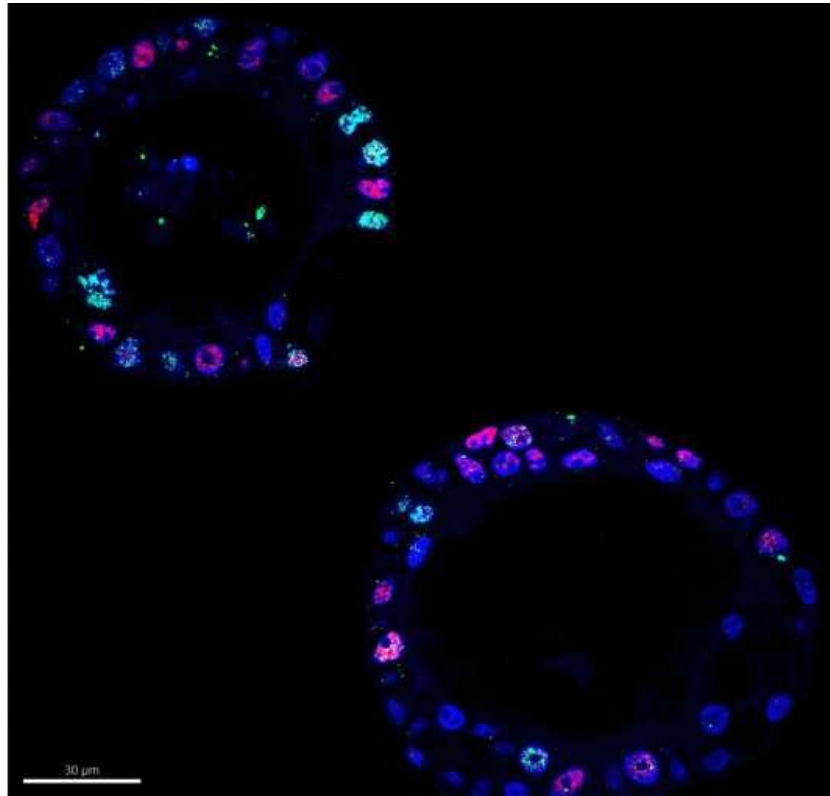
"This method provides a powerful tool for studying genes that were previously inaccessible due to their essential nature," said Associate Professor Ishida. "It also opens up new possibilities for precision breeding in agriculture, where controlled gene modification is key to improving traits without unintended consequences."

More information: Mika Yoshimura et al, Generation of viable hypomorphic and null mutant plants via CRISPR-Cas9 targeting mRNA splicing sites, *Journal of Plant Research* (2024). DOI: [10.1007/s10265-024-01597-2](https://doi.org/10.1007/s10265-024-01597-2)
Provided by [Kumamoto University](#)

MARCH 12, 2025

The secret DNA circles fueling pancreatic cancer's aggression

by [Champalimaud Centre for the Unknown](#)



Immunofluorescence images showing that cells with higher levels of the cancer-promoting MYC protein (red) also tend to exhibit high levels of DNA damage (green), suggesting that too much MYC leads to genomic stress. Credit: Vincenzo Corbo Lab

Pancreatic cancer is one of the deadliest cancers worldwide, with a five-year survival rate of 13%. This poor prognosis stems from both late detection and the cancer's notorious capacity to adapt and resist therapy.

Now, a study led by researchers at the University of Verona, University of Glasgow, and the Botton-Champalimaud Pancreatic Cancer Center uncovers a hidden driver of this adaptability: extrachromosomal DNA (ecDNA).

The findings have been published in *Nature*.

A new player in pancreatic cancer

The team found that some [pancreatic cancer](#) cells gain a major survival edge by carrying copies of critical cancer genes—such as MYC—on circular pieces of DNA that exist outside chromosomes, the structures that house most of our [genetic material](#).

Known as ecDNA, these genetic rings float freely in the [cell nucleus](#), enabling tumor cells to swiftly ramp up gene expression, change their shape, and survive in otherwise hostile environments.

"Pancreatic cancer is often called a silent killer because it's hard to detect until it's too late," says Peter Bailey, co-corresponding author and Director of Translational Research at the Botton-Champalimaud Pancreatic Cancer Center.

"We know that part of its lethality arises from the ability of [tumor cells](#) to 'shape shift' under stress. Our study shows that ecDNA forms a big part of that story."

The researchers discovered ecDNA to be surprisingly common in pancreatic tumors, particularly for oncogenes like MYC, which drives cancer growth and metabolism.

"We saw far more variability in MYC copy number when MYC was on ecDNA," explains Elena Fiorini, co-first author and senior postdoc. "Some cells carried dozens—or even hundreds—of extra MYC copies, giving them a large growth advantage under certain conditions."

"It's effectively a 'bet-hedging' strategy," adds Daniel Schreyer, co-first author and former Ph.D. student of the University of Glasgow.

"You get pockets of cells that carry very high MYC levels, which is beneficial under certain conditions, and others with fewer copies, which might do better in another environment—all within the same tumor."

Such flexibility underscores the profound intratumour heterogeneity characteristic of pancreatic cancer, where myriad sub-populations coexist and respond differently to treatment. Targeting one subset often fails against another, fueling resistance.

A key advantage of this study is that the organoids—mini-3D replicas of pancreatic tumors grown in the lab—were derived directly from patients with early-stage disease. These organoids preserve much of the genetic make-up of the original tumor, making them excellent testbeds for studying cancer. Unlike methods that artificially introduce ecDNA, these lab models reflect genuine ecDNA variants found in real tumors.

"This approach offers real-world insight into how dynamic and disordered a tumor can be," says Fiorini. "We see firsthand that even when two patients both have MYC on ecDNA, the structure of that circular DNA can differ substantially—leading to big variations in MYC expression."

Plasticity in action: Organoids in the lab

To see how ecDNA drives adaptation, the researchers grew patient-derived organoids and removed vital growth signals—such as WNT factors—and then observed how these organoids responded to the stress.

"We found that organoids bearing MYC on extrachromosomal DNA could shift their dependency on WNT," explains Antonia Malinova, co-first author and a former Ph.D. student at the University of Verona. "Essentially, cells with high levels of ecDNA became more self-sufficient, no longer needing those external signals to survive."

The study also revealed a clear link between high MYC levels and changes in tumor cell shape and behavior. When MYC ecDNA levels soared, cells morphed into more aggressive, solid structures—losing their more organized, gland-like architecture.

"What's remarkable," says co-corresponding author Vincenzo Corbo from the University of Verona, "is how rapidly these ecDNA-based copies can appear or disappear depending on the environment."

"If the cancer is under pressure—say, lacking key growth factors—cells with ecDNA can crank up MYC expression to survive. But if that pressure lifts, they can lose some of these extra DNA circles to avoid the downsides of carrying too many copies."

Indeed, expressing MYC at high levels can trigger DNA damage, forcing cancer cells to carefully balance the costs and benefits of ecDNA retention.

"That was unexpected," says Corbo. "It challenges the assumption that more MYC is always better for a cancer cell—there's a real fitness cost to maintaining such high levels."

ecDNA as a therapeutic target?

Although extrachromosomal DNA only appears in about 15% of patient samples in this study, that subset might be particularly aggressive or prone to therapy resistance. As a result, detecting or disrupting ecDNA could open new therapeutic windows.

"We might imagine a strategy that exploits the vulnerabilities introduced by ecDNA," notes Corbo. "Perhaps pushing cancer cells to dial MYC up to a point where they can't handle the DNA damage, or blocking the molecular circuits that maintain these DNA rings so cells lose them altogether."

However, the authors caution that such ideas remain early-stage. "ecDNA is a double-edged sword—helpful for quick adaptation but costly to maintain," says Corbo. "The challenge is to tip that balance in favor of the patient."

Crucially, this work broadens our understanding of genomic plasticity—challenging the notion that the genome is always "fixed."

"We knew the tumor's surroundings could drive changes, but not that WNT signaling could so directly rewrite DNA," Bailey adds. "We assumed we'd see mostly epigenetic shifts, so seeing this level of genomic re-engineering was definitely a surprise."

And with pancreatic cancer cases projected to rise in the coming years, insights into ecDNA's role could guide future strategies to intercept or exploit this genetic feature—potentially making tumors more vulnerable to treatment.

More information: MYC ecDNA promotes intratumor heterogeneity and plasticity in PDAC, *Nature* (2025). DOI: [10.1038/s41586-025-08721-9](https://doi.org/10.1038/s41586-025-08721-9)

Journal information: [Nature](#)

Provided by [Champalimaud Centre for the Unknown](#)

MARCH 11, 2025

Microplastics could be fueling antibiotic resistance

by Jessica Colarossi, [Boston University](#)

Credit: Unsplash/CC0 Public Domain

Microplastics—tiny shards of plastic debris—are [all over the planet](#). They have made their way up food chains, accumulated in oceans, clustered in clouds and on mountains, and been found [inside human bodies](#) at alarming rates. Scientists have been racing to uncover the unforeseen impacts of so much plastic in and around us.

One possible, and surprising, consequence: more [drug-resistant bacteria](#).

In a startling discovery, a team of Boston University researchers found that bacteria exposed to microplastics became resistant to multiple types of antibiotics commonly used to treat infections. They say this is especially concerning for people in high-density, impoverished areas like refugee settlements, where discarded plastic piles up and bacterial infections spread easily.

The study is published in [Applied and Environmental Microbiology](#).

"The fact that there are microplastics all around us, and even more so in impoverished places where sanitation may be limited, is a striking part of this observation," says Muhammad Zaman, a Boston University College of Engineering professor of biomedical engineering who studies [antimicrobial resistance](#) and refugee and migrant health.

"There is certainly a concern that this could present a higher risk in communities that are disadvantaged, and only underscores the need for more vigilance and a deeper insight into [microplastic and bacterial] interactions."

It's estimated that there are [4.95 million deaths](#) associated with antimicrobial-resistant infections each year. Bacteria become resistant to antibiotics for many different reasons, including the misuse and overprescribing of medications, but a huge factor that fuels resistance is the microenvironment—the immediate surroundings of a microbe—where bacteria and viruses replicate.

In the Zaman Laboratory at BU, researchers rigorously tested how a common bacteria, *Escherichia coli* (E. coli), reacted to being in a closed environment with microplastics.

"The plastics provide a surface that the bacteria attach to and colonize," says Neila Gross (ENG), a BU Ph.D. candidate in [materials science](#) and engineering and lead author of the study. Once attached to any surface, bacteria create a biofilm—a sticky substance that acts like a shield, protecting the bacteria from invaders and keeping them affixed securely.

Even though bacteria can grow biofilms on any surface, Gross observed that the microplastic supercharged the bacterial biofilms so much that when antibiotics were added to the mix, the medicine was unable to penetrate the shield.

"We found that the biofilms on microplastics, compared to other surfaces like glass, are much stronger and thicker, like a house with a ton of insulation," Gross says. "It was staggering to see."

The rate of antibiotic resistance on the microplastic was so high compared to other materials, that she performed the experiments multiple times, testing different combinations of antibiotics and types of plastic material. Each time, the results remained consistent.

"We're demonstrating that the presence of plastics is doing a whole lot more than just providing a surface for the bacteria to stick to—they are actually leading to the development of resistant organisms," Zaman says. He directs BU's Center on Forced Displacement, which has a mission to improve the lives of displaced people around the world.

