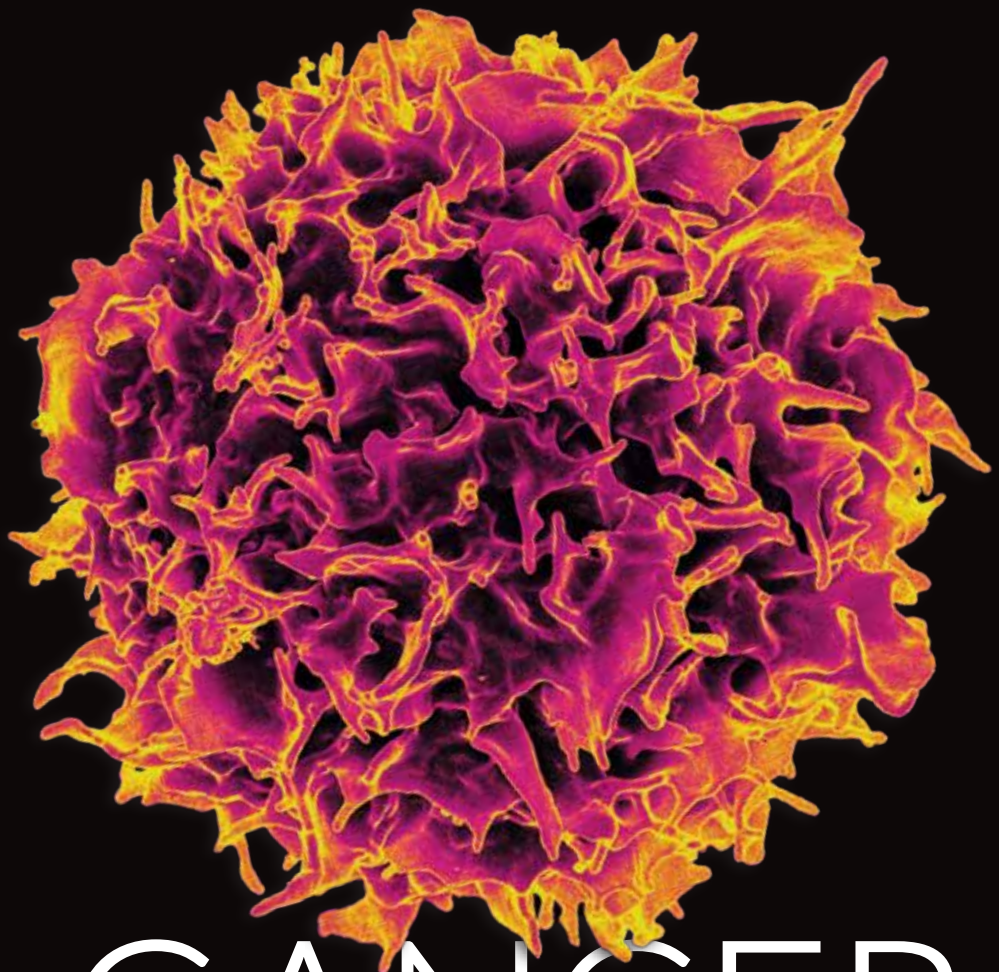
Hints of Life on Mars | The Physics of Paper Cuts

ScienceNews

MAGAZINE OF THE SOCIETY FOR SCIENCE ■ AUGUST 24, 2024



CANCER KILLER

A new treatment mobilizes T cells to vanquish tumors

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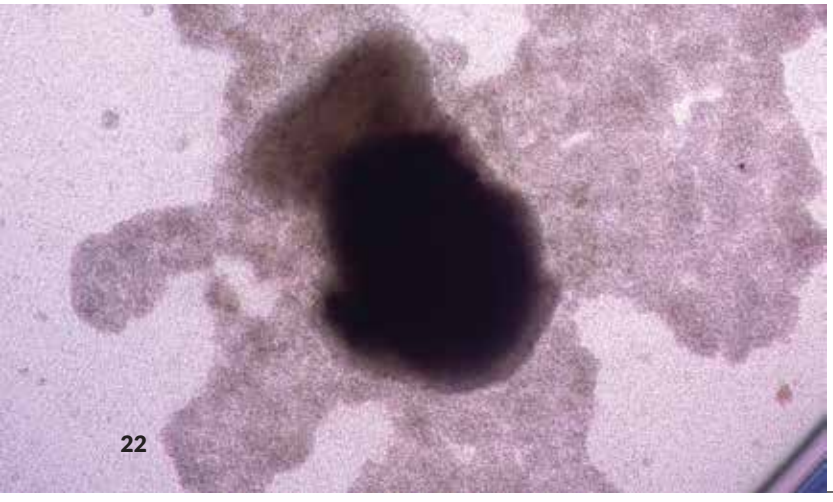

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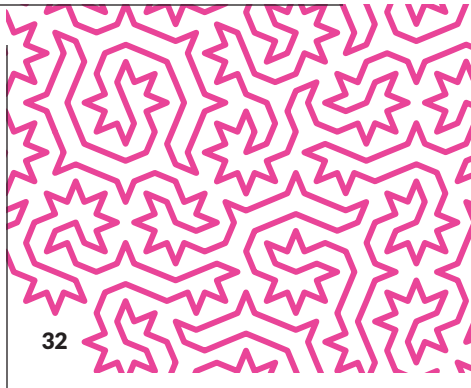
News

FROM TOP: KAMMULA LAB; S. SINGH, J. LLOYD AND F. FLICKER/*PHYSICAL REVIEW X* 2024; S.J. ENGLAND



Departments

COVER The body's immune system produces T cells (one shown in a colorized scanning electron micrograph) that can attack cancer cells. *NIAID*

A long-awaited cancer treatment reaches patients

Thanks to the pandemic, the immune system has gotten a lot of attention. When I think about all the viruses, bacteria and other invaders that the body's defenses fend off, I'm in awe, even if the nudge of a vaccine is sometimes needed to help mount the counterattack.

This issue's cover story reminds me of another reason to be in awe: The immune system not only protects against foreign threats but homegrown ones as well. On Page 22, senior writer Meghan Rosen describes a recent breakthrough in wielding the immune system against cancer. Earlier this year, the U.S. Food and Drug Administration approved the first T cell therapy for a solid tumor, sold under the name Amtagvi. To treat advanced melanoma, doctors remove tumor-infiltrating lymphocytes, a type of T cell known as TILs, from a patient's own tumor and grow these natural cancer killers by the billions in the lab. Then the battalion of T cells is injected into the patient to improve the body's odds of beating the cancer.

Oncologist Steven Rosenberg of the U.S. National Cancer Institute became intrigued by the body's potential for fighting cancer in 1968 after encountering a patient whose tumors spontaneously disappeared, presumably due to the immune system. It took decades to go from that kernel of an idea to the new TIL therapy.

Rosenberg's TIL therapy was an idea ahead of its time. In fact, it's an idea whose foundation stretches all the way back to antiquity.

Early reports of cancer suddenly going into remission after an infection date back to ancient Egypt. By the 19th century, scientists began to piece together that an awakened immune system might be at play. In 1891, New York City bone surgeon William Bradley Coley put that idea to the test by infecting patients' tumors with *Streptococcus* and *Serratia* bacteria. It appeared to work: Reportedly more than 1,000 patients saw their tumors shrink or even disappear. Many doctors, however, were wary of infecting people with potentially dangerous bacteria. Another concern was that no one really knew how or why Coley's treatment worked. And so, cancer immunotherapy stalled.

But throughout the 20th century, scientists demystified the immune system (or at least began to; it's still quite mysterious!). In 1967, for example, the year before Rosenberg's realization, immunologists discovered the existence of T cells and their role in immunity. In the last decade or so, advances have translated into wins for cancer patients. In 2011, a class of drugs known as checkpoint inhibitors, which keep cancer-fighting immune cells in attack mode, first became available. In 2017, the FDA approved the first cancer treatment that uses genetically engineered T cells from patients, called CAR T-cell therapy. This form of treatment has successfully treated blood cancers, such as leukemia. Now with TIL therapy, solid tumors are a target. So far, it's approved only for advanced melanoma, but studies suggest TIL therapy may work against other kinds of solid tumors too.

We're far from the end of the story, with many lingering questions about how the immune system fights cancer. One big question: Why do therapies often work for some patients but not others? As answers come in, we'll keep you updated.

—*Erin Wayman, Managing Editor, Print and Longform*

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Science News (ISSN 0036-8423) is published 22 times per year, bi-weekly except in May, July, October and December by the Society for Science & the Public, 1719 N Street, NW, Washington, DC 20036.
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Excerpt from the August 24, 1974 issue of *Science News*

50 YEARS AGO

Antibiotic resistance

Antibiotics have saved millions of people from life-threatening bacterial infections. But these "miracle" drugs have a serious drawback: Bacteria can build resistance to them. Resistant strains … have multiplied to the point where they may cause 50,000 to 100,000 deaths a year in American hospitals.... [The pathogens] are also becoming a health danger outside the hospital.

UPDATE: Antibiotic-resistant bacteria are now a leading cause of death worldwide. In 2019, the pathogens directly killed over 1 million people and played a role in nearly 5 million deaths (*SN: 2/26/22, p. 5*). As antibiotics lose their potency due to misuse and overuse, scientists are searching for new and diverse strategies to combat bacteria (*SN: 6/22/19, p. 15*). Those strategies include using ointments that render bacteria vulnerable to antibiotics and co-opting bacterial jumping genes to kill or weaken pathogens. Scientists also are studying how "last resort" antibiotics work, which could guide efforts to modify them as bacteria build up resistance.

Renaissance astronomer Tycho Brahe dabbled in alchemy. Instead of trying to turn cheap metals into gold, he formulated secret recipes for medicinal elixirs.

THE SCIENCE LIFE

Shedding light on Tycho Brahe's secret recipes

Artifacts from the ruins of a Renaissance-era laboratory are spilling a famous scientist's secrets.

A chemical analysis of broken glassware belonging to 16th century Danish astronomer Tycho Brahe revealed elevated levels of nine metals, researchers report July 25 in *Heritage Science*. The finding offers tantalizing clues to his work in alchemy, a precursor to modern chemistry.

The astronomer is perhaps best known for his supernova observations and for his solar system model that combined the models of Ptolemy and Copernicus. But he also dabbled in alchemy. Instead of trying to make gold from less valuable elements, he developed elixirs like the *Medicamenta tria*—a trio of medicines that contained herbs and metals.

Brahe kept his recipes secret, though, says chemist Kaare Lund Rasmussen of the University of Southern Denmark in Odense. What's known about the *Medicamenta tria* is based on secondhand accounts.

Rasmussen analyzed the chemical composition of the edges of one ceramic fragment and four glass shards from Brahe's lab on the Swedish island of Ven. Rasmussen detected high levels of mercury, copper, antimony and gold—four metals thought to have been used in the *Medicamenta tria*.

No one fragment contained all four elements. Some of those metals were found on just the exterior or interior sides, while others coated both sides. The vessels could have picked up the exterior metals from accidental splashes or from being placed inside a larger vessel containing those elements, say Rasmussen and coauthor Poul Grinder-Hansen, a historian at the National Museum of Denmark in Copenhagen.

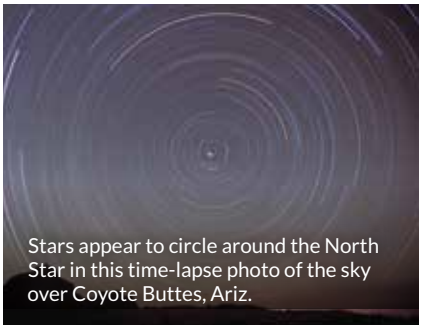
Five additional metals—nickel, zinc, tin, lead and tungsten—were found on the ceramic shard. Because they aren't in any of Brahe's known recipes, he may have used the ceramic vessel to collect waste, the researchers propose. Tin, lead, nickel and zinc were commonly used in the Renaissance world, Rasmussen says. "The most peculiar one was tungsten."

Tungsten was first purposefully isolated in 1783, nearly 200 years after Brahe's death. The metal's presence on the shard could be coincidental, Rasmussen says. Brahe may have separated tungsten from another material without realizing it.

But there is a chance that the isolation was intentional. In the first half of the 16th century, German mineralogist Georgius Agricola reported that the presence of a certain substance (later identified as tungsten) made smelting tin ore difficult. Perhaps Brahe was investigating, Rasmussen speculates.

The study is intriguing, says chemist Laure Dussubieux of the Field Museum of Natural History in Chicago. Research on ceramic vessels is common because they were often used as cookware, she says. "Much less work has been done to understand what kind of inorganic things might have been 'cooking.'" —*Skyler Ware*

SKOKLOSTER CASTLE



Stars appear to circle around the North Star in this time-lapse photo of the sky over Coyote Buttes, Ariz.

RETHINK

The North Star's age needs revising

The star marking true north is heavier than astronomers thought. At about 5.1 times as massive as the sun, the North Star is nearly 50 percent heftier than the previous estimate of 3.45 solar masses, scientists report in a study to appear in the *Astrophysical Journal*.

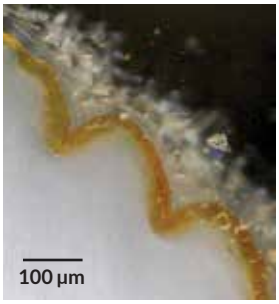
This new estimate is based on how the luminary's gravitational pull influences the motion of a close companion star. Astronomer Nancy Evans and colleagues have been tracking the companion with ground- and space-based telescopes since it was discovered in 2005. Nearly one complete orbit has now been observed, bolstering the finding's reliability. "These things take a long time," says Evans, of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Mass. The North Star's previous mass suggested the star is about 100 million years old. A higher mass means the star burns its fuel faster and thus must have formed more recently. No one has yet calculated a revised age. —*Ken Croswell*

HOW BIZARRE

Komodo dragons' iron maws

Komodo dragon teeth are ironclad. Literally.

The serrated edges and tips of the reptiles' razor-sharp chompers are layered with iron, scientists report July 24 in *Nature Ecology & Evolution*. This metal coating may reinforce each tooth, helping the Komodo dragon (*Varanus komodoensis*) tear through the flesh of deer or water buffalo.



A thin layer of iron turns the serrated edge of Komodo dragon teeth orange, as seen in this close-up image.

Paleontologist Aaron LeBlanc of King's College London and colleagues had set out to uncover what made the teeth of meat-eating dinosaurs good at cutting and used Komodo dragons as a modern comparison. The species is the biggest living lizard in the world and has small, blade-shaped teeth.

Under the microscope, the team noticed orange stains on the tips and serrated edges of tooth specimens. Chemical and structural imaging revealed that the tinge was a layer of iron. The iron is piped on top of the enamel, "sort of like icing on a cake," LeBlanc says. The teeth of some other monitor lizards as well as crocodiles and alligators also have a layer of iron along the cutting edge, though it isn't always visible by eye, the analysis found.

As for long-gone carnivorous dinosaurs, it's unclear whether their sharp tooth edges ever had an iron shield. "Iron is literally the worst element to look at in a fossilized dinosaur tooth," LeBlanc says. "It's just everywhere [in the environment]. If you bury a dinosaur tooth underground for tens of millions of years, iron is going to seep into every little bit of that tooth tissue." —*Erin Garcia de Jesús*

FROM TOP: B. PRICE; SCOTT SMITH/CORBIS DOCUMENTARY/GETTY IMAGES PLUS; A.R.H. LEBLANC *ET AL*/*NATURE ECOLOGY & EVOLUTION* 2024; USO/GETTY IMAGES

THE EVERYDAY EXPLAINED

Paper cut physics

Any way you slice it, a paper cut is painful.

