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Japan launches preprint server — but will scientists use it?

Jxiv is the latest country-specific online repository to open, but it's off to a slow start.

Dalmeet Singh Chawla

Japan has become the latest country to open an online preprint repository, in a bid to boost international exposure to the country's research. But so far, researchers haven't rushed to post on Jxiv — fewer than 40 papers have been uploaded since it launched in March — and some researchers say the platform isn't necessary.

Jxiv's supporters, however, think the platform will increase in popularity, with some suggesting researchers will warm to it because it's backed by the government. "If the government is hosting this, then it's going to stay for sure," says Guojun Sheng, an embryologist at Kumamoto University in Japan.

Japan's output of published research papers is among the highest in the world. But researchers in Japan don't often share early versions of their manuscripts on preprint servers, says Soichi Kubota, who works at the department of information infrastructure at the government-run Japan Science and Technology Agency (JST) in Tokyo.

Kubota says the JST wants to change that. It set up Jxiv to fill a gap in existing platforms, which don't accommodate all research fields — including popular ones in Japan, such as history, business and management, linguistics and interdisciplinary sciences. Vast numbers of papers that are published in Japanese are in those fields. Researchers can post manuscripts on Jxiv in English and Japanese.

India, Russia, China, Indonesia and Africa have their own dedicated repositories. Similar services that host research conducted in France and the Arab world were discontinued in 2020. Some of the most popular repositories are subject-specific, such as the original preprint server, arXiv, for physical-science and mathematics manuscripts.

Ongoing benefits

A long-running criticism of preprint servers is that, because papers are posted without standard editing or peer review, there is no process to weed out low-quality research.

Kubota acknowledges that some low-quality preprints are posted to preprint servers, but he argues that the benefits of a Japanese preprint server outweigh any downsides. The platform can help to disseminate Japanese science to a wider international audience because manuscripts are free to read. And he hopes that the Jxiv will boost collaborations between Japanese scientists and international peers.

Kubota notes that researchers often post early manuscripts on preprint servers to garner comments from peers, which acts as an informal peer review, before submitting the manuscript to a journal. This process can also reduce the workload on journal peer reviewers, he says.

But Thomas Russell, a polymer scientist with joint appointments at the University of Massachusetts, Amherst, and Tohoku University in Sendai, worries that encouraging researchers in Japan to use preprint servers will mean their manuscripts won't attract adequate scrutiny online.

"I think the Japanese are more reserved than Western cultures" when it comes to being critical in a public forum, he says.

Russell thinks that preprint servers aren't necessary to disseminate research quickly. "If it's good science, it will go through the review process and get out expeditiously," he says.

But Sheng thinks Jxiv will catch on, especially if funding agencies start requiring researchers whose work they fund to use it in the future.

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https://bit.ly/3aJf5UH

Every Single Patient in This Small Experimental Drug Trial Saw Their Cancer Disappear

A small drug trial conducted in the US found every patient treated in the experiment had their cancer successfully go into remission

Peter Dockrill

In what appears to be a very promising breakthrough for the treatment of rectal cancer, a small drug trial conducted in the US found every patient treated in the experiment had their cancer successfully go into remission.

The medication given, called dostarlimab and sold under the brand name Jemperli, is an immunotherapy drug used in the treatment of endometrial cancer, but this was the first clinical investigation of whether it was also effective against rectal cancer tumors.

The early results reported so far suggest it is surprisingly effective, with the research team saying the successful cancer remission seen in every trial patient may be unprecedented for a cancer drug intervention. "I believe this is the first time this has happened in the history of cancer," medical oncologist Luis Diaz Jr. from Memorial Sloan Kettering Cancer Center (MSK), the senior author of a new paper reporting the results, told *The New York Times*.

It's worth noting that the positive results have only been seen in 12 patients so far (the trial is ongoing), all of whom had tumors with genetic mutations called mismatch repair deficiency (MMRd), seen in a subset of approximately 5–10 percent of rectal cancer patients.

Patients with such tumors tend to be less responsive to chemotherapy and radiation treatments, which increases the need for surgical removal of their tumors.

However, MMRd mutations can also make cancer cells more vulnerable to immune response, especially it's bolstered by an immunotherapy agent – in this case, a checkpoint inhibitor, which unleashes restrictions on immune cells so they can more effectively kill cancer cells.

"When those mutations accumulate in the tumor, they stimulate the immune system, which attacks the mutation-ridden cancer cells," Diaz says. "We thought, 'Let's try it before cancer metastasizes as a first line of treatment'."

Ordinarily, patients with these kinds of rectal tumors might expect to undergo chemotherapy and radiation therapy prior to surgical removal of the cancer. Unfortunately, for many patients this gamut of treatments comes with long-lasting consequences that can last the rest of their life.

"The standard treatment for rectal cancer with surgery, radiation, and chemotherapy can be particularly hard on people because of the location of the tumor," says MSK medical oncologist Andrea Cercek, the first author of the study.

"They can suffer life-altering bowel and bladder dysfunction, incontinence, infertility, sexual dysfunction, and more."

In an amazing turn of luck, the patients who enrolled in this trial have so far completely avoided both these procedures and their associated side effects.

In the phase 2 study, patients were given dostarlimab every three weeks for six months, with standard chemoradiotherapy and surgery set to follow if tumors returned. They didn't. After six months of follow-up, all 12 patients in the trial showed a "clinical complete response", with no evidence of tumors to be seen via MRI scans, PET scans, endoscopy, and biopsy, among other tests.

"Dr. Cercek told me a team of doctors examined my tests," explains Sascha Roth, the first patient enrolled in the trial. "And since they couldn't find any signs of cancer, Dr. Cercek said there was no reason to make me endure radiation therapy."

It's worth noting that the research – funded by numerous organizations, including the pharmaceutical company GlaxoSmithKline, which manufactures Jemperli – isn't over yet,

and these are only preliminary results being reported so far.

At present, a total of 12 patients have completed the treatment and undergone at least six months of follow-up.

About three-quarters of patients so far have experienced mild or moderate side effects, including rash, itching, fatigue, and nausea – but none have so far seen a regrowth in cancer, with the median follow-up being at one year, and some patients, like Roth, being cancer-free for two years.

Ultimately, the trial is expected to include about 30 patients. When we have data on the whole group, we'll have a fuller picture of how safe and effective dostarlimab is in patients with rectal cancer, although much more study is yet needed in broader groups of patients.

Until such time, we need to treat the current results with both optimism and caution, says oncologist Hanna K. Sanoff from the University of North Carolina at Chapel Hill, who has written a commentary on the findings.

According to Sanoff, a clinical complete response to the treatment is not a surrogate for long-term cancer control, as even though checkpoint inhibitors like dostarlimab can have effects lasting years, cancer regrowth is generally expected to still occur in a minority of patients where tumors are managed non-operatively, let alone with an experimental treatment like this.

"Very little is known about the duration of time needed to find out whether a clinical complete response to dostarlimab equates to cure," Sanoff explains, noting that we also need larger-scale replication of the results to be sure of the drug's benefits, which so far have only been seen in a minority of patients with MMRd tumors.

"Whether the results of this small study conducted at Memorial Sloan Kettering Cancer Center will be generalizable to a broader population of patients with rectal cancer is also not known."

Bearing these caveats in mind, there's a lot to be hopeful for here; the researchers are already investigating whether their singular immunotherapy approach could also help patients with other tumors that have MMRd, such as some types of stomach, prostate, and pancreatic cancer. It's early days, and there's still a lot we don't know, but if further research can replicate the bright promise hinted at here, we might be witnessing the development of a new kind of cancer therapy, Sanoff says.

"Despite these uncertainties, Cercek and colleagues and their patients who agreed to forgo standard treatment for a promising but unknown future with immunotherapy have provided what may be an early glimpse of a revolutionary treatment shift," Sanoff writes.

"If immunotherapy can be a curative treatment for rectal cancer, eligible patients may no longer have to accept functional compromise in order to be cured."

The findings are reported in *The New England Journal of Medicine*.

https://bit.ly/3zuCvHG

A New Coronavirus Has Been Found Spreading Among Rodents in Sweden

Researchers have now identified a widespread and common coronavirus they've called the Grimsö virus

Carly Cassella

Bats and pangolins aren't the only wild animals harboring novel coronaviruses. Rodents like rats, mice, and voles can also carry viruses that are sometimes capable of jumping over to our own species.

(Mike Powles/Getty Images)

Among Sweden's red-backed bank voles (*Myodes glareolus*), researchers have now identified a widespread and common coronavirus they've called the Grimsö virus, after the location of its discovery.

We don't know whether the newly found virus is in any way dangerous to humans; nevertheless, the findings are a good reminder of why we need to monitor wildlife viruses, especially those carried by animals that live in close proximity to us.

"We still do not know what potential threats the Grimsö virus may pose to public health. However, based on our observations and previous coronaviruses identified among bank voles, there is good reason to continue monitoring the coronavirus amongst wild rodents," says virologist Åke Lundkvist from Uppsala University in Sweden.

Bank voles are some of the most common rodents found in Europe. Their paths often cross with our own species, and they are known hosts of the Puumala virus, which causes a hemorrhagic fever known as nephropathia epidemica in humans.

When seeking refuge from adverse weather conditions, voles are known to shelter in human buildings, and this increases the risk of us contracting a disease they carry into our households.

Even before the COVID-19 pandemic kicked off, Lundkvist and his colleagues have been trying to monitor wildlife disease among voles, to better anticipate when their viruses could spill over. Given the unrelenting pace of climate change and habitat destruction, there's every chance our interactions with voles will only increase in the future.

Between 2015 and 2017, researchers at Uppsala examined 450 wild bank voles from a site west of Stockholm called Grimsö. Testing the creatures for coronaviruses, the team found a new betacoronavirus circulating in 3.4 percent of the sample.

Betacoronaviruses are usually found amongst bats and rodents, and when they jump over to humans, they are responsible for causing the common cold and respiratory viruses like SARS-CoV-2.

The new vole virus hasn't been caught jumping over to humans just yet, but if COVID-19 has taught us anything, it's that we need increased surveillance of wildlife disease to prevent further outbreaks.

Over the course of three years, researchers in Sweden found several distinct viral strains of the Grimsö virus circulating among bank vole populations.

What's more, other closely related coronaviruses were broadly distributed amongst voles in other parts of Europe, like France, Germany, and Poland, which suggests these creatures are natural reservoirs for the disease.

The highly divergent nature of the Grimsö virus is a bad sign. It indicates the virus is easily adapted to new hosts and habitats.

The various strains found in circulation could have originally come from bank voles, or they could have jumped over from another species.

"Given that bank voles are one of the most common rodent species in Sweden and Europe, our findings indicate that Grimsö virus might be circulating widely in bank voles and further point out the importance of sentinel surveillance of coronaviruses in wild small mammalian animals, especially in wild rodents," the authors write.

Other studies have recently warned that human exploitation of wild spaces has directly increased the risk of animal disease spilling over to humans. This risk was especially notable among animals such as bats, rodents and primates, which have abundant populations and have readily adapted to human environments.

While rodents and bats have long been considered vectors of human disease, they aren't the only animals infectious disease specialists need to keep their eyes on.

Larger mammals, like wild deer, are also in close contact with human civilization, and in the northeast of the United States, roughly 40 percent of deer have been exposed to SARS-CoV-2.

Livestock, like mink, have also been rolled into the COVID-19

pandemic, and researchers are worried the virus could mutate amongst these animal hosts and reinfect us with another version of the disease down the road.

The fear ultimately led millions of farmed mink to be culled as a preventative measure. But decimating entire populations of animals is not an acceptable solution, especially in the wild. Creating more ecological upheaval will only serve to further unbalance ecosystems, stressing more animals and creating more opportunities for viruses. Improved surveillance will therefore be key.

If bad weather and habitat destruction grow worse in the future, we could be coaxing new coronaviruses right into our households.

The study was published in *Viruses*.

https://bit.ly/3Qqn5qn

How the wild jungle fowl became the chicken

New studies propose surprisingly late date, and link to rice growing, for chicken domestication

By Ann Gibbons

***Wild red junglefowl of Thailand were lured by rice grains into a life of domestication.*Rapeepong Puttakumwong/Getty Images**

From chicken biryani to khao mun gai, chicken and rice is a winning combo worldwide. But the two are more inextricably linked than even chefs realized. A pair of new archaeological studies suggest that without rice, chickens may have never existed.