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Past research has found that refugees, [asylum seekers](#), and forcibly displaced populations are at an [increased risk](#) of contracting drug-resistant infections, due to living in overcrowded camps and having heightened barriers to receiving health care.

"Historically, people have associated antibiotic resistance with patient behavior, like not taking antibiotics as prescribed. But there is nothing a person has done to be forced to live in a particular environment, and the fact is they are at a higher exposure to resistant infections," Zaman says.

That's why the environmental and social causes of drug-resistant superbugs cannot be ignored, he says. As of 2024, there were an estimated [122 million displaced people worldwide](#). According to Zaman, the prevalence of microplastics could be adding another

element of risk to already underfunded, and understudied, health systems that serve refugees.

Gross and Zaman say that the next step in their research is to figure out if their findings in the lab translate to the outside world. They hope to begin studies with research partners overseas to watch refugee camps for [microplastic](#)-related antibiotic-resistant bacteria and viruses. They also aim to figure out the exact mechanisms that allow bacteria to hold such a strong grip on plastic.

"Plastics are highly adaptable," Gross says, and their molecular composition could help bacteria flourish—but it's unclear how that happens.

One theory, she says, is that plastics repel water and other liquids, which allow bacteria to easily attach themselves. But over time, the plastics start to take in moisture. That means it's possible for microplastics to absorb antibiotics before they reach the target bacteria. They also found that even when the microplastics were removed from the equation, the bacteria they once housed kept the ability to form stronger biofilms.

"Too often, these issues are viewed from a lens of politics or international relations or immigration, and all of those are important, but the story that is often missing is the basic science," Zaman says. "We hope that this paper can get more scientists, engineers, and more researchers to think about these questions."

More information: Effects of microplastic concentration, composition, and size on *Escherichia coli* biofilm- associated antimicrobial resistance, *Applied and Environmental Microbiology* (2025). DOI: [10.1128/aem.02282-24](https://doi.org/10.1128/aem.02282-24)

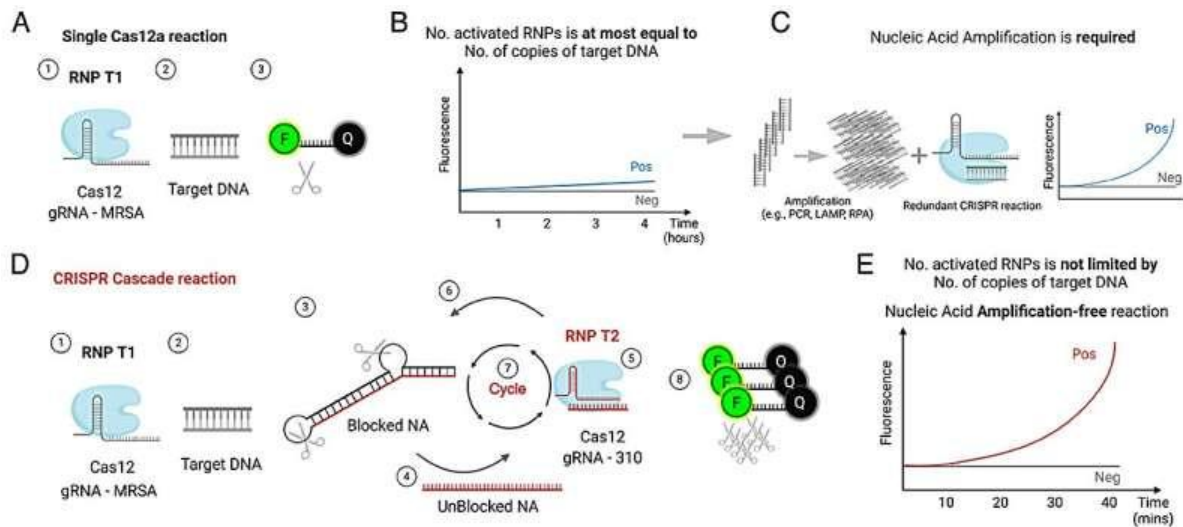
Journal information: [Applied and Environmental Microbiology](#)

Provided by [Boston University](#)

MARCH 13, 2025

CRISPR-Cascade test detects bloodstream infections in minutes without amplification

by Justin Jackson , Phys.org



CRISPR-Cascade reaction eliminating the need for pre-amplification. Credit: *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2420166122

University of Illinois at Urbana-Champaign researchers have developed a CRISPR-based diagnostic tool capable of detecting bloodstream infections in minutes without the need for nucleic acid amplification. The CRISPR-Cascade assay achieves attomolar sensitivity and incorporates an OR-gated logic function to identify multiple pathogens simultaneously through DNA from pathogens associated with bloodstream infections.

Bloodstream infections require rapid identification to prevent complications, yet standard diagnostic methods rely on [polymerase chain reaction](#) (PCR) and isothermal amplification techniques that have built-in processing times. CRISPR-based detection tools such as SHERLOCK and DETECTR have improved specificity but continue to depend on amplification, limiting their turnaround time and practicality in clinical settings.

In the study, "Amplification-free, OR-gated CRISPR-Cascade reaction for pathogen detection in blood samples," [published](#) in the *Proceedings of the National Academy of Sciences*, researchers conducted a laboratory-based investigation to determine whether a CRISPR-driven feedback loop could detect pathogenic DNA at ultra-low concentrations without amplification.

Their CRISPR-Cascade reaction utilizes two ribonucleoprotein complexes, T1 and T2, to achieve amplification-free detection of pathogenic DNA. Upon target recognition, Cas12a in the T1 complex cleaves blocked nucleic acids, triggering the release of switchable caged

RNA that activates more Cas12a enzymes in the T2 complex. This self-sustaining feedback loop enables rapid fluorescence-based detection at attomolar sensitivity within 10 minutes.

Optimizations in reaction temperature (33°C), steric hindrance strategies, and enzyme kinetics improved specificity and reduced nonspecific signal interference.

In testing, the assay successfully identified Methicillin-Sensitive *Staphylococcus aureus* (MSSA), Methicillin-Resistant *Staphylococcus aureus* (MRSA), *Escherichia coli* (E. coli), and Hepatitis B Virus in pathogen DNA-spiked [blood samples](#) within ten minutes. An OR-gated logic function enabled simultaneous detection of multiple pathogens in a single reaction, providing a rapid and scalable approach for clinical applications.

Comparisons with existing methods highlight the accelerated timeline. Traditional culturing with PCR can take 24–72 hours. PCR methods without culturing run for 3–6 hours. Rapid PCR-based methods exist that take around 1 hour.

CRISPR-Cascade, including sample preparation, requires about half an hour, making it the fastest available bloodstream infection diagnostic. There is also the potential to improve sample prep further and approach an under-15-minute mark. Potential applications include infectious disease diagnostics, point-of-care testing, and personalized medicine.

More information: Jongwon Lim et al, Amplification-free, OR-gated CRISPR-Cascade reaction for pathogen detection in blood samples, *Proceedings of the National Academy of Sciences* (2025). DOI: [10.1073/pnas.2420166122](https://doi.org/10.1073/pnas.2420166122)

Journal information: [Proceedings of the National Academy of Sciences](#)

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Scientists see the first steps of DNA unwinding

a DNA tracking strand

ATP

DNA fork nexus

N-tier

C-tier

DNA-J: A, B, C, D, E, F

Helicase domain: DNA-J (1-82), OBD (131-259), N-tier (266-355), C-tier (627-708)

b

3'-AGACCACATGG ATGTAGCGAACGATCACC

3'-GACGGACCTTAGGACTGCTGTACATCGCTTGTCTAGTGG

T₁, T₂, T₃, T₄, T₅

DNA binding loop staircase

Passive strand

Fork nexus

DNA binding loop

c

Tracking strand

Passive strand

P₀, P₁, P₂

R456, H513, K512

For the first time, scientists have witnessed the very moment DNA begins to unravel, revealing a necessary molecular event for DNA to be the molecule that codes all life. A new study from King Abdullah University of Science and Technology (KAUST), [published](#) in *Nature*, captures the moment DNA begins to unwind, allowing for all the events that follow in DNA replication.

Using [cryo-electron microscopy](#) and [deep learning](#) to observe the [helicase](#) Simian Virus 40 Large Tumor Antigen interacting with DNA, the laboratories of KAUST Assistant Professor Alfredo De Biasio and Professor Samir Hamdan provide the most detailed description yet of the very first steps of DNA replication: 15 atomic states that describe how the enzyme helicase forces the unwinding of DNA.

The achievement is not only a milestone in helicase research, but also a milestone in observing the dynamics of any enzyme at atomic resolution.

While scientists have long known the importance of helicase in DNA replication, "they did not know how DNA, helicases and ATP work together in a coordinated cycle to drive DNA unwinding," De Biasio said.

When Watson and Crick reported the [double helix](#) in 1953, they gave the scientific community a breakthrough understanding of how genetic information is stored and copied. For DNA to replicate, the helix must first unwind and break the DNA from a double strand into two single strands.

Upon binding, helicases melt the DNA, breaking the chemical bonds holding the double helix together. They then pull the two strands apart, allowing other enzymes to complete the replication. Without this first step, no DNA can be replicated. In this way, helicases are machines or, because of their size, nanomachines.

If helicases are nanomachines, then "ATP," or adenosine trisphosphate, is the fuel. Much like how burning gas drives the pistons of a car engine, burning ATP, the same fuel used to flex your muscles, causes the six pistons of a helicase to unwind DNA.

The study found that as ATP is consumed, it reduces physical constraints that allow the helicase to proceed along the DNA, unwinding more and more of the double strand. Thus, ATP consumption acts as a switch that increases the amount of entropy—or disorder—in the system, freeing the helicase to move along the DNA.

"The helicase uses ATP not to pry DNA apart in one motion, but to cycle through conformational changes that progressively destabilize and separate the strands. ATP burning, or hydrolysis, functions like the spring in a mouse trap, snapping the helicase forward and pulling the DNA strands apart," said De Biasio.

Among the many discoveries made by the KAUST scientists was that two helicases melt the DNA at two sites at the same time to initiate the unwinding. The chemistry of DNA is such that nanomachines move along a single DNA strand in one direction only. By binding at two sites simultaneously, the helicases coordinate so that the winding can happen in both directions with an energy efficiency unique to natural nanomachines.

