MEDICAL RESEARCH VOL 8

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Pasteurizing fruit smoothies could improve digestion of beneficial polyphenols

by American Chemical Society edited by Stephanie Baum, reviewed by Robert Egan

Smoothies pasteurized with pressure (left image) or heat (right image) have higher amounts of digestible polyphenols than raw smoothies. Credit: Iziar Ludwig

Drinking a smoothie is a popular way to consume fruits and vegetables, many of which are rich in micronutrients called polyphenols. If this beverage is purchased at a store, it's likely been pasteurized with heat or pressure to prevent harmful bacteria growth and extend shelf-life.

Now, a preliminary study in the *Journal of Agricultural and Food Chemistry* reports that processing smoothies with high heat could also make polyphenols easier for the gut microbiome to absorb.

Fruits and vegetables are key to a healthful human diet, partly because they contain polyphenols, which can protect against heart disease and neurodegenerative disorders. These beneficial components are released from food during digestion, making them available for absorption by the gut microbiome.

Previous research had found that food processing techniques like canning and boiling peppers and artichokes may increase the amount of polyphenols metabolized by the gut microbiota, potentially improving the health benefits of these foods. But gaps exist in scientists' knowledge of other food processing techniques. So, Iziar Ludwig and colleagues investigated how pasteurization could affect polyphenol digestion in the gut microbiome.

The researchers first prepared a smoothie made up of Granny Smith apples, green celery, green chicory, peppermint and lemon. They split up the smoothie into three parts: One was not treated, and the others underwent either high-pressure or high-temperature pasteurization.

Then, the smoothie samples were added to successive solutions meant to mimic the three stages of digestion—oral, gastric and intestinal. Post-digestion pressure- and heat-pasteurized smoothie samples had higher amounts of polyphenolic compounds (21% and

44%, respectively) available for absorption than the untreated sample (17%). The researchers attribute these results to changes in the plants' cell walls, such as softening or rupturing, induced by pasteurization that could favor the release of polyphenols into the body.

Finally, to analyze gut microbiome transformations of polyphenols, the digested samples went through a laboratory version of colonic fermentation in vials containing human feces as the microbiota source. The gut microbiota converted most polyphenols into smaller derivatives, such as phenylpropanoic acids. Some of these derivatives have previously demonstrated antidiabetic, anti-inflammatory and chemopreventive effects.

The researchers determined that the largest microbiota conversions happened in the high-temperature, post-digestion smoothie sample because it started fermentation with higher overall polyphenol levels. They say this work emphasizes how smoothie processing could lead to new beverage products with enhanced bioaccessibility.

More information: High-Pressure and Thermal Pasteurization Applied to Smoothies Enhances (Poly)Phenol Bioaccessibility along the Gastrointestinal Tract, *Journal of Agricultural and Food Chemistry* (2025). DOI: 10.1021/acs.jafc.4c09166
Journal information: Journal of Agricultural and Food Chemistry
Provided by American Chemical Society

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Waist-to-height ratio outperforms BMI in detecting the risk of fatty liver disease and liver cirrhosis

by University of Eastern Finland edited by Lisa Lock, reviewed by Robert Egan

In 6,464 multiethnic youths and adults drawn from the United States' National Health and Nutrition Examination Survey (NHANES) 2021—2023 cycle, waist-to-height ratio estimated fat mass detected the risk of fatty liver disease and liver cirrhosis better than BMI-obesity.
Credit: *Journal of the Endocrine Society* (2025). DOI: 10.1210/jendso/bvaf079
Excess fat mass estimated by waist-circumference-to-height ratio predicts the risk of liver damage better than body mass index (BMI) estimated obesity, a new study shows. Waist-to-height ratio is a cheap and universally accessible tool to detect the risk of fatty liver disease both in the young and adult population.

The study was conducted at the University of Eastern Finland, and the results were published in the *Journal of the Endocrine Society*.

In the present study, 6,464 children, adolescents and adults between 12 and 80 years of age were drawn from the United States National Health and Nutrition Examination Survey (NHANES) conducted between 2021 and 2023. Non-invasive liver scans were conducted in all participants by transient elastography, based on which their risk of liver steatosis or fibrosis was classified.

The prevalence of significant or advanced liver fibrosis was 7.1%, while 4.9% had liver cirrhosis. More than 1 in 4 (26.1%) participants had suspected liver steatosis, while less than 1% had severe liver steatosis.

Previous studies in adults have shown that BMI-diagnosed obesity is a risk factor for liver steatosis. However, recent clinical consensus statements have recommended that obesity should not be diagnosed with BMI alone but confirmed with another measure such as waist-to-height ratio.

In a recent study, waist-to-height ratio was discovered as a highly sensitive and specific predictor of dual-energy X-ray absorptiometry-measured total body fat mass and abdominal fat mass in the pediatric and young adult populations. Waist-to-height ratio cutpoints for normal, high and excess fat mass were established and have since been validated to detect the risk of type 2 diabetes and bone fracture. The present study examined if these cutpoints can predict liver steatosis and fibrosis in a multiracial population.

The prevalence of waist-to-height-ratio-estimated normal fat mass (0.40–<0.50), high fat mass (0.5–<0.53) and excess fat mass indicating obesity (≥0.53) was 20.3%, 13.6% and 64.5%, respectively. After full adjustments for covariates, normal fat mass had a 48% protective effect against liver steatosis and a 52% protective effect against liver fibrosis or cirrhosis. High fat mass predicted 63% higher odds of liver steatosis and 31% higher odds of liver fibrosis or cirrhosis. Excess fat mass predicted four-fold higher odds of liver steatosis and 61% higher odds of liver fibrosis or cirrhosis.

Waist-to-height-ratio-estimated high fat mass and excess fat mass separately predicted higher odds of liver steatosis nearly two-fold and six-fold, respectively, better than BMI-overweight and BMI-obesity. The study accounted for age, sex, systolic blood pressure, heart rate, educational status, smoking status, race, sedentary time, moderate physical activity, fasting insulin, glucose, total cholesterol and high-sensitivity C-reactive protein.

"Remarkably, the findings were consistent regardless of sex and age. In addition, the findings were similar across the studied white, Black, Mexican-American and Hispanic populations. The simple and universally accessible waist-to-height measurement is useful in clinical and public health practice for liver disease screening, prevention, diagnosis and management globally," says Andrew Agbaje, physician and associate professor (docent) of Clinical Epidemiology and Child Health at the University of Eastern Finland.

Based on his previous research, Agbaje has also developed a waist-to-height ratio clinical calculator.

More information: Andrew O Agbaje, Novel Pediatric Waist-to-height Ratio Fat Mass Cutoff Predicts Liver Steatosis and Fibrosis Better than Body Mass Index: The NHANES, *Journal of the Endocrine Society* (2025). DOI: 10.1210/jendso/bvaf079
Provided by University of Eastern Finland

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Bioengineered skin doubles burn healing speed in preclinical models

by Tel-Aviv University edited by Gaby Clark, reviewed by Robert Egan

Bioengineered artificial skin for burn treatment - stable, easy to handle, and fully autologous. Credit: Tel Aviv University
Researchers from Tel Aviv University and Sheba Tel Hashomer Medical Center have developed an innovative bioengineered skin equivalent for grafting in burn victims. The bioengineered skin produced from the patient's own cells is more stable, robust, and flexible than current treatments, making it easier to handle.

In a full-thickness wound model, it achieved wound closure in half the time of standard therapies. This pioneering study was driven by the ongoing war and the surge in severe burn injuries, which underscored the urgent need for better treatment solutions.

The paper was published in the journal *Advanced Functional Materials.*

"Surgical intervention is often essential for second-degree burns and above to restore skin, prevent infection, and save lives," explains Prof. Lihi Adler-Abramovich. "The current gold-standard treatment is 'autologous skin grafting,' in which healthy skin is harvested from another area of the patient's body and transplanted onto the burn site.

"However, this approach has significant disadvantages, in particular the need to damage healthy tissue in order to treat the injury. This becomes especially problematic in cases of extensive burns, where the availability of intact skin is limited.

"One of the most advanced alternatives, currently offered in Israel only at Sheba Medical Center, is 'cultured epidermal autograft' (CEA). Instead of removing a large skin section, a small biopsy is taken, and cells extracted from that sample are cultured in the lab to produce skin grafts for transplantation.

"While this method avoids donor-site damage, it comes with several challenges. First, the skin cells are grown on a layer of mouse-derived feeder cells, requiring strict regulation to

ensure no mouse cells remain in the graft; Second, once removed from the culture dish, the CEA shrinks by over 50%, significantly reducing yield up to 30 grafts may be needed to cover a single area, such as an arm or leg.

"Finally, the lab-grown skin consists of only the upper epidermal layer, making it extremely thin, fragile, and prone to curling at the edges."

The need for advanced solutions is particularly urgent in wartime, with many soldiers suffering from burns. For both soldiers and civilians, a durable bioengineered graft could significantly improve chances for recovery and a good quality of life.

Fluorescent staining of skin cells taken from the patient and grown on the bioengineered graft. Credit: Tel Aviv University

"Since October 2023, Sheba has treated many young people with burn injuries," says Dr. Ayelet Di Segni. "At such a time, bringing knowledge accumulated in the lab directly to the patient's bedside becomes an urgent and tangible goal. Our aim is to develop a graft that can truly transform the process of recovery."

To address this challenge, researchers from Tel Aviv University and Sheba Medical Center collaborated to develop multi-cellular, multi-layered bioengineered skin grafts designed to mimic the properties and function of natural skin, without shrinking, tearing upon contact, or relying on animal-derived additives.

"We designed a nanofiber scaffold made of a polymer called PCL, which is already FDA-approved, and combined it with a bioactive peptide—a short amino acid sequence that promotes cell adhesion, growth, and proliferation," explains Ph.D. student Dana Cohen-Gerassi.

"We then seeded this scaffold with skin cells derived from a patient's biopsy. Remarkably, the cells organized themselves naturally: fibroblasts populated one side of the scaffold, while keratinocytes grew on the other—mimicking the structure of real human skin."

Dr. Marina Ben-Shoshan, senior researcher at Sheba's Green Center for Skin Graft Engineering, adds, "Our graft is unique in that it does not shrink, and is durable, flexible, and easy-to-handle. Implantation in model animals has yielded impressive results, accelerating the healing process. While the standard treatment closes half of the burn wound in eight days, with our method, this took only four days. Moreover, we observed that essential skin structures, such as hair follicles, began to grow."

Dr. Amit Sitt from TAU's School of Chemistry adds, "The nanofiber scaffolds are made from easily available biocompatible materials and produced via a scalable spinning process. In the future, this will enable large-scale production of fiber sheets, as well as incorporation of additional substances to facilitate the healing process."

Prof. Yossi Haik of Sheba Medical Center concludes, "The bioengineered skin we've developed represents a true breakthrough in burn care. Made entirely from the patient's own cells, it is strong, flexible, easy to handle, and significantly accelerates healing.

"This is a major step towards personalized therapies that can greatly improve the recovery and quality of life of severe burn victims, both soldiers and civilians. In the next phase, we plan to conduct trials in additional models and advance the necessary regulatory processes to bring this innovative technology closer to clinical application."

More information: Dana Cohen-Gerassi et al, Stable, Easy-to-Handle, Fully Autologous Electrospun Polymer-Peptide Skin Equivalent for Severe Burn Injuries, *Advanced Functional Materials* (2025). DOI: 10.1002/adfm.202501745
Journal information: Advanced Functional Materials
Provided by Tel-Aviv University

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Ultra-processed foods may affect the brain and lead to overeating

by Janne Huovila, University of Helsinki edited by Lisa Lock, reviewed by Robert Egan

The image highlights the brain regions identified in the study as being associated with the high consumption of ultra-processed foods. Cell density is lower in the grey regions. This may point to a loss of neurons, that is, diminished brain activity in these regions. Cell density is higher in the green regions, implying the presence of inflammatory changes in the brain. Credit: University of Helsinki
Studies have linked the high consumption of ultra-processed foods with multiple diseases, including diabetes, cardiovascular and cerebrovascular disease, and dementia. A recent international study explored the connection between ultra-processed food consumption and brain structure.

The study was conducted using data from the UK Biobank, encompassing about 30,000 middle-aged individuals from the U.K. It was carried out by the University of Helsinki's O'BRAIN Lab, which studies the link between the brain and obesity, in collaboration with the Montreal Neurological Institute. The work is published in the journal *npj Metabolic Health and Disease*.

"Our findings indicate that a high consumption of ultra-processed foods is associated with structural changes in brain regions regulating eating behavior, such as the hypothalamus, amygdala and right nucleus accumbens. This may lead to a cycle of overeating. However, long-term and experimental studies are still needed to strengthen the association," says doctoral researcher Arsène Kanyamibwa of the University of Helsinki.

The study indicated that the link between ultra-processed foods and overeating cannot be accounted for solely by the resultant inflammation or obesity. Changes in the brain may also be explained by the ingredients, emulsifiers and other additives used to make ultra-processed foods.

Kanyamibwa believes that the unhealthy effects of ultra-processed foods should be given more attention as part of personal food choices, food regulation and nutrition policy alike.

He notes, however, that not all processed foods need be avoided.