The work reveals that chickens may have been domesticated thousands of years later than scientists thought, and only after humans began cultivating rice within range of the wild red jungle fowl, in Thailand or nearby in peninsular Southeast Asia, says Dale Serjeantson, an archaeologist at the University of Southampton who was not involved with the research. The studies, she says, have "dismantled many of the hoary myths about chicken origins."

Charles Darwin proposed that chickens descended from the red jungle fowl—a colorful tropical bird in the pheasant family–because the two look so much alike. But proving him right has been difficult. Five varieties of jungle fowl range from India to northern China, and small chicken bones are rare in fossil sites.

In 2020, a study of 863 living chickens' genomes confirmed that the jungle fowl *Gallus gallus spaedicus* subspecies was the ancestor of living chickens; chickens share more of their DNA with that subspecies than other types of jungle fowl. That in turn narrowed the site of domestication to Southeast Asia. Researchers have proposed fossils as early chickens dating back 8000 to 11,000 years ago in northern China and Pakistan. But genetics of living birds could not narrow the window for domestication, says geneticist Ming-Shan Wang, a postdoc at the University of California, Santa Cruz, first author of the genetic study. And they have not been able to get enough ancient DNA from fossil chickens to pinpoint the date. So paleo-anatomist Joris Peters of Ludwig Maximilian University of Munich teamed up with Greger Larson, a bioarchaeologist at the University of Oxford who is an expert on animal domestication. The duo organized an international team that began a comprehensive reevaluation of chicken bones, their dates, and records on them, from more than 600 archaeological sites around the world. In a separate study, the group directly dated chicken bones found in western Eurasia and Northern Africa.

They found the oldest bones of likely chickens came from a site called Ban Non Wat in central Thailand, where farmers grew rice 3250 to 3650 years ago, the team reports today in the *Proceedings of the National Academy of Sciences*. Farmers buried many skeletons of young members of the genus *Gallus* as grave goods along with other domesticated animals—strong evidence that these

birds were domesticated chickens, rather than wild jungle fowl. The researchers propose that the rice seeds drew wild jungle fowl to rice fields, where the birds nested in thickets at the edge of the fields and got used to humans.

As the scientists traced the trail of chicken bones across Asia into the Middle East and Africa, they found a "striking" correlation between the spread of dry rice farming, millet, and other grains—and the appearance of chickens. Chickens appeared about 3000 years ago in northern China and India, the team found, and about 2800 years ago in the Middle East and Northeast Africa. The studies finding earlier chickens were flawed, the team argues, because either the fossils were not chickens or the dates were inaccurate.

To find out when chickens first entered Europe, members of the team directly re-dated bones from 23 of the proposed earliest chickens in Europe and Asia. The first chickens in Europe were found in an Etruscan site in Italy 2800 years ago, the team reports in *Antiquity* today.

The study is backed up by historical records, too—including the Bible. "Chickens don't feature in the Old Testament," says the study's lead author Naomi Sykes, an archaeologist at the University of Exeter. "They burst onto the scene in the New Testament."

It took another 1000 years before chickens spread north to Britain (with the Romans), Scandinavia, and Iceland. The subtropical birds likely had to adapt to the colder climates, says archaeologist Julia Best of Cardiff University, who was involved in both studies.

Still, it's only recently that humans began to think of the birds primarily as food. Initially, people traded them as exotic possessions, valued for their feathers, coloring, and loud crow at first light, based on how they were depicted in art and buried as prized grave goods, Sykes says. Early chickens were smaller, she notes, and not a major source of meat. But the team's review shows that about 500 years after chickens are introduced to each new place, they lose their special status and become an ordinary food.

When researchers re-dated these chicken bones from England and Bulgaria, they found that the supposedly ancient one from Bulgaria dated instead to the 20th century. **Jonathan Rees/Cardiff University**

The studies show that "the dispersal of domestic chickens is a more recent event than has been expected in the past," says Masaki Eda, a zooarcheologist at Hokkaido University.

Still, Eda says he'd like to see follow-up research to make sure the bones in Thailand are definitely domesticated chickens, not wild junglefowl buried with humans. He also wants researchers to survey other sites in Southwest Asia to connect the dots showing where and how chickens were domesticated as rice and millet cultivation spread throughout Eurasia.

Even though chickens were domesticated later than other animals, they have become the most successful domesticated species on the planet, Larson says. Today, at 80 billion strong, they outnumber us 10 to 1. "This isn't just about chickens or rice," Sykes says. "How humans relate to chickens is a brilliant lens to understand how humans relate to the natural world."

https://bit.ly/39qd67k

Liquid platinum at room temperature: The 'cool' catalyst for a sustainable revolution in industrial chemistry

Using trace amounts of liquid platinum to create cheap and highly efficient chemical reactions at low temperatures

Researchers in Australia have been able to use trace amounts of liquid platinum to create cheap and highly efficient chemical reactions at low temperatures, opening a pathway to dramatic emissions reductions in crucial industries.

When combined with liquid gallium, the amounts of platinum required are small enough to significantly extend the earth's reserves of this valuable metal, while potentially offering more sustainable solutions for CO_2 reduction, ammonia synthesis in fertilizer production, and green fuel cell creation, together with many other possible applications in chemical industries.

These findings, which focus on platinum, are just a drop in the liquid metal ocean when it comes to the potential of these catalysis systems. By expanding on this method, there could be more than 1,000 possible combinations of elements for over 1,000 different reactions. The results will be published in the journal *Nature Chemistry* on Monday 6 June.

Platinum is very effective as a catalyst (the trigger for chemical reactions) but is not widely used at industrial scale because it's expensive. Most catalysis systems involving platinum also have high ongoing energy costs to operate.

Normally, the melting point for platinum is 1,700°C. And when it's used in a solid state for industrial purposes, there needs to be around 10% platinum in a carbon-based catalytic system. It's not an affordable ratio when trying to manufacture components and products for commercial sale.

That could be set to change in the future, though, after scientists at UNSW Sydney and RMIT University found a way to use tiny amounts of platinum to create powerful reactions, and without expensive energy costs.

The team, including members of the ARC Center of Excellence in Exciton Science and the ARC Center of Excellence in Future Low Energy Technologies, combined the platinum with liquid gallium, which has a melting point of just 29.8°C—that's room temperature on a hot day. When combined with gallium, the platinum becomes soluble. In other words, it melts, and without firing up a hugely powerful industrial furnace.

For this mechanism, processing at an elevated temperature is only required at the initial stage, when platinum is dissolved in gallium to create the catalysis system. And even then, it's only around 300°C for an hour or two, nowhere near the continuous high temperatures often required in industrial-scale chemical engineering. Contributing author Dr. Jianbo Tang of UNSW likened it to a blacksmith using a hot forge to make equipment that will last for years.

"If you're working with iron and steel, you have to heat it up to make a tool, but you have the tool and you never have to heat it up again," he said.

Liquid gallium and platinum beads in close up. **Credit: Dr Md. Arifur Rahim, UNSW Sydney.**

"Other people have tried this approach but they have to run their catalysis systems at very high temperatures all the time."

To create an effective catalyst, the researchers needed to use a ratio of less than 0.0001 platinum to gallium. And most remarkably of all, the resulting system proved to be over 1,000 times more efficient than its solid-state rival (the one that needed to be around 10% expensive platinum to work)

The advantages don't stop there—because it's a liquid-based system, it's also more reliable. Solid-state catalytic systems eventually clog up and stop working. That's not a problem here. Like a water feature with a built-in fountain, the liquid mechanism constantly refreshes itself, self-regulating its effectiveness over a long period of time and avoiding the catalytic equivalent of pond scum building up on the surface.

Dr. Md. Arifur Rahim, the lead author from UNSW Sydney, said: "From 2011, scientists were able to miniaturize catalyst systems down to the atomic level of the active metals. To keep the single atoms separated from each other, the conventional systems require

solid matrices (such as graphene or metal oxide) to stabilize them. I thought, why not using a liquid matrix instead and see what happens. "The catalytic atoms anchored onto a solid matrix are immobile. We have added mobility to the catalytic atoms at low temperature by using a liquid gallium matrix."

The mechanism is also versatile enough to perform both oxidation and reduction reactions, in which oxygen is provided to or taken away from a substance respectively.

The UNSW experimentalists had to solve some mysteries to understand these impressive results. Using advanced computational chemistry and modeling, their colleagues at RMIT, led by Professor Salvy Russo, were able to identify that the platinum never becomes solid, right down to the level of individual atoms.

Exciton Science Research Fellow Dr. Nastaran Meftahi revealed the significance of her RMIT team's modeling work. "What we found is the two platinum atoms never came into contact with each other," she said. "They were always separated by gallium atoms. There is no solid platinum forming in this system. It's always atomically dispersed within the gallium. That's really cool and it's what we found with the modeling, which is very difficult to observe directly through experiments."

Surprisingly, it's actually the gallium that does the work of driving the desired chemical reaction, acting under the influence of platinum atoms in close proximity.

Exciton Science Associate Investigator Dr. Andrew Christofferson of RMIT explained how novel these results are: "The platinum is actually a little bit below the surface and it's activating the gallium atoms around it. So the magic is happening on the gallium under the influence of platinum. "But without the platinum there, it doesn't happen. This is completely different from any other catalysis anyone has shown, that I'm aware of. And this is something that can only have been shown through the modeling."

More information: *Arifur Rahim, Low-temperature liquid platinum catalyst, Nature Chemistry (2022). DOI: 10.1038/s41557-022-00965-6. www.nature.com/articles/s41557-022-00965-6*

https://go.nature.com/39hKY6D

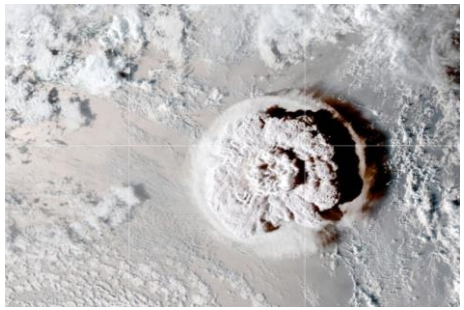
Burst of underwater explosions powered Tonga volcano eruption

Research expeditions find that the caldera's collapse exposed huge amounts of hot magma to water.

Jonathan O'Callaghan

Researchers are starting to piece together why the eruption of an underwater volcano in Tonga was so explosive — and what happened in the aftermath. Evidence gathered by two groups suggests that when the volcano's centre collapsed, it spewed an enormous amount of magma that reacted violently with water, powering several large blasts and hundreds of much smaller explosions.

The Hunga Tonga–Hunga Ha'apai volcano erupted on 15 January 2022, producing the largest atmospheric explosion in recorded history. It sent shock waves around the world and a plume of ash into the upper atmosphere.



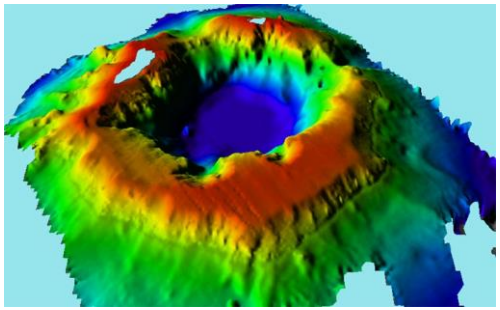
The Hunga Tonga–Hunga Ha'apai volcano eruption on 15 January produced the largest atmospheric explosion in recorded history. **Credit: NASA/GOES/NOAA/NESDIS**

In May, Shane Cronin, a volcanologist at the University of Auckland, New Zealand, led a group that sailed over the volcano's caldera, the central depression that forms when a volcano erupts, and used sonar to map its structure. They found the four-kilometre-wide caldera had dropped in depth from less than 200 metres below sea level to more than 850 metres.

"The volcano produced this enormous new caldera," says Cronin.

He estimates that some 6.5 cubic kilometres of rock were thrown out, roughly equivalent to a sphere as wide as the Golden Gate Bridge in San Francisco, California. “It was an amazing finding,” says Taaniela Kula, Tonga’s Deputy Secretary for Lands and Natural Resources in Nuku’alofa and a collaborator on the research. “It creates a better picture of the mechanism of the volcano.” The work was presented at a meeting of the European Geosciences Union (EGU) in Vienna on 26 May.

The reason for this large explosion was probably the interaction between large amounts of magma and water as the eruption began, says Cronin. “You’ve got 20-degree water and you’ve got 1,110-degree magma coming directly in contact,” he says.