Magazines, letters and books harbor a devious potential for minor self-induced agony while thin tissue paper or the thicker stuff used for postcards are less likely to offend. Scientists have now explained the physics behind why some paper is more prone to shred fingers.

In experiments with a gelatin replica of human tissue, researchers found that a thin sheet of paper tends to buckle before it can cut. Thick paper typically indents the material but doesn't pierce it: Like a dull knife blade, it doesn't concentrate force into a small enough area. A thickness of around 65 micrometers is a paper cut sweet spot—or sore spot—physicist Kaare Jensen of the Technical University of Denmark in Kongens Lyngby and colleagues report in a paper to appear in *Physical Review E*.

That makes dot matrix printer paper the most treacherous, the scientists say. (That paper is seldom used today, fortunately for pinkies and pointer fingers alike.) Paper from various magazines was a close second in the scientists' tests. (Sorry, dear reader!)

The angle of slicing also plays a role. Paper pressed straight down into the gelatin was less likely to cut than paper that cleaved across and down.

Rather than fighting paper's tendency to cut, the researchers embraced it. They designed a 3-D printed tool they call the Papermachete, which, when loaded with a strip of printer paper, acts as a knife.

The single-use blade can cut into cucumbers, peppers, apples and even chicken. The cutting-edge device could serve as a new type of cutlery with low-cost replacement blades.

Future work will study more realistic, finger-shaped materials, rather than flat sheets of gelatin, Jensen says. "Ideally you would want some test subjects, but it's hard to find volunteers." —*Emily Conover*

PLANETARY SCIENCE

Mars rover finds a major surprise

A rock might host signs of life. But can NASA get it to Earth?

BY LISA GROSSMAN

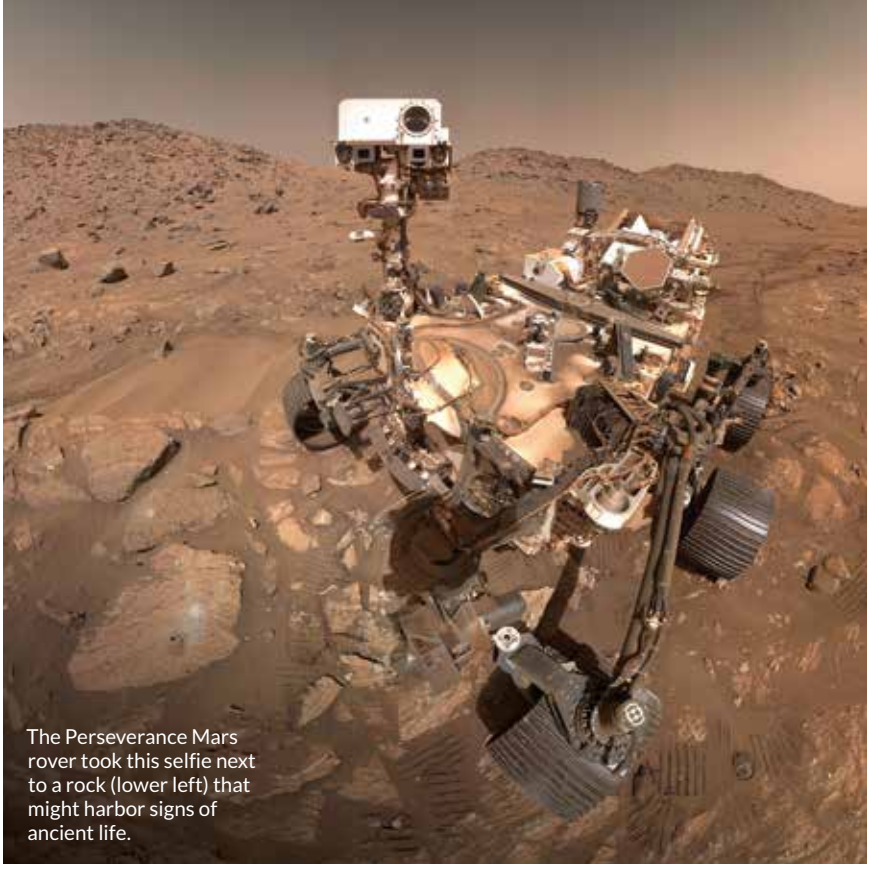
NASA's Perseverance rover has bagged its first hint of ancient microbes on Mars.

"We're not able to say that this is a sign of life," says Perseverance deputy project scientist Katie Stack Morgan of NASA's Jet Propulsion Lab in Pasadena, Calif. "But this is the most compelling sample we've found yet."

The rover, nicknamed Percy, drilled the sample on July 21 from a reddish rock dubbed Cheyava Falls. It is the first piece of Mars that Percy has examined that contains organic molecules, the building blocks of life, project scientist Ken Farley of Caltech reported July 25 in Pasadena at the 10th International Conference on Mars.

This isn't the first sign of organics on the Red Planet — the Curiosity rover detected organic molecules in Gale crater in 2014. But scientists have struggled to identify organics since Percy landed in an ancient dried-up lake called Jezero crater in 2021, Stack Morgan says.

Leopard spot–like features in this close-up image of a Martian rock resemble structures in Earth rocks that are associated with life.



The Perseverance Mars rover took this selfie next to a rock (lower left) that might harbor signs of ancient life.

Adding to the excitement, the reddish rock is speckled with little white spots with black rims. "They look like a tricolored leopard spot," Stack Morgan says.

Using instruments to identify the spots' chemical contents, Percy found that the rims contain iron phosphate. On Earth, rings with similar texture and chemistry are associated with ancient microbial life. The chemical reactions that microbes use for energy can also create the rings.

The rings "don't *require* life, of course, and that's an important caveat," Stack Morgan says. "But based on our experience with similar things on Earth, there is a possibility that life could have been involved, and these could have a biological origin."

The rock has other confusing features that muddy the picture of how it formed. It is shot through with white veins of calcium sulfate. Tiny crystals of olivine, a mineral that forms from magma, permeate these veins. The inclusion of both the spots and these volcanic features in the same rock is "a little bit mysterious," Stack Morgan says, as they point to different origins. Figuring out how the rock formed could help tell how likely it is to have had the right conditions and temperatures to host biology.

Planetary scientist Paul Byrne of Washington University in St. Louis is circumspect about the finding.

"Could this truly be a biosignature? Yes. And if it is, then it really is the kind of society-altering discovery that the discovery of truly extraterrestrial life would be," Byrne says. But it's also possible that the spots came from something other than life, "in which case all this is is an interesting example of water-rock chemistry."

The only way to find out for sure is to bring the rock home. A big part of Percy's mission is to collect samples from interesting rocks for a future spacecraft to return to Earth for study. But funding uncertainty has put the program, known as Mars Sample Return, on hold (SN: 6/15/24, *p.* 12).

"With this sample, the rationale for MSR is strengthened even more, and should, I hope, motivate NASA to commit to pulling off this project sooner rather than later," Byrne says.

The rover team is carrying on despite the budget uncertainty. "We have a mission to carry out, and a job to do: collecting compelling samples," Stack Morgan says. "It can only be our hope that the samples that we collect are compelling enough to justify the cost of Mars Sample Return. I think with this exciting sample, that really hits that home." ■

BOTH: JPL-CALTECH/NASA, MSSS

OCEANS

Metals make oxygen on the seafloor

The process may help support life in the deep ocean, scientists say

BY SID PERKINS

In an unexpected twist, metal-rich nodules found on the seafloor are generating oxygen, new research suggests. This meager but steady supply of the vital gas may help support seafloor ecosystems in areas across the world that are currently targeted for deep-sea mining, scientists say.

Researchers have long presumed that much of the dissolved oxygen in the deep sea was transported there from surface waters. Oxygen can be generated at the surface by plant life via photosynthesis or diffuse from the atmosphere as a result of wave action, says deep-sea ecologist Andrew Sweetman of the Scottish Association for Marine Science in Oban.

But new experiments, both in the lab and at the bottom of the Pacific Ocean, indicate that there are other sources for that oxygen, Sweetman and colleagues report July 22 in *Nature Geoscience*.

For years, Sweetman has been studying seafloor ecosystems thousands of meters deep in the Clarion Clipperton Zone, southeast of Hawaii. In broad areas there, metal-rich nodules that contain valuable minerals — and are thus targets for mining — litter the seabed. On several expeditions, the team's dissolved oxygen sensors suggested that the substance, rather than just being consumed by organisms, was actually, on the whole, being produced. The scientists dismissed the results as erroneous and recalibrated the instruments for their next outing.

After several expeditions yielded similarly anomalous readings, the team developed a different method of measuring dissolved oxygen — which also showed that the gas was being generated.

The data revealed that the rogue oxygen wasn't coming from bubbles trapped in equipment, nor was it seeping out of the polymer material used to make the test chambers. It also wasn't the result of natural radioactivity of metals in the nodules splitting water molecules or the breakdown of manganese oxide minerals in the nodules.

Lab tests under conditions mimicking the frigid darkness of the Pacific seafloor also indicated the concentrations of dissolved oxygen were rising, not falling, in the presence of the nodules.

"That's when we said 'My god, we have another source of oxygen,'" Sweetman says.

Further testing revealed that the nodules act like tiny batteries, producing up to 0.95 volts through an electrochemical reaction on the nodules' surface. Although it takes a little more than 1.5 volts to split seawater into hydrogen and oxygen, Sweetman suggests that under certain conditions, groupings of nodules can together produce enough voltage to do the trick.

Oxygen production seems to be happening on the surfaces of the nodules, Sweetman says. In the team's tests, the rate of oxygen production appears to be correlated with the average nodule surface area, the researchers report.

"In the bigger picture, this is just one of many processes in the deep sea that we're only now discovering," says Lisa Levin, a biological oceanographer at the Scripps Institution of Oceanography in La Jolla, Calif. More than half of the biodiversity in these ecosystems lives on the nodules, taking advantage of the hard surfaces for footholds, but also possibly to access the oxygen being generated there. It's not clear, she notes, whether the organisms living in the underlying sediments also depend on this local source of oxygen.

"It's surprising that we didn't know about this [process] before, that we've overlooked it," says geomicrobiologist Beth Orcutt of the Bigelow Laboratory for Ocean Sciences in East Boothbay, Maine.

Deep-sea mining of the metallic nodules could stir up plumes of sediment that might smother nearby unmined areas. If so, mining could reduce the production of oxygen there, Orcutt says, though it's unclear what this might do to the wider ecosystem. That reduction would be above and beyond the amount resulting from removal of the nodules themselves.

"At this point," Orcutt notes, "we don't know if oxygen production has an impact beyond the area around the nodules." ■

NOAA OCEAN EXPLORATION

Metallic nodules, like this one collected from the bottom of the North Atlantic Ocean in 2021, can produce enough voltage to split water into hydrogen and oxygen, new research suggests. The finding could have implications for deep-sea life — and mining operations.

HEALTH & MEDICINE

Deadly parasites get a new job

Engineered *Toxoplasma gondii* ferry drugs into mice's brains

BY TINA HESMAN SAEY

A mind-bending parasite may one day deliver drugs to the brain.

Toxoplasma gondii is a single-celled parasite that famously makes mice lose their fear of cats, but also can cause deadly foodborne illnesses. Now, the parasite has been engineered to deliver large therapeutic proteins to the brains of mice and into human brain cells in lab dishes, scientists report July 29 in *Nature Microbiology*.

Current methods of delivering therapies to the brain often produce unpredictable results or have a hard time penetrating the protective shield known as the blood-brain barrier. If the engineered *T. gondii* can be made safe for use in humans, it may eventually help treat a variety of neurological conditions.

Microbes such as bacteria and parasites are usually viewed as bad guys, says Sara Molinari, a bacterial synthetic biologist at the University of Maryland in College Park who was not involved with the work. But microbes have evolved "pretty sophisticated relationships with our bodies," she says. "The idea that we can leverage this relationship to instruct them to do good things for us is actually groundbreaking."

As a graduate student at Tel Aviv University, bioengineer and neuroscientist Shahar Bracha was looking for a better way to get drugs and large therapeutic proteins into the brain. Then she heard about *T. gondii* making mice behave recklessly.

The parasite, which people can get from contaminated foods and soil as well as from cat feces, has evolved to cross the blood-brain barrier. Once there, it can pump proteins into brain cells and even live quietly inside host cells for decades.

For scientists developing treatments for brain diseases, therapeutic proteins often are too big to stuff into couriers used in gene therapy — viruses. At first, the idea of using *T. gondii* to sneak big proteins into the brain sounded a little wild, says Bracha, who is now at MIT. "But the more I read about this idea, the more I could figure out an actual plan to test it."

She and colleagues teamed up with Lilach Sheiner, a *T. gondii* researcher at the University of Glasgow in Scotland, to engineer a potentially helpful version of the parasite. Their approach relies on the fact that *T. gondii* uses its own cellular machinery to unload proteins, including one called GRA16, inside host cells. Tacking on the gene for a therapeutic protein to the gene for GRA16 would result in the parasite making a fused protein, allowing the therapeutic agent to catch a ride into the host cell.

The team tested the idea using the protein MeCP2, which is mutated in people who have Rett syndrome — a genetic disorder that includes seizures and developmental delays (SN: 9/25/21, p. 14). Replacing the nonfunctional protein may be one way to treat the disorder.

Engineered *T. gondii* had no problem producing MeCP2-GRA16 proteins and unloading them into human nerve cells and brain organoids in lab dishes. Those parasites were then injected into mice. A few made their way to the brain and began pumping the protein into brain cells. Mice developed no symptoms, indicating that neither the infection nor the fused protein triggered dangerous immune system reactions.

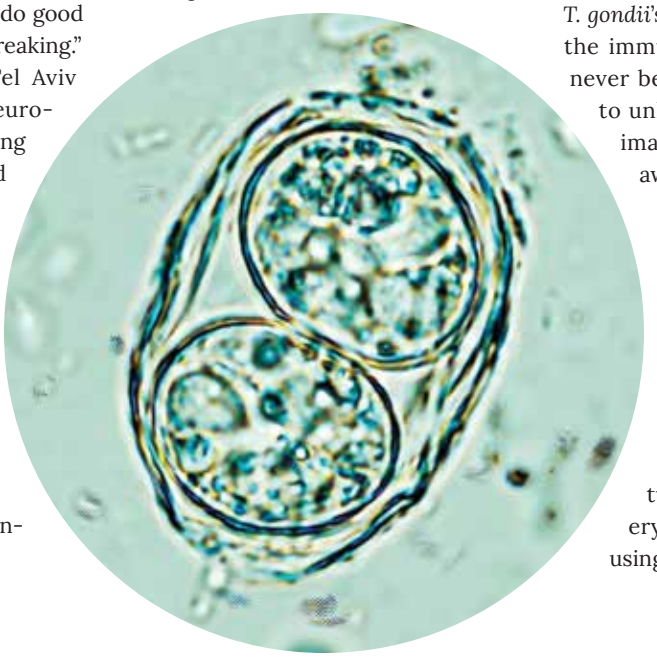
Though it is common for engineered organisms to be weakened by scientists' manipulations, the genetic changes made in this study have not neutered *T. gondii*. It could potentially still cause severe toxoplasmosis in people. Those with weakened immune systems are particularly at risk. Severe cases can damage the brain, eyes and other organs and cause hearing loss.

