GENOMICS BIOTECH VOL 7

Sugar Compound from Deep-Sea Bacteria Causes Cancer Cells to Self-Destruct

Life is not easy in the cold, lightless reaches of the South China Sea. To survive, microbes have evolved fiercely competitive and extremely resilient. Some build chemical weapons, complex molecules that help them fend off rivals. Now, scientists have found one of those weapons that may help humans fight a very different enemy: cancer.

In new study, researchers from the Chinese Academy of Sciences report the discovery of EPS3.9, a long-chain sugar made by *Spongiibacter nanhainus* and its close relatives. In lab experiments and in mice with liver cancer, EPS3.9 not only halted tumor growth but also set off a powerful immune response, showing the immune system where to strike cancer.

Like Setting Off a Flare Inside a Tumor

Researchers started looking at the bacteria in 2024, when they found that it has inhibitory effects on agricultural fungi and human pathogenic bacteria, including notorious drug-resistant pathogens. They've now focused on cancer, and also found it to be remarkably effective.

EPS3.9 works by triggering *pyroptosis* — a dramatic, "fiery" form of programmed cell death. The cell swells, bursts, and releases inflammatory molecules that act like distress signals, summoning immune cells to the site.

This is a phenomenon quite different from *apoptosis*, which is a form of programmed cell death that is crucial for normal development. Cancerous cells disrupt apoptosis and multiply in an unregulated fashion. But unlike apoptosis, which is orderly and quiet, pyroptosis is explosive, and that's a good thing..

Pyroptosis is often triggered by microbial infections and is associated with inflammation. However, in recent years, it's also emerged as a promising cancer therapy. By killing tumor cells in such a loud and messy way, it can also alert the immune system to join the attack. Cancer cells rely on evading the immune system, so this is like sounding the alarm on them.

"Our work not only provides a theoretical basis for developing more carbohydrate-based drugs but also highlights the importance of exploring marine microbial resources," said corresponding author Chaomin Sun, PhD, of the Chinese Academy of Sciences.

Cancer Treatment from the Oceans

For now, the compound destroyed cancer cells in the lab and in mice. In tests with human leukemia cells, EPS3.9 caused widespread cell death. In mice, it significantly shrank liver tumors and sparked anti-tumor immune activity.

There's a long way from this to ensuring this is safe and effective in clinical trials. Yet, it's a promising avenue.

Modern cancer therapies increasingly look to the immune system for help. Immunotherapies, such as checkpoint inhibitors and CAR-T cells, have

revolutionized treatment for some patients. Many tumors evade detection, but EPS3.9 offers a different approach — destroying, cancer cells in a way that makes them impossible to ignore. By causing the cells to erupt and spill danger signals, the compound could help alert the immune system to tumors that would otherwise fly under the radar.

Marine microbes like *Spongiibacter* are also a largely untapped resource. Life in extreme environments forces them to evolve unusual chemistry. Over the past few decades, scientists have found antibiotics, antivirals, and anticancer agents in ocean organisms, from sponges to bacteria. EPS3.9's discovery adds to that list.

If EPS3.9 proves safe and effective in humans, it could pave the way for an entirely new class of carbohydrate-based cancer therapies — treatments that don't just destroy tumors, but also rally the body's own defenses to keep the fight going. For now, a humble microbe from the ocean's depths has opened an intriguing new front in the war on cancer.

Journal Reference: Ge Liu, Yeqi Shan, Chaomin Sun. A Novel Exopolysaccharide, Highly Prevalent in Marine Spongiibacter, Triggers Pyroptosis to Exhibit Potent Anticancer Effects. *The FASEB Journal*, 2025; 39 (14) DOI: 10.1096/fj.202500412R

JUNE 24, 2025

Scientists use gene editing to correct harmful mitochondrial mutations in human cells

by Public Library of Science edited by Sadie Harley, reviewed by Robert Egan

Patient-derived liver organoids and their mitochondria (red). Credit: Martijn Koppens (CC-BY 4.0, creativecommons.org/licenses/by/4.0/)

In a step toward treating mitochondrial diseases, researchers in the Netherlands have successfully edited harmful mutations in mitochondrial DNA using a genetic tool known as a base editor. The results, published in the open-access journal *PLOS Biology*, offer new hope for people with rare genetic conditions.

Mitochondria have their own small set of DNA. Mutations in this mitochondrial DNA can lead to a wide range of maternally inherited diseases, cancer, and aging-related conditions. While the development of CRISPR technology has given scientists new ways to correct mutations in nuclear DNA, this system cannot effectively cross the mitochondrial membrane and reach mitochondrial DNA.

In the new study, the researchers used a tool called a base editor—specifically, a DdCBE (double-stranded DNA deaminase toxin A-derived cytosine base editor). This tool allows scientists to change a single letter in the DNA code without cutting it, and it works on mitochondrial DNA.

The team showed that they could effectively generate and correct mitochondrial DNA mutations in multiple disease-linked cell types in the lab. First, they engineered liver cells to carry a mitochondrial mutation that impairs energy production. Then they showed they could fix a different mutation in skin cells taken from a patient with the mitochondrial disorder Gitelman-like syndrome, restoring key signs of healthy mitochondrial function.

To help move the therapy toward clinical use, the researchers also tested the efficacy of delivering the mitochondrial base editors in mRNA form, rather than as DNA, and within lipid nanoparticles for delivery.

They showed that these approaches are more efficient and less toxic to cells than older methods like DNA plasmids. Importantly, the edits were highly specific, with minimal off-target changes detected in nuclear DNA and multiple detected in mitochondrial DNA.

"The potential of mitochondrial base editing in disease modeling and potential therapeutic interventions makes it a promising avenue for future research and development in mitochondrial medicine," the authors say.

The authors add, "Mitochondrial patients have not been able to benefit from the CRISPR revolution for so long, but recently the technology has become available with which we can finally repair mitochondrial mutations. In our study, we used this technology on human liver organoids to generate a mitochondrial disease model.

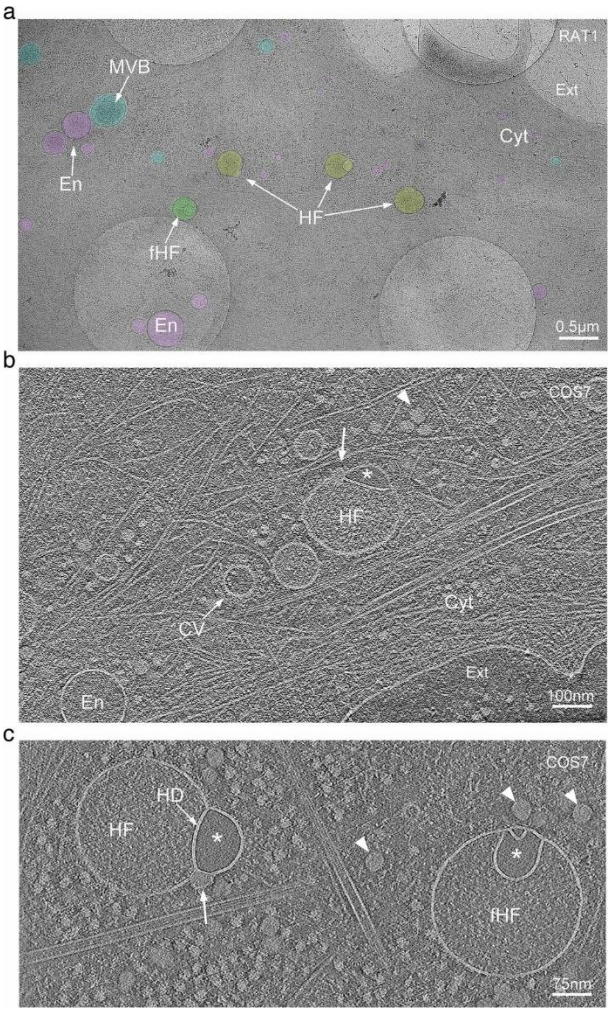
"We employed a clinic-grade technique to repair a mutation in the mitochondrial DNA of patient-derived cells."

More information: Joore IP, et al. Correction of pathogenic mitochondrial DNA in patient-derived disease models using mitochondrial base editors. *PLOS Biology* (2025). DOI: 10.1371/journal.pbio.3003207
Journal information: PLoS Biology
Provided by Public Library of Science

JUNE 25, 2025

Scientists discover unknown organelle inside our cells

by University of Virginia edited by Gaby Clark, reviewed by Robert Egan



Cryo-electron tomography observation of hemifused vesicles at the leading edge of cultured cells. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-59887-9

The discovery of an unknown organelle inside our cells could open the door to new treatments for devastating inherited diseases.

The organelle, a type of specialized structure, has been dubbed a "hemifusome" by its discoverers at the University of Virginia School of Medicine and the National Institutes of Health. This little organelle has a big job helping our cells sort, recycle and discard important cargo within themselves, the scientists say. The new discovery could help scientists better understand what goes wrong in genetic conditions that disrupt these essential housekeeping functions.