Following the eruption, researchers mapped the caldera, the central depression that forms when a volcano erupts. **Credit: Shane Cronin/University of Auckland and Taaniela Kula Tonga Geological Services**

Such a large temperature difference meant that, as the water was forced into contact with the magma by the eruption, it exploded. Each interaction pushed the water deeper into the edges of the magma, says Cronin, increasing the surface area of contact and driving further explosions in a chain reaction.

The initial depth of the caldera was also just shallow enough that the water pressure did not suppress the blast, but deep enough that the magma was fed huge amounts of water to power the interactions, resulting in several large blasts and hundreds of much smaller explosions every minute. Eyewitness accounts from the day of the eruption reported “crackling and noise like artillery fire” as far as 90 kilometres from the eruption, says Cronin. “Those aren’t sounds I’ve heard from erupting volcanoes before,” he says.

Ash grains recovered from Tonga after the eruption also suggest that there was a violent interaction between magma and water. As the seawater came into contact with the magma, it produced shock waves powerful enough to fracture the grains, said Joali Paredes-Mariño, a geological engineer at the University of Auckland, in work presented at the EGU.

Wipe out

A separate expedition by a team at New Zealand’s National Institute for Water and Atmospheric Research (NIWA) in Auckland travelled to the volcano in April, but they did not go over the caldera. They sampled ash from the sea floor around the volcano, which showed that the eruption was probably followed by dramatic pyroclastic flows, hot streams of ash and lava that rained down over the submerged sides of the caldera. The onrushing hot ash turned the surrounding sea floor into a white desert that “wiped out everything”, says voyage leader Kevin Mackay, a marine geologist at NIWA.

These flows spread underwater for thousands of square kilometres from the eruption, ripping up sea-floor cables — including those providing Tonga’s access to the Internet, which has still not been fully restored — and powering tsunamis that washed over nearby islands, reaching up to 18 metres in height. On the sea floor, nothing seems to have survived, although samples are still being analysed to work out the extent of the damage. “We don’t even think bacteria is living there,” says Mackay. “That’s how toxic we think the sediment is.”

Samples collected by the NIWA team are being used to study potential impacts on ocean oxygen levels and ocean acidification, says Sarah Seabrook, a biogeochemist at NIWA.

Not everything was decimated, however. Satellite data showed a big bloom of phytoplankton in the ocean following the eruption, which fed on nutrients released by the blast, says Seabrook. And on

nearby hills that jutted above the sea floor just 15 kilometres from the eruption, life was flourishing, says Mackay. “We expected life to be universally destroyed.”

Water-vapour plume

Other research presented at the EGU by Philippe Heinrich at the French Alternative Energies and Atomic Energy Commission near Paris showed that the pressure wave from the eruption produced a tsunami as far as the French Mediterranean coast, 17,000 kilometres away, with several centimetres in sea-level rise recorded. Luis Millán at NASA’s Jet Propulsion Laboratory in Pasadena, California, also found that the eruption sent up a water-vapour plume that reached a height of 53 kilometres, well into the stratosphere.

This plume, which has now encircled the globe, increased the water-vapour content of the stratosphere by 146 teragrams (146 trillion grams), or 10%, and will probably remain in the atmosphere for at least a year. “We haven’t seen anything like this before in the entire satellite era,” says Millán.

Some research suggests there were hints of what was to come. Thomas Walter at the German Research Center for Geosciences in Potsdam says seismology readings point to a possible partial collapse of the caldera wall in the hours before the event. “It’s a very weak hint,” he says. “But it may indicate we have first a collapse and then the explosion.”

Cronin agrees that there might have been some forewarning. Satellite imagery showed part of the protruding northern rim of the volcano falling into the sea the day before the eruption. “It could have indicated early stages of the caldera collapse,” he says. That could be a crucial tool in predicting future submarine eruptions. “If we missed the big clue that this big one was coming, then that’s obviously a lesson we’ll take forward,” says Cronin.

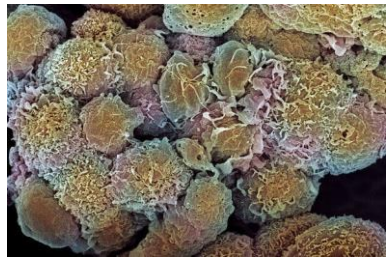
https://nyti.ms/3zwGcfV

Breast Cancer Drug Trial Results in ‘Unheard-Of’ Survival

For some patients with metastatic tumors not significantly affected by other forms of chemotherapy, the treatment halted their cancer’s growth.

By Gina Kolata

The patients had metastatic breast cancer that had been progressing despite rounds of harsh chemotherapy. But a treatment with a drug that targeted cancer cells with laserlike precision was stunningly successful, slowing tumor growth and extending life to an extent rarely seen with advanced cancers.



The new study, presented at the annual meeting of the American Society of Clinical Oncology and published on Sunday in the New England Journal of Medicine, would change how medicine was practiced, cancer specialists said.

A colored scanning electron micrograph of breast cancer cells. Patients treated with the new drug trastuzumab deruxtecan survived for 23.9 months.

Credit...Steve Gschmeissner/Science Source

“This is a new standard of care,” said Dr. Eric Winer, a breast cancer specialist, director of the Yale Cancer Center and head of the A.S.C.O. Dr. Winer was not involved with the study. He added that “it affects a huge number of patients.”

The trial focused on a particular mutant protein, HER2, which is a common villain in breast and other cancers. Drugs that block HER2 have been stunningly effective in treating breast cancers that are almost entirely populated with the protein, turning HER2-positive breast cancers from those with some of the worst prognoses into ones where patients fare very well.

But HER2-positive cases constitute only about 15 percent to 20

percent of breast cancer patients, said Dr. Halle Moore, director of breast medical oncology at the Cleveland Clinic. Patients with only a few HER2 cells — a condition known as HER2-low — were not helped by those drugs. Only a small proportion of their cancer cells had HER2, while other mutations primarily drove the cancer's growth. And that posed a problem because the cancer cells evaded chemotherapy treatments.

The clinical trial, sponsored by the pharmaceutical companies Daiichi Sankyo and AstraZeneca and led by Dr. Shanu Modi of Memorial Sloan Kettering Cancer Center, involved 557 patients with metastatic breast cancer who were HER2-low. Two-thirds took the experimental drug, trastuzumab deruxtecan, sold as Enhertu; the rest underwent standard chemotherapy.

In patients who took trastuzumab deruxtecan, tumors stopped growing for about 10 months, as compared with 5 months for those with standard chemotherapy. The patients with the experimental drug survived for 23.9 months, as compared with 16.8 months for those who received standard chemotherapy.

"It is unheard-of for chemotherapy trials in metastatic breast cancer to improve survival in patients by six months," said Dr. Moore, who enrolled some patients in the study. Usually, she says, success in a clinical trial is an extra few weeks of life or no survival benefit at all but an improved quality of life.

The results were so impressive that the researchers received a standing ovation when they presented their data at the oncology conference in Chicago on Sunday.

Trastuzumab deruxtecan was already approved for patients with HER2-positive breast cancer, but few expected it to work because other drugs for such cancers had failed in HER2-low patients.

The drug consists of an antibody that seeks out the HER2 protein on the surface of cells. The antibody is attached to a chemotherapy drug. When trastuzumab deruxtecan finds a cell with HER2 on its surface, it enters the cell, and the chemotherapy drug separates from the antibody and kills the cell. But "what is unique and distinct" about trastuzumab deruxtecan, Dr. Modi adds, is that the chemotherapy drug seeps through the cell's membrane. From there, it can move into nearby cancer cells and kill them as well.

Like all chemotherapy, trastuzumab deruxtecan has side effects, including nausea, vomiting, blood disorders and, notably, lung injuries that led to the deaths of three patients in the trials.

But, Dr. Winer said, "if I were a patient with metastatic breast cancer, and if I were to get a drug with chemotherapy's side effects, I'd prefer this drug."

Doctors have said they are planning to try the treatment in their breast cancer patients who have metastatic HER2-low cancers.

"We are all going back and looking at our patients right now," said Dr. Susan Domchek, a breast cancer specialist at the University of Pennsylvania's Abramson Cancer Center. She says that even before the Food and Drug Administration approves trastuzumab deruxtecan for HER2-low patients, she will see if the data from the new study will be enough to convince insurers to approve the drug, which has a wholesale price of about $14,000 every three weeks.

Dr. Winer emphasized that trastuzumab deruxtecan is not a drug for earlier stage breast cancer; it still must be tested in that group of patients. But that is a likely next step, as is testing the drug in other cancers and extending its strategy beyond HER2.

"This strategy is the real breakthrough," he said, explaining that it would enable researchers to zoom in on molecular targets on tumor cells that were only sparsely present.

"This is about more than just this drug or even breast cancer," Dr. Winer said. "Its real advantage is that it enables us to take potent therapies directly to cancer cells."

One patient in the current study, Mary Smrekar, age 55, of Medina, Ohio, said she felt she got a temporary reprieve from certain death.

She was diagnosed with breast cancer in 2010 and has undergone surgery, chemotherapy and radiation. Her cancer went into remission. “I thought I was free and clear,” she said.

But in 2019, the cancer came back. It had spread to her pelvis. She had chemotherapy, but this time, there was little improvement.

Two years ago, she entered the trial at its Cleveland Clinic site. Her cancer has not gone away, but the tumors stopped growing.

“I’m so happy I got another two years,” Ms. Smrekar said. “My daughter is getting married next month. I didn’t think I’d make it to the wedding.”

https://bit.ly/3NLX2f6

Concern grows that human monkeypox outbreak will establish virus in animals outside Africa

New “reservoirs” could make outbreaks common and spawn new variants

By Jon Cohen

Eleven days after being bitten by one of her pet prairie dogs, a 3-year-old girl in Wisconsin on 24 May 2003 became the first person outside of Africa to be diagnosed with monkeypox. Two months later, her parents and 69 other people in the United States had suspected or confirmed cases of this disease, which is caused by a relative of the much deadlier smallpox virus. The monkeypox virus is endemic in parts of Africa, and rodents imported from Ghana had apparently infected captive prairie dogs, North American animals, when an animal distributor in Texas housed them together.

The outbreak now underway has affected more people outside of Africa than ever before—nearly 1300 cases as of 7 June, on multiple continents, many of them men who have sex with men. But like the 2003 episode, today’s surge has raised a possibility that makes researchers gulp: Monkeypox virus could take up permanent residence in wildlife outside of Africa, forming a reservoir that could lead to repeated human outbreaks.

No animal reservoir currently exists outside of Africa, but the U.S. outbreak of 2003 was a close call, some scientists suspect, especially because nearly 300 of the animals from Ghana and the exposed prairie dogs were never found. “We narrowly escaped having monkeypox establish itself in a wild animal population” in North America, suggests Anne Rimoin, an epidemiologist at the University of California, Los Angeles, who long has studied the disease in the Democratic Republic of the Congo (DRC). In the end, however, surveys of wild animals in Wisconsin and Illinois never found monkeypox virus, none of the infected humans passed on the disease to other people, and worries about this exotic outbreak evaporated.

Will North and South America, Europe, Asia, and Australia—all of which have reported monkeypox cases in this outbreak—be similarly fortunate this time?

Viruses frequently pingpong between humans and other species. Although COVID-19 is widely thought to have resulted from SARS-CoV-2 jumping from a bat or other host into people, humans have, in “reverse zoonoses,” also infected white-tailed deer, minks, cats, and dogs with the virus. One study in Ohio found antibodies to SARS-CoV-2 in more than one-third of 360 wild deer sampled. And in past centuries, when humans carried plague and yellow fever to new continents, those pathogens created reservoirs in rodents and monkeys, respectively—which later infected humans again.

As this outbreak of monkeypox expands, the virus has an unprecedented opportunity to establish itself in non-African species, which could infect humans and provide greater opportunity for more dangerous variants to evolve. “Monkeypox reservoirs in wild animals outside of Africa is a scary scenario,” says Bertram Jacobs, a virologist at Arizona State University (ASU), Tempe, who studies vaccinia, the poxvirus that served as the smallpox vaccine and

helped eradicate that devastating virus from humans.

Public health officials in several countries have advised people who have monkeypox lesions to avoid contact with their pets until they heal. Some 80% of the cases have occurred in Europe, and the European Food Safety Authority said no pets or wild animals had been infected as of 24 May. But it added that "close collaboration between human and veterinary public health authorities is needed to manage exposed pets and prevent the disease from being transmitted to wildlife."