"In particular, processed foods of plant origin, such as frozen vegetables, can be recommended. Another good example of the benefits of processing is the pasteurization of milk. In contrast, foods high in chemically modified ingredients and additives, such as processed meat products, are problematic. The nutrition and dietary recommendations published in Finland last year offer a solid foundation for healthy eating."

More information: Filip Morys et al, Ultra-processed food consumption affects structural integrity of feeding-related brain regions independent of and via adiposity, *npj Metabolic Health and Disease* (2025). DOI: 10.1038/s44324-025-00056-3
Provided by University of Helsinki

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Q&A: Researcher discusses mapping how nutrients move through the body to treat cancer

by Katherine Fenz, Rockefeller University edited by Stephanie Baum, reviewed by Andrew Zinin

When you swallow a vitamin or eat a meal, the nutrients you've ingested flow into your stomach, break down, and enter your bloodstream. But what happens next? How do nutrients move from your arteries into the cells where they actually do their jobs? What determines whether some nutrients go to the brain, while others power your immune system instead?

There are about 5,000 different metabolites—all those nutritional end products—in human blood, and scientists still don't know how most of them make their way into cells. But this knowledge is critical for connecting the dots between what we consume and how our bodies maintain health—and for taking the guesswork out of the $200 billion supplement

industry, which revolves around the assumption that dietary elements end up where they are needed.

It also could change how we treat cancers, which suck up nutrients faster and in higher amounts than normal cells, giving them the fuel they need to grow and spread.

Kivanç Birsoy, head of the Laboratory of Metabolic Regulation and Genetics at Rockefeller University, has been mapping out nutrient highways with a meticulous curiosity and a bold vision. His lab focuses on understanding transporters—tiny protein channels that act like specialized delivery trucks, grabbing molecular cargo from your bloodstream and shuttling them into and within your cells.

In this interview, Birsoy talks about why understanding these transporters is so important to human health and disease.

You've noted that much of the current science around nutrition isn't very informative. A big part of the motivation for your research is to change that. Can you explain what you mean?

Most of the vitamins and supplements you see in stores haven't been studied in ways that actually show how they work in the body. Take vitamin C, for example. Lots of people swear it helps them fight off colds, but the studies are all over the place. Some suggest it's helpful, others say it's useless. Even when something does seem helpful, we rarely know the right dosage or who will benefit most.

The problem is that most studies are just correlations. They might show that people who take a certain supplement are healthier, but they can't prove the supplement is what made the difference. To really understand what a certain nutrient does—and doesn't do—we have to figure out how and when nutrients enter our cells and what happens to them once they're inside. That's what my lab does.

What first drew you to study the intersection of nutrition and cancer?

I was fascinated by how resourceful cancer cells are. They grow and spread at such an intense rate, far beyond what normal cells do, which means they need a lot more fuel. But the interesting thing about tumors is that they don't just rely on the fuel that is already available. They actually rewire their own metabolic machinery to grab more nutrients from their environment or to survive even when resources are scarce.

Early in my career, I realized that if we could figure out exactly what nutrients cancer cells need and how they're getting them, we might be able to cut off their supply.

Has your research suggested that targeting cancer cells' nutrients in this way will indeed be possible?

Yes, we've found some Achilles' heels in cancer cells that we think we can use to stop the growth or spread of tumors. In one study, my lab showed how cancer cells can turn on a gene that lets them suck up the amino acid aspartate from their surroundings. Cells that have this gene grow faster. Now, we're looking at drugs that interfere with a cancer's ability to produce or take in aspartate.

In other work, we discovered that some cancer cells rely heavily on an antioxidant called glutathione to protect themselves from damage and help them spread to other parts of the body. They need much more glutathione than normal cells do. When we block the transporter responsible for bringing glutathione into cancer cells, we can stop the cells from spreading.

This kind of information is vital—conventional wisdom tells people that antioxidants are good for them. And generally speaking, they are. But there are situations—like some cancers—where certain antioxidants could actually fuel disease.

By targeting these pathways with drugs, we might be able to directly kill cancer cells—or to enhance the immune system's ability to attack cancer cells, especially if we can prevent those cells from hoarding the nutrients they use to hide from immune detection.

How are you figuring out which transporters work with which nutrients?

It's a huge challenge because we're talking about thousands of different transporters, each specialized to move specific nutrients. We start by looking at genetic studies of humans. If someone has a mutation in a gene linked to a transporter, it often shows up as a problem with certain nutrient levels in their blood.

Once we identify a potential transporter or sensor, we test it by removing the gene from isolated cells or animal models. That's what we did when we discovered SLC25A39, the transporter for glutathione. Initially, we looked for proteins that responded to changes in glutathione levels. Then we confirmed that SLC25A39 was the right transporter by blocking it and seeing that cells were suddenly starved of glutathione.

It turns out SLC25A39 isn't just a transporter—it's also a sensor that helps cells keep their glutathione levels balanced, which is crucial because problems with glutathione transport have been linked to conditions like cancer, neurodegeneration, and even aging.

So these transporters aren't only important for cancer, but many other aspects of health and disease. What other areas has your lab looked at?

Recently, we found a transporter responsible for moving a vitamin-like lipid called choline into cells. Scientists knew that when a person has a mutation in a particular transporter gene, it causes the rare disease posterior column ataxia with retinitis pigmentosa (PCARP), which leads to blindness and neurodegeneration. But they didn't know why. We showed that it is because cells can't get enough choline when the transporter isn't working properly.

The best part is, this isn't just a fascinating discovery—it could also be life-changing. We're already working with doctors to design clinical trials that use high levels of choline to slow down or even stop the progression of blindness in people with this disorder.

We are also looking at how nutrient transporters move molecules into mitochondria, which are the structures within cells that act like power plants, turning nutrients into energy. We want to understand how mitochondria absorb and process these nutrients, which could be key to treating disorders linked to mitochondrial dysfunction, which also includes neurodegeneration and aging.

What keeps you excited about this field?

Many transporters are associated with diseases and drug targets. The big idea is that by mapping out how transporters work, we can develop better drugs and use nutritional supplements in more targeted ways. And we may be able to use this information to customize dietary intake to improve health outcomes. That requires a lot of basic biology research, but could ultimately impact millions of lives. We're already seeing it.

Provided by Rockefeller University

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AI tool analyzes blood DNA fragments for faster, affordable cancer monitoring

by Agency for Science, Technology and Research (A*STAR), Singapore

edited by Lisa Lock, reviewed by Robert Egan

Overview of Fragle. Credit: *Nature Biomedical Engineering* (2025). DOI: 10.1038/s41551-025-01370-3

Scientists from the A*STAR Genome Institute of Singapore (A*STAR GIS) have developed a new artificial intelligence (AI)-based method called "Fragle" that makes tracking cancer easier and faster using blood tests.

Requiring only a small blood sample, this method analyzes the size of DNA fragments in the blood to reveal distinct patterns that differentiate cancer DNA from healthy DNA, helping doctors track cancer treatment response more accurately and frequently. The research was published in *Nature Biomedical Engineering* in March 2025.

Existing methods for measuring cancer DNA in the blood, also known as circulating tumor DNA (ctDNA), often require complex and expensive DNA sequencing to screen for common cancer mutations. However, because cancer mutations vary between patients, test results can be inconsistent, making it difficult for doctors to track cancer treatment response with blood tests effectively.

Fragle uses AI to analyze the size of DNA fragments in the blood. Cancer DNA tends to exhibit different size patterns compared to healthy DNA, and the Fragle AI-model can identify these differences using very small amounts of DNA. As a result, the method allows for faster and more affordable cancer tracking.

It has also demonstrated high reliability, delivering accurate results across blood samples from hundreds of cancer patients and distinct cancer types.

Additionally, the method is versatile and compatible with most DNA profiling techniques commonly used in hospitals or offered by commercial providers.

Key benefits of Fragle:

- Faster and cheaper: Fragle offers a faster and potentially more affordable way to monitor cancer through blood tests, requiring only a small amount of DNA. Conventional commercial tests can cost over SGD $1000, whereas the estimated cost of Fragle is less than SGD $50.
- Versatile: Fragle works with widely used DNA profiling methods in hospitals and commercial labs, allowing for easy and fast adoption into existing workflows.
- Detects early signs of relapse: Fragle can identify tiny traces of cancer left after surgery and treatment (known as minimal residual disease, or MRD), helping doctors detect potential relapse early.

"Just as scientists tracked COVID-19 outbreaks by detecting viral particles in wastewater, Fragle analyzes DNA fragments in blood to monitor cancer treatment response and detect relapse early," explains Dr. Anders Skanderup, Senior Principal Scientist at A*STAR GIS Laboratory of Computational Cancer Genomics, and the lead author of this research.

"While existing methods have their strengths, they are often complex and expensive. We wanted to develop a simpler, more affordable and accessible approach—one that could support accurate monitoring without adding burden to clinical workflows. "

The team is also looking into improving Fragle's sensitivity to detect even lower levels of cancer DNA, which is critical for earlier detection of disease relapse in cancer patients. To translate these findings, the team is also collaborating with the National Cancer Center Singapore (NCCS) to identify clinical opportunities and applications. Moving ahead, the team plans to explore how Fragle can be implemented in local hospitals to improve cancer patient care.

Associate Professor Daniel Tan, Senior Consultant, Division of Medical Oncology, National Cancer Center Singapore and co-author of the study,

"We are excited to initiate studies on how methods such as Fragle can detect disease relapse earlier in local lung cancer patients."

In an ongoing study of more than 100 clinical trial patients, the GIS-NCCS team is using Fragle to monitor ctDNA levels every two months during treatment, with the aim of catching signs of relapse before they appear on routine scans. The team is also studying whether early changes in ctDNA can identify which patients are likely to have a favorable or poor response to the therapy. The goal of the study is to assess the value of incorporating ctDNA tests in routine monitoring of cancer patients during treatment.

Dr. Wan Yue, Executive Director at A*STAR GIS, "We are very excited about the potential Fragle brings, to help our health care professionals detect and track cancer more accurately and monitor treatments more effectively, leading to better cancer care for patients. It is our hope that our genomic research can be translated to benefit population health not only in Singapore, but worldwide."

More information: Guanhua Zhu et al, A deep-learning model for quantifying circulating tumour DNA from the density distribution of DNA-fragment lengths, *Nature Biomedical Engineering* (2025). DOI: 10.1038/s41551-025-01370-3
Journal information: Nature Biomedical Engineering

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New study identifies unique type of microglia associated with stroke in the I/R injured brain

by JooHyeon Heo, Ulsan National Institute of Science and Technology

Peroxiredoxin1 (Prdx1) is essential for SAM activation after stroke damage. (Left) UMAP plots showing clusters and annotations of cells identified in Prdx1+/+ and Prdx1−/− IL hemispheres after tMCAO. (Right) Representative images of TTC stained brain slices of Prdx1+/+ (n = 18) and Prdx1−/− (n = 22) mice. Credit: UNIST
A research team, affiliated with UNIST has identified a new type of microglia associated with stroke in the ischemia/reperfusion (I/R) injured brain. This breakthrough has been led by Professor Sung Ho Park and his research team in the Department of Biological Sciences at UNIST, in collaboration with a research team, led by Professor Goo Taeg Oh from Ewha Womans University.

Microglia, the primary immune cells in the central nervous system (CNS), are known to eliminate unwanted germs and debris and remove dying neurons. In this study, the research team classified a new type of microglia with enhanced antioxidant function and markers similar to those of disease-associated microglia (DAM), designated them as stroke-associated microglia (SAM).

Through animal experiments, the research team demonstrated that the presence of the typical antioxidant gene, Peroxiredoxin-1 (Prdx1), protects against acute I/R injury and is required for SAM activation and the consequent reduction of microglial cell death and inflammatory responses.

In addition, after performing transient middle cerebral artery occlusion (tMCAO) surgery to induce ischemic stroke in mice, the research team found that Prdx1−/− mice were more severely injured by acute I/R injury, as confirmed by TTC staining, neurological deficit scores, motor tests, and the survival rate, indicating that Prdx1 has a protective function.

"In this study, we have, for the first time, identified a specialized and distinctive type of microglia with enhanced antioxidant function in stroke mice," says Professor Park. "Prdx1-dependent SAM may be a potential biomarker and therapeutic target for protecting microglial function and treating brain I/R injury," He adds, "Although this new cluster will require further study, our findings provide a new perspective that Prdx1-mediated microglial heterogeneity is important in ischemic stroke."

This study has been jointly participated by Wonhyo Lee, a doctoral researcher within the Department of Biological Sciences at UNIST and Sinai Kim, a doctoral researcher within the Department of Life Sciences at Ewha Womans University, as first authors. Their findings have been published in *Redox Biology*.

More information: Sinai Kim et al, The antioxidant enzyme Peroxiredoxin-1 controls stroke-associated microglia against acute ischemic stroke, *Redox Biology* (2022). DOI: 10.1016/j.redox.2022.102347
Provided by Ulsan National Institute of Science and Technology

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JANUARY 10, 2024

Mapping brain repair and remodeling after stroke

by Karen Hopkin, Cornell University

Single-cell transcriptomic profiling of mouse brain and blood cells after transient focal cerebral ischemia. Credit: *Nature Immunology* (2024). DOI: 10.1038/s41590-023-01711-x

Researchers at Weill Cornell Medicine have cataloged the cellular response to stroke in a preclinical model, identifying the immune cells involved and the roles they may play in the days and weeks following a stroke.