"This is like discovering a new recycling center inside the cell," said researcher Seham Ebrahim, Ph.D., of UVA's Department of Molecular Physiology and Biological Physics. "We think the hemifusome helps manage how cells package and process material, and when this goes wrong, it may contribute to diseases that affect many systems in the body."

One such condition is Hermansky-Pudlak syndrome, a rare genetic disorder that can cause albinism, vision problems, lung disease and issues with blood clotting. Problems with how cells handle cargo are at the root of many such disorders.

"We're just beginning to understand how this new organelle fits into the bigger picture of cell health and disease," Ebrahim said. "It's exciting because finding something truly new inside cells is rare—and it gives us a whole new path to explore."

Tomographic reconstruction of direct hemifusome in a COS-7 cell. Direct hemifusome in a COS-7 cell reveal a dense structure embedded within the hydrophobic interior of the bilayers at the junction of HD and two heterotypic vesicles. Video is displayed at 24 fps. Scale bar: 100 nm. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-59887-9

Hello to the hemifusome

Ebrahim and her team at UVA Health worked with Bechara Kachar, MD, and colleagues Amirrasoul Tavakoli, Ph.D., and Shiqiong Hu, Ph.D., at the National Institutes of Health to

identify the organelle, which comes and goes as needed by the cell. They took advantage of UVA's expertise in cryo-electron tomography (cryo-ET)—a powerful imaging method that "freezes" cells in time—to create striking images of the organelle.

The scientists believe hemifusomes facilitate the formation of vesicles, tiny blister-like sacs that act as mixing bowls, and of organelles made up of multiple vesicles. This process is critical to cellular sorting, recycling and debris disposal, the researchers report.

"You can think of vesicles like little delivery trucks inside the cell," said Ebrahim, of UVA's Center for Membrane and Cell Physiology. "The hemifusome is like a loading dock where they connect and transfer cargo. It's a step in the process we didn't know existed."

While the hemifusomes have escaped detection until now, the scientists say they are surprisingly common in certain parts of our cells. The researchers are eager to better understand their importance to proper cellular function and learn how problems with them could be contributing to disease. Such insights, they say, could lead to targeted treatments for a range of serious genetic disorders.

"This is just the beginning," Ebrahim said. "Now that we know hemifusomes exist, we can start asking how they behave in healthy cells and what happens when things go wrong. That could lead us to new strategies for treating complex genetic diseases."

The researchers have published their findings in the journal *Nature Communications*.

More information: Amirrasoul Tavakoli et al, Hemifusomes and interacting proteolipid nanodroplets mediate multi-vesicular body formation, *Nature Communications* (2025). DOI: 10.1038/s41467-025-59887-9
Journal information: Nature Communications
Provided by University of Virginia

"CRAZY EXPERIMENT" YIELDS MICE WITH HUMAN CELLS IN MULTIPLE ORGANS

RYAN WHALEN·JUNE 19, 2025

Human-mouse chimeras have been created in recent research, in which scientists report the development of intestines, livers, and even brains within mice containing human cells.

The novel research, discussed on June 12 at the International Society for Stem Cell Research meeting in Hong Kong, involves injecting human cells into the amniotic fluid of pregnant mice. The research has not yet undergone peer review.

Hideki Masaki, a stem-cell scientist at the Institute of Science Tokyo who attended the meeting, called the work "game changing," although the researchers say that to become practically useful, their work will need to increase the ratio of human to mouse cells.

UNDERSTANDING CHIMERAS

Named after the mythical Greek creature composed of parts from several animals, real-world chimeras are organisms with more than one cellular genotype. These can arise through natural or artificial means, such as embryo fusion, organ transplants, or plant grafting.

Laboratory-made human–animal chimeras are typically created by introducing human cells into mouse or pig embryos in a dish, rather than in a living animal's womb. In most past experiments, human cells have struggled to survive under such conditions, and researchers have lacked the ability to control what types of differentiated cells emerge from the stem cells. While these experiments have provided insights into tissue development, the ultimate goal of growing full human organs for transplantation remains out of reach.

A research team—including University of Texas MD Anderson Cancer Center biomedical engineer Xiling Shen and Terasaki Institute for Biomedical Innovation developmental biologist Qiang Huang—focused on two major challenges: improving the survivability of human cells and controlling which organs they target.

Their hypothesis was that using organoids—three-dimensional human tissue models grown from more mature cells—would yield

better results than early-stage stem cells, making them more resilient in a foreign environment.

First, the scientists programmed the cells to develop into gut, liver, and brain organoids in a lab dish. They then injected these organoids into the amniotic fluid of mice at an early stage of embryonic development, allowing the pregnancies to continue to term.

INSPECTING THE RESULTS

“It’s a crazy experiment; I didn’t expect anything,” said Shen. “You get sections of the intestine that originate from injected human organoids.”

The results were evident within days, as the human cells in the amniotic fluid entered the embryos, located their target organs, and began to multiply. Each organoid sought out its intended destination—including the liver, intestines, and cortex. After birth, about 10% of the mice had human cells in their intestines, comprising roughly 1% of the intestinal cells. Human cells were also found in the brains and livers, though to a lesser extent.

Most notably, the human cells appeared to function normally and remained alive two months after the mice were born. When the team examined the liver tissue, they identified cells producing the human version of albumin, a key liver protein. The foreign cells appeared to be stable—a promising outcome for future applications.

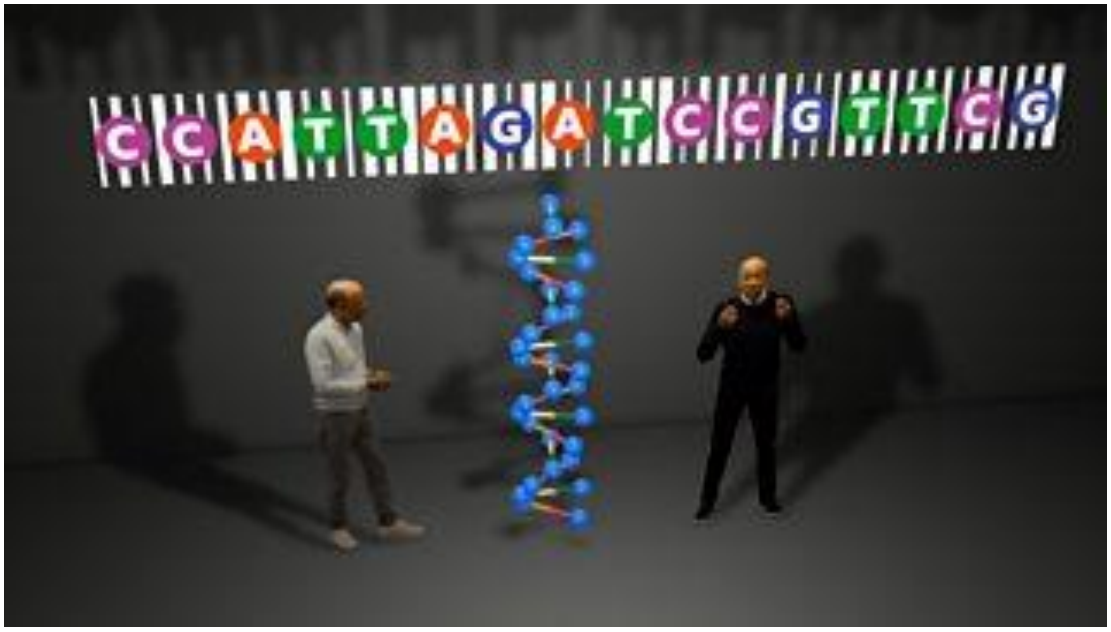
ETHICAL CONCERNS

Injecting cells into the amniotic fluid represents a major step toward making chimera creation more viable and controlled. Attendees such as Stanford researcher Hiromitsu Nakauchi praised the work, with Nakauchi noting he may adopt the method in future research. Still, the team acknowledges that much more progress is needed to

improve the number of viable human cells integrated into the developing embryos.

Ethicists continue to raise concerns about the implications of animals developing human brain cells—and the potential for human-like cognition. The researchers behind this study say the number of human cells found in the mouse brains is too low to warrant such fears at present, but acknowledge the ethical debate may intensify as the field advances.

Work begins to create artificial human DNA from scratch



How the researchers hope to create human DNA

Work has begun on a controversial project to create the building blocks of human life from scratch, in what is believed to be a world first.

The research has been taboo until now because of concerns it could lead to designer babies or unforeseen changes for future generations.

But now the World's largest medical charity, the Wellcome Trust, has given an initial £10m to start the project and says it has the potential to do more good than harm by accelerating treatments for many incurable diseases.

Dr Julian Sale, of the MRC Laboratory of Molecular Biology in Cambridge, who is part of the project, told BBC News the research was the next giant leap in biology.
"The sky is the limit. We are looking at therapies that will improve people's lives as they age, that will lead to healthier aging with less disease as they get older.
"We are looking to use this approach to generate disease-resistant cells we can use to repopulate damaged organs, for example in the liver and the heart, even the immune system," he said.
But critics fear the research opens the way for unscrupulous researchers seeking to create enhanced or modified humans.
Dr Pat Thomas, director of the campaign group Beyond GM, said: "We like to think that all scientists are there to do good, but the science can be repurposed to do harm and for warfare".
Details of the project were given to BBC News on the 25th anniversary of the completion of the Human Genome Project, which mapped the molecules in human DNA and was also largely funded by Wellcome.