The possibility that humans infected with monkeypox virus will spread it to wildlife outside of Africa "warrants serious concern," says William Karesh, a veterinarian at the EcoHealth Alliance who last week spoke about this possibility at a consultation on monkeypox research organized by the World Health Organization. For now, he says, the limited number of human cases reduces the odds. But pet rodents are a particular worry, as is the sheer number of wild ones—they make up 40% of all mammals—that frequently raid trash and could become infected by contaminated waste. "That's a lot of opportunity," he says.

Studies have yet to pinpoint the African reservoir of the monkeypox virus. Although a lab in Copenhagen, Denmark, in 1958 first identified it in research monkeys from Asia, scientists now believe the primates caught it from an African source. All human cases since the first one was reported in 1970, in the DRC (then Zaire), could be tied to the virus spilling over from animals in Africa.

So far, however, only six wild animals trapped in Africa have yielded the virus: three rope squirrels, a Gambian rat, a shrew, and a sooty mangabey monkey. Antibodies to the monkeypox virus are most abundant in African squirrels. "We still poorly understand the current reservoir other than it's rodents," says Grant McFadden, a poxvirus researcher who is also based at ASU.

But it's clear that monkeypox can infect many other kinds of animals in the wild and captivity. A 1964 outbreak in a Rotterdam, Netherlands, zoo sickened giant anteaters, orangutans, gorillas, chimpanzees, a gibbon, and a marmoset. Researchers have intentionally infected many lab animals, including rabbits, hamsters, guinea pigs, and chickens, although the virus doesn't reliably cause disease in several of them.

For many viruses, a lock-and-key relationship between viral surface proteins and receptors on host cells determines which animals it can infect; the spike protein of SARS-CoV-2, for example, latches onto angiotensin-converting enzyme 2, a protein that studs a variety of cells in humans, minks, cats, and many other species. But poxviruses don't seem to require specific host receptors, enabling many to infect a wide range of mammalian cells. Vaccinia, the smallpox vaccine virus, can even infect fruit flies in addition to cows and people, notes David Evans, a poxvirus researcher at the University of Alberta, Edmonton. Bernard Moss, a virologist at the U.S. National Institute of Allergy and Infectious Diseases (NIAID), has posited that some poxviruses have proteins on their surfaces that form a "hydrophobic face," a water-repelling area that can bind nonspecifically to hydrophilic cell membranes and initiate the infection process.

But whether a poxvirus can copy itself and, ultimately, persist in a species to create a reservoir depends on how well it fends off the host's immune attacks. Poxviruses have a relatively large complement of genes, about 200, and roughly half undermine a host's immune response. "Some viruses run and hide or are stealthy, avoiding direct contact with elements of the immune system," McFadden says. "Poxviruses by and large stand up and fight."

Their defense against host immunity appears to rely heavily on a family of genes scattered around their genomes that code for poorly understood proteins containing domains known as ankyrin repeats. Poxvirus proteins containing these repeats act as "molecular

flypaper," Evans says, glomming onto host proteins involved with coordinating the immune response. "Orthopoxviruses have these arrays of ankyrin repeats, and most of them, we don't really know what they target," Evans says. "But the bottom line is those probably hold the key to trying to understand why it is some of these viruses have the host range that they do."

Variola, the smallpox virus, appears to have lost many of these immune-evasion genes. It only persists in humans and has no animal reservoir, which was why the global vaccination campaign could eradicate it. Monkeypox is clearly more promiscuous. But the many questions that remain about it means there's no telling whether it will create reservoirs in non-African wildlife. "One of the challenges has been a lack of interest," says Lisa Hensley, a microbiologist at the U.S. Department of Agriculture who began doing monkeypox research in 2001 as part of a U.S. Army lab.

Hensley, who worked on monkeypox at NIAID for nearly a decade and collaborated with Rimoin, urges people to keep an open mind about how the virus behaves and what it might do next. "We're recognizing that this is a disease we need to worry about and that we really don't know as much as we think we know."

https://bit.ly/3NHqlQ7

Frequent Nightmares Could Be an Early Sign of Parkinson's, Study Finds

The development of nightmares later in life could be an early sign of Parkinson's disease, according to new research in older men.

Carly Cassella

Distressing dreams have long been associated with the neurological disease, especially among men, but this is the first study to investigate whether these symptoms are a warning of Parkinson's or a byproduct of the condition. Tracking the health of 3,818 older men with typical brain functioning for 12 years, researchers found those who experienced frequent nightmares were twice as likely to develop Parkinson's. Most of the diagnoses occurred within the first five years of the study.

The results suggest older adults could be screened for Parkinson's by asking them about the content of their dreams. Early interventions could then be employed to help stall the possible onset of physical symptoms, like tremors, stiffness, and slowness.

One of the biggest challenges with Parkinson's disease is early diagnosis. By the time most people figure out they've got the disease, they've already lost between 60 to 80 percent of dopamine-releasing neurons in part of their brain stem.

What's more, a previous study by the same researcher found patients with distressing dreams are five times more likely to show rapid disease progression.

"Although it can be really beneficial to diagnose Parkinson's disease early, there are very few risk indicators and many of these require expensive hospital tests or are very common and non-specific, such as diabetes," explains neurologist Abidemi Otaiku from the University of Birmingham in the UK.

"While we need to carry out further research in this area, identifying the significance of bad dreams and nightmares could indicate that individuals who experience changes to their dreams in older age – without any obvious trigger – should seek medical advice."

The link between sleep and Parkinson's is one that researchers have been investigating for several years now.

Roughly a quarter of Parkinson's patients report frequent distressing dreams from the time of diagnosis, and some report experiencing bad dreams up to 10 years before they were diagnosed.

Past studies suggest that people with Parkinson's disease are four times more likely to experience frequent nightmares than those in the general population. Parkinson's patients are also more likely to develop rapid eye movement sleep disorders, which cause dreams

to be physically reenacted during the night.

Yet until now, it hasn't been clear if these symptoms were a byproduct of Parkinson's or prodromal, which is the term scientists use for minor symptoms that appear before major symptoms arrive on the scene. The current research helps clear up that distinction by tracking a large sample of older men across more than a decade.

In the study, participants with self-reported frequent distressing dreams were two times more likely to develop Parkinson's over 12 years. What's more, in the first four years of the study, frequent distressing dreams were associated with a six-fold increase in the risk of developing the neurological disease.

Without further research to measure brain activity during sleep, it's hard to say what's going on at a biological level in Parkinson's patients who experience nightmares.

Men with Parkinson's tend to have more disturbing dreams than women with Parkinson's, but why that is remains unclear.

One hypothesis is that the late onset of nightmares is an early sign of neurodegeneration in some men.

Women are significantly more likely to experience regular nightmares early in life, but after age 65, men start to catch up.

Perhaps something is changing in the frontal cortex, which regulates emotion during sleep, as the male brain ages.

Researchers are now planning to use electroencephalography to figure out what that something might be.

The study was published in *EClinicalMedicine*.

https://bit.ly/3zqYpM6

Having Strange Dreams? They Might Be Helping Your Brain Learn Better

According to Human Brain Project experts, strange dreams may help your brain learn better

According to the National Sleep Foundation, we dream four to six times a night on average. However, since we forget more than 95% of our dreams, you will only remember a few each month.

Although we dream throughout the night, our most vivid and memorable dreams occur during rapid eye movement (REM) sleep, which begins about 90 minutes after you fall asleep. Unexpected life events, high levels of stress, and other changes can all have an effect on our dreams, making them stranger, more vivid, and memorable. The exact purpose of dreaming is still a bit of a mystery to the scientists, however recent research hopes to explain why people have strange dreams.

A new study from the University of Bern in Switzerland reveals that dreams, particularly those that seem genuine but are, on closer inspection, abnormal, help our brain learn and extract general ideas from previous experiences. The research, which was conducted as part of the Human Brain Project and published in *eLife*, offers a new hypothesis on the meaning of dreams by using machine learning-inspired methods and brain simulation.

The importance of sleep and dreams in learning and memory has long been acknowledged; the influence that a single sleepless night can have on our cognition is well documented. “What we lack is a theory that ties this together with experience consolidation, concept generalization, and creativity,” explains Nicolas Deperrois, the study’s lead author.

During sleep, we commonly experience two types of sleep phases, alternating one after the other: non-REM sleep, when the brain “replays” the sensory stimulus experienced while awake, and REM sleep when spontaneous bursts of intense brain activity produce vivid dreams.

The researchers used simulations of the brain cortex to model how different sleep phases affect learning. To introduce an element of unusualness in artificial dreams, they took inspiration from a machine learning technique called Generative Adversarial Networks (GANs). In GANs, two neural networks compete with

each other to generate new data from the same dataset, in this case, a series of simple pictures of objects and animals. This operation produces new artificial images which can look superficially realistic to a human observer.

The researchers then simulated the cortex during three distinct states: wakefulness, non-REM sleep, and REM sleep. During wakefulness, the model is exposed to pictures of boats, cars, dogs, and other objects. In non-REM sleep, the model replays the sensory inputs with some occlusions. REM sleep creates new sensory inputs through the GANs, generating twisted but realistic versions and combinations of boats, cars, dogs, etc. To test the performance of the model, a simple classifier evaluates how easily the identity of the object (boat, dog, car, etc.) can be read from the cortical representations.

"Non-REM and REM dreams become more realistic as our model learns," explains Jakob Jordan, senior author, and leader of the research team. "While non-REM dreams resemble waking experiences quite closely, REM dreams tend to creatively combine these experiences." Interestingly, it was when the REM sleep phase was suppressed in the model, or when these dreams were made less creative, that the accuracy of the classifier decreased. When the NREM sleep phase was removed, these representations tended to be more sensitive to sensory perturbations (here, occlusions).

According to this study, wakefulness, non-REM, and REM sleep appear to have complementary functions for learning: experiencing the stimulus, solidifying that experience, and discovering semantic concepts. "We think these findings suggest a simple evolutionary role for dreams, without interpreting their exact meaning," says Deperrois. "It shouldn't be surprising that dreams are bizarre: this bizarreness serves a purpose. The next time you're having crazy dreams, maybe don't try to find a deeper meaning – your brain may be simply organizing your experiences."

Reference: "Learning cortical representations through perturbed and adversarial dreaming" by Nicolas Deperrois, Mihai A Petrovici, Walter Senn and Jakob Jordan, 6 April 2022, eLife. DOI: 10.7554/eLife.76384

https://bit.ly/3xoDiYc

Evolutionary biologist suggests yawning may be a means for telling others to be more alert

Likely signals members of a social group that the yawner is not alert, so others should be

by Bob Yirka , Phys.org

Andrew Gallup, an evolutionary biologist with the Psychology and Evolutionary Behavioral Sciences Program at SUNY Polytechnic Institute in New York has published a paper in the journal *Animal Behavior* outlining research into the reason that animals yawn. He suggests there could be a variety of reasons for it but believes it mostly likely signals members of a social group that the yawner is not alert, so others should be.

Gallup has been studying yawning for several years, though it was only recently that he decided to take a more serious look at possible reasons for it. He searched for published papers involved in the study of yawning and compared what other researchers had found. He then compiled a consensus of the sorts of reasons behind yawning.

Yawning, he notes, is little more than a reflex that involves the inhalation of air, stretching of the eardrums, and a wide-open mouth, which pulls the jaw down.

In the published papers, he found researchers had ruled out the possibility of yawing providing a sudden increase in blood oxygen levels. But he also discovered evidence of yawning cooling the brain slightly. He notes that researchers have also found that initial yawns—those not instigated by seeing someone else yawn—generally occur during environmental changes. A person moving from hot to cold or vice versa, for example, or from sleep to waking.

Researchers have also found that yawning leads to an increase in cortical arousal, which could be construed as a person feeling more alert. Additionally, several researchers found evidence that yawning evolved as a means for one animal to subtly notify others nearby of their less-than-alert condition, suggesting that others should take over watching for threats.

As for why so many animals yawn when seeing someone else yawn, sometimes even members of other species, Gallup suggests the research shows it is likely a means for maintaining group alertness.

More information: *Andrew C. Gallup, The causes and consequences of yawning in animal groups, Animal Behaviour (2022). DOI: 10.1016/j.anbehav.2022.03.011*

https://bit.ly/3xJVlJQ

Most 'silent' genetic mutations are harmful, not neutral, a finding with broad implications

Once generally been assumed to be neutral, or nearly so, most synonymous mutations are shown to be strongly harmful

In the early 1960s, University of Michigan alumnus Marshall Nirenberg and a few other scientists deciphered the genetic code of life, determining the rules by which information in DNA molecules is translated into proteins, the working parts of living cells.