During a stroke, loss of oxygen leads to brain damage and cell death. It also triggers a powerful inflammatory response in which the brain's resident immune cells, along with cells recruited from the blood, infiltrate the injured tissue.

The findings, published Jan. 4 in *Nature Immunology*, could point toward novel approaches to fostering stroke recovery and provide insight into why therapies to control inflammation after a stroke haven't been successful.

"Nearly every one of us knows someone who's had a stroke. It's a huge problem," said senior author Dr. Josef Anrather, a professor of neuroscience and vice chair for research in the Feil Family Brain and Mind Research Institute at Weill Cornell Medicine. "But in terms of treatment, there is little a physician can do."

Interventions that restore blood flow to the affected brain region must be administered within hours to be effective. "So most people, more than 80%, receive no therapy at all," he said.

Understanding how immune cells contribute to repairing and remodeling the brain in the later, chronic phase after a stroke could help doctors minimize the long-term neurological consequences, including dementia and even seizures.

In 2016, Anrather and his colleagues observed that immune cells called monocytes, which are made in the bone marrow, accumulate in the brain following a stroke. Once there, they appeared to undergo a physical transformation: Some sprouted spindly arms, adopting the appearance of the brain's resident immune cells, the microglia; others grew more amorphous and amoeba-like.

But what, if anything, did this shapeshifting have to do with their behavior?

"We became interested in knowing the function of these different structural characteristics," said lead study author Lidia Garcia-Bonilla, the Finbar and Marianne Kenny Research Scholar in Neurology and an assistant professor of research in neuroscience at the Brain and Mind Research Institute, Weill Cornell Medicine.

They also wondered whether these cells were contributing to recovery or compounding the damage.

"There are always two sides to the coin," Anrather said. The same cell type might be harmful in some circumstances but helpful in others. "That might be why the clinical trials of drugs that reduce immune cell infiltration into the brain and inflammation have shown no benefit for stroke."

The most direct way to assess what a particular cell is doing is to determine which of its many genes are turned on. Working with a preclinical model, they collected immune cells at two days and 14 days after an induced stroke—the blockage of an artery in the brain. They then sequenced the RNA molecules, which encode proteins, produced by each cell. Using this approach, the researchers identified exactly each type of cell they had isolated. It also provided a readout of which genes each cell had switched on, an indication of their roles after the stroke.

The researchers first noticed that a population of microglia were rapidly proliferating. That made sense, Anrather said, "because microglia cover the territory of the brain." When their numbers are depleted by an injury, such as stroke, the cells multiply to blanket the damaged tissue.

Then they "take out the trash," Anrather said.

"For the brain to rebuild itself, you have to clean up, remove dead cells," he said. Indeed, two days after the experimental stroke, the researchers detected a cadre of microglia that switch on genes involved in clearing away cellular debris.

Joining the microglia in this effort were monocytes—white blood cells that responded to the injury. "These cells circulate continuously and don't really have a job until there is a problem, like an infection, trauma or any kind of tissue death," Anrather said. "Then they are called in to help clean up."

Once there, the researchers found, these monocytes transformed themselves into the type of cell that's needed to get the job done. "They're like little kids that get educated in the tissue," Anrather said.

After the acute clean-up phase, the immune response was restructured toward tissue remodeling. Some cellular recruits produced growth factors triggering repair while immunological "professionals" such as T cells were called in to play a neuroprotective role.

By identifying which immune cells will heed the stroke-induced distress call, the researchers provide a novel vehicle for intervention. "Because these cells know how to get to the brain," Anrather said, "you could use them as a shuttle and engineer them to deliver a therapeutic."

Furthermore, understanding precisely what these cells do when they get to the brain could be key to developing treatments that can be administered weeks or months after a stroke. "Finding a way to activate the brain's natural repair mechanism could improve the outcome for stroke patients," Garcia-Bonilla said.

More information: Lidia Garcia-Bonilla et al, Analysis of brain and blood single-cell transcriptomics in acute and subacute phases after experimental stroke, *Nature Immunology* (2024). DOI: 10.1038/s41590-023-01711-x
Journal information: Nature Immunology
Provided by Cornell University

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Repurposed cancer drugs shown to promote stroke recovery and limit brain damage

by National University of Singapore edited by Sadie Harley, reviewed by Robert Egan

Middle cerebral artery occlusion and gross neurological status upon HDACi treatment. Credit: *Glia* (2025). DOI: 10.1002/glia.70035
Stroke remains one of the leading causes of death, disability, increased economic burden and decreased quality of life around the world. Current stroke therapies are time-limited and largely focused on restoring blood flow, and there are few which address the secondary wave of inflammation that causes further injury in the hours and days after stroke.

A study by researchers from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), has shown that a class of drugs, HDACi (histone deacetylase inhibitors), protects neurons and limits brain damage following stroke by altering the gene expression of microglia, the immune cells of the brain.

HDACi are currently used or being tested as treatments for certain cancers and are also being researched for neurological conditions such as Alzheimer's disease.

The study, led by Professor S Thameem Dheen, Dr. Kevin Jayaraj and Dr. Jai S. Polepalli from the Department of Anatomy at NUS Medicine could pave the way for new treatment strategies that restore brain function after ischemic stroke.

Prof S T Dheen said the findings show tremendous potential for clinical translation and other areas of neuropathology. "HDACi are already being explored in cancer and neurodegeneration therapy. What we now show is that they can be repurposed to dampen inflammation in the brain and promote recovery in stroke, through a microglia-centric mechanism."

Published in the journal *Glia*, the study demonstrates how microglia may shift from an inflammatory state to a protective one upon HDACi treatment, ultimately reducing brain damage and improving prospects for recovery in stroke.

Prof S T Dheen (right) and Dr. Kevin Jayaraj (left) review spatial transcriptomics data derived from the laboratory models. Credit: NUS Yong Loo Lin School of Medicine
Using cutting-edge molecular techniques such as spatial transcriptomics, which allows for the simultaneous genetic profiling of microglia across multiple regions of the stroke-affected brain, the researchers investigated how these immune cells respond to stroke and treatment.

In their laboratory models, blood flow in the middle cerebral artery was blocked to simulate stroke and HDACi therapy was administered. The treated models exhibited a 60% reduction in brain damage along with improved behavioral performance and remarkable changes in microglial dynamics: instead of driving harmful neuro-inflammation in stroke-affected brains, microglia from models treated with HDACi promote brain repair and neuronal survival.

By employing spatial transcriptomics, the team mapped the expression of thousands of genes at precise locations throughout the brain, uncovering how stroke alters key genetic pathways involved in cell survival, inflammation, neuroprotection, and phagocytosis (the process of clearing debris).

HDACi treatment was found to rescue these pathways, with different brain regions displaying unique patterns of microglial response, highlighting the brain's remarkable spatial precision during recovery.

The study's co-author Professor Thiruma V. Arumugam, from the Center for Cardiovascular Biology and Disease Research, La Trobe University, Australia, added, "HDACi drugs precisely reprogram microglia in stroke-affected brain regions, transforming them from inflammatory agents to healing promoters. By targeting these immune cells, our study has the potential to address both acute damage and long-term recovery post-stroke."

"Our study demonstrates for the first time that HDACi can restore neuroprotective gene activity in microglia in a region-specific manner across the brain, including critical areas such as the hippocampus, which is responsible for memory consolidation. More importantly, we have identified alternative targets that essentially represent an out-of-the-box approach for treating stroke and other conditions where neuroinflammation plays a significant role," explained Dr. Jayaraj.

With the hope for a longer therapeutic window and a microglia-centered approach to other neurorehabilitation paradigms alongside stroke, the researchers aim next to develop therapies that act beyond the acute phase of stroke, reprogramming glial cells to support recovery, repair brain circuitry, and preserve neurological function.

More information: Kevin Jayaraj et al, Spatial Transcriptomic Analysis Reveals HDAC Inhibition Modulates Microglial Dynamics to Protect Against Ischemic Stroke in Mice, *Glia* (2025). DOI: 10.1002/glia.70035
Provided by National University of Singapore

APRIL 7, 2025

Brain blood vessel response after stroke mapped, suggesting better treatment outcomes by Aarhus University

Graphical Abstract. Credit: *Stroke* (2025). DOI: 10.1161/STROKEAHA.124.048085
Every year, millions of people around the world suffer ischemic strokes that block blood flow to a region of the brain. Restoring blood flow rapidly is decisive and can save lives. But paradoxically, it can also lead to further damage to the blood vessels in the brain.

But thanks to new Danish research, we now have new and detailed insight into what happens in the blood vessels of the brain after blood flow is restored. The paper is published in the journal *Stroke*.

"This is the first time we've looked at how the brain's blood vessels react to a stroke at the molecular level in such detail. Our results show that the blood vessels become more permeable, which makes it easier for harmful substances to enter the brain," explains Line Mathilde B. Hansen, a postdoctoral researcher at the Department of Biomedicine, who is one of the lead authors of the study.

A double-edged sword

The study also shows that reopening the blood vessels triggers a significant inflammatory response. Inflammation helps the body repair damage—but it can also exacerbate the brain damage and prolong the patient's rehabilitation.

"Inflammation is necessary, but it's about balance. If we can find a way to reduce the inappropriate effects of inflammation without interfering with the body's ability to repair itself, we can potentially help many patients to a better prognosis," explains Professor Vladimir Matchkov, the study's second lead author.

The treatment of the future

The research team behind the study has developed a publicly available web tool that researchers all over the world can use to identify significant changes in gene expression after a stroke.

"We hope that this resource will be an effective tool that will help quickly identify the key molecular signals involved and new, targeted therapies," Matchkov says.

He hopes that in the long term, researchers will be able to develop more effective and more precise forms of treatment for stroke patients.

"The goal is clear: to improve the quality of life for millions of patients all over the world," Matchkov says.

More information: Line Mathilde Brostrup Hansen et al, Spatial Transcriptomics and Proteomics Profiling After Ischemic Stroke Reperfusion: Insights Into Vascular Alterations, *Stroke* (2025). DOI: 10.1161/STROKEAHA.124.048085
Journal information: Stroke
Provided by Aarhus University

OCTOBER 18, 2023

Converting brain immune cells into neurons helps mice recover after stroke

by Kyushu University

Production of NeuroD1 in microglial cells induces their development into neurons, therefore decreasing the area of the brain with neuron loss. In scans of the mice brains, neurons are stained in red, while the dark patches represent areas with neuron loss. Credit: *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2307972120
Researchers at Kyushu University have discovered that turning brain immune cells into neurons successfully restores brain function after stroke-like injury in mice. These findings, published in *PNAS*, suggest that replenishing neurons from immune cells could be a promising avenue for treating stroke in humans.

Stroke, and other cerebrovascular diseases, occur when blood flow to the brain is affected, causing damage to neurons. Recovery is often poor, with patients suffering from severe physical disabilities and cognitive problems. Worldwide, it is one of the most common causes for a patient requiring long-term care.

"When we get a cut or break a bone, our skin and bone cells can replicate to heal our body. But the neurons in our brain cannot easily regenerate, so the damage is often permanent," says Professor Kinichi Nakashima, from Kyushu University's Graduate School of Medical Sciences. "We therefore need to find new ways to replace lost neurons."

One possible strategy is to convert other cells in the brain into neurons. Here, the researchers focused on microglia, the main immune cells in the central nervous system. Microglia are tasked with removing damaged or dead cells in the brain, so after a stroke, they move towards the site of injury and replicate quickly.

"Microglia are abundant and exactly in the place we need them, so they are an ideal target for conversion," says first author Dr. Takashi Irie from Kyushu University Hospital.

In prior research, the team demonstrated that they could induce microglia to develop into neurons in the brains of healthy mice. Now, Dr. Irie and Professor Nakashima, along with Lecturer Taito Matsuda and Professor Noriko Isobe from Kyushu University Graduate School of Medical Sciences, have shown that this strategy of replacing neurons also works in injured brains and contributes to brain recovery.

To conduct the study, the researchers caused a stroke-like injury in mice by temporarily blocking the right middle cerebral artery—a major blood vessel in the brain that is commonly associated with stroke in humans. A week later, the researchers examined the mice and found that they had difficulties in motor function and had a marked loss of neurons in a brain region known as the striatum. This part of the brain is involved in decision making, action planning and motor coordination.

The researchers then used a lentivirus to insert DNA into microglial cells at the site of the injury. The DNA held instructions for producing NeuroD1, a protein that induces neuronal conversion. Over the subsequent weeks, the infected cells began developing into neurons and the areas of the brain with neuron loss decreased. By eight weeks, the new induced neurons had successfully integrated into the brain's circuits.

At only three weeks post-infection, the mice showed improved motor function in behavioral tests. These improvements were lost when the researchers removed the new induced neurons, providing strong evidence that the newly converted neurons directly contributed to recovery.