Artwork: The aim is to build sections of human DNA from scratch

Every cell in our body, with the exception of red blood cells, contains a molecule called DNA which carries the genetic information it needs.
DNA is built from just four much smaller blocks referred to as A, G, C and T, which are repeated over and over again in various combinations. Amazingly it contains all the genetic information that physically makes us who we are.
The Human Genome Project enabled scientists to read all human genes like a bar code.
The new work that is getting under way, called the Synthetic Human Genome Project, potentially takes this a giant leap forward – it will allow researchers not just to read a molecule of DNA, but to create parts of it – maybe one day all of it - molecule by molecule from scratch.

Scientists will begin developing tools to create ever larger sections of human DNA

The scientists' first aim is to develop ways of building ever larger blocks of human DNA, up to the point when they have synthetically constructed a human chromosome. These contain the genes that govern our development, repair and maintenance.

These can then be studied and experimented on to learn more about how genes and DNA regulate our bodies.
Many diseases occur when these genes go wrong so the studies could lead to better treatments, according to Prof Matthew Hurles, director of the Wellcome Sanger Insititute which sequenced the largest proportion of the Human Genome.
"Building DNA from scratch allows us to test out how DNA really works and test out new theories, because currently we can only really do that by tweaking DNA in DNA that already exists in living systems".

BBC News
Machines at the Sanger Institute were used to sequence the human genome

The project's work will be confined to test tubes and dishes and there will be no attempt to create synthetic life. But the technology will give researchers unprecedented control over human living systems.
And although the project is hunting for medical benefits, there is nothing to stop unscrupulous scientists misusing the technology.
They could, for example, attempt to create biological weapons, enhanced humans or even creatures that have human DNA, according to Prof Bill Earnshaw, a highly respected genetic scientist at Edinburgh University who designed a method for creating artificial human chromosomes.
"The genie is out of the bottle," he told BBC News. "We could have a set of restrictions now, but if an organisation who has access to appropriate machinery decided to start synthesising anything, I don't think we could stop them"
Ms Thomas is concerned about how the technology will be commercialised by healthcare companies developing treatments emerging from the research.
"If we manage to create synthetic body parts or even synthetic people, then who owns them. And who owns the data from these creations? "
Given the potential misuse of the technology, the question for Wellcome is why they chose to fund it. The decision was not made lightly, according to Dr Tom Collins, who gave the funding go-ahead.
"We asked ourselves what was the cost of inaction," he told BBC News.
"This technology is going to be developed one day, so by doing it now we are at least trying to do it in as responsible a way as possible and to confront the ethical and moral questions in as upfront way as possible".

A dedicated social science programme will run in tandem with the project's scientific development and will be led by Prof Joy Zhang, a sociologist, at the University of Kent. "We want to get the views of experts, social scientists and especially the public about how they relate to the technology and how it can be beneficial to them and importantly what questions and concerns they have," she said.

JULY 3, 2025

New molecular tool sheds light on how cancer cells repair telomeres

by University of Pittsburgh edited by Gaby Clark, reviewed by Andrew Zinin

Human chromosomes with telomeres labeled in green and red. Credit: O'Sullivan Lab
Each time a cell divides, a small section of each chromosome's protective cap—the telomere—is worn away. Most cells use an enzyme called telomerase to help mitigate this loss, but 10% to 15% of cancers have another mechanism called the alternative lengthening of telomeres (ALT) pathway.

"ALT is found in some of the worst cancers, such as pancreatic neuroendocrine tumors, osteosarcomas and subsets of glioma," said Roderick O'Sullivan, Ph.D., professor in the Department of Pharmacology and Chemical Biology at the University of Pittsburgh and UPMC Hillman Cancer Center. "Interfering with ALT in these cancers may be a novel therapeutic approach, which represents a huge biomedical window of opportunity, but ALT has been a black box."

In a new study, published today in *Molecular Cell*, senior authors O'Sullivan and Kyle Miller, Ph.D., professor in the Department of Radiation Oncology at Emory University, and their team describe a novel tool called BLOCK-ID that offers a glimpse into the black box of ALT, bringing them one step closer to developing cancer therapies that target this process.

During cell division, the double helix of DNA unwinds to create a replication fork, allowing replication proteins access to do their job. But sometimes, this process stalls and the proteins become stuck on DNA, creating what is known as a protein barrier.

"A replication fork is like a train coming along train tracks, but if the line ends suddenly due to a protein barrier, the train will collide," said O'Sullivan. "BLOCK-ID is like an artificial barrier that allows us to monitor a collision event at one very specific part of the cell."

BLOCK-ID uses an enzyme to add a molecule called biotin to all proteins that play a role at the collision event.

Chromosome from cancer cell with normal telomeres shown in red and green (left) and chromosome from cancer cell with loss of telomere stability due to lack of TRIM24 (right). Credit: Kim et al. Molecular Cell (2025), 10.1016/j.molcel.2025.06.009

"Biotin acts like a tag that says, 'This protein has been in contact with the protein barrier,'" said O'Sullivan. "Even though proteins may move to another part of the cell, we can tell they were at the collision event because they are marked for life, allowing us to trace brief interactions that would normally be missed."

Using BLOCK-ID, the researchers identified a protein called TRIM24 as an essential player in the ALT pathway of cancer cells.

"If you remove TRIM24 from normal cells, they can tolerate it, but if you remove this protein from ALT cells, they don't like it," said O'Sullivan. "Without TRIM24, telomeres in ALT cells become a mess: they shorten, and they become destabilized and nonfunctional."

Until now, it had been thought that a protein called PML was essential for ALT because it forms a shell around telomeres, creating a specialized environment that attracts other repair proteins.

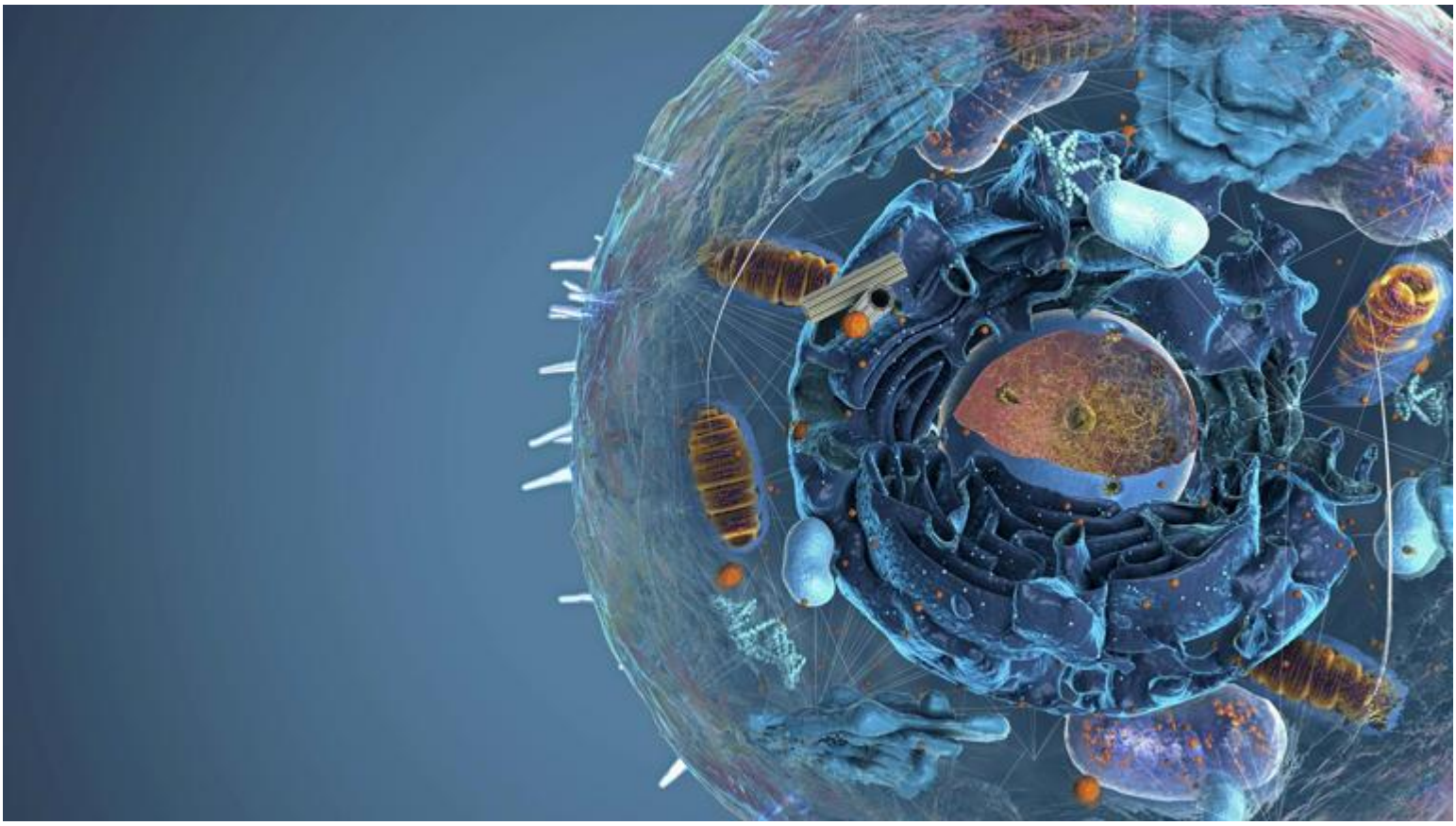
However, when the researchers molecularly tethered TRIM24 to telomeres in cancer cells lacking PML, they found that, surprisingly, these telomere repair shells still formed.

