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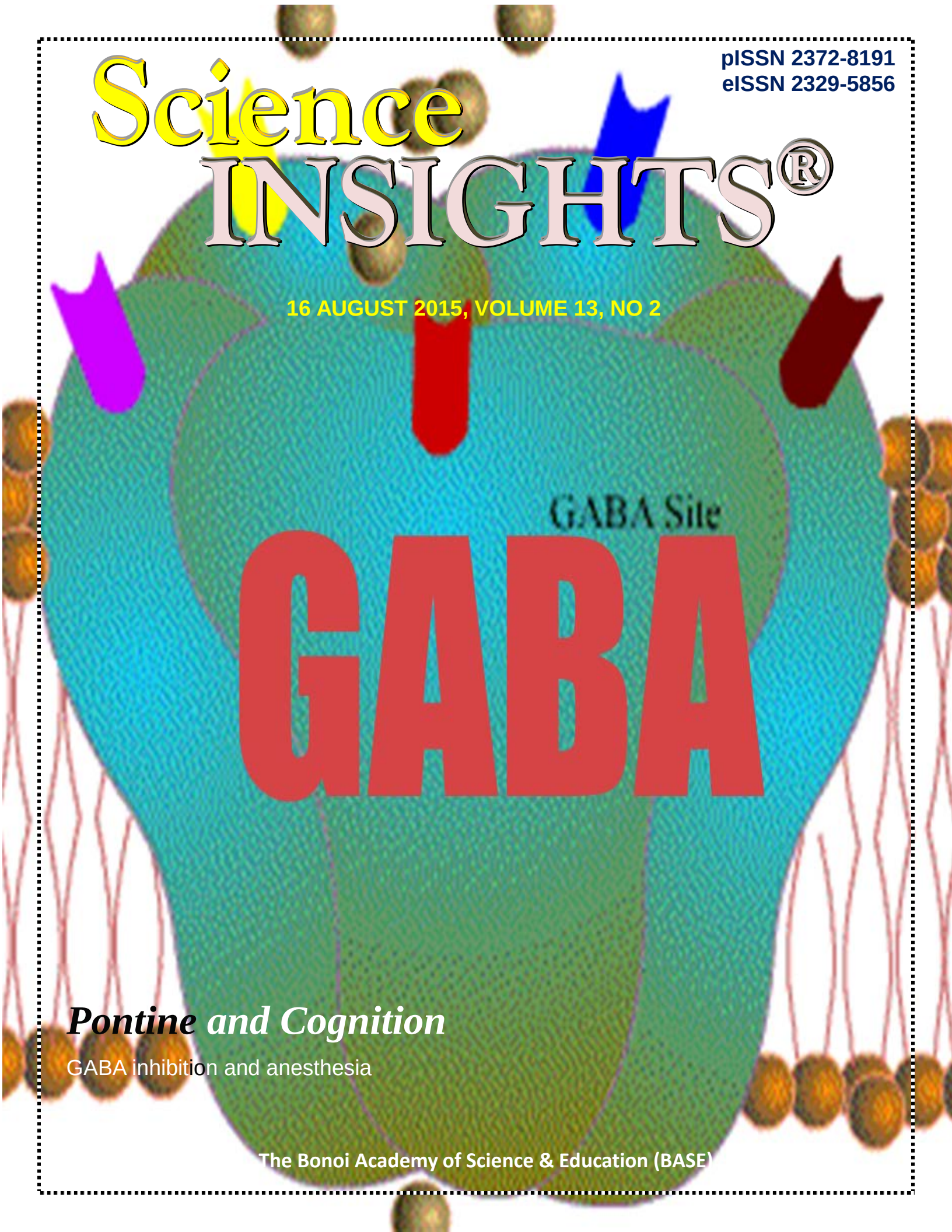


## *Pontine and Cognition*

GABA inhibition and anesthesia

The Bonoi Academy of Science & Education (BASE)