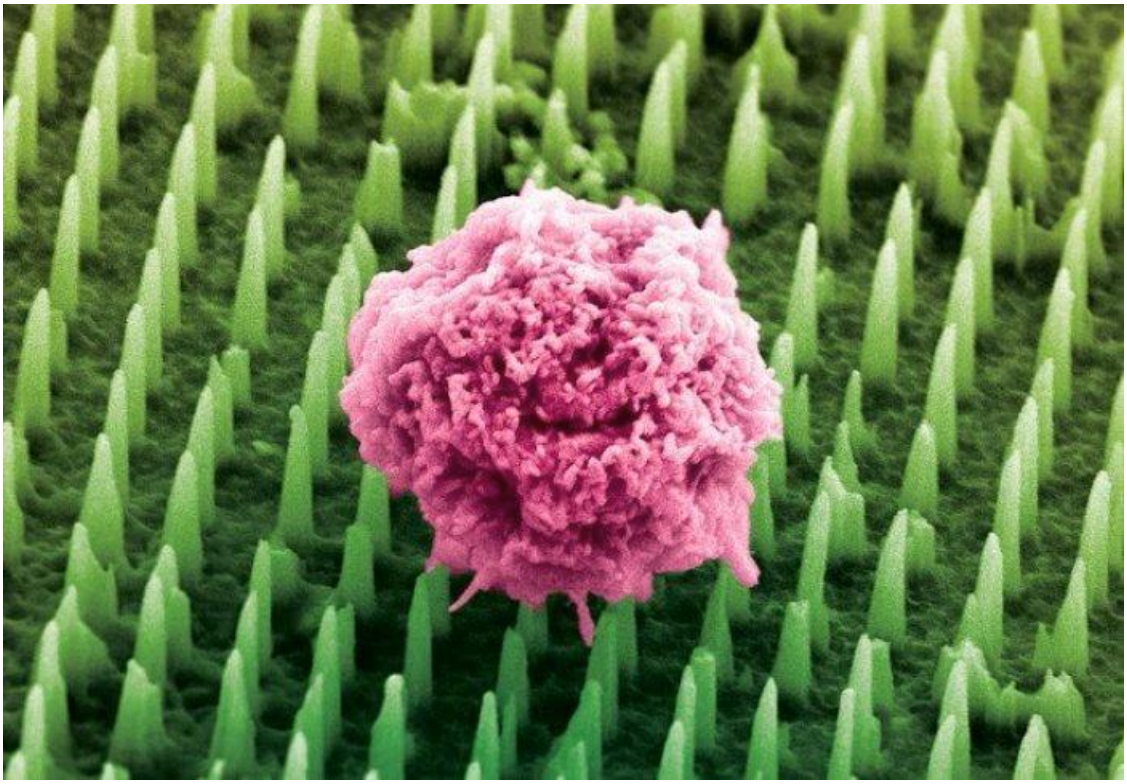
"These results are very promising. The next step is to test whether NeuroD1 is also effective at converting human microglia into neurons and confirm that our method of inserting genes into the microglial cells is safe," says Professor Nakashima.

Furthermore, the treatment was conducted in mice in the acute phase after stroke, when microglia were migrating to and replicating at the site of injury. Therefore, the researchers also plan to see if recovery is also possible in mice at a later, chronic phase.

More information: Takashi Irie et al, Direct neuronal conversion of microglia/macrophages reinstates neurological function after stroke, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2307972120
Journal information: Proceedings of the National Academy of Sciences
Provided by Kyushu University

Tens of millions of nanoneedles could replace painful cancer biopsies

King’s College London develops painless nanoneedle patch, offering real-time molecular insights for disease monitoring.



From King’s College London 17/06/25 (first released 16/06/25)

Colourised image of Nanoneedles Credit: Chippani/King’s College London

A patch containing tens of millions of microscopic nanoneedles could soon replace traditional biopsies, scientists have found.

The patch offers a painless and less invasive alternative for millions of patients worldwide who undergo biopsies each year to detect and monitor diseases like cancer and Alzheimer’s.

Biopsies are among the most common diagnostic procedures worldwide, performed millions of times every year to detect diseases.

However, they are invasive, can cause pain and complications, and can deter patients from seeking early diagnosis or follow-up tests.

Traditional biopsies also remove small pieces of tissue, limiting how often and how comprehensively doctors can analyse diseased organs like the brain.

Now, scientists at King's College London have developed a nanoneedle patch that painlessly collects molecular information from tissues without removing or damaging them.

This could allow healthcare teams to monitor disease in real time and perform multiple, repeatable tests from the same area – something impossible with standard biopsies.

Because the nanoneedles are 1,000 times thinner than a human hair and do not remove tissue, they cause no pain or damage, making the process less painful for patients compared to standard biopsies.

For many, this could mean earlier diagnosis and more regular monitoring, transforming how diseases are tracked and treated.

Dr Ciro Chiappini, who led the research published today in *Nature Nanotechnology*, said: "We have been working on nanoneedles for twelve years, but this is our most exciting development yet. It opens a world of possibilities for people with brain cancer, Alzheimer's, and for advancing personalised medicine.

It will allow scientists – and eventually clinicians – to study disease in real time like never before."

The patch is covered in tens of millions of nanoneedles.

In preclinical studies, the team applied the patch to brain cancer tissue taken from human biopsies and mouse models.

The nanoneedles extracted molecular 'fingerprints' — including lipids, proteins, and mRNAs — from cells, without removing or harming the tissue.

The tissue imprint is then analysed using mass spectrometry and artificial intelligence, giving healthcare teams detailed insights into whether a tumour is present, how it is responding to treatment, and how disease is progressing at the cellular level.

Dr Chiappini said: "This approach provides multidimensional molecular information from different types of cells within the same tissue.

Traditional biopsies simply cannot do that.

And because the process does not destroy the tissue, we can sample the same tissue multiple times, which was previously impossible."

This technology could be used during brain surgery to help surgeons make faster, more precise decisions.

For example, by applying the patch to a suspicious area, results could be obtained within 20 minutes and guide real-time decisions about removing cancerous tissue.

Made using the same manufacturing techniques as computer chips, the nanoneedles can be integrated into common medical devices such as bandages, endoscopes and contact lenses.

Dr Chippani added: “This could be the beginning of the end for painful biopsies.

Our technology opens up new ways to diagnose and monitor disease safely and painlessly – helping doctors and patients make better, faster decisions.”

The breakthrough was possible through close collaboration across nanoengineering, clinical oncology, cell biology, and artificial intelligence—each field bringing essential tools and perspectives that, together, unlocked a new approach to non-invasive diagnostics.

The study was supported by the European Research Council through its flagship Starting Grant programme, Wellcome Leap, and UKRI’s EPSRC and MRC, which enabled acquisition of key analytical instrumentation.

Creatine is safe, effective and important for everyone, longtime researcher says

Texas A&M University study reveals creatine’s role in improving cognitive function and muscle mass across all ages.

From Texas A&M University 13/06/25 (first released 09/06/25

Creatine, the supplement popular with athletes for its ability to help build strength and power, is increasingly being recognized for its broad health benefits.

The compound’s usefulness extends well beyond the gym, according to Dr. Richard Kreider, professor and director of the Exercise & Sport Nutrition Lab at Texas A&M University.

Kreider has spent more than 30 years investigating the effects of creatine, a naturally occurring compound stored in the muscle that combines with phosphate to form creatine phosphate, which is needed for cellular energy.

“When the body is stressed, like in exercise or under metabolic conditions like some diseases, creatine phosphate is needed to maintain energy in the cell, and therefore has a lot of protective and health benefits, in addition to the exercise performance effects that have been seen,” Kreider said.

How Much Creatine Do We Need?

Our bodies create about a gram per day, but it's recommended to get two to four grams of creatine per day, depending on muscle mass and activity levels.

According to Kreider, most people fall short of getting enough creatine from diet alone.

The best sources of creatine in the diet are meat and fish.

"You only get about a gram of creatine per pound of red meat or fish, like salmon, so it's expensive and takes a lot of calories to get a gram," Kreider said.

This is why supplementation matters, especially for vegetarians or vegans who do not consume enough creatine in their diet.

For athletes with performance-related goals, Kreider said it's recommended to supplement 5 grams, four times a day for a week.

Supplementation "helps load the muscle up with more energy," which makes for improved high-intensity exercise, recovery and even cognitive function.

After that, consuming 5 to 10 grams per day will maintain creatine stores and provide enough creatine for the brain.

Beyond boosting athletic performance, creatine is important for everyone as they age throughout their lives, Kreider said.

It can help older adults who lose muscle mass and cognitive function as they age, he said, and in adolescents, low dietary creatine intake is associated with slower growth, less muscle mass and higher body fat.

Is Creatine Safe?

In a comprehensive review published in February in the *Journal of the International Society of Sports Nutrition*, Kreider and colleagues analyzed 685 clinical trials on creatine supplementation to assess its safety and the frequency of reported side effects.

The analysis showed there were no significant differences in the rate of side effects for participants taking a placebo and those taking creatine.

As for anecdotal concerns like bloating or cramping, Kreider says those claims don't hold up under scrutiny, and studies have shown creatine can actually prevent cramping because it helps the body retain more fluid.

Despite the strong evidence base, Kreider said creatine has long been the subject of misconceptions and misinformation.

He’s among the members of the International Society of Sports Nutrition who recently issued a letter affirming the safety and efficacy of creatine, urging lobbyists and policymakers not to restrict access to it.

“There’s absolutely no data supporting any negative side effect anecdotally reported about creatine on the internet and in the media,” he said.

“Creatine is safe, and it’s important for everybody, not just bodybuilders and athletes.”

By Caitlin Clark, Texas A&M University Division of Marketing and Communications

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JUNE 16, 2025

Space conditions can cause gum inflammation and bone loss, say scientists

by University of Sharjah edited by Sadie Harley, reviewed by Robert Egan

Micro-CT analysis and 3D reconstructions of the left maxillary bone with ligature-induced periodontitis between the first and second molars in ground control and hindlimb unloaded (HLU) ligature-induced periodontitis mice. Credit: *Journal Periodontal Research*. DOI: 10.1111/jre.70000

Living in zero gravity can lead to periodontitis, a common and serious condition where the gums become inflamed and the bone that supports teeth starts to break down, eventually leading to tooth loss, scientists reveal in a new study.

The scientists confirm their findings in a study published in the *Journal of Periodontal Research*, in which they try to understand how simulated microgravity—the near-weightless environment astronauts experience in space—might influence the development and severity of periodontitis.

The researchers carried out their experiment in a lab in which mice were used to test the impact of periodontitis in microgravity conditions and on Earth. To simulate this, they used a special model where mice were placed in a position that mimics the effects of microgravity, and then gum disease was induced.

They write, "Six male C57BL/6J mice (3–4 months, ~30 g) were randomly divided into two groups (n=3 each): (a) ground control with ligature-induced periodontitis and (b) hindlimb unloaded with ligature-induced periodontitis.

"All procedures followed ethical approval (ACUC-02-02-2023). Mice were anesthetized (100mg/ kg ketamine/5–10mg/kg xylazine, intraperitoneally) prior to ligature placement between the first and second left maxillary molars."

The study, according to senior author Zahi Badran, University of Sharjah's professor of periodontology, has "found that mice exposed to simulated microgravity showed much worse gum inflammation and bone loss compared to mice with induced periodontitis on the ground. They had higher levels of disease markers, more severe tissue damage, and more immune cells in the affected areas."

The group of mice on the ground "showed minimal bone loss," while the group in simulated space conditions "exhibited a marked increase in CEJ-ABC distance, indicating significant bone resorption."

Similarly, the group of mice in simulated space flight "displayed a significant increase in ALP activity compared to the control group, indicating increased bone resorption and inflammation associated with periodontitis due to the change in gravity," the researchers find.

The researchers use ALP, or alkaline phosphatase activity, as a marker for several biological processes, most notably bone growth and liver function.

The research indicates that microgravity can exacerbate induced gum disease in animals, underscoring the importance of developing tailored dental prophylaxis and care strategies for future space explorers. "It also opens the door to a better understanding of how inflammation works in the body, both in space and on Earth," adds Prof. Badran.

As space travel becomes a real possibility for longer missions, including journeys to Mars, scientists are looking more closely at how space conditions affect human health. However, the authors maintain that one area that's been less studied is oral health and diseases in microgravity, especially gum disease, also known as periodontitis.

The authors stress the fact that there has been "an increased interest in astronauts and future space health, especially the effects of microgravity on various body systems."

However, they note that "to the best of our knowledge, this is the first in vivo pilot study to investigate microgravity's effects on periodontitis progression using the combination of hindlimb unloading."

Asked about the significance of the research findings for space agencies, Prof. said the study "calls for the integration of dental medicine, particularly periodontology, into astronaut/future space colonies' inhabitants' health protocols.

"Specialized prevention and treatment strategies, along with in-mission monitoring tools, will most probably be essential in the case of prolonged space stays. Simultaneously, the

model offers terrestrial benefits, providing insights into the periodontal status of immobilized bed patients, who experience similar effects of microgravity.

"This model will be extensively studied to better understand the biological pathways underlying these outcomes and to explore how periodontitis may influence other systemic diseases under microgravity."

The authors see their study as a harbinger of "a new line of multidisciplinary research on oral health and disease in microgravity" that will shed more light on space medicine in general.

They say they are determined "to replicate their model to assess additional microbiological and immunological parameters to investigate the connection between gum diseases and other systemic diseases in microgravity."

The authors are aware of the limitations of their study as its findings are based on a relatively small sample size. However, they emphasize its robustness due to the use of "the HLU model to simulate microgravity, which offers valuable insights into disease progression under space-like conditions."