"This experiment tells us how important TRIM24 is to the ALT mechanism," said O'Sullivan. "It also tells us that ALT has inbuilt redundancies. This is really important because if we are going to target ALT, we need to understand its complexities."

Other authors are listed in the manuscript.

More information: TRIM24 directs replicative stress responses to maintain ALT telomeres via chromatin signaling, *Molecular Cell* (2025). DOI: 10.1016/j.molcel.2025.06.009. www.cell.com/molecular-cell/fu … 1097-2765(25)00509-X
Journal information: Molecular Cell
Provided by University of Pittsburgh

Cells have more mini ‘organs’ than researchers thought – unbound by membranes, these rogue organelles challenge biology’s fundamentals



Specialized compartments within cells carry out specific functions.© Christoph Burgstedt/Science Photo Library via Getty Images

Think back to that basic biology class you took in high school. You probably learned about organelles, those little “organs” inside cells that form compartments with individual functions. For example, mitochondria produce energy, lysosomes recycle waste and the nucleus stores DNA. Although each organelle has a different function, they are similar in that every one is wrapped up in a membrane.

Membrane-bound organelles were the textbook standard of how scientists thought cells were organized until they realized in the mid-2000s that some organelles don't need to be wrapped in a membrane. Since then, researchers have discovered many additional membraneless organelles that have significantly changed how biologists think about the chemistry and origins of life.

I was introduced to membraneless organelles, formally called biomolecular condensates, a couple years ago when students in my lab observed some unusual blobs in a cell nucleus. Unbeknownst to me, we had actually been studying biomolecular condensates for years. What I finally saw in those blobs opened my eyes to a whole new world of cell biology.

Like a lava lamp

To get a sense of what a biomolecular condensate looks like, imagine a lava lamp as the blobs of wax inside fuse together, break apart and fuse again. Condensates form in much the same way, though they are not made of wax. Instead, a cluster of proteins and genetic material, specifically RNA molecules, in a cell condenses into gel-like droplets.

Some proteins and RNAs do this because they preferentially interact with each other instead of their surrounding environment, very much like how wax blobs in a lava lamp mix with each other but not the surrounding liquid. These condensates create a new microenvironment that attracts additional proteins and RNA molecules, thus forming a unique biochemical compartment within cells.

As of 2022, researchers have found about 30 kinds of these membraneless biomolecular condensates. In comparison, there are around a dozen known traditional membrane-bound organelles.

Although easy to identify once you know what you are looking for, it's difficult to figure out what biomolecular condensates exactly do. Some have well-defined roles, such as forming reproductive cells, stress granules and protein-making ribosomes. However, many others don't have clear functions.

Nonmembrane-bound organelles could have more numerous and diverse functions than their membrane-bound counterparts. Learning about these

unknown functions is affecting scientists' fundamental understanding of how cells work.

Protein structure and function

Biomolecular condensates are breaking some long-held beliefs about protein chemistry.

Ever since scientists first got a good look at the structure of the protein myoglobin in the 1950s, it was clear that its structure is important for its ability to shuttle oxygen in muscles. Since then, the mantra for biochemists has been that protein structure equals protein function. Basically, proteins have certain shapes that allow them to perform their jobs.

The proteins that form biomolecular condensates at least partially break this rule since they contain regions that are disordered, meaning they do not have defined shapes. When researchers discovered these so-called intrinsically disordered proteins, or IDPs, in the early 1980s, they were initially confounded by how these proteins could lack a strong structure but still perform specific functions.

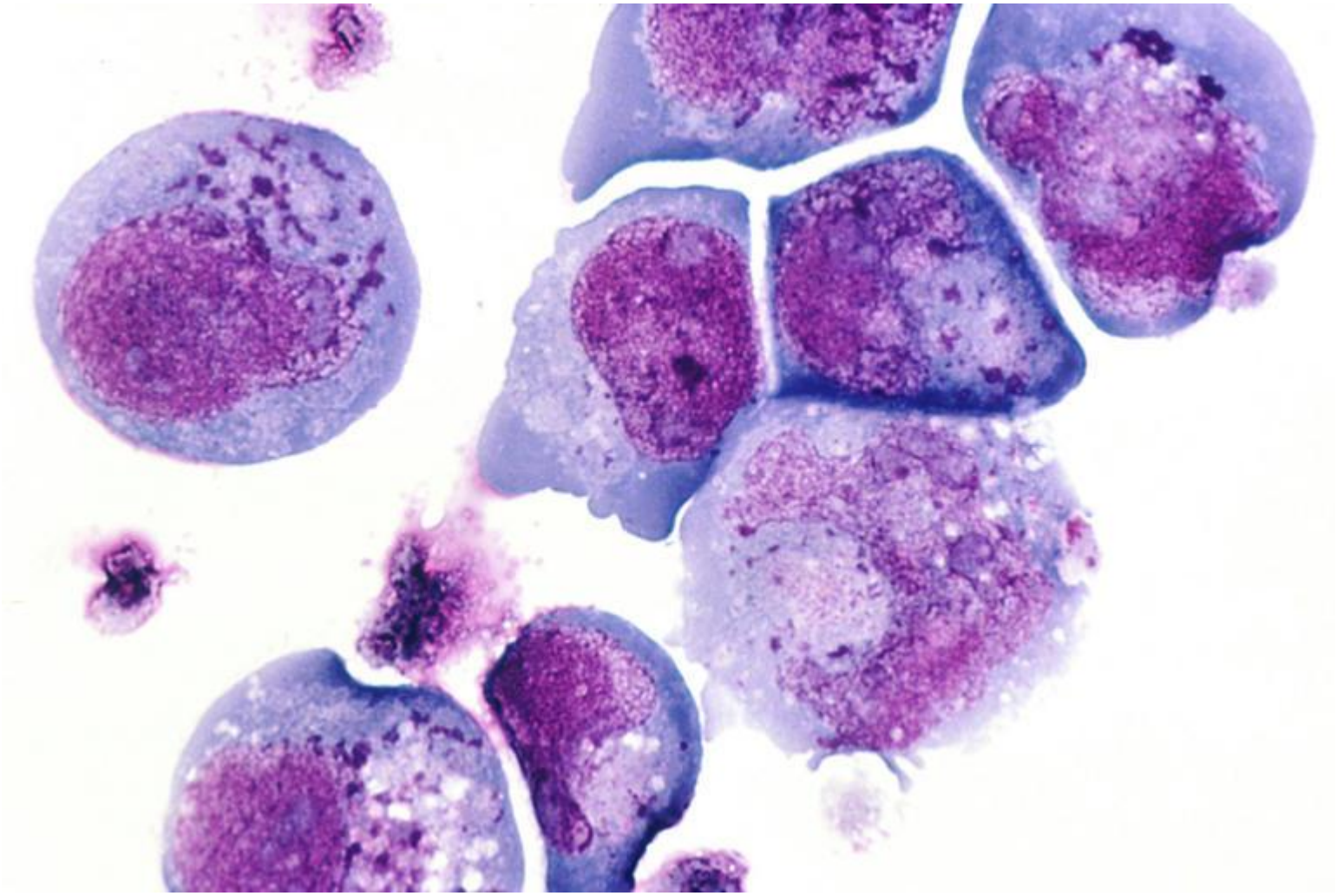
Later, they found that IDPs tend to form condensates. As is so often the case in science, this finding solved one mystery about the roles these unstructured rogue proteins play in the cell only to open another deeper question about what biomolecular condensates really are.

Bacterial cells

Researchers have also detected biomolecular condensates in prokaryotic, or bacterial, cells, which traditionally were defined as not containing organelles. This finding could have profound effects on how scientists understand the biology of prokaryotic cells.

Only about 6% of bacterial proteins have disordered regions lacking structure, compared with 30% to 40% of eukaryotic, or nonbacterial, proteins. But scientists have found several biomolecular condensates in prokaryotic cells that are involved a variety of cellular functions, including making and breaking down RNAs.

The presence of biomolecular condensates in bacterial cells means that these microbes aren't simple bags of proteins and nucleic acids but are actually more complex than previously recognized.