Science INSIGHTS®: the Real Journal of Science and Education

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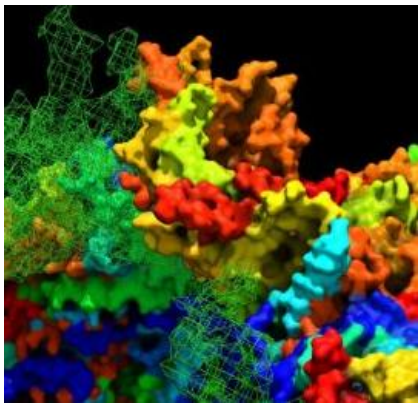
## NEWS





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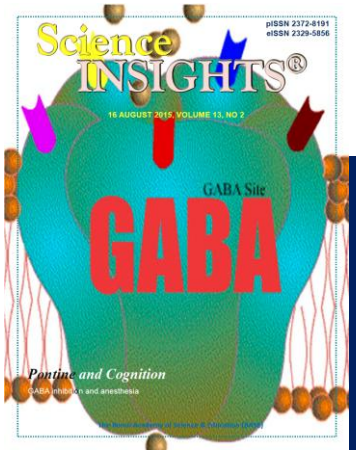


**COVER**

The GABAergic neurotransmission inhibition in the pontine reticular formation might be the mechanistic base of propofol anesthesia, and given an experimental basis of the theory of central nervous inhibition in general anesthesia. See page 483.

*Image: BASE illustrating group*

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BASE

THE BONOI ACADEMY OF SCIENCE & EDUCATION

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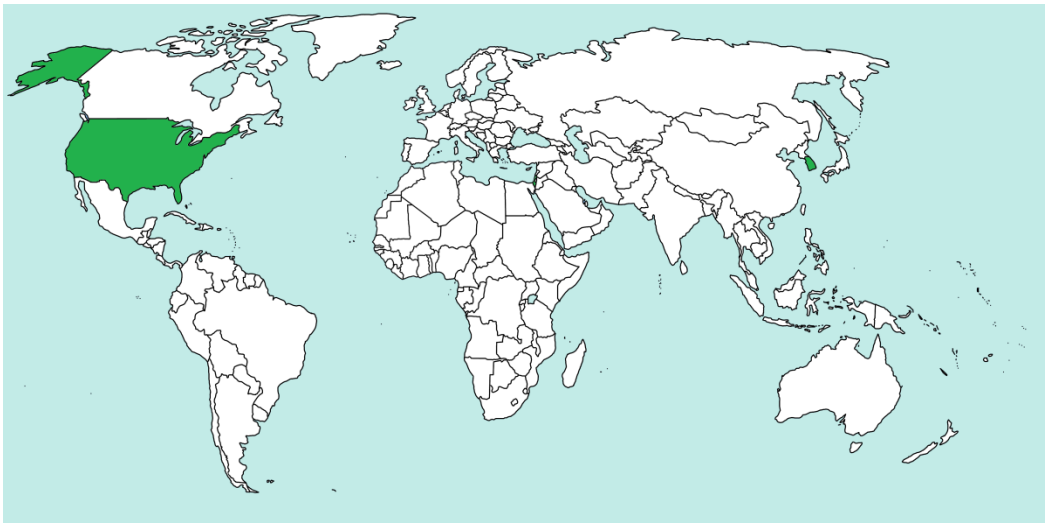
Jerusalem, ISRAEL

## Rare Writing Vanished After Unearthed



Archaeologists digging for ruins ahead of a new construction project in Jerusalem made an incredible discovery—that immediately began to vanish. During the last hours of a "salvage excavation" two months ago, the Israel Antiquities Authority stumbled upon a 2,000-year-old ritual bath when a stone suddenly disappeared into a black hole, reports Haaretz. That hole turned out to be the remains of the bath, accessible by a stone staircase, which includes an anteroom with benches and a winepress. Carved into a natural stone cave, the bath itself wasn't so unusual, but the graffiti that covered the plaster walls was. Archaeologists were therefore horrified to find the Aramaic inscriptions and paintings in mud and soot, dating to the Second Temple era from 530BC to 70AD, per Discovery News, disappearing within hours of their discovery. "The wall paintings are so sensitive that their exposure to the air causes damage to them," the IAA says, per Ynetnews. Crews quickly removed and sealed the plaster so the graffiti, along with a few carvings, can be preserved. Archaeologists say the Aramaic inscriptions are particularly special as few such writings have been found, though the script is hardly legible now. They guess at a few words, including what translates to "served" and the name "Cohen." Still, the inscriptions back up the argument that Aramaic was commonly used at the time and perhaps even the language of Jesus. The plaster also holds drawings of a boat, palm trees and other plants, and what might be a menorah—portrayals of which were then considered taboo. An IAA rep says graffiti in baths may have been "common, but not usually preserved." ■ This article originally appeared on Newser. By Arden Dier.