More information: Ahmed Bakri et al, Microgravity Exacerbates Periodontitis In Vivo, *Journal of Periodontal Research* (2025). DOI: 10.1111/jre.70000
Provided by University of Sharjah

THE BEST SOLUTION BELOW TO THE SPACE PROBLEM ABOVE

JUNE 17, 2025

Genetically modified yeast can create valuable materials from urine

by Aliyah Kovner, Lawrence Berkeley National Laboratory

edited by Lisa Lock, reviewed by Robert Egan

These optical microscopy images show the osteoyeast cells. The outline of the vacuole, the cellular organelle where calcium is accumulated to form hydroxyapatite, is fluorescing red. The calcium inside the vacuole is fluorescing green. Credit: Behzad Rad/Berkeley Lab Researchers from the Lawrence Berkeley National Laboratory (Berkeley Lab), UC Irvine, and the University of Illinois Urbana-Champaign (UIUC), have used biology to convert human urine into a valuable product. The team genetically modified yeast to take the elements present in urine and create hydroxyapatite—a calcium and phosphorus-based mineral naturally produced by humans and other animals to build bones and teeth.

Commercially manufactured hydroxyapatite is used in surgery and dentistry to repair these structures when they're broken, and the lightweight material's remarkable strength and toughness make it an excellent candidate building material and even as a replacement for some types of plastic.

Their work, recently published in *Nature Communications*, not only provides a cost-efficient pathway to produce hydroxyapatite, but also a practical mechanism for reducing the cost of wastewater treatment, an energy-efficient means of producing fertilizer, and opens the door for other yeast-based technologies that can create useful materials out of scavenged minerals.

A strange brew

The star of the show is the team's strain of Saccharomyces boulardii, a yeast closely related to the species used to brew beer and make bread. S. boulardii likes to grab minerals from its environment and store them inside a special membrane compartment.

Co-authors Yasuo Yoshikuni, head of the DNA Synthesis Science Program at the Joint Genome Institute (JGI), and Peter Ercius, staff scientist at the National Center for Electron Microscopy at the Molecular Foundry, were exploring ways to make functional biomaterials with microbes when they realized that S. boulardii was naturally performing activities similar to osteoblasts, the specialized animal cells that make hydroxyapatite and form bone.

Both the JGI and the Molecular Foundry are DOE Office of Science user facilities located at Berkeley Lab.

"The serendipitous part is this yeast already had similar molecular mechanisms," said Yoshikuni, who specializes in engineering microbes to produce fuels, chemicals, and materials at the JGI. "Just mild tweaking was sufficient to convert the yeast into a cell factory for hydroxyapatite."

The resulting organism, given the name "osteoyeast," successfully mimics osteoblasts, which are extremely difficult and costly to culture outside a body, while maintaining the low-maintenance lifestyle of yeast. From the outset, the osteoyeast represented a big return on investment by enabling cheaper hydroxyapatite production. But the team saw an opportunity to make a bigger global impact with their invention by using urine as a mineral source—inspired by an emerging trend in biotechnology aptly called "pee-cycling."

"It's kind of exactly what you think it is," said author Behzad Rad, who is Principal Scientific Engineering Associate in the Biological Nanostructures Facility at the Molecular Foundry. "People are trying to collect urine before it hits the sewer system to use the ammonia and phosphate in it for farming and other applications. These components cause environmental issues when wastewater gets into the landscape or ocean, so treatment facilities are already spending a lot of money to neutralize urine. The idea is, why don't we put it to use?"

According to Yoshikuni, pee-cycling hasn't become widespread because the cost of ammonia and phosphate are so low, there's little financial incentive to invest in new, large-

scale infrastructure that can recover these ingredients. But now, osteoyeast can make high-value hydroxyapatite out of the phosphorus (and calcium) in urine. And conveniently, the microbes also gather up the ammonia salts in their membrane compartments.

"Today, we use about 1% of the world's energy to make fertilizers from nitrogen gas," he said. "If we're able to produce both hydroxyapatite and make nitrogen fertilizer from the ammonia, we could potentially replace a significant portion of the total demand for nitrogen; saving energy while also dramatically reducing the costs at wastewater facilities."

These images taken with transmission electron microscopy (TEM) show materials inside and outside the yeast cells. The intracellular particles are composed of amorphous calcium phosphate (the components of hydroxyapatite without the complete structure) and the extracellular platelet-like crystals are crystalline hydroxyapatite. Credit: Berkeley Lab

Good bone structure

A key part of this project was confirming that the osteoyeast were accomplishing all the steps of hydroxyapatite production. Initial results indicated the project was a quick success when Isaak Müller and Alex Lin, two postdoctoral scholars at Berkeley Lab and co-first authors on the paper, spotted hydroxyapatite in the culture—but the scientists didn't find the crystalline material inside the yeast.

They could see nanoscale mineral granules gathered inside the cells, but weren't sure whether it was the yeast completing the crystal-building process, or if a separate chemical reaction was happening outside the cells. This part of the project was led by Ercius and Rad, using tools at the Molecular Foundry.

Rad used yeast strains tagged with tiny fluorescent proteins and elements to observe the yeast-gathering ingredients with optical microscopy, while Ercius employed transmission electron microscopy (TEM) to verify the granules forming in the storage membrane had the same composition as hydroxyapatite. By combining the techniques, they were able to track the entire process. Ercius also used TEM to show the hydroxyapatite is high-quality with an ideal nanostructure.

Meanwhile, Yoshikuni along with Yusuke Otani, fellow co-first author and a postdoctoral scholar at the JGI, demonstrated that the microbes can make this valuable material with impressive efficiency, producing one gram of hydroxyapatite per kilogram of urine.

"Colocalization of all these facilities was key," said Ercius. "That we were able to meet and work together so closely was really critical. I'm not a biologist, and my colleagues are not experts in materials synthesis and characterization. This work showcases what you can do when you combine scientific approaches that aren't usually done together."

Turning yellow into green

To validate that their pee-cycling endeavor is economically viable, the Berkeley Lab scientists turned to co-author Jeremy Guest, Sustainable Design Lead for the DOE Center for Advanced Bioenergy and Bioproducts Innovation at UIUC. Guest and Xinyi (Joy) Zhang, a research scientist at UIUC, performed technoeconomic analysis to simulate distributed hydroxyapatite production systems serving a city the size of San Francisco.

Factoring in the costs of culturing the osteoyeast and separating urine from the wastewater, Guest and Zhang estimate it would cost approximately $19 to make one kilogram of commercial-quality hydroxyapatite, which could be sold for $50 to $200 in the U.S. market. The entire system could generate a profit of about $1.4 million per year while reducing the chemical inputs needed to make the wastewater safe.

"It's important that we consider the potential impacts of a full-scale system," said Guest. "We can develop a new technology and demonstrate it in the lab, but is it actually feasible? Is there an opportunity for this innovation in the real world?"

The patented osteoyeast is now available to license for hydroxyapatite production, and the team is working to develop new strains that can synthesize other bio-based materials, or grab and store specific elements to enable environmentally friendly bio-mining. There are almost as many applications for this technology as there are puns to describe it.

More information: Isaak E. Müller et al, Cost-effective urine recycling enabled by a synthetic osteoyeast platform for production of hydroxyapatite, *Nature Communications* (2025). DOI: 10.1038/s41467-025-59416-8
Provided by Lawrence Berkeley National Laboratory

Researchers convert urine into bone implant material

University of California, Irvine scientists develop eco-friendly process transforming urine into valuable dental and bone implants.

From University of California – Irvine 20/06/25 (first released 17/06/25)

A research team including a materials scientist at the University of California, Irvine has engineered a yeast platform that converts human urine from wastewater into hydroxyapatite, a high-value, biocompatible substance for use in dental and bone implants, restoration of archaeological artifacts and other applications.

In a paper published recently in *Nature Communications,* the researchers offer a techno-economic analysis of the technique to transform urine – which can seriously damage watersheds – into HAp, a calcium phosphate mineral projected to hold a market value of more than $3.5 billion by 2030.

“This process achieves two goals at the same time,” said co-author David Kisailus, UC Irvine professor of materials science and engineering.

“On the one hand, it helps remove human urine from wastewater streams, mitigating environmental pollution and the buildup of unwanted nutrients; and on the other hand, it produces a material that can be commercially marketed for use in a variety of settings.”

In the *Nature Communications* paper, he and his collaborators – including scientists from Lawrence Berkeley National Laboratory, the University of Illinois Urbana-Champaign, and Japan’s Hokkaido University and Tokyo University of Agriculture and Technology – discuss how they developed and evaluated a biologically inspired system based on synthetic yeast cells they dubbed “osteoyeast” that drive the urine-to-HAp conversion.

In mammals, specialized cells called osteoblasts draw calcium phosphate from body fluids that is then processed and secreted as HAp.

Osteoblasts are not suitable for large-scale industrial HAp production, according to the researchers, so they turned to osteoyeast, which uses enzymes to break down urea and increase the pH of the surrounding environment.

This triggers tiny cavities in the yeast to accumulate calcium and phosphate that are then secreted and crystallized into HAp.

The scientists found that their method can produce as much as 1 gram of HAp per liter of urine.

“This process to yield hydroxyapatite, or bone mineral, takes less than one day,” Kisailus said.

“The fact that it uses yeast as a chassis, which is inexpensive and can be placed in large vats at relatively low temperatures – think about beer that’s made via fermentation processes and is well scaled – shows that this can be done easily without major infrastructural needs, and that has the added benefit of making it accessible to developing economies.”

Kisailus, who has a deep background in researching crystal growth mechanisms as well as making inorganic crystalline materials using biological and bio-inspired methods, said his main role in this project was to evaluate crystallization pathways in the osteoyeast platform.

According to the researchers, HAp composites are lightweight and offer significant mechanical strength, toughness and durability.

And if synthetic hydroxyapatite that had its origins in urine can be produced economically and at scale, it can serve as a renewable and biodegradable alternative to commodities like plastics and other building materials.

“I am continuing to work with Professor Yasuo Yoshikuni from Lawrence Berkeley Laboratory, a corresponding author of this paper, to make other materials using this process, including materials for energy-based applications,” Kisailus said.

“We are currently developing strategies to leverage his yeast platform with our 3D printing and structural knowledge to make multifunctional architected materials.”

The research project received financial support from the U.S. Department of Energy, the Defense Advanced Research Projects Agency and the Air Force Office of Scientific Research.

JUNE 19, 2025

Five-day vascular organoids speed tissue engineering research

by Justin Jackson, Phys.org edited by Sadie Harley, reviewed by Robert Egan

Graphical abstract. Credit: *Cell Stem Cell* (2025). DOI: 10.1016/j.stem.2025.05.014
Boston Children's Hospital scientists have unveiled a five-day approach to generate functional vascular organoids capable of supporting blood flow and in vivo engraftment.

Blood vessels are the living conduits that deliver nutrients and oxygen throughout the body, regulate hemostasis, and modulate inflammation. During development, vasculature shapes organ formation and supports postnatal tissue growth and repair, while vascular niches maintain stem cell populations.

Engineering physiologically functional vascular networks in vitro would allow detailed study of human vessel development, high-precision drug testing, and production of pre-vascularized grafts for regenerative medicine.

Recent organoid strategies produced vascular structures but depended on spontaneous mural cell emergence and required prolonged culture periods and extracellular matrix support, constraining scalability and speed required for therapeutic application.

In the study, "Rapid generation of functional vascular organoids via simultaneous transcription factor activation of endothelial and mural lineages," published in *Cell Stem Cell*, researchers designed a dual-factor program to co-differentiate induced pluripotent stem cells into endothelial and mural fates for rapid vascular-organoid assembly.

Human induced pluripotent stem cells were guided into mesodermal progenitors, combined at a 1:1 ratio, and aggregated into thousands of 250-μm vascular organoids. Investigators implanted roughly 1,000 organoids beneath the renal capsule of immunodeficient NSG mice.

A separate cohort of diabetic nude mice received the same organoid dose in a hind limb ischemia model. Pancreatic-islet studies paired 1,500 organoids with 500, 300, or 100 islet equivalents in NSG recipients.

Investigators triggered expression of transcription factors ETV2 and NKX3.1 through doxycycline-inducible constructs or chemically modified mRNA, allowing simultaneous endothelial and mural specification inside free-floating spheroids. Flow cytometry, immunofluorescence, bulk and single-cell RNA sequencing, and in-vivo imaging tracked lineage commitment.

Some organoids were embedded in collagen-Matrigel gels to gauge matrix-driven maturation, and functional vascularization was measured by perfusion assays, laser-Doppler flowmetry, and luciferase bioluminescence.

Within five days, about half of the cells in each organoid turned into blood-vessel cells bearing VE-cadherin and CD31, and those cells built hollow, tube-like networks wrapped by smooth-muscle partners.

Dropping the organoids into a collagen–Matrigel gel let them swell to nearly one millimeter and ramped up genes linked to arteries. Short, one-day doxycycline pulses pushed the vessels toward an artery-like identity, yet longer three-day pulses produced a mixed batch of artery- and vein-like cells that sprouted more readily.

After implantation, the organoids tapped into the host's circulation, restored roughly 50% of lost blood flow in injured limbs, and sharply cut tissue death.

Under the kidney-grafted capsule, organoid-derived human vessels surrounded transplanted mouse islets, letting as few as 100 islet equivalents keep blood sugar normal for 100 days.