Inclusion bodies, stained magenta in this micrograph of herpesvirus 6, are aggregates of proteins that form a type of biomolecular condensate.© National Cancer Institute/National Institutes of Health via Wikimedia Commons

Origins of life

Biomolecular condensates are also changing how scientists think about the origins of life on Earth.

There is ample evidence that nucleotides, the building blocks of RNA and DNA, can very plausibly be made from common chemicals, like hydrogen cyanide and

water, in the presence of common energy sources, like ultraviolet light or high temperatures, on universally common minerals, like silica and iron clay.

There is also evidence that individual nucleotides can spontaneously assemble into chains to make RNA. This is a crucial step in the RNA world hypothesis, which postulates that the first "lifeforms" on Earth were strands of RNAs.

A major question is how these RNA molecules might have evolved mechanisms to replicate themselves and organize into a protocell. Because all known life is enclosed in membranes, researchers studying the origin of life have mostly assumed that membranes would also need to encapsulate these RNAs. This would require synthesizing the lipids, or fats, that make up membranes. However, the materials needed to make lipids likely weren't present on early Earth.

With the discovery that RNAs can spontaneously form biomolecular condensates, lipids wouldn't be needed to form protocells. If RNAs were able to aggregate into biomolecular condensates on their own, it becomes even more plausible that living molecules arose from nonliving chemicals on Earth.

New treatments

For me and other scientists studying biomolecular condensates, it is exciting to dream of how these rule-breaking entities will change our perspective on how biology works. Condensates are already changing how we think about human diseases like Alzheimer's, Huntington's and Lou Gehrig's.

To this end, researchers are developing several new approaches to manipulate condensates for medical purposes like new drugs that can promote or dissolve condensates. Whether this new approach to treating disease will bear fruit remains to be determined.

In the long term, I wouldn't be surprised if each biomolecular condensate is eventually assigned a particular function. If this happens, you can bet that high school biology students will have even more to learn – or complain – about in their introductory biology classes.

Allan Albig receives funding from the National Institute of Health.

JULY 8, 2025

When stem cells feel the squeeze, they start building bone

by National University of Singapore edited by Gaby Clark, reviewed by Robert Egan

Asst Prof Andrew Holle (right) and Ph.D. student Gao Xu (left), first author of the research paper, discuss features on the silicon wafer containing the mold of their microchannel device. Credit: College of Design and Engineering at NUS

In a discovery that could reshape approaches to regenerative medicine and bone repair, researchers have found that human stem cells can be prompted to begin turning into bone cells simply by squeezing through narrow spaces.

The study suggests that the physical act of moving through tight, confining spaces, like those between tissues, can influence how stem cells develop. This could open new possibilities for engineering materials and therapies by guiding cell behavior using physical, rather than chemical, signals.

The research was led by Assistant Professor Andrew Holle from the Department of Biomedical Engineering in the College of Design and Engineering at the National University of Singapore (NUS), and the Mechanobiology Institute (MBI) at NUS, and was published on 8 May 2025 in the journal *Advanced Science*.

Mechanical 'memory'

Asst Prof Holle leads the Confinement Mechanobiology Lab at MBI. His lab studies how physical constraints—especially the tight spaces cells encounter as they move—affect how cells behave, function, and develop. While most earlier research in this area focused on cancer and immune cells, his team is among the first to explore how these forces affect stem cells, with the aim of applying their findings to future therapies.

The researchers focused on a type of adult stem cell known as a mesenchymal stem cell, or MSC. These cells are found in bone marrow and other tissues and are known for their ability to develop into bone, cartilage, and fat cells. Because of these properties, MSCs are widely used in research on tissue repair and regeneration.

"To test how physical forces influence stem cell fate, we developed a specialized microchannel system that mimics the narrow tissue spaces cells navigate in the body," said Asst Prof Holle.

They found that when MSCs squeezed through the smallest channels (just three micrometers wide), the pressure caused lasting changes to the cells' shape and structure. These cells showed increased activity in a gene called RUNX2, which plays a key role in bone formation. Even after exiting the channels, they retained this effect—suggesting they carry a kind of mechanical "memory" of the experience.

"Most people think of stem cell fate as being determined by chemical signals," Asst Prof Holle said. "What our study shows is that physical confinement alone—squeezing through tight spaces—can also be a powerful trigger for differentiation."

Gao Xu (front) and Asst Prof Andrew Holle (back) looking over a microscope image of their microchannel structures. Credit: College of Design and Engineering at NUS
While traditional methods of directing stem cells rely on chemical cues or growing them on stiff or soft materials, Asst Prof Holle's team believes confinement-based selection may offer a simpler, cheaper, and potentially safer alternative.

"This method requires no chemicals or genetic modification—just a maze for the cells to crawl through," he said. "In theory, you could scale it up to collect millions of preconditioned cells for therapeutic use."

Next steps

The researchers say their findings could help improve the design of biomaterials and scaffolds used in bone repair, by creating physical environments that naturally encourage the right kind of cell development. "By tuning the mechanical properties of materials, we might be able to steer stem cells more reliably toward the cell types we want," Asst Prof Holle said.

The approach could one day be used to speed up recovery from bone fractures or enhance the effectiveness of stem cell therapies.

"We'd like to test whether preconditioned cells that have gone through this mechanical selection are better at promoting healing when introduced at injury sites," Asst Prof Holle said. "That's one of the next steps."

Beyond bone repair, the research may have broader implications. MSCs are also known to migrate toward tumors, and the research team is interested in whether mechanically preconditioned cells might be better equipped to move through dense tumor tissue—a challenge that has limited the success of many current cell therapies.

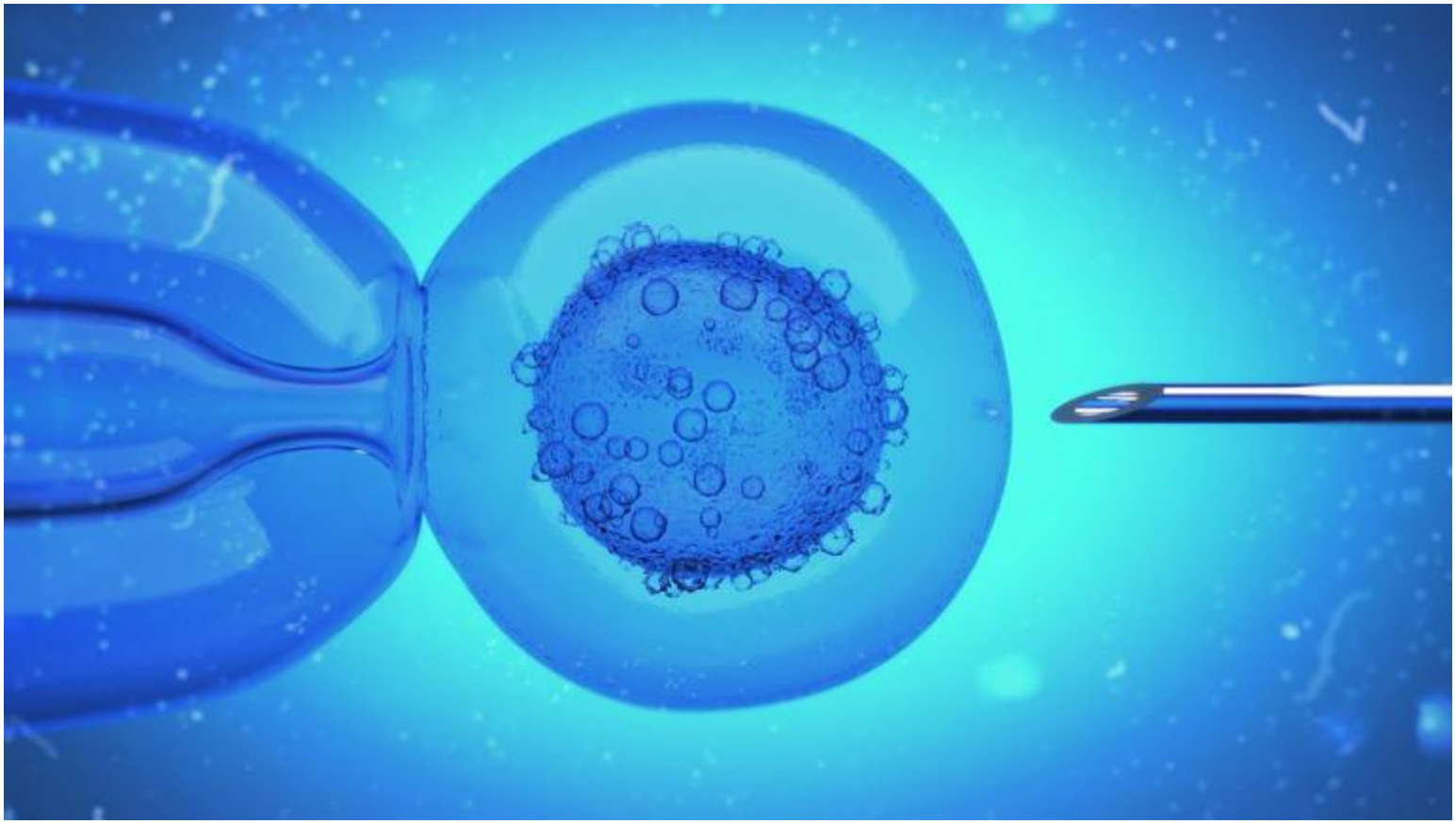
The group is also exploring whether the technique could apply to more potent stem cell types, such as induced pluripotent stem cells (iPSCs), which can develop into almost any tissue in the body.