Jerusalem, ISRAEL

## The Gate to Goliath's Hometown Was Found

An archaeological dig now in its 20th year has uncovered the entrance gate to Gath, the ancient Biblical city of the Philistines and onetime home of the giant Goliath. Before the king of Damascus destroyed it in 830 BCE, Gath was the largest city in the land for hundreds of years, reports the Jerusalem Post. The Bible refers to the massive city gate itself, in the story of David's escape from King Saul to the king of Gath. In addition to the city gate, scientists have also unearthed an "impressive fortification wall," several buildings that include a temple and iron production facility, and what the Post calls the earliest "decipherable" Philistine inscription ever found—which contains two names similar to "Goliath." "After finding a huge fortification, it's clearly the most important city of the 10th and ninth centuries," says the archaeologist in charge of the dig, per i24. The long-term dig is part of the

Ackerman Family Bar-Ilan University Expedition to Gath, a look at the archaeology and history of one of the largest "tells" (aka ancient ruin mounds) in Israel. The area in central Israel, in the Tel Zafit National Park in the Judean Foothills, has been inhabited almost continuously since the 5th millennium BCE, the researchers note in a press release.■ This article originally appeared on Newser. By Elizabeth Armstrong Moore.

**East Lansing, USA**

## Clock Was Turned Back by 3D Supernova Simulation on Star Explosions

Enormous stars collapse in ultramassive supernova explosions — now in 3D! For the first time ever, researchers have turned back the clock on a star's final moments to simulate how wrinkles in its violent collapse trigger a vast explosion. As massive stars age, they build up more and more iron in their cores, which cannot be used by the star as fuel. Eventually, when the core gets big enough, it collapses and, sometimes, incites a huge explosion. Most simulations start with a star already on the brink of collapse, with the different layers inside the star in perfect concentric rings. But models with those simplified starting conditions stubbornly refuse to blow. "Almost all supernova simulations follow about 1 second of physical time," said Sean Couch, a physicist and astronomer at Michigan State University and lead author of the new paper. "What we did that was different is, we wound the clock back 3 minutes. That's really challenging; it's never been done before. We then show this has an important and big impact on the likelihood for successful supernova explosions." Such a feat was very technologically demanding, but it proved necessary because models starting right at the collapse just wouldn't explode in a supernova, Couch said. Instead, the shock would peter out, and the collapsing star would become a black hole. "It's the difference between an onion" — the old, simplified starting point — "and cabbage," Couch told Space.com. "You slice cabbage, and there's wrinkles on the inside. It's still basically a sphere, but it's not nearly as concentrically layered as the onion will be." Those extra few moments, where the "onion" model had the chance to wrinkle into a "cabbage" more like a complex, real star before collapsing, seem to cause enough turbulence to push the system over the edge into a supernova. Just modeling those extra 3 minutes

back in time was a huge technological challenge, Couch said — the simulation on the supercomputer took about one month to complete, and they could run it only once. Therefore, the researchers chose their star carefully: one about 12 million years old, and 15 times the mass of the sun, that they thought would likely go supernova. To extend their research, the scientists are modeling four types of stars they think might lead to supernovas, and they're hoping to push the simulation even further back in time. Couch said it might be possible to understand and model the forces within a star, to go as far as an hour before the collapse. The difficulty with modeling stars is the difference in timescales, Couch said — a star evolves over the course of millions of years, but the supernova mechanism is on a millisecond scale. Incredible levels of precision and complexity are needed to understand that millisecond. "We know that we've been working with unrealistic initial conditions; it's just only come to light in the last couple of years that it matters," Couch said. "What we're learning now is that the details of these stars matter." ■ This article originally appeared on Space.com. By Sarah Lewin