More than 200,000 *T. gondii* infections are diagnosed in the United States each year, with about 5,000 to 10,000 people requiring hospitalization. An estimated 750 people die from the disease annually.

Using the parasite for drug delivery will require disabling its disease-causing mechanisms without harming *T. gondii*'s ability to quietly infect the brain. It may be impossible to make the parasite safe while retaining all the qualities that would allow it to act as a delivery van, says Sebastian Lourido, a parasitologist at the Whitehead Institute in Cambridge, Mass., who was not involved in the work.

For instance, the parasite hitches rides inside immune cells to break through the blood-brain barrier, destroying those cells as it goes. If scientists disable *T. gondii*'s ability to kill cells and subvert the immune system, the parasite may never be able to reach its destination to unload its cargo. "It's difficult to imagine how you just engineer it away," Lourido says.

Still, the study was encouraging enough for some team members to form Epeius Pharma, an Israel-based company that aims to develop *T. gondii* as a protein delivery system. Bracha and colleagues emphasize that they're just taking the first steps toward turning the parasite into a delivery vehicle and are nowhere near using it for medical treatments. ■



Scientists want to tame the deadly parasite *Toxoplasma gondii* so it can be used to deliver medications to the brains of people with neurological diseases.

TODOREAN GABRIEL/ISTOCK/GETTY IMAGES PLUS

HEALTH & MEDICINE

Bird flu has mammary glands in its sight

H5N1 infects milk-making tissue in mammals other than cows

BY ERIN GARCIA DE JESÚS

The discovery of bird flu in dairy cow milk highlighted a previously overlooked target for the H5N1 virus: mammary glands. A new study suggests it's not unique to cows.

In lab tests, mice and ferrets exposed via the nose to H5N1 isolated from a cow developed infections of the mammary glands, virologist Amie Eisfeld of the University of Wisconsin–Madison and colleagues report July 8 in *Nature*. A bird flu virus taken from an infected person in 2004 also made it to the mouse and ferret mammary glands.

Avian flu viruses typically infect the respiratory system but can also infect other tissues and organs. There were previous hints that the virus could invade mammary tissue. A study from 1953 showed that a different strain of bird flu could infect cow mammary glands. Another study found that the strain responsible for the 2009 bird flu pandemic could infect ferrets' mammary glands. Taken together with the new study, the findings suggest that the tissue unique to mammals is a more common target for the virus than originally thought.

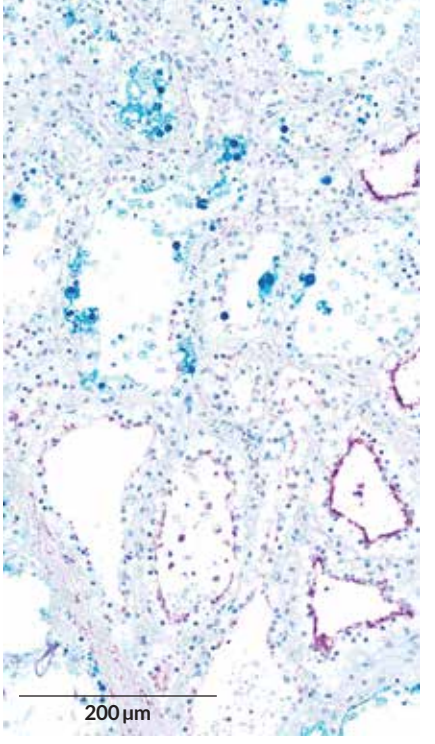
The ongoing outbreak in U.S. cows has affected more than 170 dairy herds in 13 states. Some infected cattle have no symptoms. Others develop fever and their appetite and milk production may drop.

To gain entry into cow mammary cells, the virus exploits a sugar on the cell surface, researchers report in the July *Emerging Infectious Diseases*. Once inside the mammary glands, the virus can make its way into milk. Such infections might explain how the virus is spreading among cattle. It's possible that contaminated milking equipment could carry virus from one cow's udders to another, a separate group of researchers reports in the August *Emerging Infectious Diseases*.

Bird flu has also been detected in cow respiratory tracts. Yet despite lots of virus in that part of the body, there so far doesn't seem to be much respiratory transmission, says Richard Webby, a virologist at St. Jude Children's Research Hospital in Memphis, Tenn., who was not involved in any of the work. It seems that "cows aren't a really good host for this virus unless you go directly to the udder."

In the study in *Nature*, Eisfeld's team exposed mice and ferrets to a variant of H5N1 from a cow in New Mexico. The objective: to see whether the animals developed cowlike symptoms and to understand how the virus transmits.

Bird flu infections among cows can cause dips in milk production because the virus attacks cells in mammary glands. Other mammals can get infections in the glands, too.



Cow mammary cells have a surface sugar (purple in this microscope image) that H5N1 (blue) uses to break in and cause infection.

In both mice and ferrets, the virus spread to several major organs and the mammary glands. Infected female mice could transmit the virus to pups feeding on milk, but no transmission from the mothers to healthy adults occurred through direct contact, the team found. Just one of four healthy ferrets exposed to infected animals in a neighboring cage showed signs of infection, hinting that the variant still isn't good at airborne spread.

The overall risk to people remains low, public health officials say. But U.S. farm workers have a higher risk of acquiring bird flu from cows than the public does. Four cases in dairy workers have been confirmed, but the number of infections is likely much higher, researchers report in a paper posted July 31 at medRxiv.org.

Anyone who consumes dairy is advised to avoid raw milk. But the milk on grocery store shelves remains safe to consume. A widely used pasteurization process effectively kills all H5N1 virus in milk, the U.S. Food and Drug Administration says.

Still, scientists are keeping a close eye on whether the virus is adapting in ways that could raise the risk of spread. Cow cells also have entry portals for human flus. If bird and human viruses meet up and swap genes, new versions of influenza that might better infect people could emerge. ■

FROM TOP: R.K. NELLI *ET AL/EMERGING INFECTIOUS DISEASES* 2024; HISPANOLISTIC/E+/GETTY IMAGES

ANIMALS

Poison frogs may have sexy fingers

Fingertip glands seem to exude mating-related pheromones

BY JAKE BUEHLER

During mating, some male poison frogs embrace their partner's face in a hug that is potentially laced with love potion. Glands in the amorous amphibians' fingertips may create pheromones, researchers report July 21 in *Molecular Ecology*.

Biologist Diana Abondano Almeida of Goethe University in Frankfurt and colleagues were studying chemical communication in amphibians and noticed a combination of quirks in male poison frogs. The males of some species have one markedly swollen fingertip on each hand that becomes even more bulbous during the mating season.

Mating in frogs often involves the male gripping onto the female from behind, sometimes for hours or days. Many male poison frogs grasp females by the face, with the fingers resting near the mate's mouth and nostrils. This placement, especially in concurrence with swollen fingers in some species, seemed too specific to merely be a coincidence, Almeida says.

During courtship, other amphibians use chemicals called sodefrin precursor-like factors, or SPFs. For instance, some salamanders produce these SPFs using skin glands and transfer them to their mate through close contact. Almeida's team wondered if the frogs' fingers were producing similar pheromones.

The researchers took tissue samples from the fingers of the males of two species of poison frogs: stripe-throated rocket frogs (*Leucostethus brachistriatus*) from Colombia and a lab-reared population of Anthony's poison arrow frog (*Epipedobates anthonyi*).

Using genetic analysis, the team compared the relative numbers of RNA transcripts — copies of the DNA sequence used to make proteins, including pheromones — in swollen and normal fingers. In both species, the swollen digits contained hundreds to thousands of times more SPF transcripts than unswollen ones.

Almeida and colleagues suspect that the males may be channeling these finger pharmaceuticals into the females' nostrils or skin through the prolonged contact. Given that face hugging occurs well after the frogs have paired up, the pheromones probably aren't used for attraction, Almeida says. Rather, they

A male Anthony's poison arrow frog (left) attempting to mate with a female (right) places his swollen, potentially pheromone-laced fingers close to her nostril.

ANIMALS

Some seabirds might feed off cyclones

The Desertas petrel flies toward storms, which churn up prey

BY JOSEPH POLIDORO

Tropical cyclones are synonymous with destruction. But at least one seabird appears to take advantage of them as feeding opportunities.

The Desertas petrel (*Pterodroma deserta*), a seabird native to the North Atlantic Ocean, has long been associated with oncoming storms. Now, scientists have learned that this skilled flier seems to purposely interact with cyclones, flying long distances toward them and following their wake, biologist Francesco Ventura and colleagues report in the July 22 *Current Biology*.

Desertas petrels sometimes fly toward cyclones, risking life and wing for a potential big food payout.

It's a risky gambit by the petrel, which must contend with wind speeds approaching 90 kilometers per hour and ocean swells more than eight meters high. The likely payoff: an abundance of food. The researchers found markedly high levels of chlorophyll in the stirred-up water of the storms' wakes, suggesting elevated levels of phytoplankton. These microalgae draw the birds' prey — fish and cephalopods — to the surface, which may trigger a feeding event.

The team combined GPS-tracking data for 33 petrels over four breeding seasons with data on cyclone activity during the same time span. These breeding-related foraging trips are among the longest in the animal world — a circle of about 12,000 kilometers from their colony on Bugio Island, about 400 kilometers north of the Canary Islands, toward Newfoundland and back.

Once the petrels reached about 900 kilometers from a cyclone's eye, nearly one-third of them actively flew toward the storm, the team found. Some 400 kilometers from the eye, the birds slowed down. The GPS data can't shed light on the birds' precise behavior, but it appears the petrels may drift on the ocean's surface, carried by hurricane-force winds.

Once a cyclone passed, about half of the tracked petrels followed its wake and nearly a third pursued the storm's trail for days and thousands of kilometers.

The researchers think Desertas petrels may use infrasound to locate cyclones. Storm winds and waves create this low-frequency sound, which the team says

may kick off physiological changes in the female. "[They] could induce the female to deposit eggs, or at least accelerate this process."

The finding highlights an evolving understanding of the complexity of frog courtship and mating (SN: 6/14/14, *p.* 5; SN: 3/11/23, *p.* 5). Historically, studies have focused on sound, particularly the amphibians' repertoire of croaks and creaks, says Sarah Woodley, an integrative physiologist at Duquesne University in Pittsburgh who was not involved in the new work. But in recent years, researchers have started recognizing the visual, tactile and chemical aspects of the mating process.

Frogs are sophisticated animals, Woodley says. "They are not just using one sensory modality to communicate. It's not all about calling."

There are plenty of next steps in this research, Almeida says. While the large upswing in SPF transcripts certainly hints that the fingertips are specialized pheromone factories, future studies could find and isolate these proteins and determine if and how they influence female frogs. ■

extends about 900 kilometers — the distance at which petrels began to fly toward cyclones. "We are still a long way from having conclusive evidence," says Ventura, of the Woods Hole Oceanographic Institution in Massachusetts.

Desertas petrels might not be the only species to use hurricane wakes opportunistically, Ventura says. "It's possible we're describing a process that triggers a biological response" used by sharks, tuna, turtles and marine mammals for foraging.

The findings have filled an important gap in understanding why seabirds chase storms, says marine ecologist Lesley Thorne of Stony Brook University in New York. Linking the large amounts of food in hurricane wakes with seabird behavior was "something that had not been done to date," she says. It's the kind of research that Thorne believes will help scientists figure out how wind impacts seabirds, particularly as the oceans warm. ■

ETIENNE PRACHT

A connection between making high-risk food choices and gut immunity may help explain why house sparrows are so good at colonizing new territory.

GENETICS

Why sparrows eat poop-spiked food

Scientists link risky food choices with a gut immunity gene

BY NATALIE VAN HOOSE

For animals exploring new territory, taking risks is key to survival. But eating unfamiliar foods can be dicey, since they might contain new pathogens and parasites. One avian immune system, however, seems to have a way of rolling with the punches.

Researchers have found a link between the willingness of female house sparrows to eat weird food — specifically, seed spiked with chicken poop — and the activity of a gut immunity gene, *TLR4*. The more active the gene was, the more poop-laced food the birds ate, the scientists report in the July *Brain, Behavior, and Immunity*.

TLR4 codes for a protein that warns the immune system of bacterial invaders in the gut, says disease ecologist Lynn Martin of the University of South Florida in Tampa. High gene activity means the gut is on alert, he says, so the birds seem to take more foraging risks. The findings could help to explain why house sparrows are so adept at colonizing new parts of the world, even when at risk of encountering unfamiliar disease threats.

Martin's lab has previously shown that sparrows on the fringe of populations expanding their range are more inclined to try new foods and tend to have high levels of *TLR4* activity. He and colleagues want to know whether the level of gene activity is linked to a "flexible" immune system that can seemingly fine-tune itself on the fly. Such flexibility could enable the immune system to readily counter new threats, Martin says.

In the new study, 37 house sparrows (*Passer domesticus*) caught in the Tampa area were subjected to two feeding tests. In one test, birds received seed mixed with sterilized chicken poop — mimicking the kind of unsavory material that sparrows often encounter in cities and on farms. In another, birds could choose between poop-spiked seed and normal seed. All birds were hidden from one another during the tests because sparrows take cues from one another on which foods to eat and which to avoid. Afterward, researchers analyzed *TLR4* activity in the birds' gut tissue.

The team found a direct relationship between dietary decisions and the level of gene activity in female sparrows: Those with high levels of *TLR4* activity tended to eat more spiked food. Males with high *TLR4* activity, however, opted for unspiked food. The difference may have been due to the timing of the experiment, which occurred during breeding season when females' energy needs increase, Martin says. Female sparrows generally ate more food than males in the experiment.

"As the female takes risks, [it's] going to increase the chances that a bad guy gets through," Martin says. Females with high *TLR4* activity, it seems, have guts that can handle the onslaught.

The study does a good job of connecting physiology and behavior, says ecological physiologist Sarah DuRant of the University of Arkansas in Fayetteville. But she wonders whether this gene activity is shaped by the environment, or if the birds are "preprogrammed" one way or another. "I'm not sure that's totally resolved at this point, but I think they're getting there," she says. ■

The XENONnT dark matter experiment has found neutrinos in its detector (shown).

XENON COLLABORATION

PARTICLE PHYSICS

‘Fog’ invades dark matter experiments

Neutrino sighting hints at possible limitations of future detectors

BY EMILY CONOVER

The neutrino “fog” is starting to materialize.

Lightweight subatomic particles called neutrinos have begun elbowing their way into the data of experiments not designed to spot them. Two experiments built to detect particles of dark matter have caught initial glimpses of neutrinos born in the sun, physicists report.

“That’s a triumph,” says neutrino physicist Kate Scholberg of Duke University, who was not involved with the research. The hints of these neutrinos are a long-awaited sign that the newest generation of dark matter detectors has improved sensitivity, both to dark matter and its mimics. “It’s actually a milestone,” Scholberg says.

Known as the neutrino fog, the signature suggests a new way of studying the difficult-to-detect subatomic particles. But it also points toward the beginning of the end for dark matter detectors of this type, which aim to spot the unidentified massive particles that bulk up the cosmos. As these detectors become more capable, the neutrino fog could obscure potential signs of dark matter.