"We suspect that confinement plays a role even in embryonic development," Asst Prof Holle said. "Cells migrating through crowded environments early in life are exposed to

mechanical stress that could shape their fate. We think this idea has potential far beyond just MSCs."

More information: Xu Gao et al, Confined Migration Drives Stem Cell Differentiation, *Advanced Science* (2025). DOI: 10.1002/advs.202415407
Journal information: Advanced Science
Provided by National University of Singapor

8 Children Have Been Born With 3 Biological Parents Each After Mitochondrial Transfer



By using an egg from a donor with the nuclear DNA from the intending mother, healthy children have been born with three genetic parents. - Image credit: Suliman Razvan/Shutterstock.com© IFL Science

A technique to allow women who carry diseases in their mitochondrial DNA to have healthy children has been performed successfully eight times since being legalized, two papers have announced. With one pregnancy having led to identical twins, the work has led to eight healthy babies, as well as one pregnancy underway.

We inherit most of our genes from our parents' chromosomes in the cell nucleus, with each chromosome carrying one copy from the father and one from the mother. However, a little over 0.1 percent of our genes are transmitted through the mitochondria that power the cell. It is generally thought that mitochondrial DNA is inherited entirely through the egg, i.e. from the mother, although one astonishing paper found evidence of exceptions.

Unfortunately, while mutations anywhere in the genome can have serious consequences, mitochondrial variations can carry particularly serious effects, since mitochondria provide the energy to power cells. Many aspiring mothers carrying mitochondrial diseases give up on having children, or use eggs with another woman's DNA. However, pioneering research at Newcastle University has demonstrated another way.

Almost 30 years ago researchers took a cell from a donor and transferred the mitochondria to an egg taken from a woman with mitochondrial disease. Ordinary IVF techniques were then used to fertilize the egg with sperm from the woman's partner, at which point it was implanted in the mother. The result was Alana Saarinen, hailed as the :"girl with three biological parents". Several other children were conceived this way. Like Saarinen, they have avoided the diseases their mother carried.

Nevertheless, several of these children conceived in the 1990s through what is known as cytoplasmic transfer, or mitochondrial replacement therapy, have other genetic diseases or experienced developmental disorders. It remains unclear if this was just bad luck – such conditions exist in any population – or if the process raised the risk.

Combined with the idea the work was "playing God", or could lead to undesirable applications, the process was halted for almost two decades, until a review and extensive legislative battle led to legalization by the UK Parliament in 2015.

Now the results of the first mitochondrial replacement IVFs performed with legal backing have been announced. Rather than use an ordinary cell from a donor, the process was performed through “pronuclear transfer”. The nuclear genome was taken from the mother’s egg and transferred into an egg from a donor without mitochondrial disease, which had previously had its own nuclear DNA removed. Both eggs had been fertilized with the father's sperm, prior to the transfer

None of the four boys and four girls born this way have any of the mitochondrial diseases their mothers would normally have passed on. Moreover, the babies were also healthy at birth and have so far met developmental guidelines. Illnesses some have experienced passed without unusual intervention. Nevertheless, observations are planned at least until the age of 5.

Although the children’s blood sometimes has some of their mother’s mitochondrial DNA (up to 16 percent in the highest case) the predominance of healthy DNA gives them the energy they need.

Open the Youtube video

"As parents, all we ever wanted was to give our child a healthy start in life. Mitochondrial donation IVF made that possible. After years of uncertainty this treatment gave us hope – and then it gave us our baby. We look at them now, full of life and possibility, and we're overwhelmed with gratitude. Science gave us a chance,” said the mother of one of the girls in a statement.

“This breakthrough has lifted the heavy cloud of fear that once loomed over us,” said the mother of one of the boys. The names of both families have not been released.

"Mitochondrial disease can have a devastating impact on families. [This] news offers fresh hope to many more women at risk of passing on this condition who now have the chance to have children growing up without this terrible disease,” said Professor Sir Doug Turnbull of Newcastle University, who was part of the team to develop the technique.

Efforts continue towards gene therapy tofix the mitochondrial diseases that would otherwise be transmitted, but this work is less advanced than the approach used here, leaving around 5,000 babies to be born each year with associated diseases. Other parents opt not to have children to avoid the risk.

Rather than undergoing pronuclear transfer, some mothers at lower risk of transmitting mitochondrial disease in the same program underwent ordinary IVF and preimplantation genetic testing (PGT) of embryos. This has led to 18 births within the program. Six of the mothers between the two groups had previously given birth to a child affected by mitochondrial diseases.

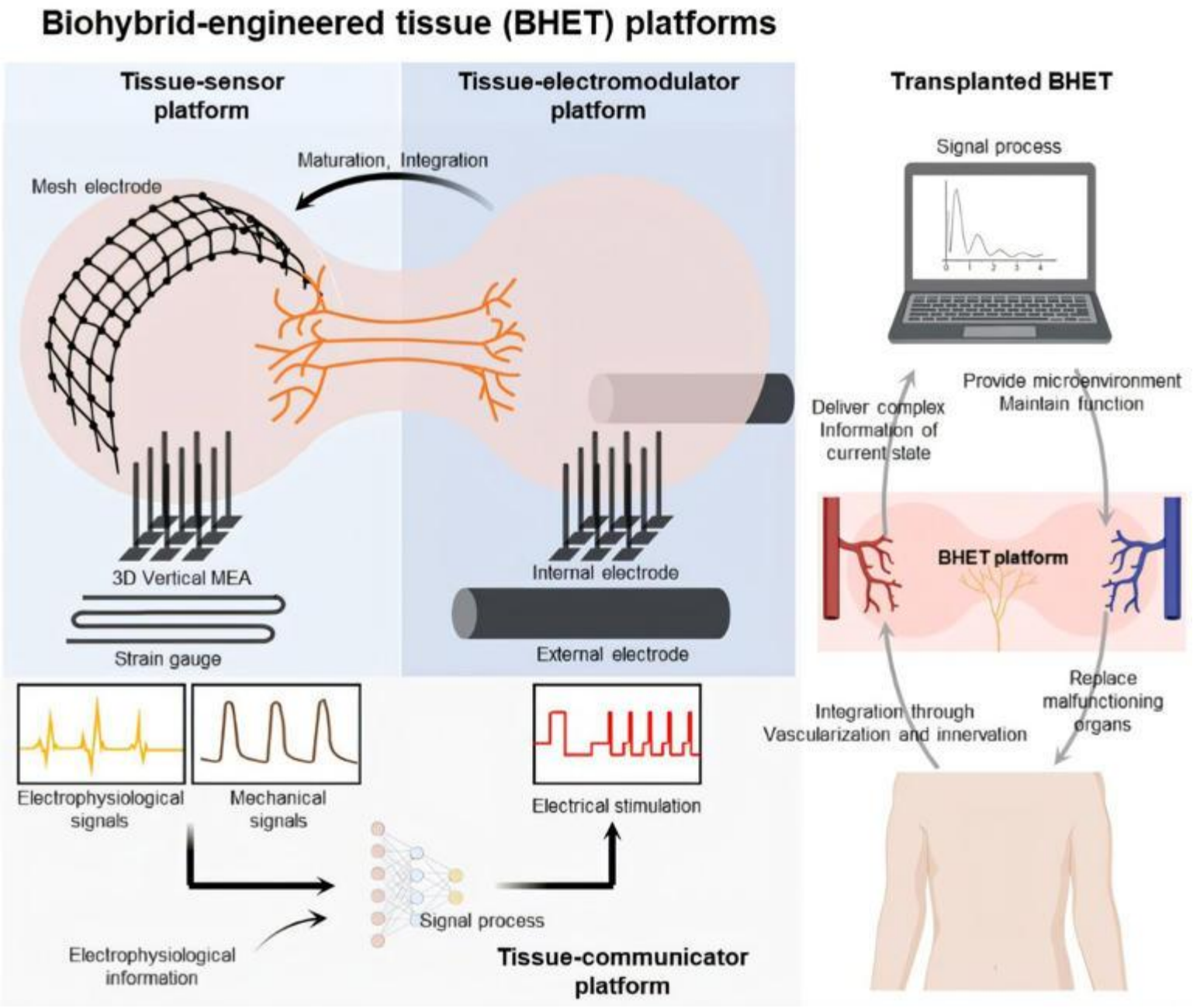
For all the benefits the pronuclear transfer provides, the proportion of mothers who experienced successful pregnancies was lower than among those who underwent PGT. The reasons for this are only partly understood.

"The published results are very valuable, but some scientists will be a little disappointed that so much time and effort has, so far, only led to the birth of 8 children," commented Professor of Reproductive Genetics at the University of Oxford Dagan Wells, who was not directly involved in the work, for Science Media Centre.