## Harrisburg, USA

## New Dinosaur's Powerful Sniffer Helped It Track Prey

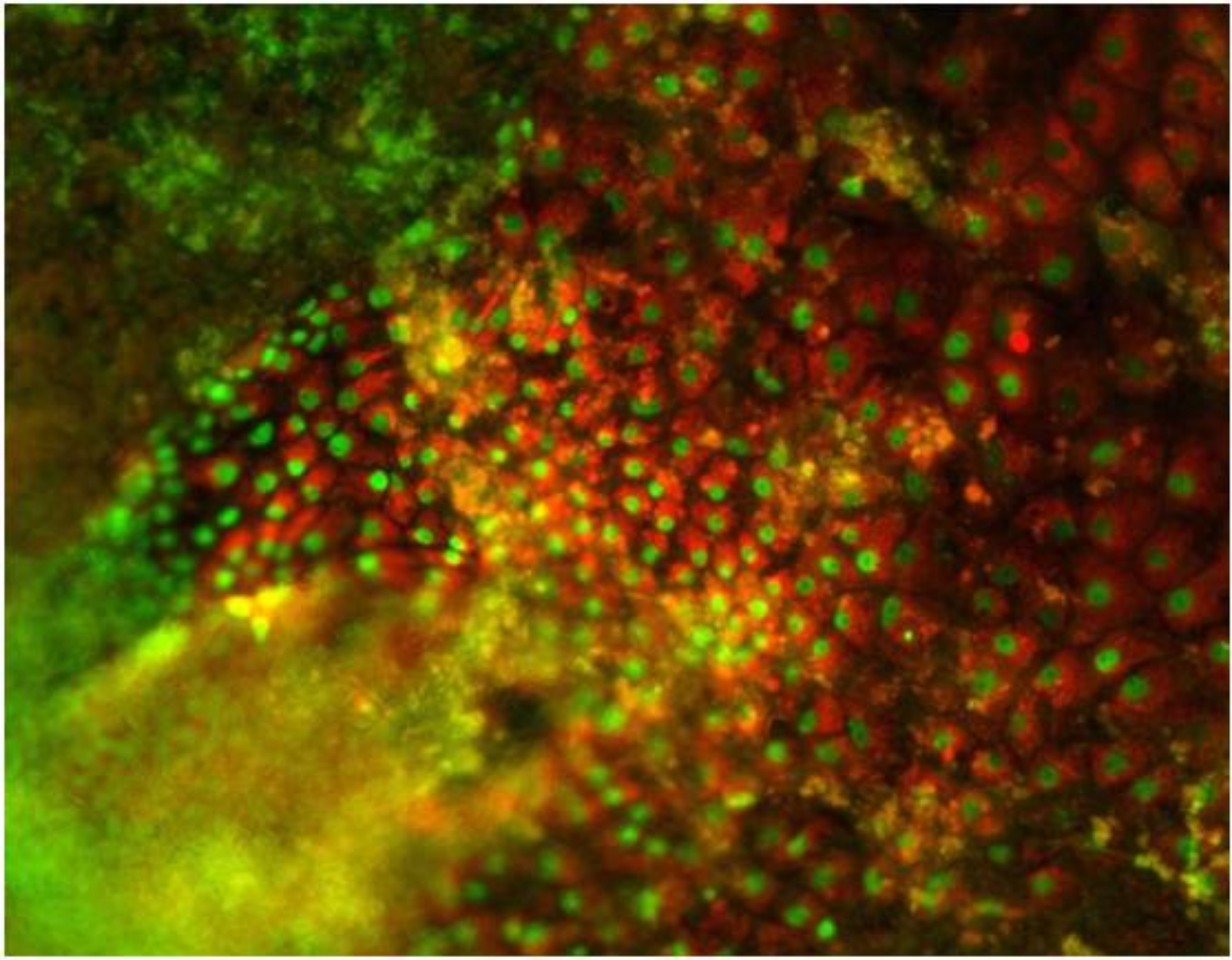
Jasinski, a doctoral candidate in the Department of Earth and Environmental Science and curator of paleontology and geology at the State Museum of Pennsylvania, was reviewing the museum's collection when he found a fossil that caught his eye. “As soon as I looked at the specimen, I could tell it was not the dinosaur it was thought to have been,” he told Live Science. The fossil was originally believed to be *Saurornitholestes langstoni*, a species within the Dromaeosauridae family. Dromaeosaurs are colloquially referred to as raptors, due to the popularization of a specific genus of dromaeosaur: *Velociraptor*. The specimen is a skull fragment with an unusually large structure in the forebrain, known as the olfactory bulb. This suggests the dinosaur had a sharp sense of smell, Jasinski said. The dinosaur's acute nose likely helped it to be a competitive predator, potentially by allowing it to hunt at night, the researchers said. This keen sense of smell could have also aided in communication — namely, by helping the dinosaur detect chemical signatures called pheromones in other dinosaurs, which is crucial for animals that live and hunt in packs. Jasinski compared the fossil to other dromaeosaurs using holotype specimens, which essentially act as the dictionary definition of a species. Holotype