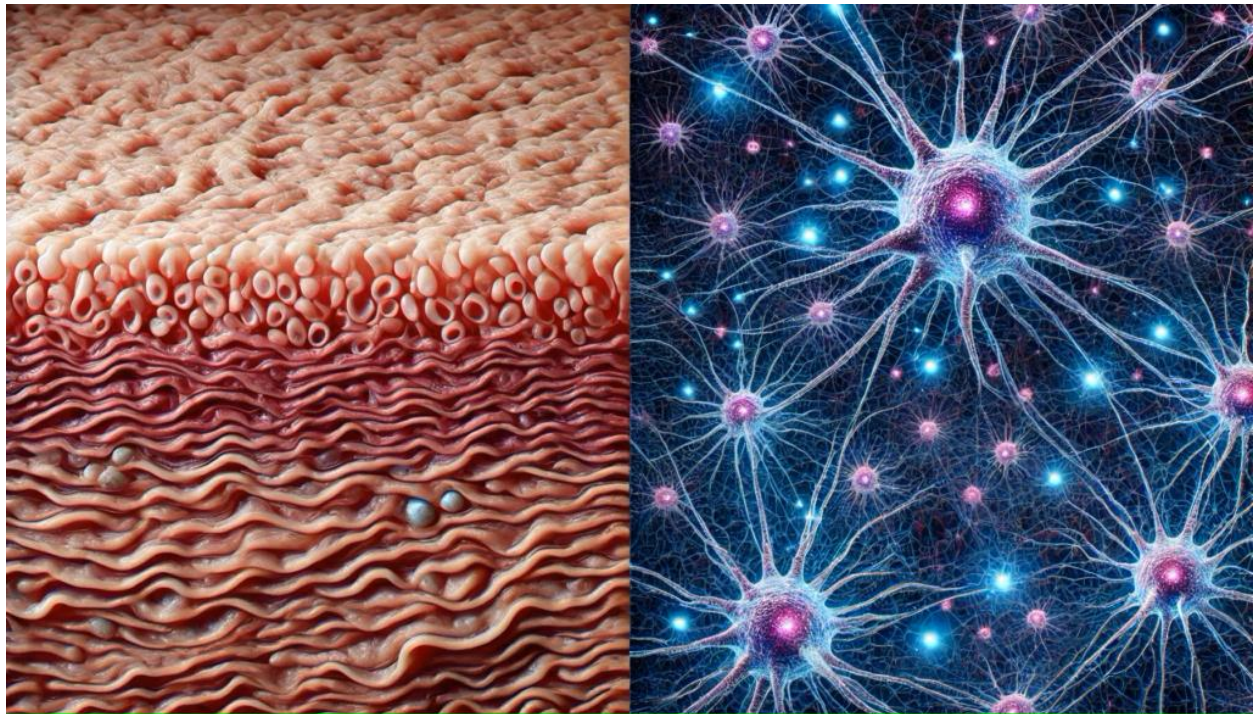
That efficiency, explains De Biasio, makes the study of DNA replication more than an attempt to answer the most fundamental scientific questions about life; it also makes helicases models for the design of new nanotechnology.

"From a design perspective, helicases exemplify energy-efficient mechanical systems. Engineered nanomachines using entropy switches could harness similar energy-efficient mechanisms to perform complex, force-driven tasks," he said.

More information: Taha Shahid et al, Structural dynamics of DNA unwinding by a replicative helicase, *Nature* (2025). DOI: [10.1038/s41586-025-08766-w](https://doi.org/10.1038/s41586-025-08766-w). www.nature.com/articles/s41586-025-08766-w

Engineers turn skin cells directly into neurons for cell therapy

MIT researchers achieved over 1,000% yield with their novel method that could lead to new therapies for spinal cord injuries or diseases.



From Massachusetts Institute of Technology 17/03/25 (first released 13/03/25)

Converting one type of cell to another — for example, a skin cell to a neuron — can be done through a process that requires the skin cell to be induced into a “pluripotent” stem cell, then differentiated into a neuron.

Researchers at MIT have now devised a simplified process that bypasses the stem cell stage, converting a skin cell directly into a neuron.

Working with mouse cells, the researchers developed a conversion method that is highly efficient and can produce more than 10 neurons from a single skin cell.

If replicated in human cells, this approach could enable the generation of large quantities of motor neurons, which could potentially be used to treat patients with spinal cord injuries or diseases that impair mobility.

“We were able to get to yields where we could ask questions about whether these cells can be viable candidates for the cell replacement therapies, which we hope they could be.”

“That’s where these types of reprogramming technologies can take us,” says Katie Galloway, the W. M. Keck Career Development Professor in Biomedical Engineering and Chemical Engineering.

As a first step toward developing these cells as a therapy, the researchers showed that they could generate motor neurons and engraft them into the brains of mice, where they integrated with host tissue.

Galloway is the senior author of two papers describing the new method, which appear today in *Cell Systems*.

MIT graduate student Nathan Wang is the lead author of both papers.

From skin to neurons

Nearly 20 years ago, scientists in Japan showed that by delivering four transcription factors to skin cells, they could coax them to become induced pluripotent stem cells (iPSCs).

Similar to embryonic stem cells, iPSCs can be differentiated into many other cell types.

This technique works well, but it takes several weeks, and many of the cells don’t end up fully transitioning to mature cell types.

“Oftentimes, one of the challenges in reprogramming is that cells can get stuck in intermediate states,” Galloway says.

“So, we’re using direct conversion, where instead of going through an iPSC intermediate, we’re going directly from a somatic cell to a motor neuron.”

Galloway’s research group and others have demonstrated this type of direct conversion before, but with very low yields — fewer than 1 percent.

In Galloway’s previous work, she used a combination of six transcription factors plus two other proteins that stimulate cell proliferation.

Each of those eight genes was delivered using a separate viral vector, making it difficult to ensure that each was expressed at the correct level in each cell.

In the first of the new Cell Systems papers, Galloway and her students reported a way to streamline the process so that skin cells can be converted to motor neurons using just three transcription factors, plus the two genes that drive cells into a highly proliferative state.

Using mouse cells, the researchers started with the original six transcription factors and experimented with dropping them out, one at a time, until they reached a combination of three — NGN2, ISL1, and LHX3 — that could successfully complete the conversion to neurons.

Once the number of genes was down to three, the researchers could use a single modified virus to deliver all three of them, allowing them to ensure that each cell expresses each gene at the correct levels.

Using a separate virus, the researchers also delivered genes encoding p53DD and a mutated version of HRAS.

These genes drive the skin cells to divide many times before they start converting to neurons, allowing for a much higher yield of neurons, about 1,100 percent.

“If you were to express the transcription factors at really high levels in nonproliferative cells, the reprogramming rates would be really low, but hyperproliferative cells are more receptive.”

“It’s like they’ve been potentiated for conversion, and then they become much more receptive to the levels of the transcription factors,” Galloway says.

The researchers also developed a slightly different combination of transcription factors that allowed them to perform the same direct conversion using human cells, but with a lower efficiency rate — between 10 and 30 percent, the researchers estimate.

This process takes about five weeks, which is slightly faster than converting the cells to iPSCs first and then turning them into neurons.

Implanting cells

Once the researchers identified the optimal combination of genes to deliver, they began working on the best ways to deliver them, which was the focus of the second Cell Systems paper.

They tried out three different delivery viruses and found that a retrovirus achieved the most efficient rate of conversion.

Reducing the density of cells grown in the dish also helped to improve the overall yield of motor neurons.

This optimized process, which takes about two weeks in mouse cells, achieved a yield of more than 1,000 percent.

Working with colleagues at Boston University, the researchers then tested whether these motor neurons could be successfully engrafted into mice.

They delivered the cells to a part of the brain known as the striatum, which is involved in motor control and other functions.

After two weeks, the researchers found that many of the neurons had survived and seemed to be forming connections with other brain cells.

When grown in a dish, these cells showed measurable electrical activity and calcium signaling, suggesting the ability to communicate with other neurons.

The researchers now hope to explore the possibility of implanting these neurons into the spinal cord.

The MIT team also hopes to increase the efficiency of this process for human cell conversion, which could allow for the generation of large

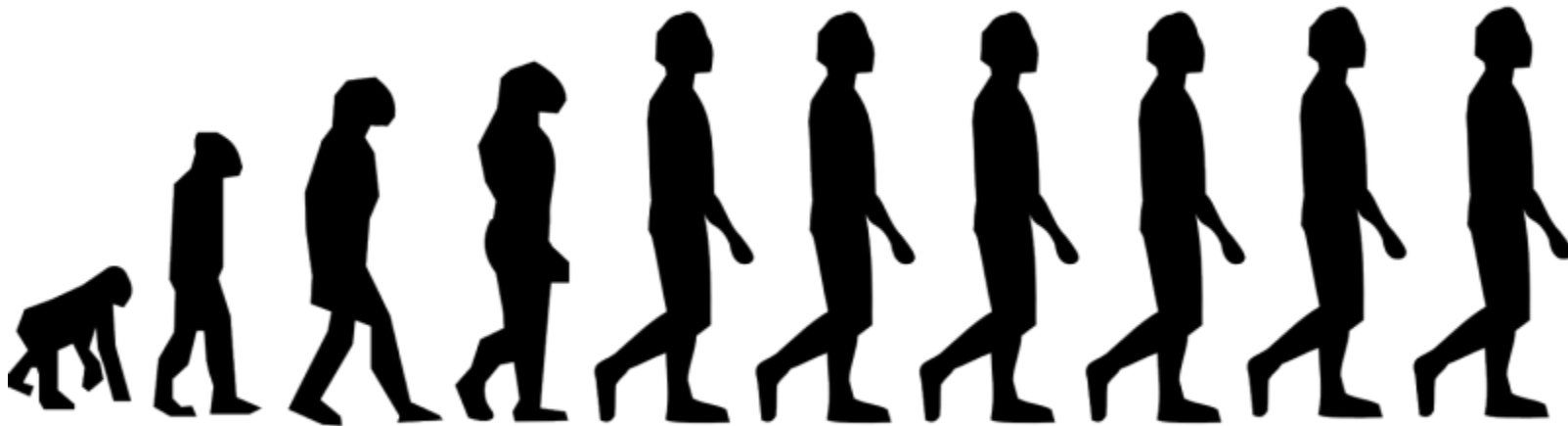
quantities of neurons that could be used to treat spinal cord injuries or diseases that affect motor control, such as ALS.

Clinical trials using neurons derived from iPSCs to treat ALS are now underway, but expanding the number of cells available for such treatments could make it easier to test and develop them for more widespread use in humans, Galloway says.

MARCH 18, 2025

Genetic study reveals hidden chapter in human evolution

by [University of Cambridge](#)



Credit: CC0 Public Domain

Modern humans descended from not one, but at least two ancestral populations that drifted apart and later reconnected, long before modern humans spread across the globe.

Using advanced analysis based on full genome sequences, researchers from the University of Cambridge have found evidence that [modern humans](#) are the result of a genetic mixing

event between two ancient populations that diverged around 1.5 million years ago. About 300,000 years ago, these groups came back together, with one group contributing 80% of the genetic makeup of modern humans and the other contributing 20%.

For the last two decades, the prevailing view in human evolutionary genetics has been that *Homo sapiens* first appeared in Africa around 200,000 to 300,000 years ago, and descended from a single lineage. However, these latest [results](#), reported in the journal *Nature Genetics*, suggest a more complex story.

"The question of where we come from is one that has fascinated humans for centuries," said first author Dr. Trevor Cousins from Cambridge's Department of Genetics. "For a long time, it's been assumed that we evolved from a single continuous ancestral lineage, but the exact details of our origins are uncertain."

"Our research shows clear signs that our evolutionary origins are more complex, involving different groups that developed separately for more than a million years, then came back to form the modern human species," said co-author Professor Richard Durbin, also from the Department of Genetics.

While earlier research has already shown that Neanderthals and Denisovans—two now-extinct human relatives—interbred with *Homo sapiens* around 50,000 years ago, this new research suggests that long before those interactions—around 300,000 years ago—a much more substantial genetic mixing took place.

Unlike Neanderthal DNA, which makes up roughly 2% of the genome of non-African modern humans, this ancient mixing event contributed as much as 10 times that amount and is found in all modern humans.