Some of the women took part in the program because they have family members with mitochondrial disease, but others have relatively mild forms of the disease themselves. The authors note there is a "theoretical risk" of pregnancy exacerbating these symptoms, but so far no related complications have been reported. The authors also note that many of the women deemed eligible for pronuclear transfer or PGT opted not to go ahead at this time after being counseled on what is involved.

The results of the program have been announced in two papers in The New England Journal Of Medicine.

From passive to intelligent: Bioengineered organs meet electronics



Classification of BHET platforms into three types based on their functional objectives: 1) tissue-sensor platforms, 2) tissue-electromodulator platforms, 3) tissue-communicator platforms. Credit: POSTECH

Bioengineered organs are no longer just structural substitutes.
A review published in *Trends in Biotechnology* introduces a groundbreaking concept: biohybrid-engineered tissue (BHET) platforms—living constructs

integrated with electronics that can monitor, modulate, and even autonomously control their own functions.

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The review outlines how recent advances in biofabrication and biomedical electronics have pushed tissue engineering onto new frontiers. The paper was authored by Dr. Uijung Yong (Future IT Innovation Laboratory, Pohang University of Science and Technology (POSTECH)), Jihwan Kim (Department of Mechanical Engineering, POSTECH), and Prof. Jinah Jang (Department of Mechanical Engineering, Convergence IT Engineering, and School of Interdisciplinary Bioscience and Bioengineering, POSTECH).

Traditional bioengineered organs have been limited in their ability to replicate the complex and dynamic nature of human organs. BHET platforms aim to change that by turning passive constructs into intelligent systems.

The authors classify BHET platforms into three main types:

- **Tissue-sensor platforms** capture real-time physiological data, such as electrical activity or metabolite levels, offering continuous insights into tissue health and function.
- **Tissue-electromodulator platforms** actively control tissue behavior using targeted electrical stimulation, accelerating tissue maturation or modulating hormone release.
- **Tissue-communicator platforms** integrate both sensing and stimulation to enable closed-loop feedback, allowing tissues to adapt autonomously to environmental cues, much like living organs do.

These systems have already shown promise in diverse applications: brain organoids learning through neural feedback, cardiac tissues synchronizing contractions with external pacing, and engineered β cells releasing insulin in response to electrical signals. Such platforms blur the line between biology and machine, turning tissues into responsive and programmable devices.

The review also explores future directions, including AI-driven control systems, conductive hydrogel electrodes, and scalable 3D bioprinting techniques that can bring intelligent tissue platforms closer to clinical applications.

"By incorporating bioelectronics into tissue engineering, we can create more functional and intelligent bioengineered organs," said Prof. Jang.

"Combining this with AI-based analytics will allow bioengineered organs to autonomously monitor and regulate their functions with unprecedented precision."

More information: Uijung Yong et al, Biohybrid-engineered tissue platforms: bridging the gap in tissue engineering, *Trends in Biotechnology* (2025). DOI: 10.1016/j.tibtech.2025.05.018

Provided by Pohang University of Science and Technology

JULY 18, 2025

Discovery of a tRNA methyltransferase with an unusual domain architecture and functional features

by Ehime University edited by Sadie Harley, reviewed by Andrew Zinin

Nucleoside sequence of T. kodakarensis $tRNA^{Trp}$. In this study, the researchers focused on the Cm modification highlighted in red. Credit: Teppei Matsuda, Ryota Yamagami, Hiroyuki Hori, Ehime university

All living organisms encode the amino acid sequences of proteins as nucleotide sequences (genetic information) in their genomic DNA. The genetic information is transcribed and subsequently translated into functional proteins.

Transfer RNA (tRNA) acts as an adaptor molecule that decodes codons on messenger RNA (mRNA) and delivers the corresponding amino acid to the ribosome, the machine of protein synthesis.

Following transcription, tRNAs undergo extensive chemical modifications, which play crucial roles in fine-tuning their structural stability and functional capacity.

Among the three domains of life, archaea are believed to have thrived in the harsh environments of early Earth, such as high temperature, high salinity, and low oxygen. To survive these extreme conditions, archaeal tRNA modifications are thought to have been diversified uniquely during evolution.

In 2019, the research group reported the nucleotide sequence of $tRNA^{Trp}$ isolated from Thermococcus kodakarensis, a hyperthermophilic archaeon. This tRNA was found to contain a 2′-O-methylcytidine (Cm) modification at position 6. However, the methyltransferase responsible for this specific modification remained unknown.

In a new study, the researchers employed comparative genomics to examine the genome of T. kodakarensis along with those of closely related archaeal species, leading to the identification of candidate genes. Among these, the team focused on the gene TK1257. The study has been published in *Nucleic Acids Research*.

Through biochemical analysis using the purified recombinant protein and high-sensitivity RNA mass spectrometry, the researchers demonstrated that the TK1257 gene product catalyzes the formation of the Cm6 modification, identifying it as a previously uncharacterized tRNA methyltransferase.

Further sequence and structural modeling analyses revealed that the enzyme contains both a THUMP domain, which recognizes and binds the 3′-end of tRNA, and a SPOUT catalytic domain with a characteristic trefoil knot structure.

This domain architecture—combining THUMP and SPOUT domains—has not been reported previously in tRNA methyltransferases. Accordingly, the researchers named this enzyme TrmTS (Transfer RNA methylation gene product with THUMP and SPOUT domains).

TrmTS exhibits substrate specificity for adenosine, cytidine, and uridine, catalyzing 2′-O-methylation at the ribose moiety of these nucleosides. Notably, it does not modify guanosine, making its substrate selectivity highly unique among known tRNA methyltransferases.

Moreover, a T. kodakarensis mutant lacking the trmTS gene exhibited impaired growth under extreme heat conditions (93°C), suggesting that the Cm6 modification contributes to the thermal stability of tRNA and plays a role in adaptation to high-temperature environments.

This study presents a novel paradigm in tRNA modification biology, identifying a tRNA methyltransferase that does not conform to existing classification schemes.

The discovery of TrmTS, with THUMP and SPOUT domains, sheds new light on the diversity and evolution of tRNA modifications and provides important insights into the molecular strategies archaea use to thrive in extreme environments.

More information: Teppei Matsuda et al, A transfer RNA methyltransferase with an unusual domain composition catalyzes 2′-O-methylation at position 6 in tRNA, *Nucleic Acids Research* (2025). DOI: 10.1093/nar/gkaf579
Journal information: Nucleic Acids Research
Provided by Ehime University

JULY 23, 2025

New insights from the 1000 Genomes Project provide most complete view to date of human genetic variation

by European Molecular Biology Laboratory edited by Stephanie Baum, reviewed by Andrew Zinin

New analysis of the 1000 Genomes sample set yields brand new insights, providing a more complete view of human genetic variation than ever before. Credit: Daniela Velasco/EMBL Completed in 2003, the Human Genome Project gave us the first sequence of the human genome, albeit based on DNA from a small handful of people. Building upon its success, the 1000 Genomes Project was conceived in 2007. The project began with the ambitious aim of sequencing 1,000 human genomes and exceeded it, publishing results gleaned from over 2,500 individuals of varying ancestries in 2015.

Together, these projects have contributed to much of our knowledge about the genetics that make us unique and underlie our biology.

Now, 10 years down the road, EMBL scientists and their collaborators have revealed exciting new insights into human biology through deeper analysis of samples from this vast resource, using methods and technologies not available a decade ago. The resulting datasets, shared in two back-to-back publications in the journal *Nature,* constitute what may be the most complete overview of the human genome to date.

"About 15 years ago, most human genome sequencing relied on 'reads' from small stretches of DNA—not enough to piece together a full genome, but sufficient to allow studies of genetic variation in larger parts of the genome," said Jan Korbel, Group Leader and Interim Head at EMBL Heidelberg, and co-senior author of the new studies.

"However, since about five years ago, it has become possible to routinely sequence human genomes with new commercially available technologies that can decode much longer stretches of DNA, allowing us to assemble the full genome of individuals and assess all parts of the genome for genetic variation."

These technologies are collectively known as long-read sequencing methods, and EMBL scientists have used them to improve our understanding of cancer development and for environmental research.

"We wanted to take advantage of the power of these new transformative sequencing techniques to learn more about human genetic variation," said Korbel.

Genetic variations—differences in DNA sequence between individuals—help make each of us unique and play an important role in health and disease. While such variations can take the form of small differences, e.g., in one or a few letters of the genetic code, they can also be much more profound, with entire long stretches of DNA being deleted, inverted, repeated, or added in certain individuals.

It is now known that such structural variations are not only common, but also play a major role in many genetic diseases, including cancer. "Maps" of such variation across the human genome are also highly clinically relevant, as they serve as a reference to understand what goes wrong under disease conditions.

The two new studies use long-read sequencing technologies to dive deeper into such structural variations across the genome. For both studies, the Korbel Group teamed up with the lab of Tobias Marschall at Heinrich Heine University Düsseldorf, Germany, which is composed of experts in genome data science.