specimens are agreed upon by scientists to be the most representative examples of an animal. Jasinski compared the skull fragment to available samples in the western United States, Canada, Mongolia, China, and Europe, but his fossil remained unique. This gave him reasonable grounds to declare that he had found something entirely new:*Saurornitholestes sullivani*. *S. sullivani*was relatively small compared to other species alive during the late Cretaceous, but its speed, agility, and impressive olfactory capability gave it a necessary advantage over other predators. It could have brought down a meal and eaten quickly before a tyrannosaur could come by and capitalize on the food. It was thriving about 8 million to 10 million years before the dinosaurs died out, when a good mix of herbivores and carnivores were coexisting. At the time, a large seaway divided North America into two major continents: Laramidia to the left of the seaway and Appalachia to the right. *S. sullivani* lived on the eastern portion of Laramidia. Most large herbivores, like duck-billed dinosaurs, would have been too large for a small dromaeosaur to take down, so packs of *S. sullivani* would target juveniles or subadults. Nick Longrich, a senior lecturer at the University of Bath, whose research focuses on the end-Cretaceous mass extinction that wiped out the dinosaurs, has discovered new dinosaur species in the same manner as Jasinski. Rummaging through forgotten museum collections is a far cry from the romanticized, Indiana Jones-esque paleontological fantasy, he said. “I’ve done fieldwork and love the badlands but it’s expensive and it’s too much of a lottery," Longrich told Live Science. "Everyone assumes it’s a great way to do science but National Geographic does not cover all the failed field expeditions." One of the main challenges is that there are gaps in our knowledge of the many species that once roamed the Earth. “The fossil record is incomplete enough that if you’re in a new area or a new time, there’s a fair chance that the dinosaurs there are going to be distinct," Jasinski said. For instance, scientists might discover a toe from a brand new species, but such subtle differences may be unrecognizable or impossible to prove. "[T]hings that we call separate species today would be very, very hard to tell apart based on their skeleton (crow versus raven, for example),” Longrich told Live Science in an email. He went so far as to suggest that because *S. sullivani* is so noticeably distinct to the naked eye, Jasinski may have identified an entirely new genus, rather than just a new species. Reviewing and reassessing fossils is more common in some collections than others, Longrich said. “Older collections have fewer new species because they are better studied … I’d be willing to bet there are a ton of new species in the smaller, more obscure fossils, and certainly in the more fragmentary stuff such as the one that [Jasinski] has found,” he added. Jasinski said he hopes his discovery will inspire others to look at neglected specimens in a new light.■ This article originally appeared on Live Science. By Kate Goldbaum