The team's method relied on analyzing modern human DNA, rather than extracting [genetic material](#) from ancient bones, and enabled them to infer the presence of ancestral populations that may have otherwise left no physical trace. The data used in the study are from the 1000 Genomes Project, a global initiative that sequenced DNA from populations across Africa, Asia, Europe, and the Americas.

The team developed a [computational algorithm](#) called cobraa that models how ancient human populations split apart and later merged back together. They tested the algorithm using simulated data and applied it to real human genetic data from the 1000 Genomes Project.

While the researchers were able to identify these two ancestral populations, they also identified some striking changes that happened after the two populations initially broke apart.

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"Immediately after the two ancestral populations split, we see a severe bottleneck in one of them—suggesting it shrank to a very small size before slowly growing over a period of one million years," said co-author Professor Aylwyn Scally, also from the Department of Genetics.

"This population would later contribute about 80% of the genetic material of modern humans, and also seems to have been the ancestral population from which Neanderthals and Denisovans diverged."

"However, some of the genes from the population which contributed a minority of our genetic material, particularly those related to brain function and neural processing, may have played a crucial role in human evolution," said Cousins.

The study also found that genes inherited from the second population were often located away from regions of the genome linked to gene functions, suggesting that they may have been less compatible with the majority genetic background. This hints at a process known as purifying selection, where natural selection removes harmful mutations over time.

Beyond human ancestry, the researchers say their method could help to transform how scientists study the evolution of other species. In addition to their analysis of human evolutionary history, they applied the cobraa model to genetic data from bats, dolphins, chimpanzees, and gorillas, finding evidence of ancestral population structure in some but not all of these.

"What's becoming clear is that the idea of species evolving in clean, distinct lineages is too simplistic," said Cousins. "Interbreeding and genetic exchange have likely played a major role in the emergence of new species repeatedly across the animal kingdom."

So who were our mysterious human ancestors? Fossil evidence suggests that species such as *Homo erectus* and *Homo heidelbergensis* lived both in Africa and other regions during this period, making them potential candidates for these ancestral populations, although more research (and perhaps more evidence) will be needed to identify which genetic ancestors corresponded to which fossil group.

Looking ahead, the team hopes to refine their model to account for more gradual genetic exchanges between populations, rather than sharp splits and reunions. They also plan to explore how their findings relate to other discoveries in anthropology, such as [fossil evidence](#) from Africa that suggests early humans may have been far more diverse than previously thought.

"The fact that we can reconstruct events from hundreds of thousands or millions of years ago just by looking at DNA today is astonishing," said Scally. "And it tells us that our history is far richer and more complex than we imagined."

More information: A structured coalescent model reveals deep ancestral structure shared by all modern humans, *Nature Genetics* (2025). DOI: [10.1038/s41588-025-02117-1](https://doi.org/10.1038/s41588-025-02117-1)

Journal information: [Nature Genetics](#)

Provided by [University of Cambridge](#)

MARCH 26, 2025

A breakthrough moment: Researchers discover new class of antibiotics

by [McMaster University](#)



A new class of antibiotics has been identified by McMaster University researchers. Credit: McMaster University

The last time a new class of antibiotics reached the market was nearly three decades ago—but that could soon change, thanks to a discovery by researchers at McMaster University.

A team led by researcher Gerry Wright has identified a strong candidate to challenge even some of the most drug-resistant bacteria on the planet: a [new molecule](#) called lariocidin. The findings were [published](#) in the journal *Nature* on March 26, 2025.

The discovery of the all-new class of antibiotics responds to a critical need for new antimicrobial medicines, as bacteria and other microorganisms evolve new ways to withstand existing drugs. This phenomenon is called antimicrobial resistance—or AMR—and it's one of the top global public health threats, according to the World Health Organization.

"Our old drugs are becoming less and less effective as bacteria become more and more resistant to them," explains Wright, a professor in McMaster's Department of Biochemistry and Biomedical Sciences and a researcher at the university's Michael G. DeGroote Institute for Infectious Disease Research. "About 4.5 million people die every year due to antibiotic-resistant infections, and it's only getting worse."

Wright and his team found that the new molecule, a lasso peptide, holds great promise as an early drug lead because it attacks bacteria in a way that's different from other antibiotics. Lariocidin binds directly to a bacterium's protein synthesis machinery in a completely new way, inhibiting its ability to grow and survive.

"This is a new molecule with a new mode of action," Wright says. "It's a big leap forward for us."

Lariocidin is produced by a type of bacteria called *Paenibacillus*, which the researchers retrieved from a soil sample collected from a Hamilton backyard.

The research team allowed the soil bacteria to grow in the lab for approximately one year—a method that helped reveal even the slow-growing species that could have otherwise been missed. One of these bacteria, *Paenibacillus*, was producing a new substance that had strong activity against other bacteria, including those typically resistant to antibiotics.

"When we figured out how this new molecule kills other bacteria, it was a breakthrough moment," says Manoj Jangra, a postdoctoral fellow in Wright's lab.

In addition to its unique mode of action and its activity against otherwise drug-resistant bacteria, the researchers are optimistic about lariocidin because it ticks a lot of the right boxes: it's not toxic to [human cells](#), it's not susceptible to existing mechanisms of antibiotic resistance, and it also works well in an animal model of infection.

Wright and his team are now laser-focused on finding ways to modify the molecule and produce it in quantities large enough to allow for clinical development. Wright says because this new molecule is produced by bacteria—and "[bacteria](#) aren't interested in making new drugs for us"—much time and resources are needed before lariocidin is ready for market.

"The initial discovery—the big a-ha! moment—was astounding for us, but now the real hard work begins," Wright says. "We're now working on ripping this molecule apart and putting it back together again to make it a better drug candidate."

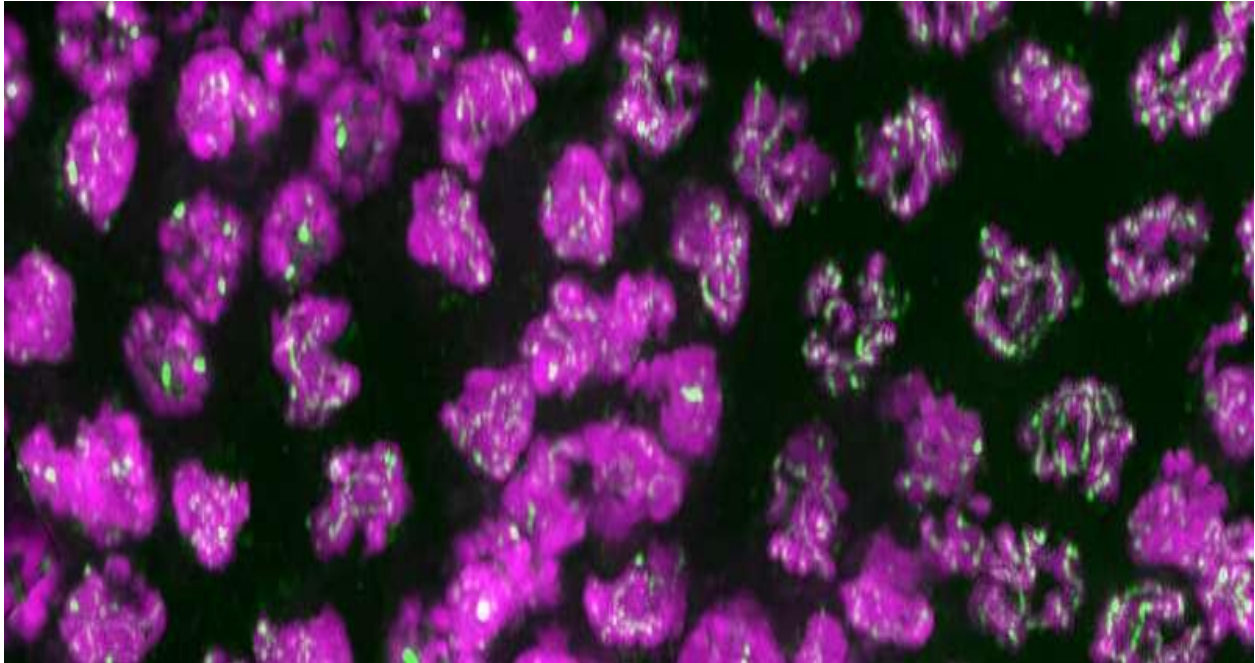
More information: Gerard Wright, A broad-spectrum lasso peptide antibiotic targeting the bacterial ribosome, *Nature* (2025). DOI: [10.1038/s41586-025-08723-7](https://doi.org/10.1038/s41586-025-08723-7). www.nature.com/articles/s41586-025-08723-7

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

APRIL 10, 2025

Cell biologists discover two proteins are key to proper transfer of genetic material

by [University of California - Santa Cruz](#)



PCH-2 (green) localizes to meiotic chromosomes (magenta) as they undergo meiotic crossover recombination. Credit: Bhalla Lab

The biological research of UC Santa Cruz's Needhi Bhalla to determine the molecular motions at the heart of heredity has yielded a new discovery: The proper transfer of genetic materials depends on two key proteins that choreograph the delicate dance between chromosomes when sexual-reproduction cells divide.

When cells split to create eggs and sperm, they must undergo a crucial process called "meiotic crossover recombination." This mechanism ensures that [genetic material](#) is properly shuffled between chromosomes, preventing errors that could lead to disorders such as miscarriages, infertility, birth defects, and even cancer.

This process also results in the endearing transfer of traits that parents see in their children. And beyond contributing to parental pride, Bhalla says meiotic crossover recombination is fundamental for human evolution by promoting [genetic diversity](#). That's why the identification of two specific proteins that play central roles in controlling how and where these crossovers happen is so significant.

"Thirty percent of miscarriages are because the embryo doesn't have the correct number of chromosomes," said Bhalla, a professor of molecular, cell, and developmental biology (MCD Bio). "Because meiotic crossover recombination is essential to get the right number of chromosomes, you'd think it was a stable and predictable process. But it's actually an incredibly delicate and responsive mechanism that is very heavily regulated to look straightforward."

Chromosomal crossing guards

Through [lab studies](#) on the roundworm *C. elegans*, Bhalla's team discovered that a protein known as PCH-2 plays an important role in regulating crossover events. While scientists have long recognized its importance, the protein's precise function hasn't been well understood.

The [new study](#), now published in *eLife*, shows that PCH-2 acts against crossover formation in a controlled manner at different stages of cell division. Initially, it limits the number of potential crossover sites, preventing an excessive number of crossovers from forming too early. Later, it ensures that at least some crossovers occur, a process known as crossover assurance, the researchers found.

As Bhalla explains, every cell undergoing the sexual-reproduction process of meiosis must make critical decisions regarding crossover events. Hundreds of potential crossover sites exist within a [single cell](#), but only a limited number become actual crossovers.

This [selection process](#) is crucial for maintaining genetic integrity. If crossovers fail to occur properly, essential genetic information can be lost, mutations can arise, or chromosomes can partition incorrectly—leading to dire consequences for the organism.

The study further revealed that PCH-2 interacts with another protein, HIM-3, which helps organize chromosomes during meiosis. Together, these proteins fine-tune the crossover process, ensuring both efficiency and accuracy.

"The placement of crossovers is just as crucial as their presence. If crossovers occur near the ends of chromosomes, they tend to be less stable than those positioned more internally," Bhalla said. "Our findings highlight the necessity of precise control over both crossover number and distribution."