They identified three-letter units in DNA sequences, known as codons, that specify each of the 20 amino acids that make up proteins, work for which Nirenberg later shared a Nobel Prize with two others.

Occasionally, single-letter misspellings in the genetic code, known as point mutations, occur. Point mutations that alter the resulting protein sequences are called nonsynonymous mutations, while those that do not alter protein sequences are called silent or synonymous mutations.

Between one-quarter and one-third of point mutations in protein-coding DNA sequences are synonymous. Ever since the genetic code was cracked, those mutations have generally been assumed to be neutral, or nearly so.

But in a study scheduled for online publication June 8 in the journal *Nature* that involved the genetic manipulation of yeast cells in the laboratory, University of Michigan biologists show that most synonymous mutations are strongly harmful.

The strong non-neutrality of most synonymous mutations—if found to be true for other genes and in other organisms—would have major implications for the study of human disease mechanisms, population and conservation biology, and evolutionary biology, according to the study authors.

"Since the genetic code was solved in the 1960s, synonymous mutations have been generally thought to be benign. We now show that this belief is false," said study senior author Jianzhi "George" Zhang, the Marshall W. Nirenberg Collegiate Professor in the U-M Department of Ecology and Evolutionary Biology.

"Because many biological conclusions rely on the presumption that synonymous mutations are neutral, its invalidation has broad implications. For example, synonymous mutations are generally ignored in the study of disease-causing mutations, but they might be an underappreciated and common mechanism."

In the past decade, anecdotal evidence has suggested that some synonymous mutations are nonneutral. Zhang and his colleagues wanted to know if such cases are the exception or the rule.

They chose to address this question in budding yeast (Saccharomyces cerevisiae) because the organism's short generation time (about 80 minutes) and small size allowed them to measure the effects of a large number of synonymous mutations relatively quickly, precisely and conveniently.

They used CRISPR/Cas9 genome editing to construct more than 8,000 mutant yeast strains, each carrying a synonymous, nonsynonymous or nonsense mutation in one of 21 genes the researchers targeted.

Then they quantified the "fitness" of each mutant strain by measuring how quickly it reproduced relative to the nonmutant strain. Darwinian fitness, simply put, refers to the number of offspring an individual has. In this case, measuring the reproductive rates of the yeast strains showed whether the mutations were beneficial, harmful or neutral.

To their surprise, the researchers found that 75.9% of synonymous mutations were significantly deleterious, while 1.3% were significantly beneficial.

"The previous anecdotes of nonneutral synonymous mutations turned out to be the tip of the iceberg," said study lead author Xukang Shen, a graduate student research assistant in Zhang's lab.

"We also studied the mechanisms through which synonymous mutations affect fitness and found that at least one reason is that both synonymous and nonsynonymous mutations alter the gene-expression level, and the extent of this expression effect predicts the fitness effect."

Zhang said the researchers knew beforehand, based on the anecdotal reports, that some synonymous mutations would likely turn out to be nonneutral. "But we were shocked by the large number of such mutations," he said. "Our results imply that synonymous mutations are nearly as important as nonsynonymous mutations in causing disease and call for strengthened effort in predicting and identifying pathogenic synonymous mutations."

The U-M-led team said that while there is no particular reason why their results would be restricted to yeast, confirmations in diverse organisms are required to verify the generality of their findings.

The other authors of the *Nature* study are Siliang Song of the U-M Department of Ecology and Evolutionary Biology and Chuan Li of Stanford University.

More information: *Jianzhi Zhang, Synonymous mutations in representative yeast genes are mostly strongly nonneutral, Nature (2022). DOI: 10.1038/s41586-022-04823-w. www.nature.com/articles/s41586-022-04823-w*

https://bit.ly/3NOhqMM

Research Shows That Playing Video Games Increases Your Intelligence

A new study finds that playing video games boosted children's intelligence by 2.5 IQ points

In today's world, video games are only becoming more popular. As of 2020, more than 200 million Americans play video games in the United States alone. That means that approximately 65 percent of American adults play video games.

Since the 1970s, video games have sparked debate. Concerns have been raised by parents and children's advocates that violent video games can influence young players to commit violent acts in real life.

However, video games are also thought to be beneficial to both the mind and the body. Action video game players had higher hand-eye coordination and visuomotor abilities than nonplayers. According to a recent study, playing video games might even boost your intelligence.

Researchers at Sweden's Karolinska Institutet examined how children's screen habits link with how their cognitive abilities grow over time. They discovered that youngsters who spent more time than average playing video games increased their IQ more than the average, however TV watching or social media had no effect. The results have been published in the journal *Scientific Reports*.

Children are spending an increasing amount of time in front of devices. It is fiercely discussed how this impacts their health and if it has a positive or detrimental influence on their cognitive abilities. Researchers from Karolinska Institutet and Vrije Universiteit Amsterdam investigated the relationship between screen usage and intellect over time for this study.

The research included over 9,000 boys and girls from the United States. The children were nine or ten years old when they took a

battery of psychological tests to assess their general cognitive ability (intelligence). The children and their parents were also asked how much time they spend watching television and movies, playing video games, and using social media.

Followed up after two years

Just over 5,000 of the children were followed up after two years, at which point they were asked to repeat the psychological tests. This enabled the researchers to study how the children's performance on the tests varied from one testing session to the other and to control for individual differences in the first test. They also controlled for genetic differences that could affect intelligence and differences that could be related to the parent's educational background and income.

On average, the children spent 2.5 hours a day watching TV, half an hour on social media, and 1-hour playing video games. The results showed that those who played more games than the average increased their intelligence between the two measurements by approximately 2.5 IQ points more than the average. No significant effect was observed, positive or negative, of TV-watching or social media.

"We didn't examine the effects of screen behavior on physical activity, sleep, wellbeing, or school performance, so we can't say anything about that," says Torkel Klingberg, professor of cognitive neuroscience at the Department of Neuroscience, Karolinska Institutet. "But our results support the claim that screen time generally doesn't impair children's cognitive abilities and that playing video games can actually help boost intelligence. This is consistent with several experimental studies of video-game playing."

Intelligence is not constant

The results are also in line with recent research showing that intelligence is not a constant, but a quality that is influenced by environmental factors.

"We'll now be studying the effects of other environmental factors and how the cognitive effects relate to childhood brain development," says Torkel Klingberg.

One limitation of the study is that it only covered US children and did not differentiate between different types of video games, which makes the results difficult to transfer to children in other countries with other gaming habits. There was also a risk of reporting errors since screen time and habits were self-rated.

The study was financed by the Swedish Research Council and the Strategic Research Area Neuroscience (StratNeuro) at Karolinska Institutet. The researchers report no conflicts of interest.

Reference: "The impact of digital media on children's intelligence while controlling for genetic differences in cognition and socioeconomic background" by Bruno Sauce, Magnus Liebherr, Nicholas Judd and Torkel Klingberg, 11 May 2022, Scientific Reports.
DOI: 10.1038/s41598-022-11341-2

https://bit.ly/3O6tLM7

Scientists grew living human skin around a robotic finger

The advance brings Terminator-like cyborgs a small step closer to reality

By Maria Temming

The Terminator may be one step closer to reality.

Researchers at the University of Tokyo have built a robotic finger that, much like Arnold Schwarzenegger's titular cyborg assassin, is covered in living human skin. The goal is to someday build robots that look like real people — albeit for more altruistic applications.

Living human skin covering a robotic finger can bend with the finger (shown) and self-heal. **Shoji Takeuchi**

Super realistic-looking robots could more seamlessly interact with humans in medical care and service industries, say biohybrid

engineer Shoji Takeuchi and his colleagues June 9 in *Matter*. (Whether cyborgs masked in living tissue would be more congenial or creepy is probably in the eye of the beholder.)

To cover the finger in skin, Takeuchi and colleagues submerged the robotic digit in a blend of collagen and human skin cells called dermal fibroblasts. The mixture settled into a base layer of skin, or dermis, covering the finger. The team then poured a liquid containing human keratinocyte cells onto the finger, which formed an outer skin layer, or epidermis.

After two weeks, skin covering the finger measured a few millimeters thick — comparable to the thickness of human skin.

The lab-made skin was strong and stretchy enough to withstand the robotic finger bending. It could also heal itself: When researchers made a small cut on the robotic finger and covered it with a collagen bandage, the skin's fibroblast cells merged the bandage with the rest of the skin within a week.

Researchers at the University of Tokyo covered this robotic finger in living human skin to pave the way for ultrarealistic cyborgs.

"This is very interesting work and an important step forward in the field," says Ritu Raman, an MIT engineer who also builds machines with living components. "Biological materials are appealing because they can dynamically sense and adapt to their environments."

For instance, she'd like to see a future version of the living robot skin embedded with nerve cells to make robots more aware of their surroundings.

But a robot can't wear this lab-grown skin suit out and about just yet, Raman notes. The skin-covered robotic finger spent most of its time soaking in sugar, amino acids and other ingredients that skin cells need to survive. A Terminator or other cyborg wearing this skin would have to bathe often in a broth of nutrients or use some other complex skin care routine.

https://bit.ly/3aNqwL5

Are we born with a moral compass?

Young infants can make and act on moral judgments, shedding light on the origin of morality

For millennia, philosophers have pondered the question of whether humans are inherently good. But now, researchers from Japan have found that young infants can make and act on moral judgments, shedding light on the origin of morality.

In a study recently published in *Nature Human Behaviour*, researchers from Osaka University, in collaboration with Otsuma Women's University, NTT Communication Science Laboratories, and the University of Tokyo, revealed that eight-month-old infants can punish antisocial behavior exhibited by a third party. Thus, the motivation driving punishment might be intrinsic as opposed to learned.

Punishment of antisocial behavior is found in only humans, and is universal across cultures. However, the development of moral behavior is not well understood. Further, it can be very difficult to examine decision-making and agency in infants, which the researchers at Osaka University aimed to address.

"Morality is an important but mysterious part of what makes us human," says lead author of the study Yasuhiro Kanakogi. "We wanted to know whether third-party punishment of antisocial others is present at a very young age, because this would help to signal whether morality is learned."

To tackle this problem, the researchers developed a new research paradigm. First, they familiarized infants with a computer system in which animations were displayed on a screen. The infants could control the actions on the screen using a gaze-tracking system such that looking at an object for a sufficient period of time led to the destruction of the object. The researchers then showed a video in which one geometric agent appeared to "hurt" another geometric

agent, and watched whether the infants "punished" the antisocial geometric agent by gazing at it.

"The results were surprising," says Kanakogi. "We found that preverbal infants chose to punish the antisocial aggressor by increasing their gaze towards the aggressor."

To verify their findings, the researchers conducted three control experiments to exclude alternative interpretations of the infants' gazing behaviors. "The observation of this behavior in very young children indicates that humans may have acquired behavioral tendencies toward moral behavior during the course of evolution," says Kanakogi. "Specifically, the punishment of antisocial behavior may have evolved as an important element of human cooperation."

This new paradigm for studying decision-making in a social context could be an important turning point in infant cognitive research. In particular, while much previous research on infant cognition has used observations from third parties, and thus examined passive responses to events, the eye-gaze paradigm allows for the observation of active decision-making in infants. Thus, this research model may be useful in uncovering additional information about cognitive abilities in preverbal infants.

More information: *Yasuhiro Kanakogi, Third-party punishment by preverbal infants, Nature Human Behaviour (2022). DOI: 10.1038/s41562-022-01354-2. www.nature.com/articles/s41562-022-01354-2*

https://bit.ly/39hGwVu

Samples of the asteroid Ryugu are scientists' purest pieces of the solar system

Analysis reveals the asteroid was evolving about 5 million years after the solar system's start

By Liz Kruesi

Samples of the asteroid Ryugu are the most pristine pieces of the solar system that scientists have in their possession.

A new analysis of Ryugu material confirms the porous rubble-pile asteroid is rich in carbon and finds it is extraordinarily primitive (*SN: 3/16/20*). It is also a member of a rare class of space rocks known as CI-type, researchers report online June 9 in *Science*.

The 31 milligrams of dust and debris from asteroid Ryugu seen in this photo, along with several other samples, are the most pristine pieces of the solar system scientists have ever studied. **JAXA**

Their analysis looked at material from the Japanese mission Hayabusa2, which collected 5.4 grams of dust and small rocks from multiple locations on the surface of Ryugu and brought that material to Earth in December 2020 (*SN: 7/11/19*; *SN: 12/7/20*). Using 95 milligrams of the asteroid's debris, the researchers measured dozens of chemical elements in the sample and then compared abundances of several of those elements to those measured in rare meteorites classified as CI-type chondrites. Fewer than 10 meteorites found on Earth are CI chondrites.