### Jerusalem, ISRAEL

## Functional Liver Cells from Stem Cells

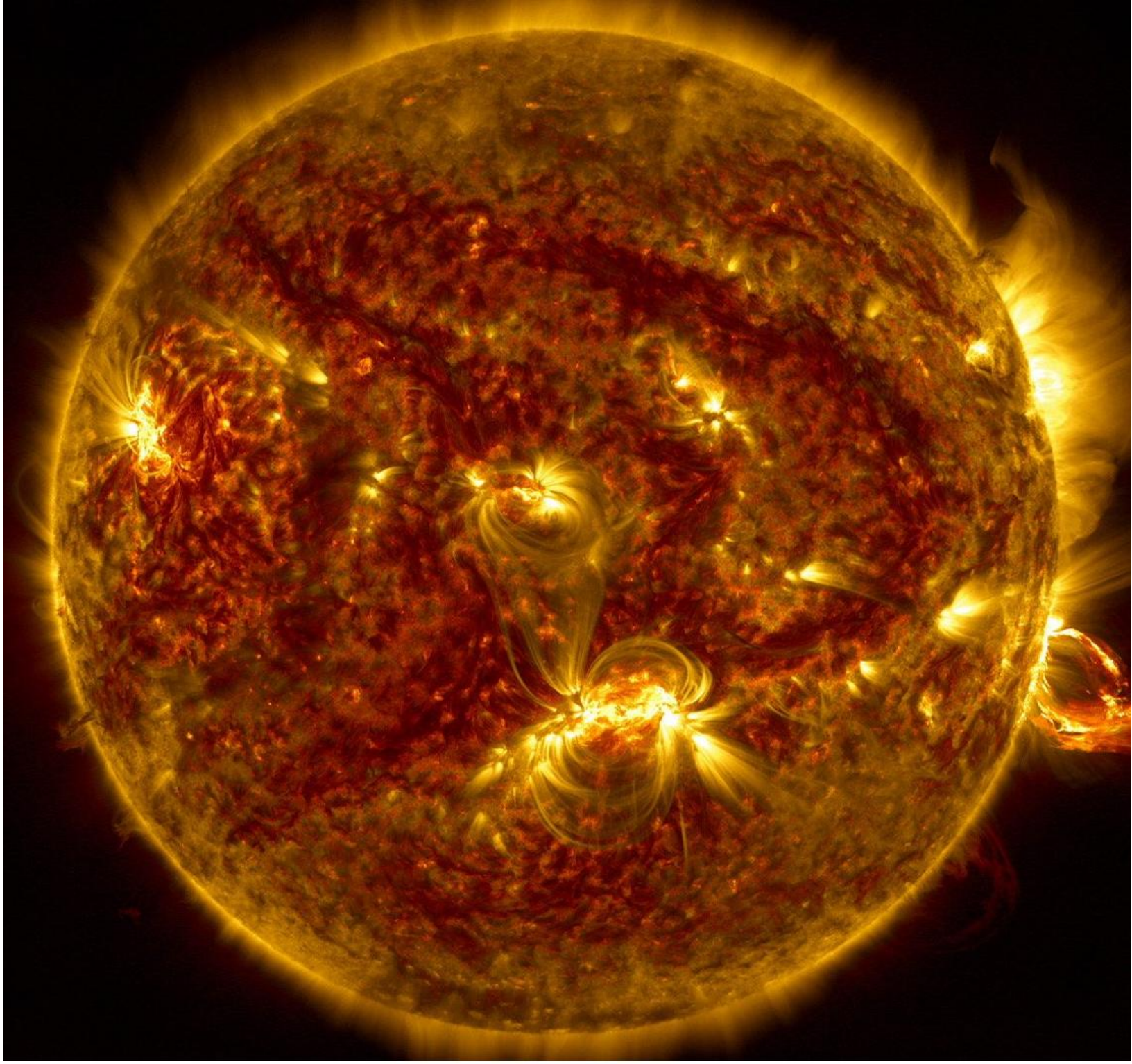
The liver plays a critical role in human metabolism. As the gatekeeper of the digestive track, this massive organ is responsible for drug breakdown and is therefore the first to be injured due to overdose or misuse. Evaluating this drug-induced liver injury is a critical part of pharmaceutical drug discovery and must be carried out on human liver cells. Regretfully, human liver cells, called hepatocytes, are in scarce supply as they can only be isolated from donated organs. Now, in research published on the cover of the July edition of Hepatology, scientists from the Hebrew University of Jerusalem's Alexander Grass Center for Bioengineering report that they produced large amounts of functional liver cells from human embryonic and genetic engineered stem cells. "This is quite a revolution for pharmaceutical drug discovery," said Prof. Yaakov Nahmias, the study's senior author. "While other groups have been able to produce liver cells before us, their cells showed little functional activity, and could not be reliably used for drug discovery. In fact, up until now stem cell-derived hepatocytes showed little ability to predict clinical outcome." The limited availability of functional hepatocytes for drug testing is a major bottleneck bringing pharmaceutical companies to spend $1 billion/year on liver cells