Impact on human health

One of the most promising applications of this research is in the development of molecular diagnostics. Similar to how cancer diagnostics allow for early detection and treatment decisions, Bhalla said the discoveries her team made could pave the way for genetic tests that assess infertility risks or the likelihood of recurrent miscarriages.

Such a [diagnostic tool](#) could provide crucial information for patients and physicians, enabling them to explore fertility interventions such as in vitro fertilization, surrogacy, or other reproductive-assistance options.

"This intricate, highly regulated process ensures the successful continuation of life across generations," Bhalla said.

More information: Bhumi Patel et al, The conserved ATPase PCH-2 controls the number and distribution of crossovers by antagonizing their formation in *Caenorhabditis elegans*, *eLife* (2025). DOI: [10.7554/eLife.102409.3](https://doi.org/10.7554/eLife.102409.3)

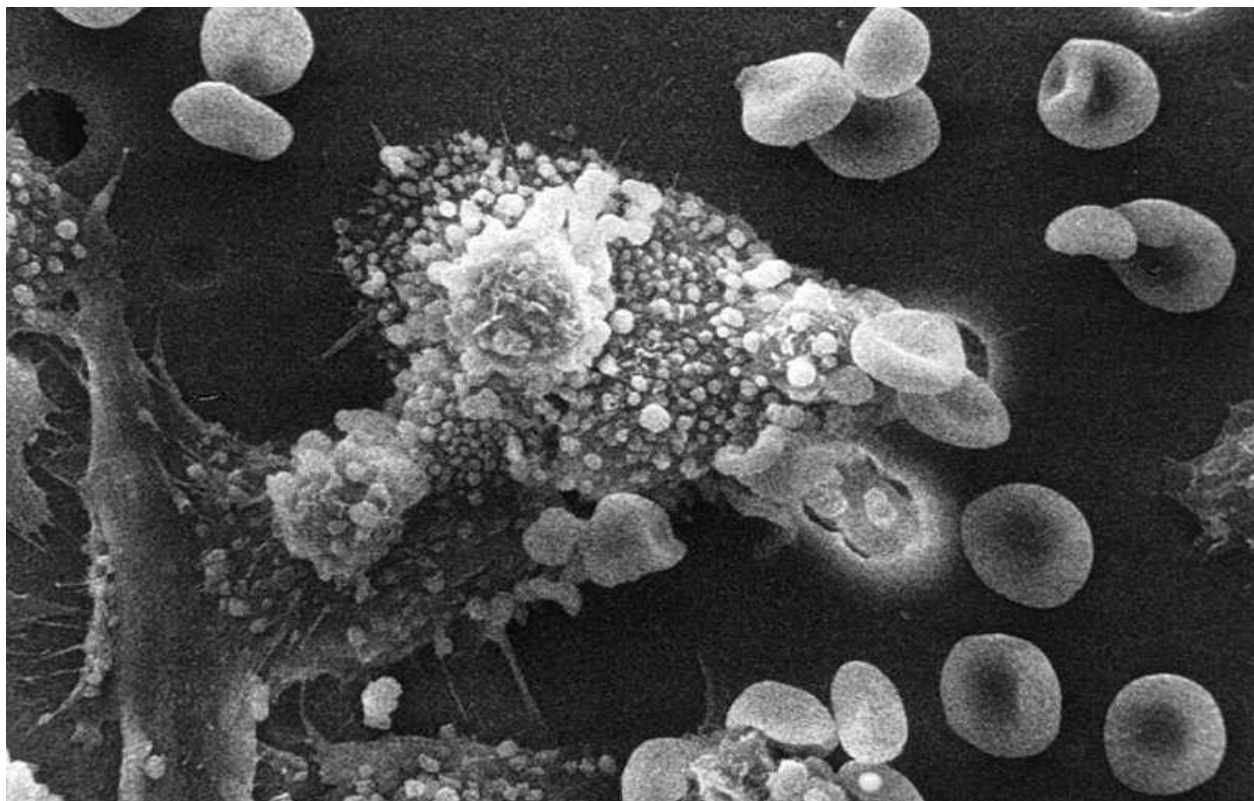
Journal information: [eLife](#)

Provided by [University of California - Santa Cruz](#)

APRIL 10, 2025

Master switch gene can turn immune cells into cancer eradicators

by [Weizmann Institute of Science](#)



Macrophages killing a cancer cell. Credit: Susan Arnold and Raowf Guirguis / National Cancer Institute

To grow, cancer tumors must hijack the immune system for their needs. One of the main tricks that most tumors use is to manipulate a type of immune cell called a macrophage, causing it to protect the tumor from the rest of the immune system, recruit blood vessels and help the cancer spread to other tissues.

Now researchers in Prof. Ido Amit's lab at the Weizmann Institute of Science have used state-of-the-art gene editing and single-cell and AI technologies to identify a master switch that turns macrophages into cancer helpers.

Based on this discovery, the team developed a new therapy that was shown to be effective in mice with bladder tumors, one of the most common types of cancer in humans and one for which only limited therapeutic innovations are currently available. The discovery is presented in a paper [published](#) in the journal *Cancer Cell*.

"Macrophages are highly versatile cells, sort of a 'Swiss knife' of the [immune system](#), capable of activating multiple types of functions for different tasks and in different situations," explains Amit, a faculty member of Weizmann's Systems Immunology Department.

These cells have the potential to be highly effective cancer eradicators that can perform multiple antitumor functions, such as promoting anticancer inflammation or alerting the rest of the immune system to the dangers posed by [tumor cells](#). That's precisely the reason most solid cancers need to convert macrophages to their side in order to develop.

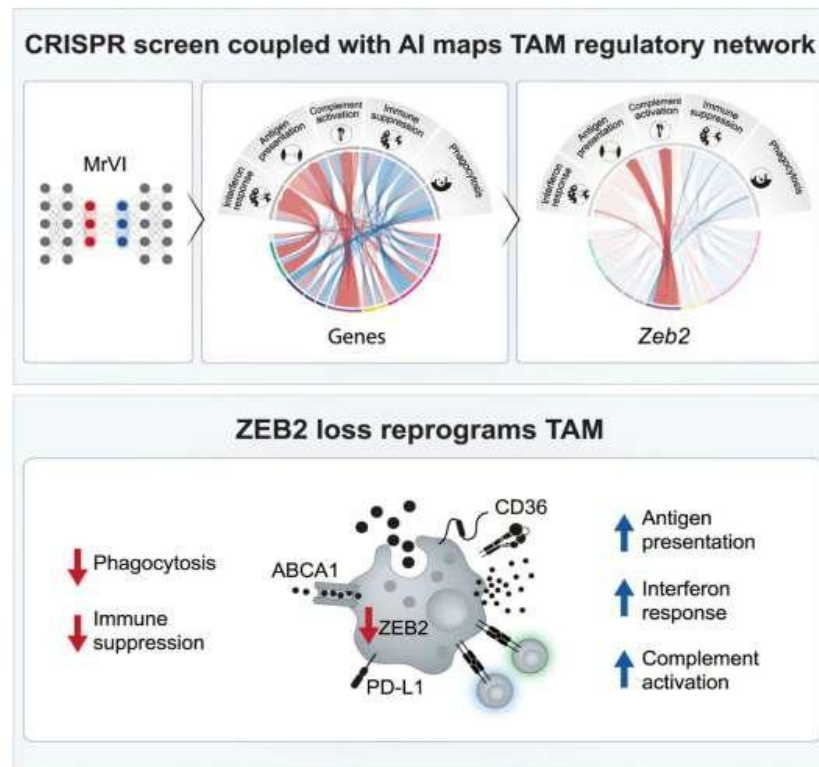
"By doing that, the tumors protect themselves from the macrophages' 'nasty' side, and also turn on macrophage functions that help them grow, such as suppressing the activity of other immune cell types and encouraging blood vessel growth for supplying oxygen to the tumor."

Indeed, recent studies have revealed a strong link between the activation mode of tumor macrophages—whether these cells fight the tumor or help it grow—and cancer patients' survival. Considering this significance, many studies have searched for ways to reprogram macrophages back to their anticancer mode.

"Those efforts failed because they separated macrophages into two very general categories—protumor and antitumor," Amit says. "Today we know that this categorization misses much of the complexity of macrophage function."

The new study, led by Dr. Fadi Sheban, took a more nuanced approach to analyzing macrophage functions. "We started the research by analyzing datasets of macrophages from human tumor samples and looking at the many different functions of these cells," Sheban says. "This analysis enabled us to identify 120 genes suspected of playing a role in activating the macrophages' various protumor functions."

The next step was to develop a system capable of screening these 120 potential role-playing genes to identify the genes that are most important for the tumor's ability to hijack macrophage activity. Amit and the team relied on their advanced single-cell technologies, capable of studying cellular function at single-cell resolution, in combination with CRISPR-Cas9 gene editing.



Credit: *Cancer Cell* (2025). DOI: 10.1016/j.ccell.2025.03.021

The combined technology provided them with the ability to delete individual macrophage genes in a single macrophage, one by one, from the list of suspected genes and see how this changed the properties and function of the macrophage at single-cell resolution.

"Using our newly developed platform, we were able to study the effects of all 120 suspected genes on the function of individual macrophage cells. This phase of the study included sequencing over 100,000 edited macrophage cells in total," says Sheban.

The result was a detailed dataset of how the different regulatory switches activate or deactivate various macrophage functions. "It was a complete mess. At first, we couldn't tell which genes were the most important ones and which macrophage activity they controlled," recalls Sheban.

To make sense of the empirical data, Amit and the team used a deep learning tool developed by departmental colleague Prof. Nir Yosef. The tool, called MrVI, simplified the data into a functional map showing both how the different regulatory switches, each represented as a point on the map, influence macrophage functions and how similar the effects of the various regulators are to one another.

"Using MrVI, we were able to understand which gene deletions changed the functions of the macrophages in a way that made them fight the tumor," says Sheban.

One gene, called Zeb2, stood out on the map, as it completely modified the macrophages' tumor-supporting activities. This gene had never been studied in tumor macrophages

before. "We understood that a macrophage with a Zeb2 activates all the protumor functions and deactivates all the antitumor programs, and that silencing this gene achieves the exact opposite," adds Sheban. "In other words, we found the master switch for reprogramming macrophages so that they will fight cancer."

More in-depth research into the gene showed that the protein encoded by Zeb2 works by changing the physical structure of the genome, known as the epigenome, thereby determining which other genes will be "open," that is, available for translation into proteins, and which will be inactive, or "closed." "Zeb2 opens all the protumor genes in the macrophages and closes all the antitumor [genes](#). By removing it, we can obtain the opposite effect," says Sheban.

Experiments conducted in tissue culture and in mice showed that silencing Zeb2 converts macrophages into the antitumor mode. "We also did another analysis of data from human patients and found that patients with a high expression of Zeb2 are at a much higher risk of having more aggressive cancer."

The next step was to try to turn this discovery into a potential therapy. To do so, Amit and the team collaborated with Prof. Marcin Kortylewski from the City of Hope National Medical Center in California, U.S., who developed a unique DNA molecule designed to attach itself to macrophages and be swallowed by them.