The XENONnT experiment at the Gran Sasso National Laboratory in Italy saw signs of neutrinos that had been produced in the sun, physicists reported July 10 in L’Aquila, Italy, at the International Workshop on the Identification of Dark Matter. The PandaX-4T experiment at the China Jinping Underground Laboratory in Liangshan saw similar evidence, researchers reported at the workshop July 8 and in a paper submitted July 15 to arXiv.org.

The result “opens [a] new door of using our detectors to study neutrinos and searching for associated new physics phenomena,” says physicist Ning Zhou of Shanghai Jiao Tong University, a PandaX deputy spokesperson.

In the nuclear fusion processes that power the sun, multitudes of neutrinos are produced in a variety of reactions (*SN*: 9/20/14, *p.* 32). Some of the most energetic come from the radioactive decay of boron-8, a type of boron created during the fusion process. Scientists had long predicted that those neutrinos are prevalent enough and have the appropriate energies to be seen in dark matter detectors. That’s what the two dark matter detectors have found.

Each experiment houses several metric tons of liquid xenon. If a dark matter particle crashes into the nucleus of a xenon atom, the experiments can detect that nucleus recoiling in response, revealing dark matter’s presence. But neutrinos can also slam into atomic nuclei, causing similar recoils.

This type of interaction, in which a neutrino knocks into an entire atomic nucleus rather than an individual proton or neutron, was first glimpsed in 2017 by the COHERENT neutrino detector, using neutrinos from a laboratory source (*SN*: 9/2/17, *p.* 7). The two new experiments mark not only the first signs of nucleus-thwacking by neutrinos in dark matter detectors, but also the first signs of such thwacking by neutrinos from the sun.

In the future, detecting solar neutrinos via the nuclei they knock around could help physicists understand the particles better. For example, scientists could study the neutrino signal to look for what detectors might be missing: hypothetical “sterile” neutrinos that wouldn’t interact with matter at all, aside from gravitational forces (*SN*: 11/20/21, *p.* 8). Dark matter detectors might also spot neutrinos from other sources, such as nearby exploding stars.

“It’s very cool to see that we can turn this detector into a neutrino observatory,” says physicist Michael Murra of Columbia University, a member of the XENONnT collaboration.

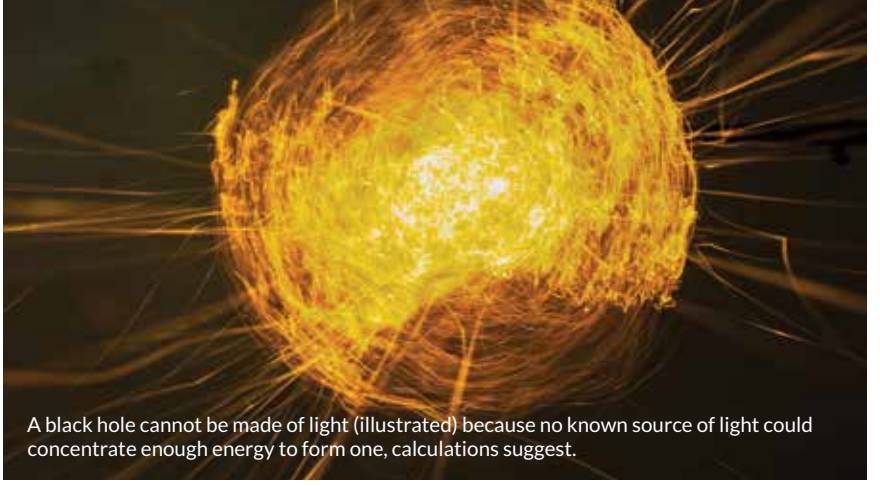
Neutrinos aren’t yet hindering dark matter detection. The solar neutrino signal would obscure only low-mass dark matter particles, which fall below the mass range that these detectors scrutinize most carefully for dark matter. There’s still a long way to go before neutrinos start to swamp dark matter detection of higher masses.

The next generation of dark matter detector should still be able to search for dark matter. But further improvement will start to become difficult. Scientists could move to detectors that measure the direction of the incoming particles to help determine if they are neutrinos or dark matter. That would let scientists look for dark interactions originating away from the sun, banishing solar neutrinos from their data. ■

QUANTUM PHYSICS

Pure light can't make black holes

Particles and antiparticles would sap too much energy



A black hole cannot be made of light (illustrated) because no known source of light could concentrate enough energy to form one, calculations suggest.

BY EMILY CONOVER

Quantum physics has put the kibosh on black holes forming from pure light, theoretical physicist Eduardo Martín-Martínez and colleagues report in the July 26 *Physical Review Letters*.

Matter is responsible for black holes, which often form when a star's core implodes. But matter isn't necessarily required to create a black hole. According to Einstein's general theory of relativity, black holes could form from concentrated energy alone.

A black hole thought to be made from light is called a kugelblitz. That concept has been jangling around in physicists' brains for decades. But actually producing a kugelblitz seems to be a no-go. "No known source in the current universe would be able to produce it, neither artificial or natural," says Martín-Martínez, of the University of Waterloo in Canada.

In general relativity, gravity results from matter curving spacetime. If enough mass is packed into one region, the spacetime can curve so dramatically that it forms a region within which it's impossible to escape — a black hole. Since energy and mass are equivalent in general relativity, that means energy can curve spacetime just as matter can, which suggests that a black hole could form without matter.

The concept is an interesting thought, "especially if we want to produce something like this in the laboratory," says theoretical physicist Juan García-Bellido of Universidad Autónoma de Madrid. Scientists have considered whether lasers could form a black hole, and even proposed using a kugelblitz to power a spacecraft.

Alas, calculations reveal that any attempt at a kugelblitz would fail, Martín-Martínez says. "You are not going to get even close."

Where light energy is highly concentrated, pairs of electrons and their positively charged antimatter partners begin to form. The duos would escape, taking energy with them. This quantum effect would prevent the energy levels needed to form a black hole.

Creating a kugelblitz in a lab would require light intensities over 10^{50} times that of state-of-the-art laser pulses, the team estimates. (That's a mind-bogglingly large factor — a 1 followed by 50 zeroes.) In nature, the brilliantly luminous centers of active galaxies are likewise vastly too dim.

The kibosh applies to kugelblitzes ranging from a fraction of a nanometer to 100 million meters wide. Even outside that range, a kugelblitz would still be very unlikely, Martín-Martínez says.

But García-Bellido notes a possible loophole: Conditions in the early universe could have allowed something akin to a kugelblitz. ■

ANIMALS

Pollination via static electricity

Birds do it. Bees do it. Even butterflies and moths do it.

As lepidopterans fly, their wings accumulate enough static electricity to potentially pull pollen from nearby flowers. Scientists measured the electrostatic charges of 269 moths and butterflies representing 11 species. A charge of about 50 picocoulombs — the average of a European peacock butterfly (shown) — can move 100 pollen grains at least six millimeters, simulations show. The finding suggests that these butterflies and other lepidopterans with similar amounts of charge can pollinate flowers without having to land on the blooms, ecologist Sam England of the Natural History Museum in Berlin and a colleague report in the July *Journal of the Royal Society Interface*.

Butterflies and moths join bees and hummingbirds on the list of organisms capable of electrostatic pollination. The diversity of this small, growing group hints the phenomenon may be widespread, England says. — *Anna Gibbs*

FROM TOP: BASEM GAMAL/GETTY IMAGES; S.J. ENGLAND

PLANETARY SCIENCE

Hidden lunar quakes revealed

The finding may influence future trips to the moon

BY LISA GROSSMAN

A new look at decades-old data from the NASA Apollo missions has uncovered evidence of tens of thousands of previously unrecognized moonquakes. The finding could reveal details about the moon's inner workings and have implications for future human missions.

"There were more tectonic events on the moon; it's more tectonically active than considered before," says planetary seismologist Keisuke Onodera of the University of Tokyo. By meticulously examining the shapes of seismic waves recorded on the moon, Onodera found 22,000 never-before-seen moonquakes, he reports in the July *Journal of Geophysical Research: Planets*.

In the 1960s and 1970s, the Apollo missions that landed on the moon brought along two kinds of seismometers: one to measure longer-period seismic waves that originate deep underground and one to measure shorter-period waves that begin closer to the surface or that carry more energy.

The seismometers draw the shape of the waves that shake the ground—some are squat and dampen quickly while others are long and taper out. Based on the shapes, scientists can learn about the origins of the quake.

Some of those seismometers took data nearly continuously from 1969 through 1977, recording about 13,000 seismic events (SN: 6/8/19, *p.* 7). But most of the data from the short-period seismometers were so contaminated with other sources of waves, they were almost unusable at the time.

"These are 50-year-old data that people had to deal with basically by hand," says Ceri Nunn, a lunar seismologist who is based in California. "You'd print them out on a crappy old dot matrix printer and draw it up by hand."

So lunar scientists knew that they were probably missing some moonquakes from that time period. But nobody had actually sat down and cleaned up the data to find out how many, until Onodera turned his attention to it last year.

"The most surprising thing is I detected 22,000—a much larger number of events than the original dataset," Onodera says. The new quakes bring the total known number to 35,000. "That's something nobody expected," he says.

Onodera looked at the graph of each individual seismic event by eye, and categorized them one by one based on shape. Other lunar scientists were impressed by this low-tech meticulousness.

"It's natural intelligence, I would say, not artificial intelligence," says planetary geophysicist Raphaël Garcia of ISAE-SUPAERO in Toulouse, France. "I'm sure it's a huge amount of work. He reprocessed everything."

Most of the newly identified quakes were from external sources like extreme temperature changes or impacts, including times when NASA deliberately dropped rocket boosters or lunar modules on the moon's surface to see what would happen. But some were shallow moonquakes that reflect motions originating in the upper few kilometers of the moon's crust. These quakes are the ones most likely to give information about the moon's inner workings.

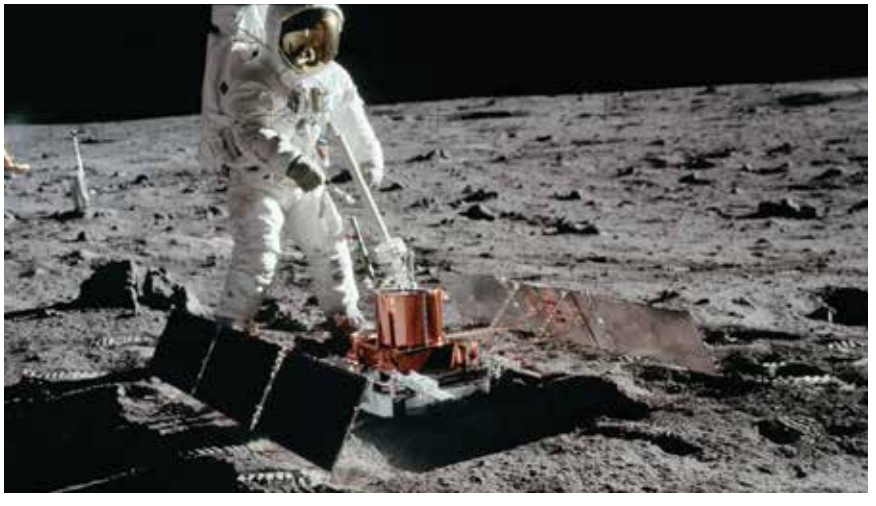
Previous studies had identified 28 such quakes over the eight years of observations. Onodera found 46 more, significantly increasing the total number of known shallow moonquakes.

He also found that these shallow quakes seemed to be more common in the northern hemisphere, near the Apollo 15 landing site, than near the more southerly Apollo 14 and 16 sites. Gravity data from the NASA GRAIL probes, which smashed into the lunar surface in 2012, showed that solidified magma streams surround the Apollo 15 site as well. The shallow moonquakes may form when the moon's crust contracts around these dense intrusions, Onodera suggests.

Getting a better handle on lunar quakes' frequency and strength will be important in planning human trips to the moon and possibly building structures there. Seismic data can help measure the depth of lunar soil, which can set limits for how much shaking lunar habitats need to withstand, and indicate where the safest landing sites might be.

Lunar scientists should soon have much more data to work with. NASA and its commercial partners are planning to send a pair of seismometers to the farside of the moon in 2025. And the Chinese Chang'e 7 mission will send a seismometer to the lunar south pole in 2026.

"It's kind of a golden age for planetary seismology," says Garcia, who is one of the lead investigators for the 2025 mission. ■



A NASA astronaut places a seismometer on the moon during the Apollo 11 mission in 1969. Now, a reanalysis of Apollo-era seismic data has found thousands of previously missed lunar quakes.

NASA

ARCHAEOLOGY

Quakes added to Pompeii death toll

Building collapses killed people sheltering from a volcano's fury

BY CAROLYN GRAMLING

This skeleton's fractures suggest that the person was crushed by the house he sheltered in when Mount Vesuvius erupted in A.D. 79. The explosion likely caused quakes that toppled the house.

POMPEII ARCHAEOLOGICAL PARK

In A.D. 79, a massive volcano in southern Italy explosively awoke, leading to one of the ancient world's deadliest natural disasters. Ash and gas from the eruption killed at least 1,500 people in the city of Pompeii. Now, an analysis suggests that powerful earthquakes concurrent with the eruption may have been yet another killer, researchers report July 17 in *Frontiers in Earth Science*.

Previous excavations of Pompeii have revealed residents fully encased in ash, their preserved bodies telling a powerful tale of a swift, scalding end. In nearby Herculaneum, people who sought shelter in stone boathouses may have survived the heat only to slowly suffocate from volcanic gases (SN: 2/29/20, p. 5).

In the most recent analysis, volcanologist Domenico Sparice of the Istituto Nazionale di Geofisica e Vulcanologia in Naples and colleagues studied a collapsed building in Pompeii, as well as the skeletons of two people found within the rubble. The individuals had injuries similar to those caused by collapsing buildings during modern earthquakes, the team reports.

Mount Vesuvius' eruption nearly 2,000 years ago ejected thick clouds of superhot gases, ash and rock into the stratosphere — a suffocating, scalding mix that swiftly fell back to Earth and blanketed nearby Roman cities. Adding to the destruction, the volcano also sent pyroclastic flows, dense currents of hot gas and rock, speeding down its slopes toward the cities closest to its feet.

An eyewitness to the event, Pliny the Younger, described the eruption in a series of letters from his vantage point in Misenum, across the Bay of Naples from the volcano. In one letter, he wrote of "earth tremors" felt at Misenum that became "so violent that everything felt as if it were being shaken and turned over."

Such strong seismic shocks caused by the force of the eruption, Sparice says, may have forced Pompeii's inhabitants to make a deadly choice: Seek shelter from the eruption inside buildings made unstable by powerful quakes or flee outside into the scalding ash.

To learn more about what role the quakes may have played in the death toll, Sparice and colleagues turned to two newly excavated rooms in a house found in an area of Pompeii known as the Insula of the Chaste Lovers. The walls were decorated with unfinished frescoes, while piles of mortar were found leaning against garden walls and resting on the kitchen counter. Vesuvius had apparently interrupted the building's renovations.

The two individuals found in the house were both male and around 55 years old when they died. Their skeletons were lying near large blocks of masonry — remnants of a crumbled partition wall. Multiple rib fractures, as well as severe fractures to pelvic, arm and facial bones, suggest that the men experienced powerful crushing forces. One man was huddled on his left side, his left hand protecting his head, as if he had been trying to take cover.