Mice that received 300 islet equivalents recovered normal glucose, and about half of those given 100 islet equivalents kept blood sugar normal for 100 days.

The authors conclude that orthogonal transcription-factor programming offers a scalable path to tailor-made vascular organoids capable of rapid engraftment and tissue rescue, suggesting future avenues for treating ischemic injury, improving cell-therapy survival and a potentially durable diabetes therapy.

Written for you by our author Justin Jackson, edited by Sadie Harley , and fact-checked and reviewed by Robert Egan —this article is the result of careful human work. We rely on readers like you to keep independent science journalism alive. If this reporting matters to you, please consider a donation (especially monthly). You'll get an **ad-free** account as a thank-you.

More information: Liyan Gong et al, Rapid generation of functional vascular organoids via simultaneous transcription factor activation of endothelial and mural lineages, *Cell Stem Cell* (2025). DOI: 10.1016/j.stem.2025.05.014
Journal information: Cell Stem Cell

JUNE 23, 2025

Ecnoglutide yields superior, sustained reduction in body weight: Study

by Elana Gotkineedited by Stephanie Baum, reviewed by Robert Egan

For adults with obesity or overweight without diabetes, the novel cyclic adenosine monophosphate-biased glucagon-like peptide 1 receptor agonist known as ecnoglutide yields a superior and sustained reduction in body weight versus placebo, according to a study published online June 21 in *The Lancet Diabetes & Endocrinology* to coincide with the annual meeting of the American Diabetes Association, held from June 20 to 23 in Chicago.

Linong Ji, M.D., from the Peking University People's Hospital in Beijing, and colleagues examined the efficacy and safety of once-weekly ecnoglutide versus placebo for the treatment of overweight or obesity. Participants, aged 18 to 75 with overweight or obesity, without diabetes, were randomly assigned to receive subcutaneous ecnoglutide (1.2, 1.8, or 2.4 mg; 166, 166, and 167 participants, respectively) or volume-matched placebo (165 participants), once weekly.

The researchers found that the least-square mean percentage change in body weight at week 40 was −9.1%, −10.9%, and −13.2% in the ecnoglutide 1.2-, 1.8-, and 2.4-mg groups, respectively, versus 0.1% in the placebo group. The proportion of participants who achieved at least a 5% reduction in body weight at week 40 was 77%, 84%, and 87% in the ecnoglutide 1.2-, 1.8-, and 2.4-mg groups, respectively, versus 16% in the placebo group. Treatment-emergent adverse events were observed in 93% of each ecnoglutide dose group and in 84% of the placebo group.

"These findings suggest ecnoglutide is a potent therapeutic option for individuals with overweight or obesity, particularly considering its extended dosing range enabling personalized weight management strategies," the authors write.

The study was funded by Hangzhou Sciwind Biosciences, which is developing ecnoglutide.

More information: Linong Ji et al, Efficacy and safety of a biased GLP-1 receptor agonist ecnoglutide in adults with overweight or obesity: a multicentre, randomised, double-blind,

placebo-controlled, phase 3 trial, *The Lancet Diabetes & Endocrinology* (2025). DOI: 10.1016/S2213-8587(25)00141-X

Tricia M-M Tan, Is biased agonism helpful in the treatment of obesity with the GLP-1 receptor analogues?, *The Lancet Diabetes & Endocrinology* (2025). DOI: 10.1016/S2213-8587(25)00157-3

More Information
Journal information: The Lancet Diabetes & Endocrinology

AI · HEALTHCARE
June 30, 2025

The Path to Medical Superintelligence

by Dominic King & Harsha Nori

The Microsoft AI team shares research that demonstrates how AI can sequentially investigate and solve medicine's most complex diagnostic challenges—cases that expert physicians struggle to answer.

Benchmarked against real-world case records published each week in the New England Journal of Medicine, we show that the Microsoft AI Diagnostic Orchestrator (MAI-DxO) correctly diagnoses up to 85% of NEJM case proceedings, a rate **more than four times higher than a group of experienced physicians.** MAI-DxO also gets to the correct diagnosis more cost-effectively than physicians.
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As demand for healthcare continues to grow, costs are rising at an unsustainable pace, and billions of people face multiple barriers to better health – including inaccurate and delayed diagnoses. Increasingly, people are turning to digital tools for medical advice and support. Across Microsoft's AI consumer products like Bing and Copilot, we see over 50 million health-related sessions every day. From a first-time knee-pain query to a late-night search for an urgent-care clinic, search engines and AI companions are quickly becoming the new front line in healthcare.

We want to do more to help -and believe generative AI can be transformational. That's why, at the end of 2024, we launched a dedicated consumer health effort at Microsoft AI, led by clinicians, designers, engineers, and AI scientists. This effort complements Microsoft's broader health initiatives and builds on our longstanding commitment to partnership and innovation. Existing solutions include RAD-DINO which helps accelerate and improve radiology workflows and Microsoft Dragon Copilot, our pioneering voice-first AI assistant for clinicians.
For AI to make a difference, clinicians and patients alike must be able to trust its performance. That's where our new benchmarks and AI orchestrator come in.

Medical Case Challenges and Benchmarks

To practice medicine in the United States, physicians need to pass the United States Medical Licensing Examination (USMLE), a rigorous and standardized assessment of clinical knowledge and decision making. USMLE questions were among the earliest benchmarks used to evaluate AI systems in medicine, offering a structured way to compare model performance – both against each other and against human clinicians.

In just three years, generative AI has advanced to the point of scoring near-perfect scores on the USMLE and similar exams. But these tests primarily rely on multiple-choice questions, which favor memorization over deep understanding. By reducing medicine to one-shot answers on multiple-choice questions, such benchmarks overstate the apparent competence of AI systems and obscure their limitations.

At Microsoft AI, we're working to advance and evaluate clinical reasoning capabilities. To move beyond the limitations of multiple-choice questions, we've focused on sequential diagnosis, a cornerstone of real-world medical decision making. In this process, a clinician begins with an initial patient presentation and then iteratively selects questions and diagnostic tests to arrive at a final diagnosis. For example, a patient presenting with cough and fever may lead the clinician to order and review blood tests and a chest X-ray before they feel confident about diagnosing pneumonia.

Each week, the New England Journal of Medicine (NEJM) – one of the world's leading medical journals – publishes a Case Record of the Massachusetts General Hospital, presenting a patient's care journey in a detailed, narrative format. These cases are among the most diagnostically complex and intellectually demanding in clinical medicine, often requiring multiple specialists and diagnostic tests to reach a definitive diagnosis.

How does AI perform? To answer this, we created interactive case challenges drawn from the NEJM case series – what we call the Sequential Diagnosis Benchmark (SD Bench). This benchmark transforms 304 recent NEJM cases into stepwise diagnostic encounters where models – or human physicians – can iteratively ask questions and order tests. As new information becomes available, the model or clinician updates their reasoning, gradually narrowing toward a final diagnosis. This diagnosis can then be compared to the gold-standard outcome published in the NEJM.

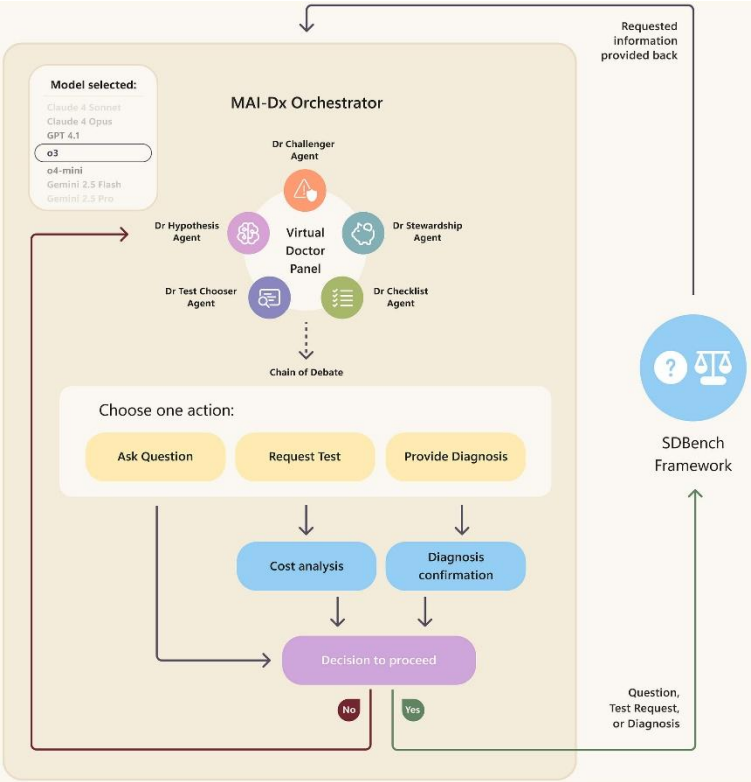
Each requested investigation also incurs a (virtual) cost, reflecting real-world healthcare expenditures. This allows us to evaluate performance across two key dimensions: diagnostic accuracy and resource expenditure. You can watch how an AI system progresses through one of these challenges in this short video.

Walkthrough of how MAI-DxO works through a case to reach a diagnosis

Getting to a Correct Diagnosis

We evaluated a comprehensive suite of frontier generative AI models against the 304 NEJM cases. The foundation models tested included GPT, Llama, Claude, Gemini, Grok, and DeepSeek.

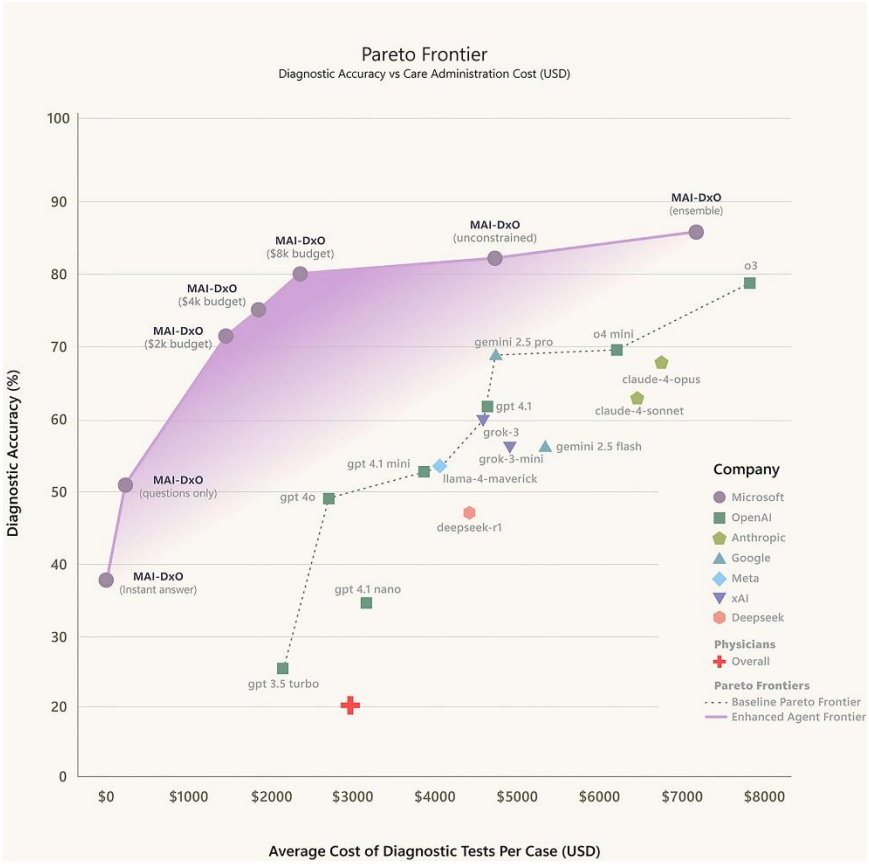
Beyond baseline benchmarking, we also developed **the Microsoft AI Diagnostic Orchestrator (MAI-DxO),** a system designed to emulate a virtual panel of physicians with diverse diagnostic approaches collaborating to solve diagnostic cases. We believe that orchestrating multiple language models will be critical to managing complex clinical workflows. Orchestrators can integrate diverse data sources more effectively than individual models, while also enhancing safety, transparency, and adaptability in response to evolving medical needs. This model-agnostic approach promotes auditability and resilience, key attributes in high-stakes, fast-evolving clinical environments.



The MAI-Dx Orchestrator turns any language model into a virtual panel of clinicians: it can ask follow-up questions, order tests, or deliver a diagnosis, then run a cost check and verify its own reasoning before deciding whether to proceed.

MAI-DxO boosted the diagnostic performance of every model we tested. The best performing setup was MAI-DxO paired with OpenAI's o3, which correctly solved 85.5% of the NEJM benchmark cases. For comparison, we also evaluated 21 practicing physicians from the US and UK, each with 5-20 years of clinical experience. On the same tasks, these experts achieved a mean accuracy of 20% across completed cases.

MAI-DxO is configurable, enabling it to operate within defined cost constraints. This allows for explicit exploration of the cost-value trade-offs inherent in diagnostic decision making. Without such constraints, an AI system might otherwise default to ordering every possible test – regardless of cost, patient discomfort, or delays in care. Importantly, we found that MAI-DxO delivered *both* higher diagnostic accuracy and lower overall testing costs than physicians or any individual foundation model tested.