This comparison confirmed Ryugu is a CI-type chondrite. But it also showed that unlike Ryugu, the meteorites appear to have been altered, or contaminated, by Earth's atmosphere or even human handling over time. "The Ryugu sample is a much more fresh sample," says Hisayoshi Yurimoto, a geochemist at Hokkaido University in Sapporo, Japan.

The researchers also measured the abundances of manganese-53 and chromium-53 in the asteroid and determined that melted water ice reacted with most of the minerals around 5 million years after the solar system's start, altering those minerals, says Yurimoto. That water has since evaporated, but those altered minerals are still present in the samples. By studying them, the researchers can learn more about the asteroid's history.

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Scientists Found Superworms That Love Eating Styrofoam, And It Could Be a Good Thing

Larvae of Zophobas morio darkling beetles – are eager to dine on polystyrene: their gut enzymes could be key to improved recycling

Issam Ahmed, AFP

Packing material, disposable cutlery, CD cases: Polystyrene is among the most common forms of plastic, but recycling it isn't easy and the vast majority ends up in landfills or finds its way to the oceans where it threatens marine life.

Scientists at Australia's University of Queensland have now discovered that superworms – the larvae of *Zophobas morio* darkling beetles – are eager to dine on the substance, and their gut enzymes could hold the key to higher recycling rates.

Chris Rinke, who led a study that was published in the journal *Microbial Genomics* on Thursday, told AFP previous reports had shown that tiny waxworms and mealworms (which are also beetle larvae) had a good track record when it came to eating plastic, "so we hypothesized that the much larger superworms can eat even more."

Superworms grow up to two inches (five centimeters) and are bred as a food source for reptiles and birds, or even for humans in countries such as Thailand and Mexico.

Rinke and his team fed superworms different diets over a three week period, with some given polystyrene foam, commonly known as styrofoam, some bran, and others not fed at all.

Polystyrene in the gut of a worm. **(University of Queensland)**

"We confirmed that superworms can survive on a sole polystyrene diet, and even gain a small amount of weight – compared to a starvation control group – which suggests that the worms can gain energy from eating polystyrene," he said. Although the polystyrene-reared superworms completed their life cycle, becoming pupae and then fully developed adult beetles, tests revealed a loss of microbial diversity in their guts and potential pathogens.

These findings suggested that while the bugs can survive on polystyrene, it is not a nutritious diet and impacts their health.

Next, the team used a technique called metagenomics to analyze the microbial gut community and find which gene-encoded enzymes were involved in degrading the plastic.

Bio-upcycling

One way to put the findings to use would be to provide superworms with food waste or agricultural bioproducts to consume alongside polystyrene. "This could be a way to improve the health of the worms and to deal with the large amount of food waste in Western countries," said Rinke.

But while breeding more worms for this purpose is possible, he envisages another route: creating recycling plants that mimic what the larvae do, which is to first shred the plastic in their mouths then digest it through bacterial enzymes. "Ultimately, we want to take the superworms out of the equation," he said, and he now plans more research aimed at finding the most efficient enzymes, then enhancing them further through enzyme engineering.

The breakdown products from that reaction could then be fed to other microbes to create high-value compounds, such as bioplastics, in what he hopes would become an economically viable "upcycling" approach.

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New Device Purifies Saltwater Over a 1000 Times Faster Than Standard Industrial Equipment

The future of desalination: Using a Teflon-like membrane to purify water

Water scarcity is a growing problem around the globe. In Africa alone, it is estimated that about 230 million people will face water shortages by 2025, with up to 460 million living in water-stressed regions.

Water covers 70% of Earth, so it is easy to assume that it will always be abundant. However freshwater is very scarce. One technology designed to help produce more freshwater is desalination plants. Water desalination is the process of removing salt from seawater to produce fresh water that can be processed further and safely used. A desalination plant converts about half of the water it receives into drinkable water.

Although seawater desalination is a well-established way of producing drinking water, it comes with a high energy cost. Researchers have successfully filtered salt from water for the first time using fluorine-based nanostructures. These fluorous nanochannels are more effective than conventional desalination technologies because they operate quicker, use less pressure, are a more effective filter, and use less energy.

You've probably seen how effortlessly wet ingredients slide across a nonstick Teflon-coated frying pan if you've ever used one. Fluorine, a lightweight ingredient that is inherently water-repellent, or hydrophobic, is a crucial component of Teflon. Teflon can also be used to enhance the flow of water by lining pipes with it. Associate Professor Yoshimitsu Itoh of the University of Tokyo's Department of Chemistry and Biotechnology, as well as his colleagues, were intrigued by this behavior. Thus, they were inspired to investigate how fluorine pipelines or channels may work on a different scale, the nanoscale.

"We were curious to see how effective a fluorous nanochannel might be at selectively filtering different compounds, in particular, water and salt. And, after running some complex computer simulations, we decided it was worth the time and effort to create a working sample," said Itoh. "There are two main ways to desalinate water currently: thermally, using heat to evaporate seawater so it condenses as pure water, or by reverse osmosis, which uses pressure to force water through a membrane that blocks salt. Both methods require a lot of energy, but our tests suggest fluorous nanochannels require little energy and have other benefits too."

The researchers developed test filtration membranes by chemically manufacturing nanoscopic fluorine rings that were stacked and implanted in an otherwise impenetrable lipid layer, similar to the organic molecules found in cell walls. They developed multiple test samples with nanorings ranging in size from 1 to 2 nanometers. A human hair is almost 100,000 nanometers wide for comparison. Itoh and his colleagues evaluated the presence of chlorine ions, one of the major components of salt (the other being sodium), on either side of the test membrane to determine the effectiveness of their membranes.

"It was very exciting to see the results firsthand. The smaller of our test channels perfectly rejected incoming salt molecules, and the larger channels too were still an improvement over other desalination techniques and even cutting-edge carbon nanotube filters," said Itoh. "The real surprise to me was how fast the process occurred. Our sample worked around several thousand times faster than typical industrial devices, and around 2,400 times faster than experimental carbon nanotube-based desalination devices."

As fluorine is electrically negative, it repels negative ions such as the chlorine found in salt. But an added bonus of this negativity is that it also breaks down what is known as water clusters, essentially loosely bound groups of water molecules, so that they pass through the channels quicker. The team's fluorine-based water desalination membranes are more effective, faster, require less energy to operate, and are made to be very simple to use as well, so what's the catch?

"At present, the way we synthesize our materials is relatively

energy-intensive itself; however, this is something we hope to improve upon in upcoming research. And, given the longevity of the membranes and their low operational costs, the overall energy costs will be much lower than with current methods," said Itoh. "Other steps we wish to take are of course scaling this up. Our test samples were single nanochannels, but with the help of other specialists, we hope to create a membrane around 1 meter across in several years. In parallel with these manufacturing concerns, we're also exploring whether similar membranes could be used to reduce carbon dioxide or other undesirable waste products released by industry."

Reference: "Ultrafast water permeation through nanochannels with a densely fluorous interior surface" by Yoshimitsu Itoh, Shuo Chen, Ryota Hirahara, Takeshi Konda, Tsubasa Aoki, Takumi Ueda, Ichio Shimada, James J. Cannon, Cheng Shao, Junichiro Shiomi, Kazuhito V. Tabata, Hiroyuki Noji, Kohei Sato and Takuzo Aida, 12 May 2022, Science. DOI: 10.1126/science.abd0966

https://bit.ly/3mG9WiT

The secret carbon decisions plants are making about our future

Plants make their own "secret" decisions about how much carbon to release back into the atmosphere via a previously unknown process

by Liz McGrath, University of Western Australia

New research from The University of Western Australia has revealed that plants make their own "secret" decisions about how much carbon to release back into the atmosphere via a previously unknown process, a discovery with "profound implications" for the use of plants as carbon stores.

Professor Harvey Millar, from UWA's School of Molecular Sciences and an author of the study published today in *Nature Plants*, said the findings mean plants of the future could be designed to meet the world's food needs while also aiding the environment.

"Every school student learns about photosynthesis, the process by which plants use sunlight, water, and carbon dioxide to create oxygen and energy in the form of sugar," said Professor Millar, Director at the ARC Centre of Excellence in Plant Energy Biology.

"But a plant doesn't grow as fast as the carbon it takes in by photosynthesis because it releases up to half of that carbon again as CO_2 in the process of plant respiration. This stops plants being the best sinks for carbon they could be and limits how much they are able to help lower atmospheric CO_2."

A carbon sink is anything that absorbs more carbon from the atmosphere than it releases.

Professor Millar said deciding when and how much CO_2 to lose is a secret that plants keep locked away inside parts of the cell called mitochondria where CO_2 release takes place.

"Our research, led by Ph.D. candidate and Forrest Scholar Xuyen Le, discovered this CO_2 release decision is governed by a previously unknown process, a metabolic channel that directs a product of sugar called pyruvate to be oxidized to CO_2 or kept to make plant biomass," Professor Millar said.

"We found that a transporter on mitochondria directs pyruvate to respiration to release CO_2, but pyruvate made in other ways is kept by plant cells to build biomass—if the transporter is blocked, plants then use pyruvate from other pathways for respiration," Le said.

Professor Millar said the research shows that plants can differentiate and choose one pyruvate source over another to use for CO_2 release. This secret process breaks the normal rules of biochemistry, where the next step in a process does not know the origin of the product from the step before.

"Understanding the plant's respiration secret to use a metabolic channel to prioritize carbon release over keeping it to make biomass provides a new opportunity to influence the decision at the last moment," he said.

"This could be done by limiting this channeling to respiration or making new channels to direct carbon inside mitochondria back towards biomass production and so limiting CO_2 release from plants."

"It shows that current discussions around carbon net zero and the role that crops, forests and grasslands can play, should also include conversations on what happens inside plants, alongside global financial decisions."

UWA researchers are now involved in long term international partnerships to find better ways to use energy from respiration in order to redirect carbon to biomass without limiting a plant's ability to grow and protect itself from pathogens or harsh environments.

More information: *Xuyen H. Le et al, Metabolic evidence for distinct pyruvate pools inside plant mitochondria, Nature Plants (2022). DOI: 10.1038/s41477-022-01165-3*

https://wb.md/3xsZEYi

'DIY' Artificial Pancreas Systems Found to Be Safe, Effective

Open-source automated insulin delivery systems appear to be both effective and safe in adults and children, new research finds.

Miriam E. Tucker

Automated insulin delivery (AID) system, also known as closed-loop systems or an artificial pancreas, link an insulin pump and a continuous glucose monitor (CGM) with an algorithm that automatically adjusts insulin delivery to optimize glycemic control.

Prior to the availability of commercial AID systems, Dana Lewis, a patient with type 1 diabetes, and her partner co-developed an algorithm that could link older versions of an insulin pump and CGM.

In 2015, they made the code and all related materials open-source, so that anyone who wanted to create their own AID system could do so. Today thousands of people worldwide with type 1 diabetes are using the systems, which are sometimes called "do-it-yourself (DIY)" AID systems although the approach has been community-based.

AID systems are not approved by any regulatory body, and despite several nonrandomized studies demonstrating their effectiveness and safety, there is still concern among some health professionals about their safety. In 2019, the US Food and Drug Administration (FDA) warned against the use of any nonapproved devices or algorithms. (Now, though, at least one open-source AID system algorithm is under FDA review.)

Aimed at addressing those concerns, CREATE (Community Derived Automated Insulin Delivery) is the first randomized controlled clinical trial to compare an open-source AID system to insulin pump therapy and CGM (without any communication between the two) in patients with type 1 diabetes, most of whom were naive to AID systems.

Doctors Uncomfortable With Open Source; Study Provides Reassurance

The findings were presented June 6 at the American Diabetes Association 82nd Scientific Sessions by Martin I. de Bock, PhD, FRACP, a pediatric endocrinologist and senior lecturer at the University of Otago, Christchurch, New Zealand.

The study compared the most commonly used open-source AID system (using the OpenAPS algorithm from a version of AndroidAPS implemented in a smartphone with the DANA-i insulin pump and Dexcom G6 CGM) to any insulin pump plus CGM as a comparator group.

The open-source AID system led to a significant reduction in A1c with no major safety issues.