Enhancing the human pangenome

The first study looks at 1,019 genomes from the 1000 Genomes Project dataset, spread across 26 populations from five continents. Using long-read sequencing methods and teaming up with Siegfried Schloissnig from the Institute of Molecular Pathology (IMP) Vienna, Austria, the researchers created detailed maps of structural variations across the genomes of these individuals. In addition to generating new biological knowledge, with this new information, they could expand by more than twentyfold the 44-genome reference graph published by the Human Pangenome Reference Project in 2023.

For this study, the researchers also collaborated with Ewan Birney's team and Sarah Hunt at EMBL-EBI, as well as Bernardo Rodríguez Martín from the Centre for Genomic Regulation (CRG), Spain, among others.

"The original 1000 Genomes Project created a map of genome locations that are variable in the human population, and this enabled us to systematically search for regions associated with common diseases," said Hunt. "That first map was built from short variants, but we already know of cases where longer variants are associated with disease. The new map from this study is more precise and deeper than other structural variant maps created so far and will enable us to seek new disease links."

The second study uses a much smaller sample set of only 65 individuals but combined several powerful sequencing methods to put together genomes that are more complete than any ever sequenced before. For several chromosomes, the researchers assembled end-to-end sequences, a remarkable feat considering that human chromosomes can be hundreds of millions of base pairs (i.e. "letters") long. This study was carried out in

collaboration with researchers from several leading US institutes, who together formed part of the Human Genome Structural Variation Consortium.

"The Human Genome Structural Variation Consortium brings together people who are experts in different techniques and genomic areas and shows the power of international collaboration to drive discovery," said Hunt. "This work reveals new biological insights by shining a light on parts of the genome we could not previously see and has created a toolkit for the analysis of further genomes."

Korbel believes the studies strongly complement each other.

"One study uses less sequencing power, but a much larger cohort. The other uses a smaller cohort, but much more sequencing power per sample. This led to complementary conclusions," he said.

Such complete datasets have tremendous clinical relevance, since they serve as references against which genetic variations in disease can be identified and checked. In an additional experiment, the researchers showed that using the larger dataset of 1,019 genomes as a reference significantly improved the accuracy of identifying disease-associated variants compared to previous methods.

The datasets also yielded interesting new biological insights. For example, the study with 1,019 samples helped elucidate a new mechanism by which transposons—sometimes called jumping genes—can help move stretches of DNA to new locations within the genome, giving rise to new variants.

The 65-genome dataset, on the other hand, helped scientists understand certain sections of the genome that are very difficult to study using traditional methods, such as centromeres. Centromeres are the spots where two strands of the chromosome attach to each other when cells divide (forming the well-known X-shape), and disruptions in them have been linked to many disorders, including immune disorders and cancer.

"These two studies underscore the crucial role of repetitive DNA in shaping the human genome, uncovering a reservoir of genetic variation within regions that were largely missed in previous reference datasets due to their repetitive and complex nature," said Bernardo Rodríguez-Martín, former member of the Korbel group, now Group Leader at the CRG and co-senior author of one of the studies.

A new resource for genome biologists

The new datasets have been made publicly available to researchers worldwide to analyze and use. The studies also forced innovation in the form of new genomic analysis methods, which the scientists created to analyze data at a scale much greater than previous studies had attempted.

"Through these studies, we have created a comprehensive and medically-relevant resource that can now be used by researchers everywhere to better understand the origins of human genomic variation, and see how it is affected by a plethora of different factors," said Marschall, Professor at Heinrich Heine University Düsseldorf and co-senior author on the two studies.

"This is a great example of collaborative research opening up new vistas in genomic science and a step towards a more complete human pangenome."

More information: Complex genetic variation in nearly complete human genomes, *Nature* (2025). DOI: 10.1038/s41586-025-09140-6. www.nature.com/articles/s41586-025-09140-6

Structural variation in 1,019 diverse humans based on long-read sequencing, *Nature* (2025). DOI: 10.1038/s41586-025-09290-7. www.nature.com/articles/s41586-025-09290-7
Journal information: Nature
Provided by European Molecular Biology Laboratory

JULY 23, 2025

Floating babies, cosmic radiation and zero-gravity birth: What space pregnancy might actually involve

by Arun Vivian Holden, The Conversation edited by Gaby Clark, reviewed by Andrew Zinin

Timeline of development. P_0 to P_{10} are probabilities of successfully completing the processes of ejaculation P_0, ovulation P_1, fertilization P_2, blastocyst formation P_3, implantation P_4, gastrulation P_5, placentation P_6. Credit: *Experimental Physiology* (2025). DOI: 10.1113/EP092290

As plans for missions to Mars accelerate, so do questions about how the human body might cope. A return trip to the red planet would give more than enough time for someone to become pregnant and even give birth. But could a pregnancy be conceived and carried safely in space? And what would happen to a baby born far from Earth?

Most of us rarely consider the risks we survived before birth. For instance, about two-thirds of human embryos do not live long enough to be born, with most losses happening in the first few weeks after fertilization; often before a person even knows they're pregnant. These early, unnoticed losses usually happen when an embryo either fails to develop properly or to implant successfully in the wall of the womb.

Pregnancy can be understood as a chain of biological milestones. Each one must happen in the right order and each has a certain chance of success. On Earth, these odds can be estimated using clinical research and biological models. My latest research explores how these same stages might be affected by the extreme conditions of interplanetary space.

Microgravity, the near-weightlessness experienced during spaceflight, would make conception more physically awkward but probably wouldn't interfere much with staying pregnant once the embryo has implanted.

However, giving birth, and looking after a newborn, would be far more difficult in zero gravity. After all, in space, nothing stays still. Fluids float. So do people. That makes delivering a baby and caring for one a much messier and more complicated process than on Earth, where gravity helps with everything from positioning to feeding.

At the same time, the developing fetus already grows in something like microgravity. It floats in neutrally buoyant amniotic fluid inside the womb, cushioned and suspended. In fact, astronauts train for spacewalks in water tanks designed to mimic weightlessness. In that sense, the womb is already a microgravity simulator.

But gravity is only part of the picture.

Radiation

Outside Earth's protective layers, there's a more dangerous threat: cosmic rays. These are high-energy particles—"stripped-down" or "bare" atomic nuclei—that race through space at nearly the speed of light. They're atoms that have lost all their electrons, leaving just the dense core of protons and neutrons. When these bare nuclei collide with the human body, they can cause serious cellular damage.

Here on Earth, we're protected from most cosmic radiation by the planet's thick atmosphere and, depending on the time of day, tens of thousands to millions of miles of coverage from Earth's magnetic field. In space, that shielding disappears.

When a cosmic ray passes through the human body, it may strike an atom, strip its electrons, and smash into its nucleus, knocking out protons and neutrons and leaving behind a different element or isotope. This can cause extremely localized damage—meaning that individual cells, or parts of cells, are destroyed while the rest of the body might remain unaffected. Sometimes the ray passes right through without hitting anything. But if it hits DNA, it can cause mutations that increase the risk of cancer.

Even when cells survive, radiation can trigger inflammatory responses. That means the immune system overreacts, releasing chemicals that can damage healthy tissue and disrupt organ function.

In the first few weeks of pregnancy, embryonic cells are rapidly dividing, moving, and forming early tissues and structures. For development to continue, the embryo must stay

viable throughout this delicate process. The first month after fertilization is the most vulnerable time.

A single hit from a high-energy cosmic ray at this stage could be lethal to the embryo. However, the embryo is very small—and cosmic rays, while dangerous, are relatively rare. So a direct hit is unlikely. If it did happen, it would probably result in an unnoticed miscarriage.

Pregnancy risks

As pregnancy progresses, the risks shift. Once the placental circulation—the blood flow system that connects mother and fetus—is fully formed by the end of the first trimester, the fetus and uterus grow rapidly.

That growth presents a larger target. A cosmic ray is now more likely to hit the uterine muscle, which could trigger contractions and potentially cause premature labor. And although neonatal intensive care has improved dramatically, the earlier a baby is born, the higher the risk of complications, particularly in space.

On Earth, pregnancy and childbirth already carry risks. In space, those risks are magnified—but not necessarily prohibitive.

But development doesn't stop at birth. A baby born in space would continue growing in microgravity, which could interfere with postural reflexes and coordination. These are the instincts that help a baby learn to lift its head, sit up, crawl, and eventually walk: all movements that rely on gravity. Without that sense of "up" and "down," these abilities might develop in very different ways.

And the radiation risk doesn't go away. A baby's brain continues to grow after birth, and prolonged exposure to cosmic rays could cause permanent damage—potentially affecting cognition, memory, behavior and long-term health.

So, could a baby be born in space?

In theory, yes. But until we can protect embryos from radiation, prevent premature birth, and ensure babies can grow safely in microgravity, space pregnancy remains a high-risk experiment—one we're not yet ready to try.

More information: Arun V. Holden, Spaceborne and spaceborn: Physiological aspects of pregnancy and birth during interplanetary flight, *Experimental Physiology* (2025). DOI: 10.1113/EP092290