"We used this molecule as bait and connected it to a small silencing RNA molecule. Once swallowed by the macrophage, the RNA molecule silences the Zeb2 gene specifically," explains Sheban. The researchers used this newly developed molecule to treat mice with bladder cancer: They injected the molecule into the tumor area and found that the therapy reprogrammed the macrophages to fight the tumor, and that the tumors shrank significantly.

"Now the goal is to develop this approach into a novel cancer treatment for humans," summarizes Amit. "Our study has also demonstrated how advanced technologies can provide an in-depth, high-resolution understanding of the way various immune system players function in different diseases, and how this understanding has the potential to become the foundation of new therapies for patients."

More information: ZEB2 is a Master Switch Controlling the Tumor-Associated Macrophage Program, *Cancer Cell* (2025). DOI: [10.1016/j.ccell.2025.03.021](https://doi.org/10.1016/j.ccell.2025.03.021). [www.cell.com/cancer-cell/fulltext/S1535-6108\(25\)00122-9](https://www.cell.com/cancer-cell/fulltext/S1535-6108(25)00122-9)

Journal information: *Cancer Cell*

Provided by [Weizmann Institute of Science](#)

Beyond the Double Helix: Strange New DNA Structures Discovered in Ape Genomes

BY PENN STATEMAY 16, 2025



Scientists have uncovered the locations of mysterious DNA shapes across great ape genomes, potentially reshaping our understanding of genetic function and evolution. **Researchers utilized recently published telomere-to-telomere genomes of humans, chimpanzees, bonobos, gorillas, and two orangutans to predict where DNA sequences might form alternative structures beyond the traditional double helix.**

Certain DNA sequences can adopt structures that differ from the familiar double helix. These alternative conformations, known as non-B DNA, have been linked to the regulation of cellular processes and genome evolution. However, because non-B DNA often occurs in repetitive regions of the genome, it has historically been difficult to accurately read and assemble their sequences.

Now, a research team led by biologists at Penn State has made significant progress by systematically predicting the locations of non-B DNA structures across the genomes of

great apes. This marks a critical first step toward understanding the roles these structures play in biological function and evolution. Non-B DNA has already been associated with genetic diseases and cancer.

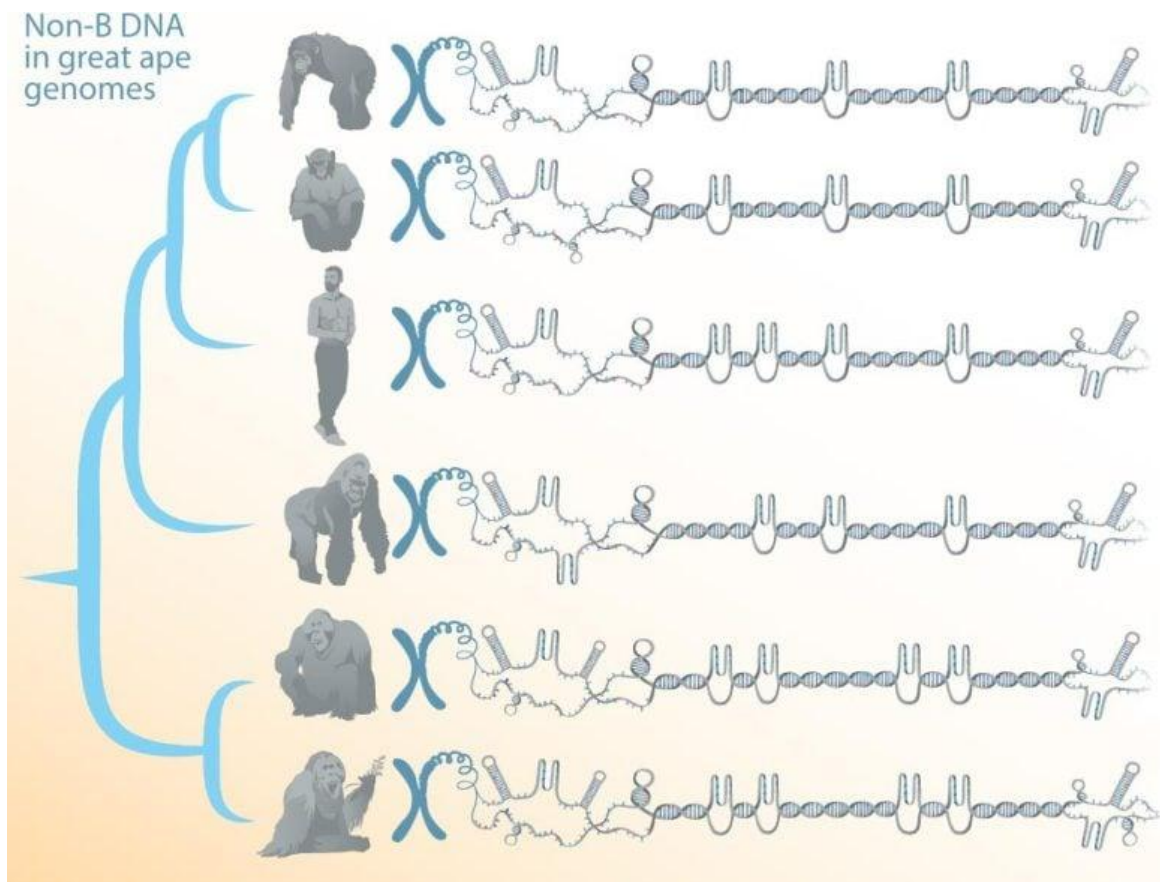
This breakthrough was made possible by recently completed telomere-to-telomere (T2T) genome assemblies, which provide complete, gap-free sequences for humans and other great apes. These assemblies overcome previous limitations caused by highly repetitive DNA regions. The new study, published in *Nucleic Acids Research*, reveals that non-B DNA structures are enriched in the newly sequenced genomic regions and points to potential previously unknown functions.

“When the human genome was first published in 2001, it actually wasn’t complete,” said Kateryna Makova, Verne M. Willaman Chair of Life Sciences, professor of biology at Penn State and the leader of the research team. “About 8% of the genome, largely repetitive DNA, was left undetermined because the available technology and computational algorithms were unable to reconstruct these regions. In 2022 and [2023](#), a massive effort by the [Telomere-to-Telomere consortium](#) filled in these gaps for the human genome, and this year, [we did the same for all the great apes](#).”

The Challenge of Repetitive DNA

For most genomes that have been sequenced, researchers used short-read DNA sequencing technologies. These techniques work by first breaking genomes into millions of tiny segments, which can be sequenced and then must be painstakingly reassembled like the world’s most complicated jigsaw puzzle.

“Much of the genome is made up of repetitive DNA, which could take the form of hundreds or even thousands of copies of the same short sequence back-to-back along a chromosome,” said Linnéa Smeds, a postdoctoral researcher in biology at Penn State and the first author of the paper. “This is a problem for assembling genomes from short reads, because there are so many puzzle pieces that look the same. The T2T genomes overcome this using new long-read sequencing technologies, allowing us to sequence the genomes in fewer longer segments. This way we can explore these regions for interesting functional elements, like non-B DNA, for the first time.”



New research predicts the location of DNA sequences that can form structures besides the canonical double helix — non-B DNA — in the recently released telomere-to-telomere genomes of the great apes, finding that non-B DNA is enriched in newly deciphered genomic regions, including telomeres and centromeres. Image shows evolutionary relationships among the great apes (left) including chimpanzee, bonobo, human, gorilla, and two orangutan species (from top to bottom), and illustrations of representative chromosomes (right) with canonical helical and non-B DNA. Credit: Dani Zemba and Makova laboratory, Penn State

Non-B DNA can take many forms, including bent DNA, hairpins, G-quadruplexes (G4s), and Z-DNA based on certain sequence motifs, which tend to be repetitive. These structures have recently been implicated in several cellular processes, such as DNA replication initiation during cell division, gene expression regulation, and the function of telomeres — the caps at the ends of chromosomes — and centromeres, chromosomal structures that play a crucial role during cell division.

The research team searched the T2T genomes for these sequence motifs to identify all potential non-B forming regions in the genomes of human, chimpanzee, bonobo, gorilla, two orangutan species and siamang, a lesser ape used as an outgroup.

A Genome-Wide View of Structural Motifs

“We now have a complete picture of the motifs that are prone to non-B DNA formation for these genomes,” Smeds said.

The research team found that newly deciphered sequences in the genomes are enriched for non-B motifs and that the patterns of non-B DNA distribution were largely similar across the ape species. The gorilla genome, known to have a higher percentage of repetitive DNA, also contained a higher number of potential non-B DNA motifs.

Non-B DNA also tends to have higher mutation rates and can be unstable, which could lead to DNA breakpoints and allow for chromosomal rearrangements, which the researchers suggested may be important for genome evolution and in certain genetic disorders.

“Recently, a type of repetitive DNA, known as satellite DNA, was shown to be the breakpoint of a translocation of chromosome 21 that is associated with one type of Down Syndrome,” Smeds said. “We found motifs for Z-DNA, a type of non-B DNA, to be 97 times more frequent in this region than the rest of the genome, which could indicate a role of non-B DNA in these types of chromosomal rearrangements, but additional research would be required to validate this relationship.”

Analyzing only a small number of motifs for now, the researchers experimentally confirmed that non-B DNA structures actually form but emphasized that the vast majority will require additional confirmation.

“The formation of non-B DNA structures at a given motif is almost certainly going to be context-dependent,” Makova said. “It could depend on cell type, developmental stage, and genomic context, including DNA modifications like methylation. There has been a recent shift in how we think about the function of the genome to go beyond sequence to include structure. We hope our study will serve as a springboard for additional studies of the function of these novel structural characteristics in the genome.”

Reference: “Non-canonical DNA in human and other ape telomere-to-telomere genomes” by Linnéa Smeds, Kaivan Kamali, Iva Kejnovská, Eduard Kejnovský, Francesca Chiaromonte and Kateryna D Makova, 14 April 2025, *Nucleic Acids Research*.

[DOI: 10.1093/nar/gkaf298](https://doi.org/10.1093/nar/gkaf298)

In addition to Makova and Smeds, the research team includes Kaivan Kamali, computer scientist at Penn State at the time of the study; Francesca Chiaromonte, Dorothy Foehr Huck and J. Lloyd Huck Chair in Statistics for the Life Sciences and professor of statistics at Penn State; and Iva Kejnovská and Eduard Kejnovský at the Institute of Biophysics of the Czech Academy of Sciences. The U.S. National Institute of General Medical Sciences and the Grantová Agentura České Republiky funded the research.

The Telomere-to-Telomere (T2T) consortium is an open, community-based effort to generate the first complete assembly of a human genome.

Release of the first human genome assembly was a landmark achievement, and after nearly two decades of improvements, the current human reference genome (GRCh38) is the most accurate and complete vertebrate genome ever produced. However, no one chromosome has yet been finished end to end, and hundreds of gaps persist across the genome.