"The acceptance [among clinicians] of open-source systems is diverse and complicated, [with varying] personal comfort levels of seeing someone using an AID system that has no regulatory approval," de Bock told *Medscape Medical News*.

"This is one of the reasons that it was so important to conduct the CREATE trial for the many thousands of open-source AID users. Given that the trial demonstrated safety and efficacy using the most robust scientific methodology available — a long-term randomized controlled trial — it may go some way to provide assurance for providers when they are seeing people using an open-source automated system," he said.

Asked for comment, session moderator Diana Isaacs, PharmD, CDCES, an endocrine clinical pharmacist at the Cleveland Clinic, Ohio, told *Medscape Medical News:* "There has been concern that these systems aren't safe, so showing the safety is important. I think people deserve choice. As long as they're safe, patients should be able to use what they want to use, and we should support them."

Isaacs pointed out that an advantage of open-source systems over current commercial AIDs for patients is the ability to customize glucose targets, but in CREATE, those targets were established in the protocol by the investigators.

"I think it's nice having the data, although in the trial they had specific requirements. They had a target range and active insulin time that they were recommending. So it's a little different than true DIY where you don't really have those guidelines you have to follow. It is exciting, it's very interesting, but I wouldn't say it's a true mirror of the real world."

Open-Source Systems Improved Time-in-Range, No Safety Issues

For the CREATE study, 100 participants were enrolled, including 50 children aged 7-15 years and 50 adults aged 16-70 years. All participants had been using insulin pumps for at least 6 months. Most of the children and about two thirds of the adults were also using CGMs, but just 6% of the children and 18% of the adults had prior experience with AID systems.

Baseline A1c in children was 7.5% and in adults was 7.7%.

After a 4-week run-in, all patients were randomized to the open-source AID or insulin pump plus CGM for 6 months.

The final group analyzed consisted of 42 patients in the open-source AID group and 53 patients in the comparator group.

The primary outcome, the adjusted mean difference in percent time-in-range (glucose of 70-180 mg/dL) during the final 2 weeks of the 6-month trial, showed a significant difference of 14% ($P < .001$) with open-source AID compared with pump plus CGM only.

Time-in-range in the open-source AID group rose from 61.2% to 71.2%, while it actually dropped slightly in the comparator group, from 57.7% to 54.5%.

The proportion of patients achieving time-in-range > 70% with open-source AID was 60% versus just 15% with pump plus CGM.

Glycemic improvements with open-source AID were significant for adults and children and were greater for those with higher baseline A1c levels. The effect was immediate and sustained throughout the study period, "which is super-pleasing, because there was a worry that the technical burden of open source might be [leading to] dropout, but we didn't see that. It was sustained right through to the end of the trial," de Bock commented.

Hypoglycemic rates didn't differ between groups, and there were no episodes of severe hypoglycemia or diabetic ketoacidosis.

No More Waiting: What Is the Future of Open-Source AID?

When the open-source APS was first developed, users coined the motto: "We are not waiting." But now that the "wait" is over and several commercial AIDs have been approved by regulatory bodies, with others still in the pipeline, will people still use open-source systems?

There are no current data on people moving from DIY to commercial systems. However, de Bock said, "For most who undertook an open-source option, the precision of the settings that they can use and enjoy would mean that most would likely stick to

their open source."

Isaacs agrees: "I actually don't think it's going to go away in the near future, because the FDA has very specific criteria for where these [formally approved] devices can be in terms of their target ranges and requirements versus with open source you can really customize. So I still think there's going to be a subset of people who want that customization, who want the lower targets."

Dana Lewis, the originator of the DIY system and a CREATE co-author, told *Medscape Medical News*: "I don't believe there has been a fall-off, and in fact, I think open-source AID has continued to have ongoing uptake as awareness increases about options and as more pumps and CGMs become interoperable with various open-source AID choices."

"I think uptake increasing is also influenced by the fact that in places like Europe, Asia, and Australia there are in-warranty on-the-market pumps that are compatible and interoperable with open-source AID. I think awareness of AID overall increases uptake of commercial and open source alike," she said.

"Clinicians, as emphasized in recent position statements, must maintain support of the person with diabetes, irrespective of the mode of treatment they are on...Healthcare providers should be encouraged to learn from the experiences of the people who have stuck with open-source AID or switched, so that they can inform themselves of the relative strengths and benefits of each system," de Bock advised.

Lewis noted: "We are seeing increasing awareness and comfort in endocrinologists from the community perspective, and we do hope that this study helps increase conversation and awareness of the safety and efficacy of open-source AID systems as an option for people with diabetes."

In fact, the team published an article specifically about clinicians' experience in CREATE. "The learning curve is similar across AID technology," she observed.

Findings of a 6-month continuation phase of CREATE, in which all participants used the open-source AID, are scheduled to be presented in September at the European Association for the Study of Diabetes (EASD) 2022 annual meeting.

The study was funded by the Health Research Council of New Zealand, with hardware support from SOOIL Developments, South Korea; Dexcom; and Vodafone New Zealand. de Bock has reported receiving honoraria and/or research funding from Novo Nordisk, Sanofi, Pfizer, Medtronic, Lilly, Ypsomed, and Dexcom. Isaacs has reported serving as a consultant for LifeScan, Lilly, and Insulet, and as a speaker for Dexcom, Medtronic, Abbott, and Novo Nordisk. Lewis has reported no relevant financial relationships.

ADA 2022 Scientific Sessions. Presented June 6, 2022. Abstract 286-OR.

https://bit.ly/3OeKOf5

The Length of a Day Oscillates Every 6 Years, And We May Finally Know Why

How we think about our planet's center may need to be seriously updated.

Michelle Starr

New evidence suggests that, instead of consistently rotating faster than Earth's spin, the solid inner core oscillates – spinning first in one direction with respect to the surface far above, then the other, changing direction every six years.

This not only has implications for our understanding of the inner workings of our home world, it can also neatly explain a mystery that has perplexed scientists for some time: an oscillating variation in the length of Earth's day, with a period of 5.8 years.

"From our findings, we can see the Earth's surface shifts compared to its inner core, as people have asserted for 20 years," said geophysicist John E. Vidale of the University of Southern California, Los Angeles (UCLA).

"However, our latest observations show that the inner core spun slightly slower from 1969-71 and then moved the other direction from 1971-74. We also note that the length of a day grew and

shrank as would be predicted. The coincidence of those two observations makes oscillation the likely interpretation."

Although our understanding of Earth's core has developed a lot in recent decades, there's still a lot we don't know. We can't just go there and take a gander at it; everything we know, we've gleaned from indirect observations, such as seismic waves propagating and bouncing through the entire planet.

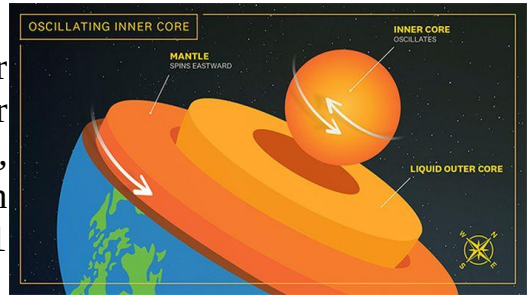
But this is still a very effective tool. Scientists have been able to ascertain that Earth's inner core is probably a hot, dense ball of solid iron, measuring roughly 2,440 kilometers (1,516 miles) across, a little bigger than the size of Pluto.

Evidence also suggests that it demonstrates superrotation, rotating faster than Earth itself.

Researchers first detailed this phenomenon in 1996, with an estimated superrotation rate of 1 degree per year. Vidale and his colleague, Wei Wang, also of UCLA, later revised the rate down to 0.29 degrees per year, using data from underground nuclear tests conducted at the Russian Novaya Zemlya testing site in the 1970s.

In the new research, they went back in time, adding two tests conducted below Amchitka Island in 1971 and 1969. And that revealed something odd.

The data suggested that, rather than superrotating, Earth's inner core was subrotating – that is, spinning more slowly than Earth's rotation, by about 0.1 degrees per year.



A diagram illustrating Vidale and Wang's model. **(Edward Sotelo/USC)**

This, the researchers said, was consistent with oscillation. When in the full swing of its spin, the inner core superrotates, but then it slows down before speeding up again.

"The idea the inner core oscillates was a model that was out there, but the community has been split on whether it was viable," Vidale said.

"We went into this expecting to see the same rotation direction and rate in the earlier pair of atomic tests, but instead we saw the opposite. We were quite surprised to find that it was moving in the other direction."

The six-year periodicity of the oscillation neatly matches other oscillations for which we don't have a confirmed explanation.

Earth's days undergo time variations of plus or minus 0.2 seconds every six years or so, too, and Earth's magnetic field also oscillates with a six-year period. In amplitude and phase, they match the periodicity of the model Vidale and Wang derived for the oscillations of Earth's inner core.

This all means it will require more data to unravel, which could be tricky. The facility that recorded the data from the nuclear tests, the US Air Force's Large Aperture Seismic Array, closed in 1978, and underground nuclear testing is nowhere near as prolific as it used to be.

But further advances in sensor technology could mean that the detailed data needed to probe Earth's inner core isn't so far into the future; the results so far offer a tantalizing hint that Earth's insides are a bit more complex than we knew.

"The inner core is not fixed – it's moving under our feet, and it seems to [be] going back and forth a couple of kilometers every six years," Vidale said.

"One of the questions we tried to answer is, does the inner core progressively move, or is it mostly locked compared to everything else in the long term? We're trying to understand how the inner core formed and how it moves over time – this is an important step in better understanding this process."

The research has been published in *Science Advances*.

https://bit.ly/3NOXt8G

Monkeypox spreading via direct, physical contact, CDC says as US cases hit 45

CDC worked to raise awareness, dispel concerns of airborne transmission.

Beth Mole

The US has now identified 45 monkeypox cases scattered across 15 states and the District of Columbia, while the multinational outbreak has reached more than 1,300 confirmed cases from at least 31 countries. No deaths have been reported.

In a press briefing Friday, US health officials provided updates on efforts to halt the spread of the virus and dispel unfounded concerns that the virus is spreading through the air.

To date, no cases of airborne transmission have been reported in the outbreak, which has almost entirely been found spreading through sexual networks of men who have sex with men. Monkeypox may spread through large, short-range respiratory droplets, and health care providers are encouraged to mask and take other precautions during specific procedures, such as intubation. But the general potential for spread via smaller, long-range aerosols is more speculative and theoretical.

"Monkeypox is not thought to linger in the air and is not typically transmitted during short periods of shared airspace," Centers for Disease Control and Prevention Director Rochelle Walensky said in the briefing. There's no evidence to suggest its spreading by having a casual conversation, passing someone in a store, or touching the same item, such as a doorknob, she noted.

Officials are seeing that the current outbreak is spreading through "close, sustained physical contact," she added. "This is consistent with what we've seen in prior outbreaks and what we know from decades of studying this virus and closely related viruses."

The CDC is still collecting clinical data on some of the country's 45 cases, but of those with data, all are related to direct physical contact, such as sex, CDC officials said. Most are linked to international travel.

"Everyone reports a type of close contact that can be associated with direct, skin-on-skin contact," Jennifer McQuiston, deputy director of CDC's Division of High Consequence Pathogens and Pathology, said in the briefing. "It's often difficult to separate out what a face-to-face [respiratory] droplet transmission might look like compared to direct skin-on-skin contact because people are very intimate and close with one another. But all of our patients have reported direct skin-on-skin contact."

Officials were eager to clarify the points after The New York Times ran a controversial story earlier this week emphasizing the potential for airborne transmission while drawing comparisons to communication failures earlier in the COVID-19 pandemic. Virologists and health experts have already noted that evidence of airborne transmission for monkeypox is thin at best—and clearly not the primary mode of transmission. The article also can increase stigma around the infection, some said, which health authorities have been working hard to avoid.

Real concerns

Moreover, as Walensky noted, unlike the novel coronavirus, which public health officials and virologists scrambled to understand during the mushrooming pandemic, experts have decades of experience with monkeypox. The virus was first identified in monkeys in 1958, and the first human case was seen in 1970. There have been periodic outbreaks in Central and West Africa, where the virus is endemic and exists in animals. For instance, separate from the multinational outbreak, there have been more than 1,400 confirmed and suspected cases in endemic countries this year, including 66 deaths.

While airborne transmission is not a significant concern, health

officials are racing to contain the current outbreak and urging people to take it seriously. Earlier this week, the World Health Organization called on countries to "make every effort to identify all cases and contacts to control this outbreak and prevent onward spread."