Taken together, that evidence suggests the men took shelter from and survived the initial hot rain of gas and ash, which lasted about 18 hours. Some ash did penetrate the house, probably through cracks in doors and windows. But the chunks of wall rest on top of that ash, rather than below it. Sparice's team hypothesizes that powerful quakes toppled the house's partition walls, crushing the men, after the ashfall had dwindled.

Those killer earthquakes may have been the result of the collapse of the volcano's central crater, the team says, which heralded the onset of the volcano's final, deadliest phase. Pyroclastic currents of hot gas, ash and molten rock then swept across the region, burying Pompeii beneath a 3-meter-thick layer of sediment.

The findings confirm "what archaeologists have assumed was the reality," in part due to Pliny the Younger's account, says archaeologist Kevin Dicus of the University of Oregon in Eugene. "I appreciate the evidence-based approach. It takes us from assuming that earthquake tremors were just as destructive at Pompeii to providing a methodology to measure this theory."

The analysis also "gives us a better picture of what the people at Pompeii went through on that day, and why some people chose to stay and ride it out," Dicus says. "It was clearly already a hellscape outside. The ash cloud turned day to night, rock and ash were raining on them. Now we can add a violently trembling ground to the mix."

Such studies also help revise the picture of who was trapped by the eruption, Dicus says. Scientists had once thought that it was mostly the old, the infirm or the enslaved who could not escape the destruction. "We are starting to realize that a true cross section of the population is represented in the bones and body casts," he says. ■

GENETICS

Mammoth DNA preserved in 3-D

The 'chromoglass' reveals the extinct animal's gene activity

BY TINA HESMAN SAEY

Beef jerky and some woolly mammoths have at least one thing in common: Drying turns their DNA into super-tough glass.

This glassy DNA is so stable that it preserved the three-dimensional structure of chromosomes in one woolly mammoth for 52,000 years, researchers report in the July 11 *Cell*. The finding gave researchers an unprecedented look at the extinct animal's genetic instruction book, or genome, even revealing genes that were turned on and off before the mammoth died, says genomicist and neuroscientist Cynthia Pérez Estrada. If well-preserved samples of other mammoths can be found, glimpses at gene activity may help scientists understand how the extinct animals functioned, not just how they looked.

The detailed survey of the mammoth genome was made possible after scientists figured out how to adapt a technique dubbed Hi-C, which looks for the 3-D structure of DNA packed into a cell's nucleus (SN: 9/5/15, *p.* 18).

"I've known about Hi-C for a while now. I just never could think of a way that you would apply it to ancient DNA," says Christina Warinner, a biomolecular archaeologist at Harvard University who was not involved in the research.

That's because DNA crumbles over time. It was hard to imagine that the tiny bits of ancient DNA could retain the shape of chromosomes, Warinner says. And Hi-C usually requires fresh, intact samples.

Even Pérez Estrada's colleagues, who work on 3-D DNA structure with her at Baylor College of Medicine in Houston, weren't convinced such a technique could work on degraded samples. She thought it could, so she tested Hi-C on turkey bones left over after Thanksgiving dinner, on tissue from a dried-out roadkill mouse she found on her way to work, and on a piece of leather from her bag.

"All of those experiments were fascinating, because it actually showed that the structure of the DNA is pretty resilient," Pérez Estrada says. "Despite the cooking, and despite the sun and the environment when talking about the mouse, the structure of the DNA was still there."

But she didn't know whether the structure could hold up for thousands of years. So she teamed up with Marcela Sandoval-Velasco, then at the University of Copenhagen. Sandoval-Velasco had been working on ancient DNA for years and was interested in probing its 3-D structures. She brought a bag full of wonders — museum specimens of insects, fish, reptiles, birds and other animals — to Houston for testing, Pérez Estrada says. And Pérez Estrada visited Copenhagen, where the researchers probed ancient polar bear skulls and a mummified wolf.

56
chromosomes
The total number that woolly mammoths had

The experiments often failed. The Hi-C method used on fresher samples wouldn't work for ancient samples, so the scientists created a new version, dubbed PaleoHi-C.

That's how research often goes — slow, says Sandoval-Velasco, who is now at the National Autonomous University of Mexico in Cuernavaca. "It's iterative. It's full of failures, and it's about not giving up." Teamwork helps too, she says. Over 50 scientists with different areas of expertise came together for the study.

After years of partial success and failure, the team got access to skin from the head of a woolly mammoth that died in Siberia about 52,000 years ago. The mammoth was freeze-dried and preserved in permafrost.

Rapid drying had locked the ancient DNA into a tight molecular state similar to that of glass, called chromoglass. The geneticists and a team of theoretical physicists deduced that the chromoglass structure prevented the pieces of DNA from drifting away from each other.

In unconventional experiments with lab-made beef jerky, the team found that such glassy DNA can remain stable for at least a year at room temperature and stand up to varied insults including being microwaved, run over with a car, smashed with a fastball and blasted with a shotgun.

The mammoth's glassy DNA locked its chromosomes into place. For the first time, the researchers could count the number of chromosomes a mammoth

Scientists examine the skin of a woolly mammoth that died 52,000 years ago in Siberia. Permafrost and freeze-drying turned DNA in the animal's skin cells into a tough 3-D structure.

LOVE DALÉN/STOCKHOLM UNIV.

had: 56, or 28 pairs, just like elephants, Baylor geneticist Erez Lieberman Aiden said July 2 during a news conference. Mammoths also had the same basic chromosome structure as elephants.

Chromosomes stuffed into the nucleus resemble a skein of yarn after a cat has played with it. The snaggled appearance belies the carefully orchestrated structure within.

Genes that are turned on are moved to one subcellular compartment like dancers taking the dance floor, while genes that are turned off are relegated to wallflower status in another compartment. Examining the compartments in skin cells, the researchers found 425 genes that were active in mammoths but not in elephants and 395 genes turned on in elephants but not in mammoths.

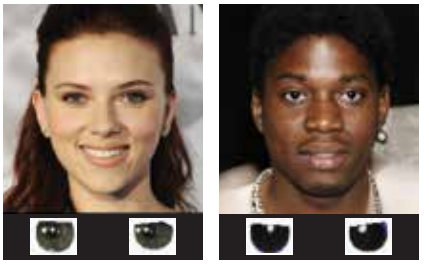
Take *EGFR*, a gene that helps regulate skin and hair growth. The gene was active in elephants but a wallflower in mammoths. In people, switching off the gene leads to long, thick eyelashes and excessive hair growth. That suggests that keeping the gene off the dance floor may have helped mammoths grow their shaggy coats.

The team examined the DNA of a second mammoth, which was killed by a saber-toothed tiger about 39,000 years ago and was buried by human hunters, probably to preserve the meat. The hunters never went back for their prize, Aiden said, but the researchers found that the mammoth also had chromoglass, which preserved loops, compartments and other 3-D structures in the DNA. Quick drying by freezing or high temperatures in arid conditions might produce similar DNA glass in other natural or created mummies, the team suggests.

Warinner predicts that "a lot of scientists are going to read this and start to think, 'Could we apply [PaleoHi-C] to our own questions? Could this solve questions or problems that we have been stuck on for a long time?'"

There will be a learning curve to apply a technique that researchers who study ancient DNA didn't even know they could use, Warinner says. The study "opens up a lot of new doors in the field, in a direction that we just haven't been looking before." ■

ADEJUMOKE OWOLABI



The image of actress Scarlett Johansson, left, is a real photo while the right image is AI-made, an analysis of eye reflections (inset) reveals.

ARTIFICIAL INTELLIGENCE

The eyes can betray fake portraits

Twinkling eyes offer a potential way to suss out AI-generated images of people.

In real images, light reflections in the eyeballs match up, showing, for instance, the same number of windows or ceiling lights. But in fake images, there's often an inconsistency in the reflections. "The physics is incorrect," says observational astronomer Kevin Pimbblet of the University of Hull in England.

Pimbblet and colleagues used a computer program to detect the reflections in images of real and AI-generated people, then took the reflections' pixel values — which represent the intensity of light at a given point — to calculate the Gini index. This calculation, which is often used to study galaxies, indicates how light is distributed across an image.

The difference in the indices between the left and right eyeball is the clue to an image's authenticity, the team reported July 15 in Hull at a meeting of the Royal Astronomical Society. For about 70 percent of the fake images the researchers examined, this difference was much greater than the difference for real images. In real images, there tended to be no, or close to no, difference. The approach is no silver bullet for detecting fakery, Pimbblet says. But it could be part of a battery of tests — at least until AI learns to get reflections right. — *Ananya*

CHEMISTRY

Element 120 may be within reach

To expand the periodic table, it might be time to go titanium. A new study lays the groundwork for a search for element 120, to be made by slamming titanium ions into a californium target. If produced, the new element would have an atomic nucleus brimming with 120 protons and would occupy a new row of the periodic table.

In a proof-of-principle experiment, scientists created two atoms of the known element livermorium, element 116, by focusing a beam of titanium ions onto a target of plutonium. The experiment took 22 days' worth of data, nuclear scientist Jacklyn Gates reported July 23 in Lemont, Ill., at the Nuclear Structure 2024 meeting. A similar experiment aimed at creating element 120 would take about 10 times as long, Gates, of Lawrence Berkeley National Laboratory in California, and colleagues predict. — *Emily Conover*

HEALTH & MEDICINE

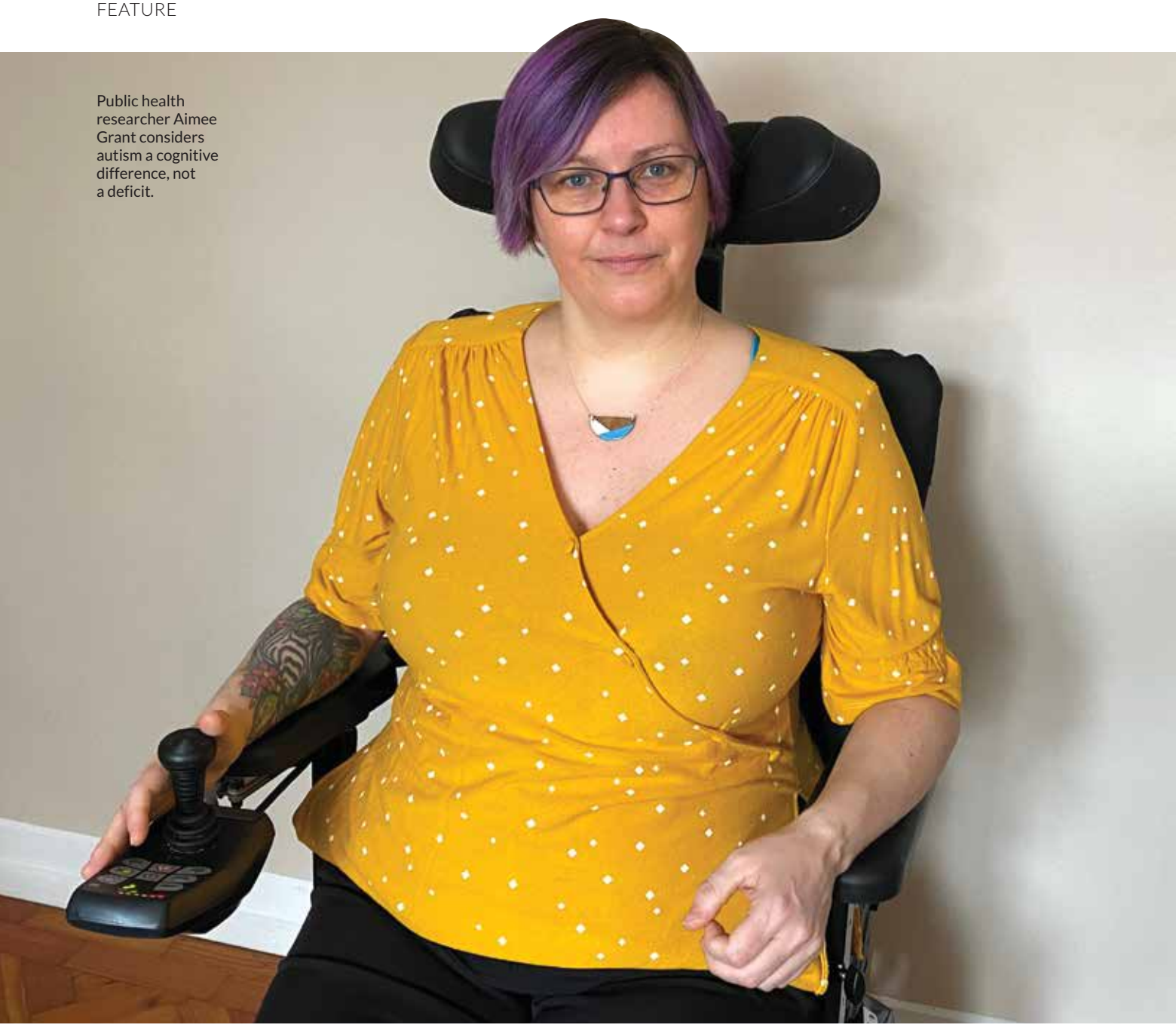
PrEP shots show promise

Zero: That's the number of new HIV infections among young women and teen girls who took a twice-yearly preventive medicine.

Researchers tested a new version of pre-exposure prophylaxis, or PrEP, in a clinical trial of HIV-negative women and teens ages 16 to 25 in South Africa and Uganda. The trial compared a twice-yearly injection of the antiviral drug lenacapavir with a daily PrEP pill that contains two different antiviral drugs.

There were no new infections among the more than 2,100 women and girls who received the shots, researchers with the pharmaceutical company Gilead Sciences report July 24 in the *New England Journal of Medicine*. There were 16 new infections among the nearly 1,100 people taking Truvada, the daily PrEP pill.

Young women and teen girls in sub-Saharan Africa are at high risk for contracting HIV. On average, about 75 percent of the 4,000 young women and adolescent girls who became infected globally each week in 2023 were from the region, the United Nations reports. Barriers to using PrEP include stigma and difficulty keeping a daily regimen. The shots may make maintaining protection easier, says epidemiologist Amrita Rao of the Johns Hopkins Bloomberg School of Public Health. — *Aimee Cunningham*



Public health researcher Aimee Grant considers autism a cognitive difference, not a deficit.

MATTHEW ARTHUR

REIMAGINING Autism Research

Aimee Grant focuses on well-being rather than treating autism as a disease to cure **By Saima S. Iqbal**

Before becoming a researcher, Aimee Grant worked for six years as a caregiver in Cornwall, England, supporting autistic adults in group homes. But only after befriending an autistic colleague at a sociology conference more than a decade later did she realize she was autistic herself.

The stereotypical view of autism as a male brain impairment made it difficult for Grant to make sense of her internal world. From an early age, she struggled to pick up on important social cues and found the sounds, sights and scents in her environment distractingly painful. But like many children of her generation, she says she grew accustomed to either dismissing or disguising her discomfort. It was by listening to some of the stories of her female peers that Grant saw that the label could fit.

Receiving a diagnosis in 2019 prompted her to "reframe [my] entire life," she says. She began working with her mind rather than against it. She no longer felt the same pressure to seem as nonautistic as possible with friends and family members, and she began to make use of accommodations at work, such as a light filter for her computer monitor.

Today, as a public health researcher at Swansea University in Wales, Grant aims to uncover the lived experience of autistic people. Many scientists and clinicians see autism as a developmental disorder that hinders a person's ability to understand and communicate with others. Grant believes that their work often obscures the heterogeneity of autism. And because many studies view autism as a disease, they overlook the reality that autistic people can feel more disabled by widespread misunderstanding and a lack of accommodations than by autism itself.