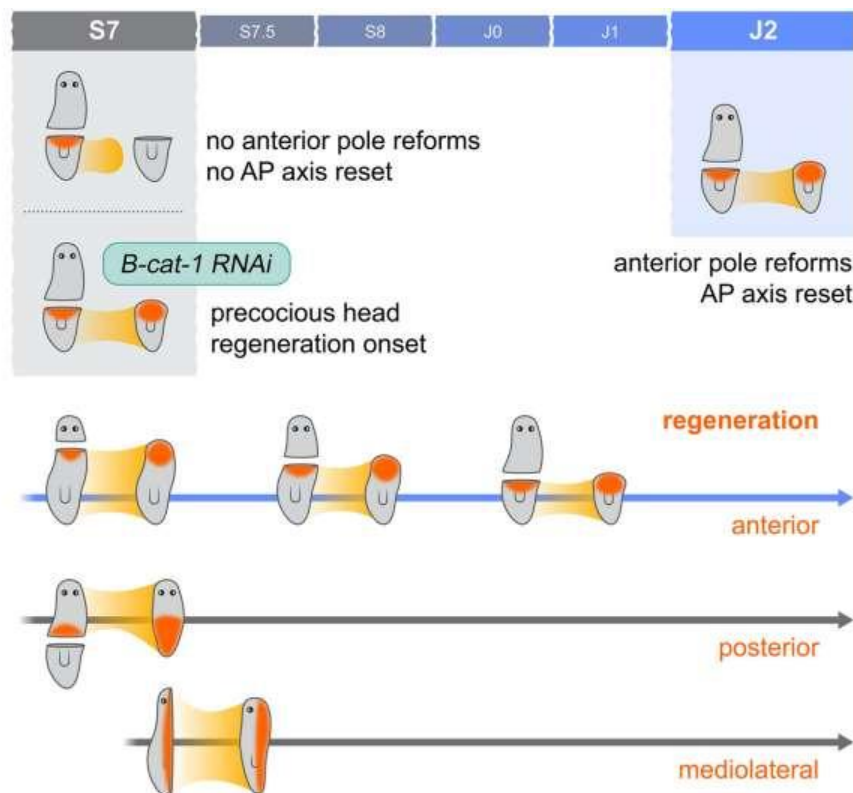
These unresolved regions include segmental duplications, ribosomal rRNA gene arrays, and satellite arrays that harbor unexplored variation of unknown consequence.

We aim to finish these remaining regions and generate the first truly complete assembly of a human genome. The ultimate goal of this effort is to drive technology to dramatically increase the throughput of complete, high quality telomere-to-telomere assemblies from diploid human genomes.

APRIL 23, 2025

Stem cells need positional signals to drive regeneration, flatworm study reveals

by Justin Jackson , Phys.org



Establishment of whole-body regeneration competence during *S. polychroa* development. Credit: *Current Biology* (2025). DOI: 10.1016/j.cub.2025.03.065

Scientists at the National Cancer Institute and partnering institutions have discovered that *Schmidtea polychroa*, a flatworm capable of regenerating lost tissue, develops this ability progressively during early life stages. Whole-body regeneration emerges during specific embryonic and juvenile stages, with head regeneration limited until the organism gains the capacity to reset its body's main axis. Stem-like cells are necessary for tissue growth yet insufficient on their own to trigger full regeneration.

Regeneration encompasses biological processes that replace tissues during normal maintenance or after injury. Some aquatic invertebrates such as hydrozoans, planarians, and acoels can regenerate entire bodies from mere tissue fragments. Certain fish, amphibians, and reptiles can regrow lost appendages.

Regenerative abilities change throughout an organism's life. In many species, embryos and juveniles regenerate more readily than adults. Aging has been associated with reduced regeneration in structures such as the mouse heart and digit tip, *Xenopus* limbs and tail, and *Drosophila* imaginal disks.

Even highly regenerative animals like tunicates and sponges show reduced ability as they age. These changes have been linked to stem cell exhaustion, loss of cellular plasticity, epigenetic alterations, and metabolic shifts. Gains in regenerative ability during adulthood have also been observed in sponges, crinoids, ctenophores, annelids, tunicates, and some vertebrates such as *Xenopus* tadpoles and certain lizards.

Planarian flatworms retain whole-body regenerative capacity into adulthood. Their regenerative ability depends on adult pluripotent stem cells, called neoblasts, which are distributed throughout the body. Neoblasts respond to injury through position-specific signaling from surrounding tissues and generate new tissues during maintenance, asexual reproduction, and regeneration.

In the study, "Developmental onset of planarian whole-body regeneration depends on axis reset," [published](#) in *Current Biology*, researchers conducted a developmental analysis to determine when and how regeneration competence emerges in the flatworm *Schmidtea polychroa*.

Staged embryos and juveniles of *S. polychroa* were bisected along the anterior-posterior axis to test regeneration at defined developmental stages. Anterior and posterior fragments were assessed for their ability to regenerate missing tissues.

Gene expression was tracked using in situ hybridization, a labeling method that binds to RNA transcripts to show where genes are active. Tissue samples were prepared using whole-mount microscopy techniques to preserve spatial context.

Irradiation was applied to identify whether regenerative ability depended on radiation-sensitive progenitor cells. Knockdown experiments using RNA interference targeted Wnt signaling components to test axis reset mechanisms.

Whole-body regeneration developed progressively during late embryonic and early juvenile stages. Posterior tissues regenerated from anterior fragments at earlier stages, while regeneration of head structures from posterior fragments was delayed until after hatching.

Stage-dependent recovery of head regeneration was associated with the capacity to reset the body's anterior-posterior axis. Irradiation-sensitive cells were necessary but not sufficient for regeneration alone. Knockdown of the Wnt pathway effector β -catenin-1 restored head regeneration in otherwise non-competent fragments.

Results reveal that whole-body regeneration is not an inherent, default property of possessing stem cells but instead depends on developmental cues that enable axis reset. The ability to regenerate a head only emerged after embryos gained competence to reset anterior-posterior polarity. Fragments containing functional progenitor cells still failed to regenerate unless specific polarity signals were activated.

Axis reset emerges as a critical gatekeeper in whole-body regeneration, with direct manipulation of signaling pathways enabling regeneration in fragments previously unable to recover. Findings point to regeneration as a conditional capability, one that may be switched on or off depending on developmental state and molecular context.

Broader strategies to induce regeneration in less regenerative animals may require restoring not just stem cell presence, but also the injury-induced cues that trigger polarity establishment and tissue identity. Results may challenge assumptions that regenerative loss is irreversible and suggest new targets for restoring tissue-forming potential.

Mammals, including humans, have limited regenerative capacity and are restricted to replacing select tissues and cell types.

Repair in mammals often proceeds through scarring, a process that rapidly seals wounds without restoring original tissue architecture. This may reflect an evolutionary trade-off in larger or more complex organisms, where fast tissue sealing through fibrosis can ensure immediate survival, even at the cost of long-term function or structural integrity.

Greater understanding of the requirements for [regeneration](#) in worms and other regenerating species brings science closer to the goal of one day reverse-engineering regenerative responses in therapeutic settings.

More information: Clare L.T. Booth et al, Developmental onset of planarian whole-body regeneration depends on axis reset, *Current Biology* (2025). DOI: [10.1016/j.cub.2025.03.065](https://doi.org/10.1016/j.cub.2025.03.065)

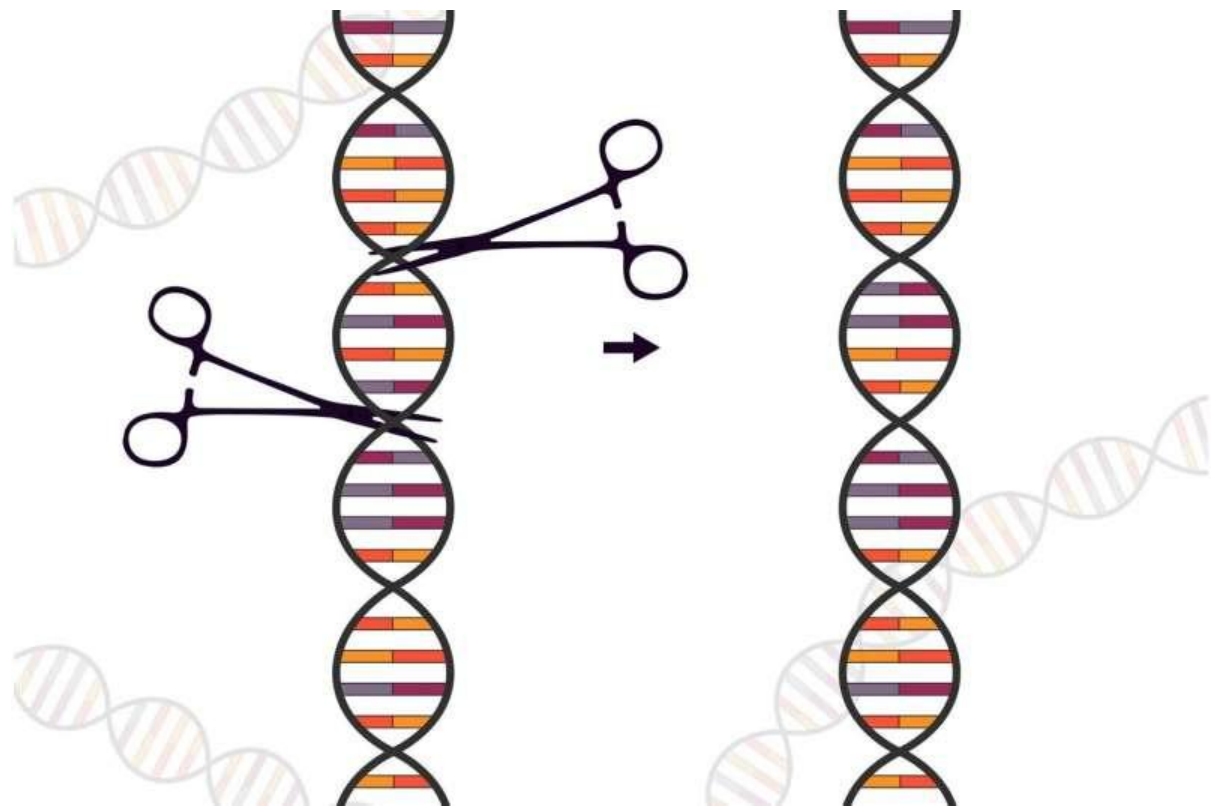
Journal information: [Current Biology](#)

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APRIL 23, 2025

Engineering 'bespoke enzymes': Machine learning expands CRISPR toolbox

by [Mass General Brigham](#)



Credit: Pixabay/CC0 Public Domain

Genome editing has advanced at a rapid pace with promising results for treating genetic conditions—but there is always room for improvement. A new paper by investigators from Mass General Brigham showcases the power of scalable protein engineering combined with machine learning to boost progress in the field of gene and cell therapy.

In their study, the authors developed a machine learning algorithm—known as PAMmla—that can predict the properties of approximately 64 million [genome-editing](#) enzymes. The work could help reduce off-target effects and improve editing safety, enhance editing efficiency, and enable researchers to predict customized enzymes for new therapeutic targets. The results are [published](#) in *Nature*.

"Our study is a first step in dramatically expanding our repertoire of effective and safe CRISPR-Cas9 enzymes. In our manuscript, we demonstrate the utility of these PAMmla-predicted enzymes to precisely edit disease-causing sequences in primary [human cells](#) and in mice," said corresponding author Ben Kleinstiver, Ph.D., Kayden-Lambert MGH Research Scholar associate investigator at Massachusetts General Hospital (MGH).

"Building on these findings, we are excited to have these tools utilized by the community and also apply this framework to other properties and enzymes in the genome editing repertoire."