Comparison of AI powered diagnostic agents by accuracy and average diagnostic test cost per case. Top performing agents appear toward the top left quadrant, reflecting higher accuracy and lower cost. The lower dotted line represents the performance range of the best individual foundation models. The purple line traces the performance of MAI-DxO across different configurations. The red cross indicates the average performance of 21 practicing physicians.

What's Next?

Physicians are typically characterized by the breadth or depth of their expertise. Generalists, like family physicians, manage a wide array of conditions across ages and organ systems. Specialists, such as rheumatologists, focus deeply on a single system, disease area or even condition. No single physician, however, can span the full complexity of the NEJM case series. AI, on the other hand, doesn't face this trade-off. It can blend both breadth and depth of expertise, demonstrating clinical reasoning capabilities that, across many aspects of clinical reasoning, exceed those of any individual physician.

This kind of reasoning has the potential to reshape healthcare. AI could empower patients to self-manage routine aspects of care and equip clinicians with advanced decision support for complex cases. Our findings also suggest that AI reduce

unnecessary healthcare costs. U.S. health spending is nearing 20% of US GDP, with up to 25% of that estimated to be wasted – per having little influence on patient outcomes.
Of course, our research has important limitations. Although MAI-DxO excels at tackling the most complex diagnostic challenges, further testing is needed to assess its performance on more common, everyday presentations. Clinicians in our study worked without access to colleagues, textbooks, or even generative AI, which may feature in their normal clinical practice. This was done to enable a fair comparison to raw human performance.

A novel aspect of this work is its attention to cost. While real-world health costs vary across geographies and systems, and include many downstream factors that we don't account for, we apply a consistent methodology across all agents and physicians evaluated to help quantify high level trade-offs between diagnostic accuracy and resource use.

For us, this is just the first step. We're energized by the opportunities ahead. Important challenges remain before generative AI can be safely and responsibly deployed across healthcare. We need evidence drawn from real clinical environments, alongside appropriate governance and regulatory frameworks to ensure reliability, safety, and efficacy. That's why we're partnering with leading health organizations to rigorously test and validate these approaches—an essential step before any broader roll out.

Together with our partners, we strongly believe that the future of healthcare will be shaped by augmenting human expertise and empathy with the power of machine intelligence. We are excited to take the next steps in making that vision a reality.

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Further information:
SD Bench and MAI-DxO are research demonstrations only and are not currently available as public benchmarks or orchestrators. You can find more detail on the underlying methodology and results in a pre-print paper published alongside this blog. We are in the process of submitting this work for external peer review and are actively working with partners to explore the potential to release SDBench as a public benchmark.
Acknowledgments:
We are grateful to NEJM Group for permission to use the NEJM cases in the research reported in this blog post. The research described here has benefited from the insights

of many people. We are grateful to the authors named on the arXiv paper and the wider team at MAI. We also thank further colleagues both inside and outside of Microsoft for sharing their insights including Bryan Bunning, Nando de Freitas, Andrija Milicevic, Hoifung Poon, David Rhew, Karén Simonyan, Eric Topol, and Jim Weinstein. Gianluca Fontana and Kevin Hawkins (Prova Health) provided support on the health economics and outcomes section.

View Publication

Q&A

Is this AI safe to use for healthcare?

The work presented here is not yet approved for clinical use and would only be approved after rigorous safety testing, clinical validation, and regulatory reviews. For now, this represents exciting initial research. At the heart of any plans to deploy this technology in the real world is our commitment to safety, trust, and quality ensuring that any healthcare solutions are clinically grounded, ethically designed, and transparently communicated.

Will AI replace doctors?

While AI is becoming a powerful tool in healthcare, our team of practicing clinicians believes AI represents a complement to doctors and other health professionals. While this technology is advancing rapidly, their clinical roles are much broader than simply making a diagnosis. They need to navigate ambiguity and build trust with patients and their families in a way that AI isn't set up to do. Clinical roles will, we believe, evolve with AI giving clinicians the ability to automate routine tasks, identify diseases earlier, personalize treatment plans, and potentially prevent some diseases altogether. For consumers, they will provide better tools for self-management and shared decision making.

What is an AI orchestrator?

In the context of generative AI, an orchestrator is like a digital conductor helping to coordinate multiple steps in achieving a complex task. In healthcare, the role of orchestration is crucial given the high stakes of each decision. Our orchestrator sits above underlying language models making sure each point in getting a diagnosis is handled systematically, reducing the risk in future of errors and offering the necessary stability, consistency and transparency to ultimately build trust from users.

Why have you looked at costs?

We initially wanted to understand whether the AI was simply requesting excessive diagnostic workups to reach the right diagnosis. What we found was that our Orchestrator was able to reach the correct answer with much less money spent on testing. In some ways this is not a surprise as diagnostic over-testing is recognized as

being a widespread challenge, accounting for millions of unnecessary tests annually in the US. This work suggests AI creates an opportunity for clinicians – and consumers – to reach a faster, more accurate diagnosis while reducing costs.

JULY 3, 2025

A new drug causes nerve tissue to emit light, enabling faster, safer surgery

by Michael Haederle, University of New Mexico

edited by Stephanie Baum, reviewed by Robert Egan

Intraoperative nerve images at 500 mg bevonescein dose. Paired intraoperative nerve images from 4 different patients at 500 mg bevonescein dose. WLR images (**A**–**D**) and the same field of view seen with fluorescence signal overlayed on WLR (**E**–**H**). Nerves on the surgical field surface (solid yellow arrows) appear yellowish/green compared to adjacent non-nerve tissue (reddish). There is white surgical gauze visible in the left lower quadrant of **A**. Nerve not on the surgical field surface (dashed yellow arrows) are more easily discernible in **F**, **G**, **H** compared to **B**, **C**, **D**. WLR – white light reflectance; Paired –white light reflectance with fluorescence overlay. The Visualization Scoring System utilized the WLR and Paired images. The SBR analysis utilized the WLR and FL (grayscale) images.
Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-60737-x
When surgeons dissect tissue to remove a tumor or make a repair, they must work cautiously, relying on electrophysical monitors and their own anatomical knowledge to avoid cutting nerves, which could complicate the patient's recovery.

A University of New Mexico surgeon has helped develop and test a first-of-its-kind drug that binds to nerve tissue and fluoresces (emits light), enabling surgeons to better see the nerves they're trying to work around.

A newly published study in *Nature Communications* reports that bevonescein—a short chain of amino acids attached to a fluorescing molecule—was safe to use and highlighted longer stretches of nerves than would be visible to the naked eye, improving the odds of operating without causing injury.

"The way that I explain this drug to patients is that I think if we can help surgeons see things better, they can do faster, more efficient, safer surgery," said Ryan Orosco, MD, an associate professor and otolaryngologist (head and neck surgeon) in the UNM School of Medicine who co-authored the paper.

The journal article reported on a small Phase 1–2 study of the drug, which was tested on 27 cancer patients to evaluate its safety and efficacy.

"The trial was for patients having a neck dissection to remove lymph nodes or a parotid surgery or a thyroid surgery," he said. "In all of those cases, there are cranial nerves that are important to identify, work around and protect."

A larger Phase 3 study currently underway includes patients at UNM Hospital and is expected to be completed by this summer, Orosco said. It will assess whether use of the imaging agent meaningfully improves overall surgical outcomes, something the initial trial was not designed to determine.

Orosco's involvement in the development of the drug dates back to his ENT residency at the University of California, San Diego, where he spent a year-long research fellowship in the lab of Quyen Nguyen, MD, Ph.D. She had worked closely with the late biochemist Roger Tsien, Ph.D., who won the Nobel Prize in 2008 for discovering green fluorescent protein, enabling the development of methods to "tag" specific molecules and tissue types, such as cancer cells.

Nguyen's research eventually led to the development of bevonescein. Orosco, who went on to do a head and neck cancer fellowship at Stanford before joining the UCSD faculty, played a role in developing the clinical trial protocol and performed many of the surgeries in the study.

He joined the UNM faculty in late 2022 and now serves as the national principal investigator for the Phase 3 trial of the drug, which now includes 10 sites.

Patients in the trials receive an IV infusion of the drug prior to surgery, but it is quickly cleared by the kidneys, Orosco said.

"We can image them five, six, seven, eight hours later, and it still stays bound to the nerves, but it flushes out of the body within 12 hours."

In the operating room, surgeons use microscopes with special lights and filters that illuminate the surgical site at a specific frequency that causes the drug to fluoresce. The nerves appear as wormlike yellowish-green structures that thread through the surrounding tissue.

An upcoming phase of the research will evaluate the use of specially modified headband-mounted magnifying loupes of the sort that surgeons wear, rather than the microscope.

"Testing those loupes in a spinoff trial is a critical and practical step toward real-world implementation," Orosco said.

If the Phase 3 trial shows clear clinical benefit from the use of bevonescein during head and neck surgery, it could win FDA approval, leading to wider use in surgical procedures throughout the body.

"Once the FDA has approved it for a certain indication, then it'll be on the shelves," he said. "Surgeons can also use it off-label for whatever they want. Then the big question is, how does that go? Who starts using it and in which types of surgeries?"

More information: Yu-Jin Lee et al, Intraoperative nerve-specific fluorescence visualization in head and neck surgery: a Phase 1 trial, *Nature Communications* (2025). DOI: 10.1038/s41467-025-60737-x
Journal information: Nature Communications
Provided by University of New Mexico

JULY 3, 2025

Destabilizing microtubules to boost platelet production from iPS cell-derived megakaryocytes

by Kyoto University edited by Lisa Lock, reviewed by Robert Egan

Single-cell time-lapse imaging reveals heterogeneous and asynchronous platelet biogenesis/release by terminally differentiating imMKCLs under static in vitro culture conditions. Credit: *PLOS One* (2025). DOI: 10.1371/journal.pone.0326165
A collaborative research team led by Dr. Thorsten Schlaeger (Boston Children's Hospital) Emiri Nakamura and Professor Koji Eto (Department of Clinical Application) has identified microtubule (MT) destabilization as a promising strategy to enhance platelet production from human iPS cell-derived immortalized megakaryocyte progenitor cell lines (imMKCLs). The work is published in *PLOS One*.

Platelet transfusions are essential for managing thrombocytopenia and bleeding disorders, yet donor-derived platelets face limitations such as short shelf life, supply shortages, and immune incompatibility.

To address these critical issues, the Eto Lab has developed imMKCLs—conditionally immortalized megakaryocyte lines derived from human iPS cells—which can be expanded and matured to produce functional platelets. However, platelet yields remain suboptimal under static culture conditions.

Using single-cell time-lapse imaging, the research team observed that imMKCLs exhibit asynchronous and heterogeneous platelet production, with only a minority of cells releasing large numbers of platelet-like particles (PLPs). A high-content chemical genetics screen identified MT-destabilizing agents, particularly vinca alkaloids such as vincristine (VCR), as potent enhancers of proplatelet extension formation.

VCR treatment on day three of differentiation significantly increased PLP output, especially under turbulence-enhanced culture conditions using the VerMES bioreactor. These findings demonstrate that timed microtubule destabilization enhances platelet biogenesis from iPS cell-derived megakaryocytes without compromising function.

Further analysis revealed an inverse correlation between MT content and platelet yield. Compared to static cultures, imMKCLs cultured under turbulent flow showed reduced MT staining and higher platelet productivity. VCR addition further boosted yields, with optimal effects observed when applied on day 3, after polyploidization but before proplatelet formation. Early or late VCR treatment diminished efficacy, highlighting a critical time-window for intervention.

Importantly, platelets produced under VCR treatment retained key functional properties. Flow cytometry and confocal imaging confirmed responsiveness to activation agonists, low Annexin V binding, and the ability to spread on fibrinogen-coated surfaces. In vivo experiments using thrombocytopenic NSGS-SGM3 mice demonstrated that VCR-treated iPS cell-derived platelets restored hemostasis effectively, although higher VCR doses slightly reduced platelet persistence and marginal band structure.

This study underscores the role of MT dynamics in megakaryocyte maturation and platelet biogenesis. By leveraging FDA-approved compounds like VCR, the researchers present a practical method to enhance platelet yields from iPS cell-derived sources. These insights pave the way for scalable, cost-effective platelet production systems for transfusion medicine, with future work aimed at elucidating the underlying mechanism of MT modulation and its role during maturation.

More information: Emiri Nakamura et al, Association of microtubule destabilization with platelet yields in terminally differentiating hiPSC-derived megakaryocyte lines, *PLOS One* (2025). DOI: 10.1371/journal.pone.0326165
Journal information: PLoS ONE
Provided by Kyoto Univers

JULY 7, 2025

Quantum enhancement discovery could improve medical technologies

by University of Glasgow edited by Lisa Lock, reviewed by Robert Egan

Experimental configuration. Credit: *Science Advances* (2025). DOI: 10.1126/sciadv.adw4820

Technologies such as biomedical imaging and spectroscopy could be enhanced by a discovery in research that involved several institutions, including the University of Glasgow. Scientists have found that two-photon processes, which have applications in the study of Alzheimer's disease and other nervous system disorders, can be strengthened by quantum light at far higher levels than previously thought possible.

The processes normally require high-intensity light but this can cause samples to be damaged or bleached.

It was suggested many years ago—and has since been demonstrated—that entangled photon pairs could overcome this limitation. However, it has been widely believed that this quantum enhancement only survives for very faint light, raising doubts about the usefulness of the approach.