In line with the thinking of the neurodiversity movement that emerged in the 1990s, Grant views autism as a cognitive difference, rather than a deficit: an alternative way of being in the world just as deserving of understanding and acceptance as any other. "I would say I'm disabled because of a range of different things, including being autistic," she explains. (Grant has dyslexia and uses a wheelchair.) "But were I in a different environment, I don't think I'd necessarily be disabled by being autistic — I think it's those kinds of neurotypical expectations that can make life quite difficult."

So Grant is asking a different research question: What might autistic people need?

She's among a growing group of neurodivergent researchers whose science seeks to better serve its participants. Large surveys conducted in the United States and the United Kingdom suggest that the majority of autistic people would choose to spend research dollars on actionable studies on well-being versus studies of the basic science of autism. At conferences and in private Facebook groups, researchers trying to shift science's focus now number in the hundreds.

Grant's current work centers on autistic parents who give birth. Through extensive surveys and interviews, she's studied the barriers some autistic parents face in breastfeeding. She's also identified ways clinicians can temper the pain of their patients' pregnancy loss, such as by using clear and direct language or including partners or patient advocates. On a YouTube channel she helped launch last year, autistic people share details of pregnancy and parenting. And she's cofounded the Autistic Health Research Network, a small but international association of researchers seeking to better health care outcomes in the autistic community.

A passion for improving lives powers Grant's research and outreach, says Karen Henry, a lecturer in midwifery at the University of Suffolk in England. Both Henry and Grant are part of the U.K.-based Maternity Autism Research Group. "I don't know how she has enough hours in the day."

The needs of autistic parents

Grant's work aims not only to serve study participants, but also to amplify their voices. By aggregating personal accounts, her research gives participant testimonies weight they often lack on their own, Henry says.

In one breastfeeding study, published last November in *Maternal & Child Nutrition*, Grant's team surveyed 152 autistic birthing parents in the United Kingdom. Nearly 70 percent of participants enjoyed breastfeeding overall. But many reported dealing with pain roughly half the time or more. One parent likened the feeling of the let-down reflex that gets breast milk flowing to "an old-fashioned telephone ringing in my breasts."

Still, most remained committed to breastfeeding, which the World Health Organization recommends women do exclusively for at least six months. The parents came up with creative solutions to ease their discomfort, including wearing clothing that exposed less of their sensitive skin, wearing nipple shields and distracting themselves with videos or games on their phones.

Parents who received support from health care professionals, such as midwives or lactation consultants, tended to have a much easier time with breastfeeding. But nearly half of study participants had a negative interaction with at least one clinician, either struggling to access services,

UNSUNG CHARACTERS

This article is part of a *Science News* series highlighting people of science — past and present — who we believe should be better known. Watch for more of these stories, and send your ideas to editors@sciencenews.org

receiving incomplete or conflicting health information or even feeling that their struggles were flat-out dismissed.

These struggles are not unique to parents with autism, of course. In the United Kingdom, just 1 percent of all mothers meet the WHO's six-month recommendation, according to the latest available data. Grant and colleagues attribute this low rate to structural impediments, such as inadequate support for parents and aggressive campaigning by the formula industry, not to a lack of trying on the part of parents.

Grant says she has always wanted to "change perceptions about groups," especially those who face stigma. Her work broadly aims "to help the wider public recognize just how hard that group is working."

To shed light on things about autistic people that might not be known by policy makers, Grant has communicated her findings to the public in news articles and at conferences. The YouTube channel she helped launch now features more than 100 clips of autistic parents and maternity experts sharing their knowledge.

"My work has a purpose: to make lives better for marginalized groups."

AIMEE GRANT

In 2022, Grant won a $3 million grant for an expansive study characterizing the broad reproductive health care needs of autistic people with wombs, from menstruation to menopause. The project will recruit 100 participants, interviewing them every six months for a total of five years.

"There's a lot more questions than answers at the moment," Grant says. Some of her team's questions: How can individuals manage the discomfort of a period cramp or of ultrasound gel? What contraceptives do participants use, and what are their experiences? Are there differences in how autistic people sense and communicate bodily pain to health care professionals compared with what the research says of nonautistic people?

A project of such size and duration will identify areas where autistic people's health care needs are not being met, Grant predicts. It may also uncover positives of the autistic experience, as well as new avenues for research. Her team plans to keep the interviews loosely structured to "give people the space to talk about the things that are important to them."

The team aims to capture the diversity within the community by partnering with autism organizations that serve individuals of various ethnic backgrounds and learning abilities, by paying participants for their time and for sign language interpreters if needed, and by allowing participants to choose to respond to questions through a video call, on the phone or via email. The researchers, who are all autistic, will also lean on their own neurodivergent perspectives to anticipate hurdles and solutions, such as putting text in fonts and colors that are easier to read and using inclusive language that accounts for nonbinary and transgender people with wombs.

Grant is "one of those practice-what-you-preach people," says Rebecca Ellis of Swansea, a research assistant working on the project. "She is continually making sure that she can be as inclusive as possible and amplify the voices that get heard the least."

Keeping an open mind

Grant doesn't claim to have the single answer on what research on autism should look like; she's committed to having an open mind. "I'm sure in 10 years we'll have even more of a social model of autism," she says, referring to the view of autism as a disability constructed in large part by society, "and where we are now will seem outdated." For now, she's helping to get different perspectives in the room, collecting evidence for the theory that one's environment can be more disabling than one's difference.

Grant's path to science may be part of what makes her work so unconventional.

Growing up, she did not expect to become a researcher. Her father was a firefighter, and her mother a housewife. In school, she just kept pursuing "the next thing that was interesting." She attributes where she is today in large part to chance.

She pursued a Ph.D. in social policy at Cardiff University, where she studied competing political narratives around disability-benefit users, debunking a prominent myth that claimants were exploiting the welfare system. After completing that work, she needed to find a job near her home to reserve a spot on a waiting list for much-needed surgery. She worked in Cardiff as a research assistant, studying how well the National Health Service's smoking cessation programs work, and then was asked to shift her focus to maternity. After her own autism diagnosis, she began to focus on autistic parents.

Along the way, she tended to be drawn to and stick with jobs with a social justice ethos. "My work has a purpose: to make lives better for marginalized groups," she says. "It's almost painful for me to do research that isn't in those areas." ■

Explore more

- Find Aimee Grant on YouTube at @AutismMenstruationToMenopause

Saima S. Iqbal is a health and medicine writer based in New York City.

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A ‘living drug’ that uses patients’ own T cells to treat solid tumors gains FDA approval

By Meghan Rosen

THE BODY’S CANCER FIGHTERS

STEVE GSCHMEISSNER/SCIENCE SOURCE

Toni English's medical team was giddy.

It was six weeks after English had completed an experimental cancer treatment, and she had arrived at the Orlando Health Cancer Institute in Florida with her husband to see the results of her latest scan.

Her team gathered in a patient exam room on the second floor of the institute. English could sense the excitement. Someone held up a phone, ready to take English's picture. Her oncologist stood near a computer screen and pointed to an image. "Here's the picture of your lungs before treatment," he said. In English's left lung, the bulbous white splotch of a tumor was clearly visible — about the size of a nectarine.

Then the oncologist showed English her most recent scan. That white spot was gone. "It was history," English says. The team waited for a reaction. English stayed silent for a moment and then said, "Well, good! Isn't that what we were expecting?"

English, who is in her 60s, had mucosal melanoma, a rare form of the disease — and it can be deadly. Five years after receiving a diagnosis, only about a quarter of patients are still alive. English's melanoma had become metastatic, creeping beyond its initial home in her nose to her lungs, kidney and brain.

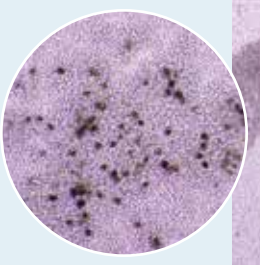
Existing therapies can shrink these kinds of tumors and keep the cancer under control, but they don't help every patient. Over the last three years, English had been trying a nightmarish carousel of treatments including surgery, radiation and drugs that boost the immune system. Looking back on that time, "it was pretty rough," she says, but "I was just doing what I had to do." Still, the cancer persisted, and English thought she was out of options — until her doctor told her about a clinical trial for the new drug.

The trial was testing a treatment developed by the company Iovance Biotherapeutics, and it was unlike anything English had tried: a "living drug" made up of immune cells called T cells. Tumor-infiltrating lymphocyte therapy, or TIL therapy, takes cancer-targeting T cells from a patient's own tumor, grows them to the billions in the lab and then infuses them back into the body. This massive influx zeroes in on and attacks cancer cells and, in some cases, appears to wipe out every last one.

Now, six years after English saw her promising scan, TILs are available for patients beyond clinical trials or early access programs. In February, the U.S. Food and Drug Administration approved Iovance's TIL therapy, called lifileucel, brand name Amtagvi, for advanced melanoma. Though other T cell–based therapies that engineer patients' cells have been approved for blood cancers, this is the first time the FDA has approved a T cell therapy for a solid tumor. Such tumors make up some 90 percent of new cancer cases worldwide and may kill more than 550,000 people in the United States this year.

Amtagvi didn't work for everyone with advanced melanoma — not by a long shot. English was one of the lucky ones. The FDA based its approval on 73 people, including English, who were part of a larger clinical trial. Of those 73, just three saw their cancer disappear. But nearly a third of the patients saw some benefit. Though the number may sound

T cells to the rescue After about a week of growing in the lab, tumor-infiltrating lymphocytes from a uveal melanoma tumor (right) expand in number and surround the tumor. The TILs form a halo around cancer cells (dark speckles, below), destroying the tumor.



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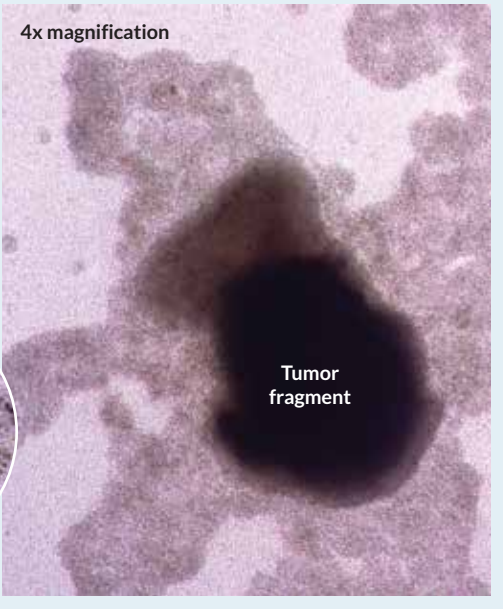


KAMMULA LAB

"The very mutations that cause the cancer are likely to be the Achilles' heel for treatment."

STEVEN ROSENBERG

low, TIL therapy can be a lifesaver for some people. And as scientists get a better handle on which patients will benefit and which T cells are most powerful, outcomes should only improve, says cancer surgeon Udai Kammula of the University of Pittsburgh.

The drug's approval has cracked the door open to a potential wide world of TIL therapies, Kammula says. Dozens of TIL trials around the world, including three from Kammula's team, are testing treatment variations and more types of cancer, including breast, pancreatic and colorectal cancers, some of the deadliest forms of the disease.

Oncologist Steven Rosenberg, chief of the Surgery Branch of the National Cancer Institute in Bethesda, Md., pioneered the technology. He began treating patients with TILs in the late 1980s. Rosenberg has now seen dozens of people survive more than a decade cancer-free. "That's pretty convincing evidence that cure is possible," he says.

The rise of TIL therapy

Scientists today know that our immune systems can attack cancer, but when Rosenberg started working at the National Cancer Institute in 1974, the idea was dogged with doubts. Most scientists just didn't think our immune systems could tell the difference between a healthy cell and a cancerous one.

Rosenberg wasn't so sure. In 1968, he saw a patient who had undergone surgery more than a decade earlier to remove most of his cancer-ridden stomach. Tumors also riddled his liver and lymph nodes, but his doctors couldn't operate on them, and he hadn't received any further treatment.

While operating on the patient during an unrelated gallbladder surgery, Rosenberg noticed that the man's cancer had entirely disappeared. Somehow, he had fully recovered from cancer without additional treatment. "One of the rarest events in medicine," Rosenberg wrote in a 2021 editorial that chronicled the history of cancer immunotherapies.

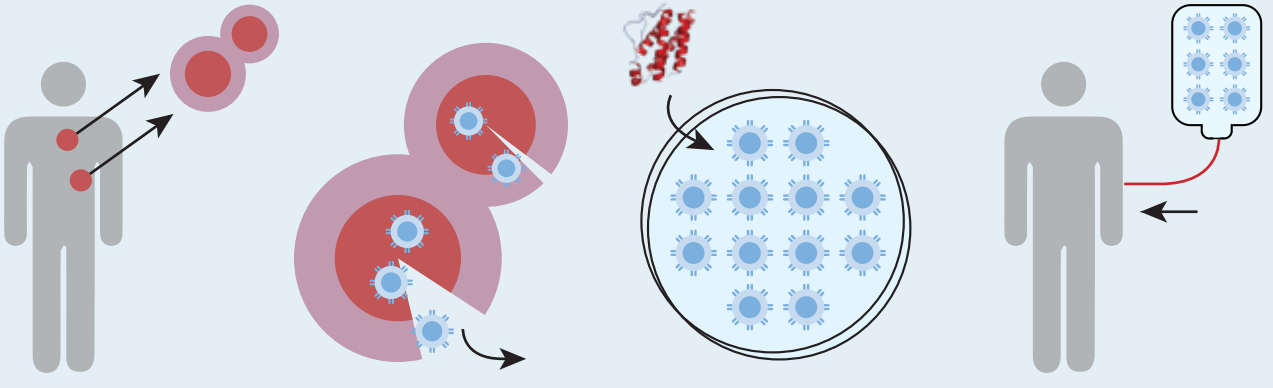
That remarkable recovery stuck in his mind. The man's immune system had probably hunted down and destroyed the cancer, Rosenberg thought. The case helped put him on a path toward understanding the immune system's cancer-fighting powers. And "what better place to look for cells doing battle against cancer than within the cancer itself?" he says.

Scientists now know that a variety of factors can suppress T cells' natural tumor-fighting abilities. So our immune systems sometimes need help to quash cancer.

In 1988, after years of experiments in the lab and the clinic, Rosenberg's team reported a breakthrough. In a trial of 20 people with melanoma that had spread from the skin to other places in the body, tumors shrank in more than half of participants treated. The patients had received TILs, cells surgically removed from their tumors and expanded to large numbers in the lab, along with infusions of interleukin-2, or IL-2, a molecule that helps the cells grow. The work "demonstrated for the first time that lymphocytes could be used as a living drug for treating cancer," Rosenberg says.

His team's results inspired a decades-long effort

TIL therapy in action Immunotherapy harnesses the body's immune system to attack cancer. In TIL therapy, doctors collect tumor-infiltrating lymphocytes, a type of T cell, from a patient's cancer (Steps 1 and 2) and grow billions of them in the lab (3). The patient undergoes chemotherapy to prepare the body to accept the infusion of T cells, which are injected into the bloodstream (4). SOURCE: MOFFITT CANCER CENTER



1. Resection
A surgeon removes part of a patient's tumor.

2. Extraction
Scientists extract tumor-infiltrating lymphocytes, or TILs, from the tumor.

3. Expansion
TILs are cultured in the lab with interleukin-2 (red squiggles), a molecule that boosts cell growth.

4. Infusion
The patient receives billions of TILs to bolster the immune response against cancer cells.

FROM TOP: NCI; B. PRICE

to improve TIL therapy. It's an idea that was ahead of its time, says Jae Park, a hematologist-oncologist at Memorial Sloan Kettering Cancer Center in New York City. And while researchers were getting TIL off the ground, Rosenberg's team and others were also working on other ways to harness T cells to fight cancer.