CRISPR-Cas9 enzymes can be used to edit genes at locations throughout the genome, but there are limitations to this technology. Traditional CRISPR-Cas9 enzymes can have off-target effects, cleaving or otherwise modifying DNA at unintended sites in the genome. The newly published study aims to improve this by using machine learning to better predict and tailor enzymes to hit their targets with greater specificity.

The approach also offers a scalable solution. Other attempts at engineering enzymes have had a lower throughput and typically yielded enzymes in quantities that were lower by orders of magnitude.

One of the key elements of utilizing CRISPR-Cas9 technologies is that the enzymes must locate and bind to a short DNA sequence called a protospacer adjacent motif (PAM). Researchers used machine learning to predict the PAMs of millions of Cas9 enzymes, identifying a set of novel engineered Cas9 enzymes that would have the best on-target activity and specificity. The researchers conducted proof-of-concept experiments in human cells and a mouse model of retinitis pigmentosa, finding that the bespoke enzymes had greater specificity.

"A major outcome of this work is the creation of this PAMmla model that can now be used by researchers to predict customized enzymes that are uniquely tuned for their specific use cases," said lead author Rachel A. Silverstein, Ph.D. candidate, NSERC postgraduate scholar and 2024 Albert J. Ryan Fellow in the Kleinstiver lab at MGH.

"The result of this model is that we now have an enormous toolbox of safe and precise Cas9 proteins that can be utilized for a variety of research and therapeutic applications."

More information: Michael Wheeler, Psychedelic control of neuroimmune interactions governing fear, *Nature* (2025). DOI: [10.1038/s41586-025-08880-9](https://doi.org/10.1038/s41586-025-08880-9). www.nature.com/articles/s41586-025-08880-9

The researchers have made a web tool to allow others to use the PAMmla model, which is available at pammla.streamlit.app/

Journal information: *Nature*

Provided by [Mass General Brigham](#)

This baby boy was treated with the first personalized gene-editing drug

The one-off treatment highlights the promise of a new type of gene editing and the challenges of using it to treat extremely rare genetic diseases.

May 15, 2025



KJ Muldoon, a baby treated with a personalized gene-editing drug, relaxes with his parents and siblings. CHILDREN'S HOSPITAL OF PHILADELPHIA

Doctors say they constructed a bespoke gene-editing treatment in less than seven months and used it to treat a baby with a deadly metabolic condition.

The rapid-fire attempt to rewrite the child's DNA marks the first time gene editing has been tailored to treat a single individual, according to [a report](#) published in the *New England Journal of Medicine*.

The baby who was treated, Kyle “KJ” Muldoon Jr., suffers from a rare metabolic condition caused by a particularly unusual gene misspelling.

Researchers say their attempt to correct the error demonstrates the high level of precision new types of gene editors offer.

“I don’t think I’m exaggerating when I say that this is the future of medicine,” says Kiran Musunuru, an expert in gene editing at the University of Pennsylvania whose team designed the drug. “My hope is that someday no rare-disease patients will die prematurely from misspellings in their genes, because we’ll be able to correct them.”

The project also highlights what some experts are calling a growing crisis in gene-editing technology. That’s because even though the technology could cure thousands of genetic conditions, most are so rare that companies could never recoup the costs of developing a treatment for them.

In KJ’s case, the treatment was programmed to correct a single letter of DNA in his cells.

“In reality, this drug will probably never be used again,” says Rebecca Ahrens-Nicklas, a physician at the Children’s Hospital of Philadelphia, who treats metabolic diseases in children and who led the overall effort to treat the child.

That effort involved more than 45 scientists and doctors as well as pro bono assistance from several biotechnology companies. Musunuru says he cannot estimate how much it cost in time and effort.

Eventually, he says, the cost of custom gene-editing treatments might be similar to that of liver transplants, which is around \$800,000, not including lifelong medical care and drugs.

The researchers used a new version of CRISPR technology, called base editing, that can replace a single letter of DNA at a specific location.

Previous versions of CRISPR have generally been used to delete genes, not rewrite them to restore their function.

The researchers say they were looking for a patient to treat when they learned about KJ. After he was born in August, a doctor noted that the infant was lethargic. Tests found he had a metabolic disorder that leads to the buildup of ammonia, a condition that’s frequently fatal without a liver transplant.

CRISPR will get easier and easier to administer. What does that mean for the future of our species?

In KJ’s case, gene sequencing showed that the cause was a misspelled letter in the gene CPS1 that stopped it from making a vital enzyme.

The researchers approached KJ's parents, Nicole and Kyle Muldoon, with the idea of using gene editing to try to correct their baby's DNA. After they agreed, a race ensued to design the editing drug, test it in animals, and get permission from the US Food and Drug Administration to treat KJ in a one-off experiment.

The team says the boy, who hasn't turned one yet, received three doses of the gene-editing treatment, of gradually increasing strength. They can't yet determine exactly how well the gene editor worked because they don't want to take a liver biopsy, which would be needed to check if KJ's genes have really been corrected.

But Ahrens-Nicklas says that because the child is "growing and thriving," she thinks the editing has been at least partly successful and that he may now have "a milder form of this horrific disease."

"He's received three doses of the therapy without any complications, and is showing some early signs of benefit," she says. "It's really important to say that it's still very early, so we will need to continue to watch KJ closely to fully understand the full effects of this therapy."

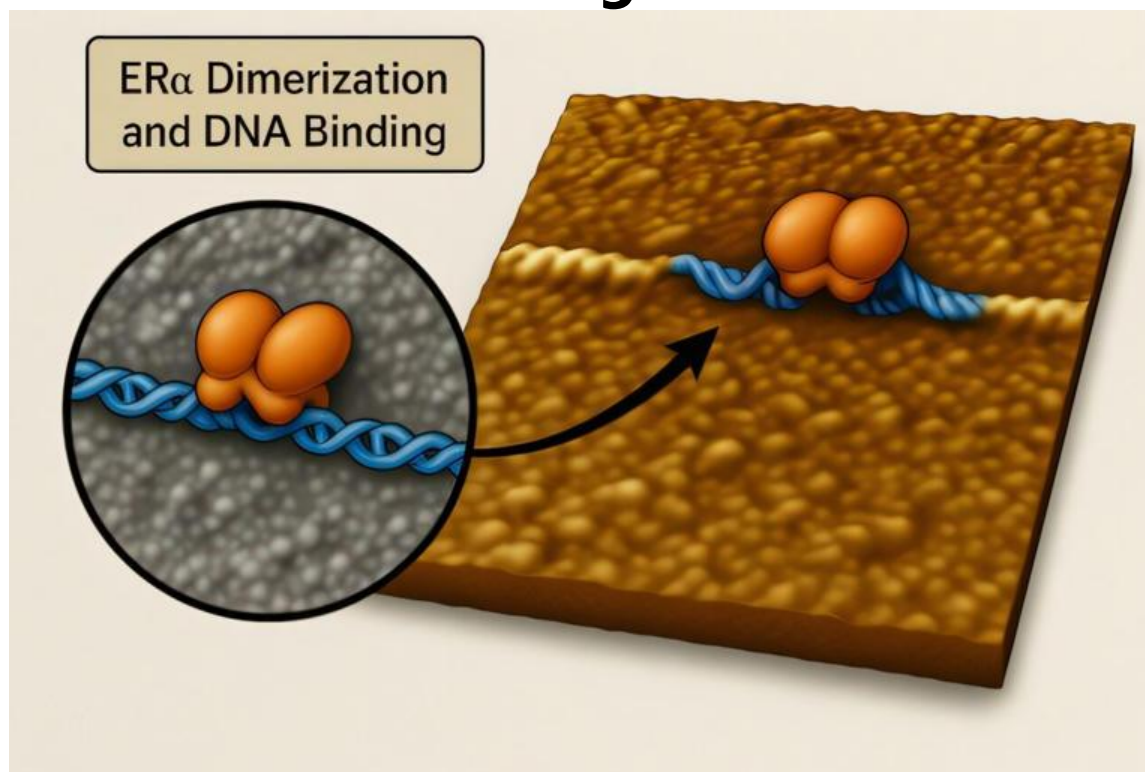
The case suggests a future in which parents will take sick children to a clinic where their DNA will be sequenced, and then they will rapidly receive individualized treatments. Currently, this would only work for liver diseases, for which it's easier to deliver gene-editing instructions, but eventually it might also become a possible approach for treating brain diseases and conditions like muscular dystrophy.

The experiment is drawing attention to a gap between what gene editing can do and what treatments are likely to become available to people who need them.

So far, biotechnology companies testing gene editing are working only on fairly common gene conditions, like sickle cell disease, leaving hundreds of ultra-rare conditions aside. One-off treatments, like the one helping KJ, are too expensive to create and get approved without some way to recoup the costs.

The apparent success in treating KJ, however, is making it even more urgent to figure out a way forward. Researchers acknowledge that they don't yet know how to scale up personalized treatment, although Musunuru says initial steps to standardize the process are underway at his university and in Europe.

High-speed imaging captures mechanics of hormone-driven gene activation



How estrogen receptor binds DNA. This illustration shows the estrogen receptor alpha (ER α , in orange) attaching to DNA (in blue) as a pair, or dimer. The image is based on real-time, high-speed atomic force microscopy (HS-AFM) data, showing how ER α recognizes and binds specific DNA sequences to activate genes. The close-up highlights the dimer sitting on the DNA strand—a key step in hormone-driven gene regulation. Credit: Richard Wong

Scientists at Nano Life Science Institute (WPI-NanoLSI), Kanazawa University, have captured real-time footage showing how a key hormone receptor activates genes, offering a clearer view of one of the most fundamental processes in biology.

Using high-speed atomic force microscopy (HS-AFM), Richard Wong and colleagues at Kanazawa University directly visualized how the estrogen receptor alpha (ER α) binds to DNA and switches on genes in response to the hormone estrogen.

Their findings, [published](#) in *ACS Nano*, reveal new molecular details of hormone signaling, with important implications for diseases like breast cancer.

Estrogen receptors play a critical role in controlling gene activity in many tissues. When estrogen binds to ER α , the protein changes shape, forms a dimer (a molecular pair), and attaches to specific regions of DNA called estrogen response elements (EREs).

Although the importance of this process has been known for decades, it had never before been observed unfolding at the single-molecule level in real time.

To capture this, the researchers used HS-AFM to scan individual ER α molecules interacting with DNA. They compared the behavior of ER α with and without estrogen present. Their experiments showed that ER α could bind to DNA without estrogen but did so less precisely and less stably. When estrogen was present, ER α molecules dimerized more efficiently and exhibited targeted, stable binding to ERE sequences.

"Our study shows that estrogen acts like a molecular matchmaker," says Wong. "It not only triggers ER α to find the right DNA sequence but also stabilizes its grip, ensuring accurate gene activation."

Based on these observations, the team proposed a new "ligand-induced dimerization" (LID) model explaining how hormones fine-tune the dynamic behavior of receptors at the DNA level.

This work provides direct visual evidence of how molecular signals from hormones lead to precise gene control—a fundamental advance that could guide new strategies for treating hormone-driven diseases.

More information: Goro Nishide et al, Zooming into Gene Activation: Estrogen Receptor α Dimerization and DNA Binding Visualized by High-Speed Atomic Force Microscopy, *ACS Nano* (2025). DOI: [10.1021/acsnano.4c14943](https://doi.org/10.1021/acsnano.4c14943)

Provided by Kanazawa University