However, the new study by researchers in Scotland and Italy saw evidence of quantum enhancement which worked at nearly 10 times higher light intensity levels.

The research could pave the way for new technology which offers increased signal strengths without sacrificing quantum enhancement.

The study was carried out by researchers at Strathclyde, the University of Glasgow, Università dell'Insubria in Como, and Istituto di Fotonica e Nanotecnologie del CNR in Milan. It has been published in the journal *Science Advances*.

Dr. Lucia Caspani, former senior lecturer (and now visiting researcher) at Strathclyde's Institute of Photonics and lead researcher in the project, said, "We have been able to demonstrate that quantum effects can still provide an advantage well beyond the level of low intensity.

"This could significantly expand the role of quantum light in applied technologies, notably within the field of biosensing.

"Our research could lay the groundwork for the next generation of quantum-enhanced sensing approaches."

The researchers made experimental and theoretical explorations of two-photon processes and compared the quantum physics results with those of an experiment using classical, non-quantum, light.

The theoretical and experimental results were well-matched, indicating that the two-photon processes driven by quantum light are more efficient than their classical counterpart, even at higher intensities where quantum enhancement has been expected to fade.

More information: Thomas Dickinson et al, Quantum-enhanced second harmonic generation beyond the photon pairs regime, *Science Advances* (2025). DOI: 10.1126/sciadv.adw4820
Journal information: Science Advances
Provided by University of Glasgow

JULY 10, 2025

A one minute scan of your foot could help prevent amputation: Here's how

by Christian Heiss, The Conversation edited by Owen Ferguson, reviewed by Andrew Zinin

Credit: Unsplash/CC0 Public Domain

Imagine having blocked arteries in your legs and not knowing it. At first, there may be no symptoms at all. Just occasional fatigue, cramping or discomfort—symptoms easy to dismiss as aging or being out of shape.

But as blood flow worsens, a small cut on your foot might not heal. It can turn into an ulcer. In the worst cases, it can lead to amputation. This condition is called peripheral artery disease (PAD)—and it's far more common than many realize.

PAD affects around one in five people over the age of 60 in the UK, and is especially prevalent in people with diabetes, high blood pressure or kidney disease.

PAD is rarely an isolated issue: it's usually a sign of widespread atherosclerosis, the build-up of fatty deposits that can also narrow arteries in the heart and brain.

It also significantly increases the risk of heart attacks, strokes and other conditions linked to poor blood flow to vital organs. Research shows that a large proportion of people diagnosed with PAD will die within five to ten years, most often due to these complications.

Early detection is key to reducing the impact of PAD, and I've been working with colleagues to develop a faster, simpler way to diagnose it.

PAD testing

Doctors can check circulation in the feet by comparing blood pressure in the toe with that in the arm. The result is known as the toe–brachial index (TBI). The trouble is that the test needs a toe-sized cuff, an optical sensor and a doctor who knows how to use the equipment.

Many GP surgeries and foot clinics don't have this kit. And in many people, especially those with diabetes or stiff arteries, the test doesn't always give a clear or reliable result.

Our research team asked a simple question: could we turn a routine ultrasound scan into a quick, reliable way to measure blood flow in the foot?

Most hospitals, and many community clinics, already have handheld ultrasound probes, which use Doppler sound to track how blood flows through vessels.

This works through the Doppler effect: as blood moves, it changes the pitch of the sound waves. Healthy blood flow creates a strong, steady "swoosh", while a narrowed or blocked artery produces a faint or disrupted sound. Doctors are trained to hear the difference and use these sound patterns to spot circulation problems, especially in conditions like PAD.

But my research team wondered whether a computer could do more than listen: we wanted to know whether it could convert the shape of that Doppler "wave" into a number that mirrors the TBI.

To investigate, we scanned the feet of patients already being treated for PAD—150 feet in all. For each artery, we used Doppler ultrasound to measure how quickly blood surged with each heartbeat, a pattern known as the acceleration index. We then compared these results to the standard toe–brachial index, the traditional test that measures blood pressure in the toe.

A one-minute scan, a nearly perfect match

The acceleration index alone was able to predict the standard toe–brachial index with 88% accuracy. Using a simple formula, we converted that Doppler reading into an "estimated TBI"—a number that closely mirrored the conventional result. It needed no toe cuff, no optical sensor and it took under a minute to perform.

Even more encouraging, estimated TBI rose in tandem with traditional TBI results after treatment. When patients underwent angioplasty—a procedure to reopen blocked arteries—their estimated TBI increased almost identically to the measured TBI. That means this scan doesn't just help diagnose PAD; it could also be used to track recovery over time.

Crucially, our approach works with equipment that's already widely available. We repeated the experiment using a basic pocket Doppler: the kind many GPs and podiatrists have tucked in a drawer.

While it wasn't quite as precise as hospital-grade ultrasound, the results were still strong. With some additional software refinement, doctors could soon assess foot circulation quickly and accurately using tools they already own, without adding time to a busy clinic schedule.

Why early detection matters

Because early diagnosis of PAD changes everything. It can mean the difference between losing a foot, keeping your mobility and living longer with a better quality of life. It can shorten hospital stays and reduce the risk of heart attack and stroke.

But right now, too many people with PAD aren't diagnosed until they already have chronic limb-threatening ischaemia—the most severe form of the disease. This condition occurs when blood flow to the legs or feet becomes critically low, depriving tissues of oxygen. It can cause constant foot pain (especially at night), wounds that won't heal and, in advanced cases, tissue death (gangrene) and the risk of amputation. Without urgent treatment to restore circulation, chronic limb-threatening ischaemia can be life-threatening.

Part of the problem is that the tools used to diagnose PAD are often slow, expensive or too complicated for routine use. That's why a simple, cuff-free Doppler scan that provides a reliable estimate of toe–brachial index is so promising. It uses equipment that many clinics already have, takes less than a minute and delivers immediate results—offering a faster, easier way to spot poor circulation before serious damage is done.

We're now looking at ways to automate the measurement so that it can be used even by non-specialists. We're testing it in various clinics with different patient groups and exploring its performance over time. But the evidence so far suggests that this could become a key part of vascular care—not just in hospitals, but in GP surgeries, diabetes clinics and anywhere else early intervention could save a limb.

Blocked arteries don't need to stay hidden. With the right tools, we can find them earlier, treat them faster and protect people from the devastating consequences of late diagnosis.

Provided by The Conversation

JULY 23, 2025

Myosin-binding protein-C is critical in maintaining heart health, study shows

by University of Missouri edited by Stephanie Baum, reviewed by Andrew Zinin

No one can live without a heart pumping blood to the rest of the body. New research from the University of Missouri School of Medicine reveals more information about this vital function and how it's related to certain heart diseases and conditions.

In a heartbeat, cardiac muscle cells contract to push blood out to the body, then relax to allow the heart to fill again. This is possible because muscle proteins are organized into sarcomeres, which are small structural units of muscle located inside muscle cells. When a muscle contracts, the parts of a sarcomere "shorten" and come closer together. Each cardiac muscle cell can have over 5,000 sarcomeres, which compounds both the shortening and relaxation events.

"This process appears to be regulated by myosin-binding protein-C (cMyBP-C), which is a heart muscle protein," study author Kerry McDonald said. "Our study investigated its role in cardiac muscle contraction. Without this protein, muscle contraction occurred at a higher rate, especially when the heart was under increased stress."

The study is published in the *Journal of General Physiology*.

According to the research, the protein seems to sense stress on the muscle cells and adjusts sarcomere shortening—and consequently, muscle contraction—based on how hard the heart needs to work. If cMyBP-C is not present or is mutated, it decreases the cell's ability to properly adjust the strength of muscle contraction.

"This protein seems fundamental to heart performance and cardiovascular health," McDonald said. "In fact, alterations to this protein are linked to diseases like heart failure and hypertrophic cardiomyopathy (HCM)."

HCM is a condition where cardiac muscles become thicker than usual, which makes it harder for the heart to pump blood and to fully relax, causing the muscles to contract more often. Mavacamten, a recently developed medication, helps treat HCM and could treat other cardiac-related diseases.

The medication targets sarcomeres and reduces their activity, which then reduces the rate of cardiac muscle contraction. In the study, mavacamten was useful in mice without cMyBP-C for regulating the sarcomere shortening process.

"This study demonstrates the potential benefit of focusing on cMyBP-C in targeted therapies, which can improve quality of life for patients with heart disease," McDonald said.

Dr. McDonald is a professor and the chair of Medical Pharmacology and Physiology at the Mizzou School of Medicine. He is also a Bolm Distinguished Professor, and a Bolm Distinguished Chair in Cardiovascular Health.

More information: Kerry S. McDonald et al, Myosin binding protein-C modulates loaded sarcomere shortening in rodent permeabilized cardiac myocytes, *Journal of General Physiology* (2025). DOI: 10.1085/jgp.202413678
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The A to K of vitamins: What you need and where to get it

by Dan Baumgardt, The Conversation edited by Gaby Clark, reviewed by Andrew Zinin

Credit: Unsplash/CC0 Public Domain
The late, great comedian Barry Humphries (of Dame Edna fame) once spoke whimsically about the health benefits of kale. Just one fistful, he joked, contained enough essential vitamins, minerals and trace elements to keep you in a sedentary position in the bathroom for two whole days. Apparently, it wasn't tasty enough to justify a second helping.

In a world where "superfoods" are relentlessly marketed for their supposed ability to deliver all the nutrients we need, it's worth asking: which vitamins really are essential? And aside from kale (which I actually rather like), what foods help us meet our daily needs?

Vitamin A

Let's start at the top. Vitamin A—also known as retinol—is found in foods like eggs, oily fish and dairy products. It plays a crucial role in keeping your skin and immune system healthy.

But it's probably most famous for supporting vision. Vitamin A binds with light-sensitive pigments in the rod and cone cells of your retina, helping you to see, particularly in low light.

A deficiency in vitamin A, though uncommon in wealthy countries, can lead to serious vision problems and even blindness. Another source of vitamin A is beta-carotene, found in colorful fruits and vegetables like carrots, peppers, spinach and pumpkin. Your body converts beta-carotene into vitamin A, which is why we associate carrots with seeing in the dark.

Vitamin B

The B vitamins are a family of eight different nutrients, each with its own number and role.

B1 (thiamin) helps the nervous system and aids digestion. People with chronic alcoholism are especially at risk of deficiency, which can lead to Wernicke-Korsakoff syndrome, a serious neurological disorder that affects memory and movement.

B2 (riboflavin) and B3 (niacin) support similar functions, while B9 (folate) and B12 (cobalamin) are essential for red blood cell production. A lack of either can lead to anemia.

Folate is especially important in early pregnancy, helping to prevent neural tube defects like spina bifida. That's why it's recommended for people who are pregnant or trying to conceive.

You'll find B vitamins in everything from beans and legumes to meat, fish and dairy; a wide-ranging family of nutrients in a wide-ranging variety of foods.

Vitamin C

The go-to vitamin when we're under the weather, whether from a virus or a hangover, vitamin C (ascorbic acid) is known as the "healing" vitamin for good reason. It promotes wound healing, supports tissue repair and helps maintain blood vessels and bones.

A deficiency in vitamin C causes scurvy—a condition once common among sailors—with symptoms like fatigue, bruising, depression and gum disease.

Fortunately, vitamin C is found in many different fruits and vegetables, especially citrus fruits. That's why 19th-century British sailors were given limes to prevent scurvy, earning them the nickname "limeys."

Vitamin D

Vitamin D is essential for bones, teeth and muscles. It can be absorbed through diet, especially from oily fish, eggs and meat, but your body also makes it in the skin, thanks to sunlight.

In the summer, most people get enough vitamin D from being outside. But in the winter months, diet and, if needed, supplementation become more important.

Deficiency is more common, especially in areas with limited sun exposure. It can lead to soft, weakened bones and symptoms like bone pain, fractures and deformities—including the classic bow-legged appearance. In children, this condition is known as rickets; in adults, it's called osteomalacia.

Vitamin E

Often overlooked, vitamin E helps protect cells, supports vision and bolsters the immune system. You'll find it in nuts, seeds and plant oils and it's usually easy to get enough through a varied diet.

Vitamin F (Sort of)

Not actually a vitamin, "vitamin F" is just a nickname for two omega fatty acids: alpha-linolenic acid (ALA) and linoleic acid (LA). These essential fats support brain function, reduce inflammation, and help maintain healthy skin and cell membranes. Since they're technically not vitamins, we'll let them quietly bow out.

Vitamin K

No, you didn't miss vitamins G through J: they were renamed over the years. But vitamin K is real, and crucial for blood clotting.

Deficiencies are more common in children, and can lead to bruising and bleeding that's hard to stop. Supplements are effective and given after birth.

Most adults get enough through foods like leafy greens and grains.

And the winner is...

All these vitamins are important—and all are found in a wide range of everyday foods. But which single food provides the widest variety?

Kale, oily fish and eggs come in strong at second, third and fourth. But number one is: liver.

Yes, liver. The stuff of childhood dread and overcooked school dinners. But it's also rich in vitamins A, B, D and K. So rich in vitamin A, in fact, that it's advised to eat it only once a week to avoid vitamin A toxicity, and not at all if you're pregnant. Sometimes, you just can't win.

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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

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