One method that took off faster than TIL therapy is called CAR T-cell therapy, for chimeric antigen receptor T cells. Using genetic engineering, scientists modify a patient's own T cells so they can recognize a specific cancer cell signal. These customized cells can hunt down certain cancers like a pack of hounds with the scent of prey in their noses. Since 2017, the FDA has approved a half dozen CAR T-cell therapies for certain leukemias, lymphomas and multiple myeloma, which develops inside the bone marrow (SN: 7/7/18, p. 22).

But trying to engineer designer T cells that recognize and lock onto cells from solid tumors has been a thorny challenge. It's tricky to find a unique molecular signal on the tumor cells that clearly shouts "cancer" to the T cells. So far, the therapy has been approved only for liquid cancers, like those of the blood.

"Efforts to use CAR T-cells in solid tumors have been uniformly unsuccessful," Kammula says.

Hunting down cancer

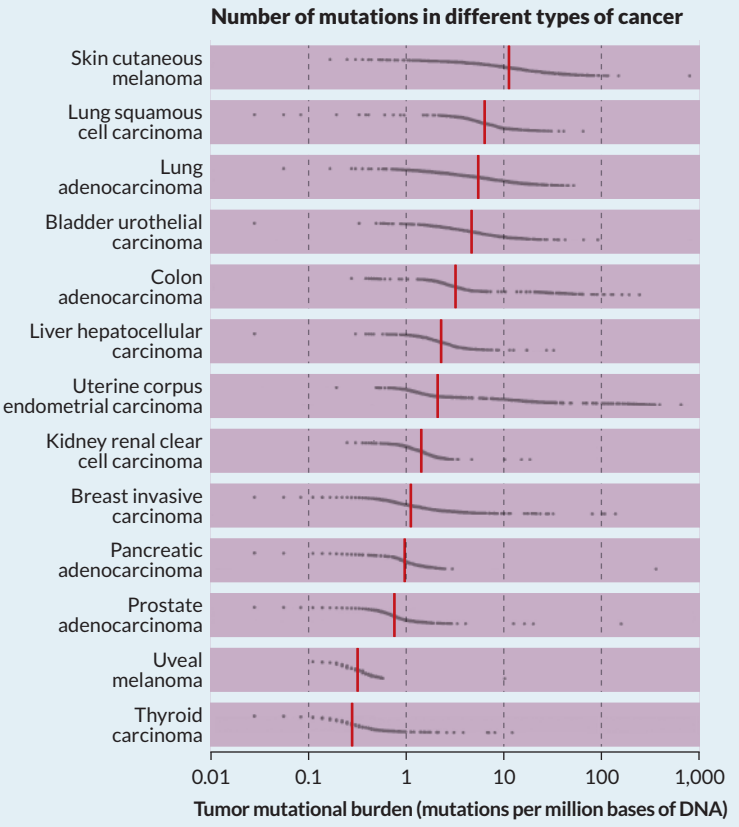
CAR T-cell therapy probably wouldn't have worked for English's melanoma, or any disease like hers. But that's where TIL can come in.

"TIL therapy is a relatively primitive treatment," says Marco Donia, an oncologist at the University of Copenhagen Herlev Hospital and Gentofte Hospital in Denmark. The therapy approved by the FDA doesn't rely on genetic engineering nor a predefined molecular target. It's just a messy mix of T cells grown from a patient's tumor.

In fact, as CAR T-cells and a related therapy called T-cell receptor therapy emerged, "people started to think that TIL would be obsolete," says Sylvia Lee, an oncologist at Fred Hutchinson Cancer Center in Seattle. "It was not as sophisticated or as elegant as these fancier ways to create designer T cells."

Scientists simply surgically remove part of a patient's tumor, grow vast quantities of T cells from the tumor over about a month, and then infuse the cells back into the patient's bloodstream. TILs have an innate tumor-detecting ability and can kill cancer cells, sometimes eliminating the disease. But how exactly everything works — and why it sometimes doesn't — is something scientists don't completely understand, Lee says.

Vulnerable mutations Some cancers carry more genetic mutations, called the tumor mutational burden, than other cancers, though this can vary from person to person. Skin cutaneous melanomas, for example, tend to have far more mutations than uveal melanomas, which affect the eye. Here, dots represent patient samples and red lines represent the median number of mutations. Having many mutations may make a cancer more susceptible to TIL therapy. SOURCE: Y. RAO *ET AL/FRONT. ONCOL.* 2022



One aspect of TIL biology seems clear: Tumor-infiltrating cells have a sort of sixth sense for the mutated proteins that can twist a healthy cell's fate toward cancer. Some of these mutated proteins, unleashed by simple tweaks to a cell's DNA, fail to keep cell growth in check; others get growth galloping like a horse touched by spurs.

"The very mutations that cause the cancer are likely to be the Achilles' heel for treatment," Rosenberg says. That's especially relevant for cancers loaded with mutations, like melanomas that form in the skin.

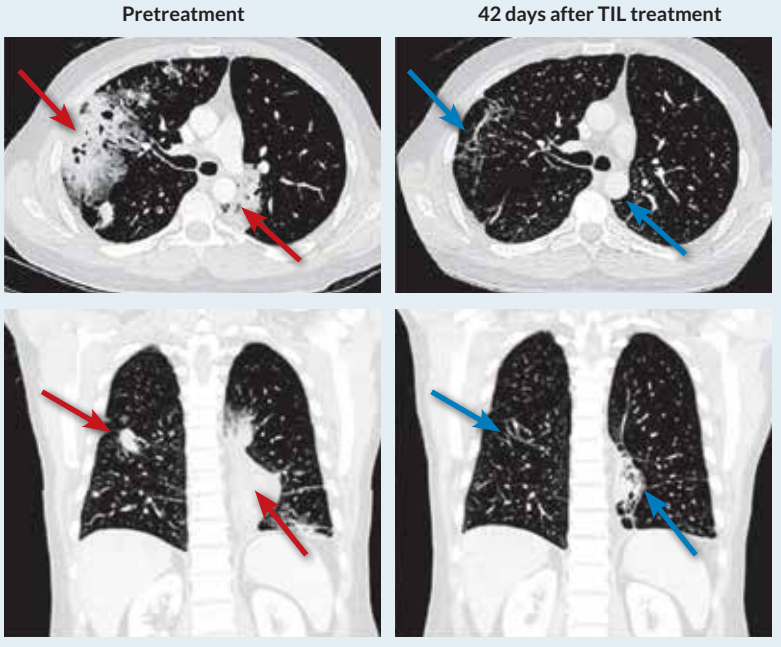
If you rank cancers by mutation level, these melanomas, called cutaneous melanoma, tend to top the list. Not far behind are lung cancer and bladder cancer, which make them promising targets for TIL, says Michael Poch, a urologic oncologist at Moffitt Cancer Center in Tampa, Fla. He's currently recruiting participants for a TIL clinical trial in people with bladder cancer.

It's still early days. His team will first test the

32
percent
Portion of patients who saw their tumor shrink or disappear with the drug Amtagvi

B. PRICE

Before and after
The drug lifileucel, sold as Amtagvi, has been approved for use against melanoma. But this form of TIL therapy shows promise against other solid tumors too. In a small clinical trial of 28 patients with non-small cell lung cancer, six participants, or 21 percent, saw their tumors shrink after taking the drug. These CT scans show the drug's effectiveness against one man's tumors (shown from two angles).



treatment's safety in about a dozen patients. But, like many other clinical trials under way, it's taking TIL in new directions — in this case, with a different type of cancer.

Kammula is steering into territory that's even less familiar. Rather than tackle another cancer chockfull of mutations, Kammula did an about-face. He's trying TIL therapy on uveal melanomas. Unlike skin melanomas, these cancers arise in the eye. But they neither carry many mutations nor teem with T cells.

By testing uveal melanoma samples in the lab, Kammula's team could identify which ones likely contain cancer-fighting T cells. That let the researchers predict how well people will respond to TIL, they reported in April in *Nature Communications*. It's an approach that could give doctors a better idea of who might benefit most from treatment and is being tested in a clinical trial expected to be completed in 2027.

Kammula thinks what his team learns from uveal melanoma could serve as a blueprint for treating other cancers. But he notes that improvements in TIL therapy could take many forms — including how best to create an environment in the body where the cancer-fighting cells can thrive.

Amtagvi and most other TIL therapies in the works require knocking down a patient's immune system before giving them the expanded batch of T cells. "If you're going to reboot and redevelop the immune system," he says, "you've got to get rid of the old one."

That takes chemotherapy; later, patients receive a drug to soup up their newly infused TIL. Honing this process could one day make TIL therapy easier for patients, Kammula says. Right now, it's no cakewalk. "There's a risk of infection, there's a risk of death," he says. "It's a tough treatment." And it's what English went through in her clinical trial in Orlando.

Not for everyone

English's cancer began as a sinus infection. At least, that's what she thought. It was spring 2015, and her nose felt irritated and dried out, perhaps bothered by pollen. Then came the nosebleeds.

It was no big deal at first, says English, an indefatigable optimist with a soft Southern accent. But the nosebleeds began coming more frequently, and they got more severe. She could actually see that something was growing out of her nostril. It was large, it was black and it was cancer.

The tumor stretched up into her nose, pressed against her right eyeball and filled her sinuses, like an invasive fungus flexing its fingers throughout her face. A surgeon operated and removed everything but a tiny spot near her tear duct. English has since learned that people with tumor masses as large as hers often have to have part of their face cut away. But her surgeon promised he wouldn't take her eye. Later, radiation zapped the remaining spot, and scans three months, six months and nine months afterward looked good. English seemed to be in the clear.

Then came her 12-month scans. Almost a year to the day after she had completed radiation, the cancer came back. This time, doctors found spots on her lungs, right kidney and brain. English couldn't believe it. "It was just everywhere," she says.

Doctors got her started on immunotherapy with drugs called checkpoint inhibitors, which rev up the immune system's cancer-fighting abilities (SN: 7/11/15, p. 14). "These medications are great," Lee says. "They've transformed the care of melanoma over the past 10 years."

But about half of melanoma patients relapse after treatment or don't respond at all, she says. The

drugs didn't work for English. A different kind of therapy, called gamma knife radiosurgery, had destroyed the tumors in her brain, but even after two kinds of immunotherapy, scans showed cancer still simmering in her kidney and lungs. She asked her oncologist, "What are we going to do now?"

For English and other trial participants, tumor-infiltrating lymphocytes were a last-ditch treatment. English received her TILs on April 2, 2018, a date that stands out in her mind, though the treatment was largely uneventful. She remembers a nurse hanging up the IV bag that delivered more than 7 billion cells into her veins. After the TILs had infused into her body, nurses wheeled English's bed to the hospital's intensive care unit for the next step. That's when things got difficult. Every eight to 12 hours for about two days, English received a high dose of IL-2, which ramps up TIL growth.

It's a crucial part of the process, but rife with side effects. The medication can cause high fevers, chills, dangerously low blood pressure, kidney problems and fluid to leak from the blood vessels, among other issues.

English doesn't recall much from that time in the hospital. The treatment left her feeling weak, and sleeping at night was difficult. In the shower, her hair fell out by the handful. But about four days later, English's strength had built up enough that she could walk laps in the hospital's halls. She was healthy enough to discharge. Six weeks later, at English's follow-up visit, she saw the scans showing that her lung tumor had vanished. And six months after TIL therapy, all traces of cancer were gone.

Those drastic results weren't the norm. Of the 73 participants whose data the FDA considered, just 23 people — about 32 percent — saw their tumors shrink or disappear completely. "We'd love that to be 99 or 100 percent," says Allison Betof Warner, an oncologist at Stanford University School of Medicine who wasn't involved with the trial. But, she says, the results are among the best researchers have seen for melanoma that has continued to advance even after treatment with immunotherapy drugs.

What stands out to Brian Gastman, the executive vice president of medical affairs at Iovance, is how long patients who do well on the treatment can stay healthy — in some cases, years.

In a longer-term analysis of a larger group of trial participants, 48 of 153 people responded to Amtagvi and nearly half of them were still alive at the study's four-year follow-up, researchers reported in 2023 at the ESMO Immuno-Oncology Congress. "We know that people are alive today because of this drug," Gastman says. Scientists still can't predict the end point of Amtagvi's tumor-fighting effects, he says. "We haven't even gotten there yet. We have no idea."

Looking ahead

After Amtagvi's approval in February, cancer centers around the country began preparing to offer patients the drug. As of May, Iovance reported that more than 100 patients had enrolled for Amtagvi therapy. The company has also taken steps to gain approval elsewhere, including in the European Union, the United Kingdom, Canada and Australia.

Scientists are also trying to make Amtagvi work in a larger proportion of advanced melanoma patients. An ongoing clinical trial, for example, is combining the therapy with checkpoint inhibitor drugs. Early results suggest this combo can increase the number of people who benefit from TIL. Of 22 metastatic melanoma patients who received the combo treatment, nearly 64 percent showed some response, researchers reported in May at the annual meeting of the American Society of Clinical Oncology. "It's a very exciting time to be in the field," Poch says.

As for Rosenberg, who has been at the forefront of cell therapy research for decades, finally seeing FDA approval for a TIL therapy felt gratifying, he says. Still, Amtagvi's high price tag — $515,000 per patient — is one barrier to widespread availability, Rosenberg wrote in a recent editorial in *Science*. And he still thinks about the people for whom TIL doesn't work. You go into one patient's room and they're responding to treatment, Rosenberg says, but in the next room over, there's a patient who's not. "It's a roller coaster," he says. His team and others are working to figure it out — and how to tailor TILs to other solid tumors. "That's 100 percent of what we're doing now," he says.

English's last scan was August 2, and she's still cancer-free more than six years after receiving her TILs. Her next scan is in February. "Hopefully I'm still going to be negative for a long, long time," she says.

In the time since her treatment, English has picked up a new passion: supporting others with mucosal melanoma. She helped build a website about the disease, coaches people who've been newly diagnosed and facilitates weekly Zoom calls for patients and caregivers where she shares her treatment experiences. "Being able to share that and motivate and help other people on their journey," she says, "is why I get up every day." ■

"Hopefully I'm still going to be negative for a long, long time."

TONI ENGLISH

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Explore more

- Steven A. Rosenberg. "Lymphocytes as a living drug for cancer." *Science*. July 5, 2024.

Turning to Stone
Marcia Bjornerud
FLATIRON BOOKS, $28.99

BOOKSHELF

What can stones tell us? More than most can imagine

Marcia Bjornerud sits in the basement of a soon-to-be-demolished building at Lawrence University in Appleton, Wis. The sole faculty member remaining in a depleted geology department, she sorts through castaway lab equipment, books and rocks. Anything she doesn't save is destined for the dumpster. One of her student helpers moves a display case, revealing a hidden door leading to a secret storage room crammed with crates of granite.