"The risk of monkeypox becoming established in non-endemic countries is real," WHO Director-General Tedros Adhanom Ghebreyesus said.

While the outbreak continues to largely be seen in men and, specifically, men who have sex with men, the virus can spread to and infect anyone. There have already been a small number of cases identified in women. "WHO is particularly concerned about the risks of this virus for vulnerable groups, including children and pregnant women," Tedros said.

In Friday's briefing, Walensky and other federal health officials highlighted some of their work to contain the outbreak. That starts with efforts to raise awareness about the disease and what it looks and feels like. Cases can't be tested, treated, or traced unless people know what to look for.

In this outbreak, monkeypox appears to be mainly presenting—but not entirely—as it has in the past: an illness developing five to 21 days after prolonged physical contact with an infected person. Usually, monkeypox begins as a flu-like illness before progressing to include a telltale rash with lesions all over the body, concentrating on the extremities, including the face, palms of the hands, and soles of the feet. The lesions begin as flat but then become raised, filled with fluid, and scab over. The lesions contain large numbers of the virus, and direct contact with them, their fluid, or materials contaminated by the lesions, is how the virus spreads. A person is thought to be no longer contagious when all lesion scabs fall off, and a fresh layer of intact skin has formed.

US cases

But, in this current outbreak, there are some unique aspects of the infections, and the CDC and other health agencies are working on getting the word out on the nuanced differences. In many cases, the rash begins in the genital and anal areas. Sometimes, cases see this rash before flu-like symptoms or are never developing flu-like symptoms. In some cases, the rash spreads to the rest of the body, but sometimes it doesn't, or the spread is relatively limited.

Clinicians have also reported seeing proctitis, CDC's McQuiston noted, which is a painful rectum inflammation. Additionally, localized rashes in the genital and anal areas have been mistaken for common sexually transmitted infections (STIs), including herpes, syphilis, and gonorrhea. The CDC urges health providers to consider monkeypox when conducting STI testing and not rule out monkeypox even if a person is positive for an STI. Some of the monkeypox cases have occurred as co-infections with STIs.

Otherwise, the CDC is looking to expand testing capacity for monkeypox. There are currently 69 labs around the country capable of performing about 1,000 tests per day for *Orthopoxvirus* (the genus of virus to which monkeypox belongs). Positive *Orthopoxvirus* cases are considered presumptive monkeypox cases and the CDC performs confirmatory testing.

Federal health officials are also working with health departments and the CDC to offer treatments, trace contacts, and offer vaccines to those at high risk. So far, the federal government has provided vaccine and treatment resources to 16 states and jurisdictions.

While the CDC presumes that some community transmission is occurring in the US, so far, most of the identified cases still appear to be linked to international travel. Seventy-five percent or more are linked to international travel exposure, McQuiston said. Though she didn't give specific numbers, she said some US cases are contacts of other cases.

"There are some individuals in the United States—it's not many,

just a few—who are not sure how they acquired monkeypox, and that might suggest that there is some community transmission happening at levels that are below what's coming to the attention of public health officials," McQuiston said. But, so far, there's no clustering in a geographical area that would suggest a localized outbreak with community transmission. She said that the unlinked cases could be linked to an imported case that hasn't been identified. That's why awareness and testing are so key.

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New Treatment Repairs Heart Damage After a Heart Attack With No Side Effects

Following a heart attack, cardiac progenitor cells produce healthy tissue

A heart attack, also known as a myocardial infarction, occurs when a part of the heart muscle does not get enough blood. The longer it goes without restoring blood flow, the more damage is done to the heart muscle.

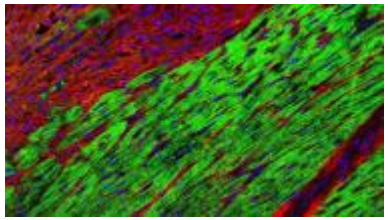
The most common cause of a heart attack is coronary artery disease. A strong spasm, or abrupt constriction, of a coronary artery, which may cut off blood supply to the heart muscle, is another, although less frequent reason.

The human body is incapable of rebuilding damaged tissue following a heart attack due to the heart's incapacity to produce new muscle. Treatment with cardiac progenitor cells, however, could result in the production of functional heart cells in injured regions. A global team introduced this new treatment method in *Nature Cell Biology* on May 12th. Clinical trials should begin within the next two years.

How can heart function be restored after a heart attack? With an estimated 18 million deaths worldwide from cardiovascular diseases each year, according to the World Health Organization (WHO), this is a focus of worldwide research. Treatment using an enhanced pool of human pluripotent stem cell-derived ventricular progenitors, or HVPs for short, might be one viable approach. In a study published in the journal *Nature Cell Biology*, an international team comprised of the Technical University of Munich (TUM) and its university hospital Klinikum Rechts der Isar, the Swedish Karolinska Institutet, the Swedish biotech startup Procella Therapeutics, and the biopharmaceutical company AstraZeneca evaluated this approach.

Heart muscle cells and blood vessels die as a result of many heart diseases. They are replaced by fibrotic scar tissue, which worsens cardiac function. Some animals, particularly amphibians and fish, can heal such injury — a talent that an adult human's heart lacks almost entirely. Stem cell treatment is one experimental strategy for regenerating missing cardiac tissue.

Previous research used heart cells derived from stem cells, specifically cardiomyocytes. However, numerous side effects occurred, including abnormal heartbeats and deadly arrhythmia.



A tissue section shows that already after fourteen days cardiac progenitor cells (green) almost completely colonize damaged areas in the heart. **Credit: Poch et al., Nature Cell Biology**

Cardiac progenitor cells instead of differentiated heart cells

In contrast, the team working with Karl-Ludwig Laugwitz, Professor of Cardiology at TUM, is investigating human ventricular progenitor cells. These cells play a crucial role in the formation of the heart during development. Over time, they differentiate into the various cell types in the heart, including cardiomyocytes. The team has succeeded in producing large numbers of such HVPs from human embryonic pluripotent stem cells. "This represents the culmination of two decades of our work trying to find the ideal cell to rebuild the heart," says Kenneth R. Chien, Professor of

Cardiovascular Research at Karolinska Institutet.

Complex molecular mechanisms

With these cells, the scientists studied the complex molecular processes involved in the repair of damaged areas of the heart muscle. “In laboratory investigations, we were able to show how HVPs can, in a sense, track down damaged regions in the heart, migrate to injury sites, and mature into working heart cells. They also actively prevent the formation of scar tissue by cross-talking with fibroblasts, as we call the cells that form the structural framework for the non-functional connective tissue,” says Prof. Laugwitz, who heads the First Medical Department of TUM’s Klinikum Rechts der Isar.

Successful treatment of pig hearts

As the next step, the interdisciplinary team used pigs to study the effectiveness of treating a damaged heart with HVPs. Physiologically, pig hearts are quite similar to those of humans. As a result, experiments with pigs are often conducted shortly before the start of studies in human patients. The results show that damage to the heart can be reliably repaired even in large animals with no serious side effects observed. “The treatment successfully demonstrated the formation of new cardiac tissue and importantly, improved cardiac function and reduced scar tissue,” says Dr. Regina Fritsche-Danielson, Head of Research and Early Development at AstraZeneca.

Researchers aim at starting clinical studies within the next two years

In the coming months and years, the scientists plan to translate their current research findings to develop a treatment for heart patients. An important intermediate step in the development of hypoimmunogenic lines of HVPs. Currently, it is necessary to inactivate the recipient’s immune system to prevent it from destroying the cell treatment. Hypoimmunogenic cells would eliminate the need for this step because they would not be identified as foreign bodies to the recipient. Further research will be conducted on hypoimmunogenic cells and possible side effects. The aim is to start clinical studies on the therapeutic use of HVPs within the next two years.

“The new insights on the therapeutic use of HVPs represent a milestone in the treatment of diverse patients with serious heart failure,” says Prof. Karl-Ludwig Laugwitz. “Especially older patients with coexisting conditions, for whom major heart surgery would represent an excessive strain, would benefit from treatment with HVPs.”

Reference: “Migratory and anti-fibrotic programmes define the regenerative potential of human cardiac progenitors” by Christine M. Poch, Kylie S. Foo, Maria Teresa De Angelis, Karin Jennbacken, Gianluca Santamaria, Andrea Bähr, Qing-Dong Wang, Franziska Reiter, Nadja Hornaschewitz, Dorota Zawada, Tarik Bozoglu, Ilaria My, Anna Meier, Tatjana Dorn, Simon Hege, Miia L. Lehtinen, Yat Long Tsoi, Daniel Hovdal, Johan Hyllner, Sascha Schwarz, Stefanie Sudhop, Victoria Jurisch, Marcella Sini, Mick D. Fellows, Matthew Cummings, Jonathan Clarke, Ricardo Baptista, Elif Eroglu, Eckhard Wolf, Nikolai Klymiuk, Kun Lu, Roland Tomasi, Andreas Dendorfer, Marco Gaspari, Elvira Parrotta, Giovanni Cuda, Markus Krane, Daniel Sinnecker, Petra Hoppmann, Christian Kupatt, Regina Fritsche-Danielson, Alessandra Moretti, Kenneth R. Chien, and Karl-Ludwig Laugwitz, 12 May 2022, Nature Cell Biology. DOI: 10.1038/s41556-022-00899-8

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Large Study Found a Strange Link Between Eating Fish And Skin Cancer

New research suggests that as with all things, too much good fish could also be a bad thing

Tessa Koumoundouros

More than 3 billion people around the world rely on fish for food. Fish are a favored source of proteins and healthy fats in highly recommended diets, like Mediterranean and Nordic.

But new research suggests that as with all things, too much good fish could also be a bad thing.

A large, long-term study of almost 500,000 people, found people

who eat more fish than the equivalent of half a can of tuna a day were 22 percent more likely to contract a malignant melanoma.

"Melanoma is the fifth most common cancer in the [US] and the risk of developing melanoma over a lifetime is one in 38 for White people, one in 1,000 for Black people, and one in 167 for Hispanic people," explains Brown University dermatologist Eunyoung Cho.

It's important to note that this doesn't at all mean we should avoid eating fish. This study shows a trend, not an underlying cause, which means researchers have not directly demonstrated that eating more fish increases your risk of skin cancer. Also, even if there does prove to be a direct link, the benefits of eating fish would still likely outweigh total avoidance.

However, such a strong link within a big sample size, that makes sense in the wider context of our current environment, does beg for further investigation.

"Although the results are from a cohort study, which means they are observational and hence do not imply causation, they cannot be ignored," says University of Newcastle dietitian Clare Collins, who was not involved in the study. "The role of contaminants that may be present in some fish needs to be considered."

It is well established that toxins in our environment, including those that we know directly cause cancer like heavy metals, build up through the food chain.

For example, Mercury emitted through industrial processes like burning coal finds its way into our waterways where microbes break it down into methylmercury.

This is taken up by plankton and ends up accumulating in the tissues of the shrimp that eat those plankton, then the fish that eat the shrimp, and so on, getting more concentrated the higher up the food chain it goes. This is known as biomagnification.

"We speculate that our findings could possibly be attributed to contaminants in fish, such as polychlorinated biphenyls, dioxins, arsenic, and mercury," says Cho.

"Previous research has found that higher fish intake is associated with higher levels of these contaminants within the body and has identified associations between these contaminants and a higher risk of skin cancer."

The researchers, led by Brown University epidemiologist Yufei Li, used data from the USA NIH-AARP Diet and Health Study, from participants recruited between 1995 and 1996. They collated this with the National Death Index and state cancer registries and found the risk of melanoma was 22 percent higher in those who ate around 43 grams of fish a day compared to those who ate the median amount (around 3 grams per day).

This link was linear, meaning the amount of tuna consumed increased the cancer incidence, and it was consistent across several demographic and lifestyle factors after also considering other risks like mole count, hair color, history of severe sunburn, and sun-related behaviors.

The intake of fish was only calculated at the start of the study though, so this may have changed over the participants' lifetime though.

These findings in no way reduce other well-established causes of skin cancer. "It is critical that we don't confuse or cloud the prevention message," CEO of Melanoma Institute Australia Matthew Browne cautioned in a comment about the study. "The scientific evidence is clear – sun exposure is the single biggest risk factor for developing melanoma."

But as levels of these contaminants increase thanks to intensifying land use and even climate change (mercury concentrations in some waterways has been increasing as rainfall increases) this potential cause of skin cancer shouldn't be neglected. Li and colleagues call for further investigation.

This study was published in *Cancer Causes & Control*.