Bjornerud is exhausted and dizzy. She's grappling with her department's collapse, the sleep deprivation of early motherhood and a strained marriage to a terminally ill husband decades her senior. She empathizes with the forgotten granites. They have persisted for over a billion years, though geologists' interpretations of them have changed. Life is the same, she realizes. "The past is immutable, but its meaning changes with time."

This story and reflection is one of many in Bjornerud's latest book, *Turning to Stone*—part memoir, part geology explainer, part meditation on science and society. Bjornerud, now a tenured structural geologist at the same university (which eventually replenished its geology department), stitches together seemingly disparate topics to tell the tales of rocks that helped her "understand what it means to be an Earthling."

Bjornerud's life scaffolds each chapter; the rocks set the scene. The book is largely chronological, from Bjornerud's childhood to the present day. Each chapter features a titular rock type that holds some significance to her life. Sandstone, for instance, shaped her childhood in ways she didn't understand until she was a full-fledged geologist. In the part of Wisconsin in which Bjornerud grew up, the rock had once formed the foundation of the Big Woods of *Little House in the Big Woods* fame. The forests were logged and cleared for agriculture, leaving behind sandy soil that was never meant to host more than pines. Increasing amounts of fertilizer, needed to produce "a reasonable harvest," seeped through the porous sandstone into aquifers, contaminating the groundwater that provided most households in her community with drinking water, she writes.

Bjornerud's eloquent storytelling, complete with tantalizing geologic controversies, entices readers to turn the page—and learn complex science concepts along the way. Take the loads of granite Bjornerud unearthed in the secret room. How did these rocks form? In the early 20th century, some vocal geologists posited that sedimentary rocks morphed into granite through some cryptic chemical process. But experiments beginning in the 1920s conducted by geologist Norman Bowen revealed how Earth's mantle contained all the necessary ingredients to yield a variety of rocks. He found that, depending on how melted mantle cooled, rocks ranging from basalt to granite could form.

Throughout the narrative, Bjornerud sprinkles tidbits about the people in her orbit. She describes her marriages in varying levels of detail and drops snippets about her children and adopted Ojibwe sister. But readers interested in learning more about these people's lives may leave wanting more. They are not the central characters. Bjornerud and Earth are.

When Bjornerud came of age during the 1980s, geology was "redefining itself as a more rigorous, quantitative science." Numerical modeling and lab experiments were gaining favor over "old-school" geology, which relied mostly on field observations. Bjornerud was small, young and a woman—she didn't fit the mold of what a geologist looked like. She realized that she could not speak of "field experiences as transcendent spiritual epiphanies" if she wanted to be taken seriously.

But now, Bjornerud feels free to reverently describe her connection to the rocks she studied. "I feel lucky to have spent enough time in the company of rocks to understand their language," she writes. Diamictites from the Norwegian archipelago of Svalbard told her of ancient ice sheets. Pseudotachylyte from New Zealand's South Island hinted at past earthquakes.

The view that Earth is impassive has paved the path to environmental catastrophe and cultural anomie, Bjornerud writes. "We don't remember who we really are." In this book, readers will see the world through her eyes, and perhaps accept her invitation into a geocentric world view, "in which rocks are raconteurs, companions, mentors, oracles, and sources of existential reassurance." —*Alka Tripathy-Lang*

In her new book, structural geologist Marcia Bjornerud speaks of rocks, such as those in the Norwegian archipelago of Svalbard (shown), as companions, storytellers and mentors.

BDPHOTO/GETTY IMAGES

VIRTUAL TELEPORTATION IS ALREADY HERE

Science fiction has inspired plenty of today's tech. But one development many of us would really value remains elusive. It's the "Beam me up, Scotty" teleportation seen on *Star Trek*. At the flick of a switch, people appear to break down into their constituent atoms then stream to some distant destination where they flawlessly reassemble. Unfortunately, right now, science suggests there's no reason to believe we can do that. But virtual human teleporting? That's already here.

Doctors can "holoport" to the International Space Station to give distant patients a virtual exam. Students can now "beam" to archaeological sites to learn excavation techniques—without ever leaving their classroom. And holoportation technology could be used for much more.

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Talk of the tauonium

Scientists propose a hunt for tauonium, a hypothetical variety of atom that would consist of a tau lepton and its antimatter counterpart, an antitau, ***Emily Conover*** *reported in "Tauonium"* (SN: 6/29/24, p. 5).

Reader **Hal Heaton** asked why tauonium would be classified as an atom, considering it wouldn't have typical atomic features: electrons and a nucleus of protons and neutrons.

Tauonium would be part of a class called exotic atoms, **Conover** says. These are similar to the standard atoms on the periodic table but with at least one constituent replaced by another particle. For example, an electron can be replaced with a heavier relative, such as a muon. Or a neutron can be replaced with another particle, such as a hyperon, which contains a strange quark.

In the case of tauonium, a hydrogen atom's electron is replaced with a negatively charged tau lepton, and its proton is replaced with a positively charged antitau, **Conover** says.

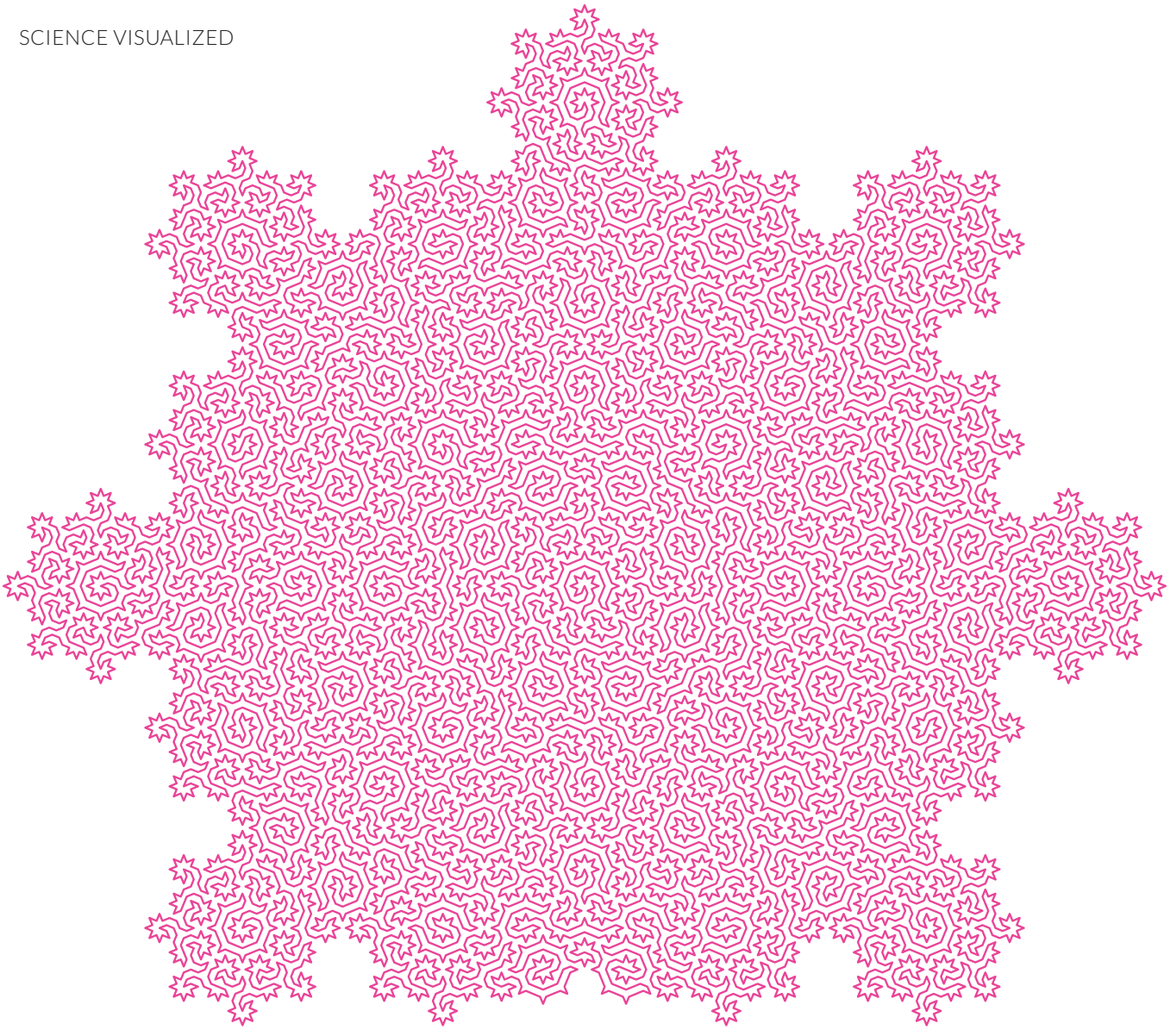
Reader **Guy DeWhitney** asked why the article states that scientists want to "search" for tauonium. "Create" or "invent" seem to be more appropriate descriptions, **DeWhitney** says.

It's true that tauonium would be created in the process that scientists propose. But "invented" is not quite accurate. Theoretical physicists previously came up with the concept of tauonium, as well as a description for how the atom would behave, **Conover** says.

Several readers wondered how stable tauonium would be.

Tauonium would likely decay very quickly, says physicist **Yu-Jie Zhang** of Beihang University in Beijing. Its estimated average lifetime is about 20 quadrillionths of a second.

The atom's tau and antitau particles would orbit one another briefly before eventually colliding and annihilating one another, releasing energy in the process, **Conover** says.



Connecting the dots on quasicrystal surfaces

This maze of jagged curls looks like something out of the world's hardest puzzle book. How fast do you think you can solve it?

Stuck? Don't worry. It's actually more of a connect-the-dots puzzle. The labyrinthine pink path is the shortest nonintersecting route to connect every point on a kaleidoscopic, "quasicrystalline" surface, researchers report July 10 in *Physical Review X*.

Shobhna Singh, a theoretical physicist at Cardiff University in Wales, and colleagues examined a type of pattern known as an Ammann-Beenker tiling, which fills a 2-D space using square- and rhombus-shaped tiles. Like some kaleidoscope images, these tilings are organized, and some parts of the pattern are symmetrical. But the pattern in an Ammann-Beenker tiling doesn't repeat itself regularly. The atoms in certain types of quasicrystals — ordered but nonrepeating chemical structures — adopt a similar geometry (*SN: 2/24/24, p. 8*).

The researchers found a path that touches every tile corner in an Amman-Beenker tiling, without crossing itself, before ending back where it started. Called Hamiltonian cycles, such pathways form a closed loop that you can trace without picking up your finger. Try it!

Solving a Hamiltonian cycle for even one type of tiling is no small feat. But this particular cycle — and possibly others — could help address scientific challenges. For example, it could make certain quasicrystals more efficient catalysts, substances that reduce the energy required for a chemical reaction. In theory, if molecules involved in the reaction arranged themselves along the Hamiltonian path of such a quasicrystal, they could attach to the surface of the quasicrystal with maximum efficiency.

Moving forward, the team will search for Hamiltonian cycles on other tilings and look for ways to apply such cycles to existing challenges, Singh says. "The most interesting application could be one which we have not thought about." — *Skyler Ware*

S. SINGH, J. LLOYD AND F. FLICKER/*PHYSICAL REVIEW X* 2024

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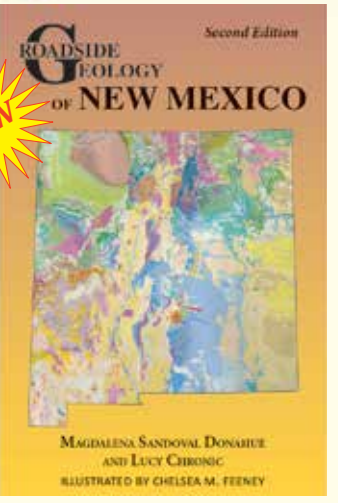

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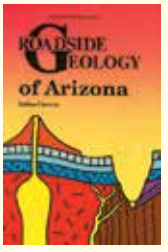

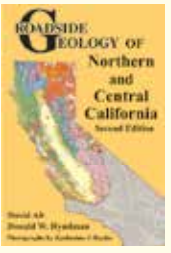

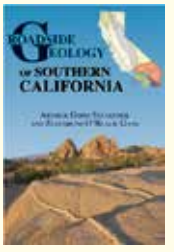

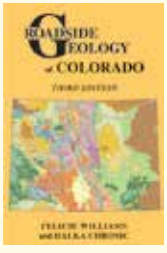

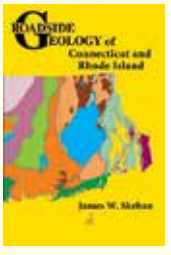

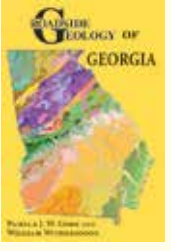

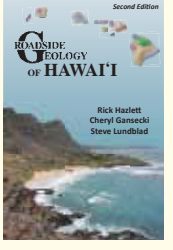

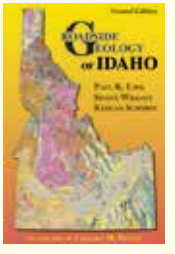

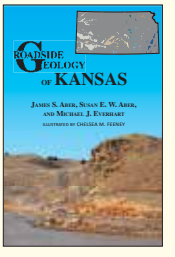

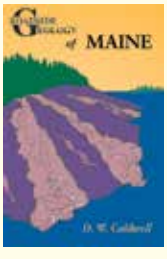

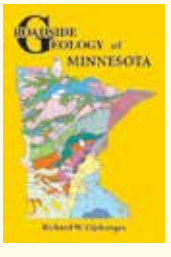

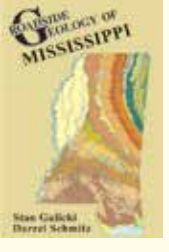

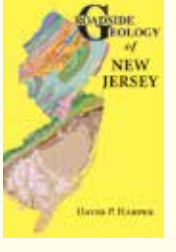

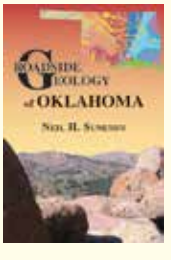

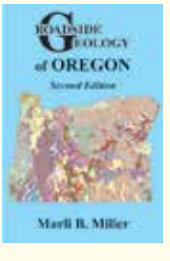

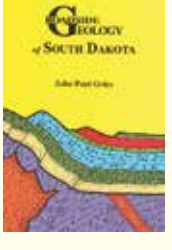

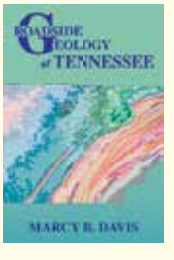

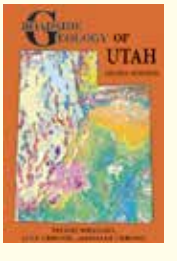

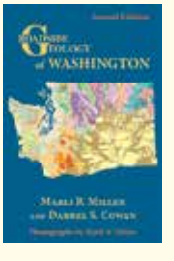

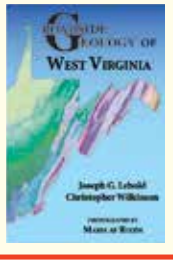

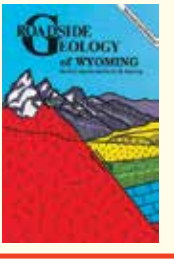

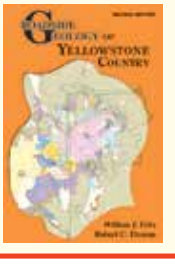

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