alone. "Our ability to produce an unlimited supply of functional liver cells from human pluripotent stem cells can change all that," said Nahmias. The breakthrough came with the birth of Nahmias' baby girl earlier this year. "I watched her feeding just moments after birth, and realized this is the first time her liver started working," said Nahmias. "Nobody had thought of mimicking this part of human development before, so that's exactly what we did." The team went on to discover that the bacteria populating the infant gut moments after birth produce vitamin K2 and bile acids that activate the fetal liver's dormant drug metabolism program. The groundbreaking work further demonstrated that liver cells produced from either embryonic stem cells or genetically engineered skin cells, can detect the toxic effect of over a dozen drugs with greater than 97% accuracy. "The implications for liver biology and drug discovery are quite staggering," said Prof. Oren Shibolet, Head of the Liver Unit at the Tel-Aviv Sourasky Medical Center, who was not involved in this study. "The method provides access to unlimited amounts of functional liver cells and is likely to critically improve our ability to predict drug toxicity, which was previously limited by the unavailability of liver cells. Furthermore, as gut bacteria develop differently in infants delivered by caesarean section, the mode of delivery can possibly affect newborns' liver maturation. Current practice is to routinely administer Vitamin K to newborns. The data presented suggest that parents abstaining from this practice may cause liver maturation and drug metabolism in their children to develop quiet differently."

## Providence, USA

## A New Super Material That Can Withstand



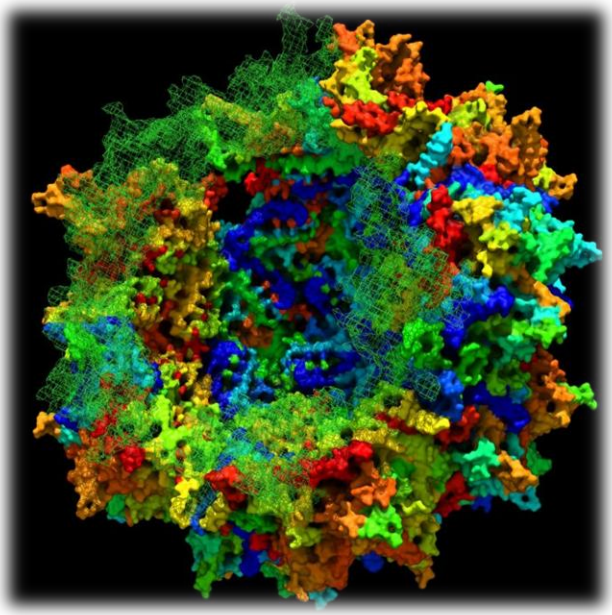
## Temperatures More Than 7,460 Degrees

A new substance, unlike any on Earth, could have one of the highest melting points we've ever seen, theoretically withstanding temperatures of more than 7,460 degrees Fahrenheit. To put that into perspective, this is about 180F warmer than the liquid iron and nickel outer core of Earth, about 2/3 the temperature of the surface of the sun, and almost 360F higher than the current record holder of the highest experimentally-recorded melting point — the temperature at which a substance turns from a solid into a liquid. That is, however, if the team can successfully synthesize it. There is no other compound like this on Earth, and it doesn't occur naturally, study researcher Axel van de Walle, of Brown University, told Tech Insider in an email. These types of materials are tricky to study in a lab given that, well, you'd have to replicate mind-bogglingly scorching temperatures — think surface of the sun hot — to understand their heat-resistant properties. So scientists rely on computers to simulate what would happen to different combinations of substances under a variety of con-

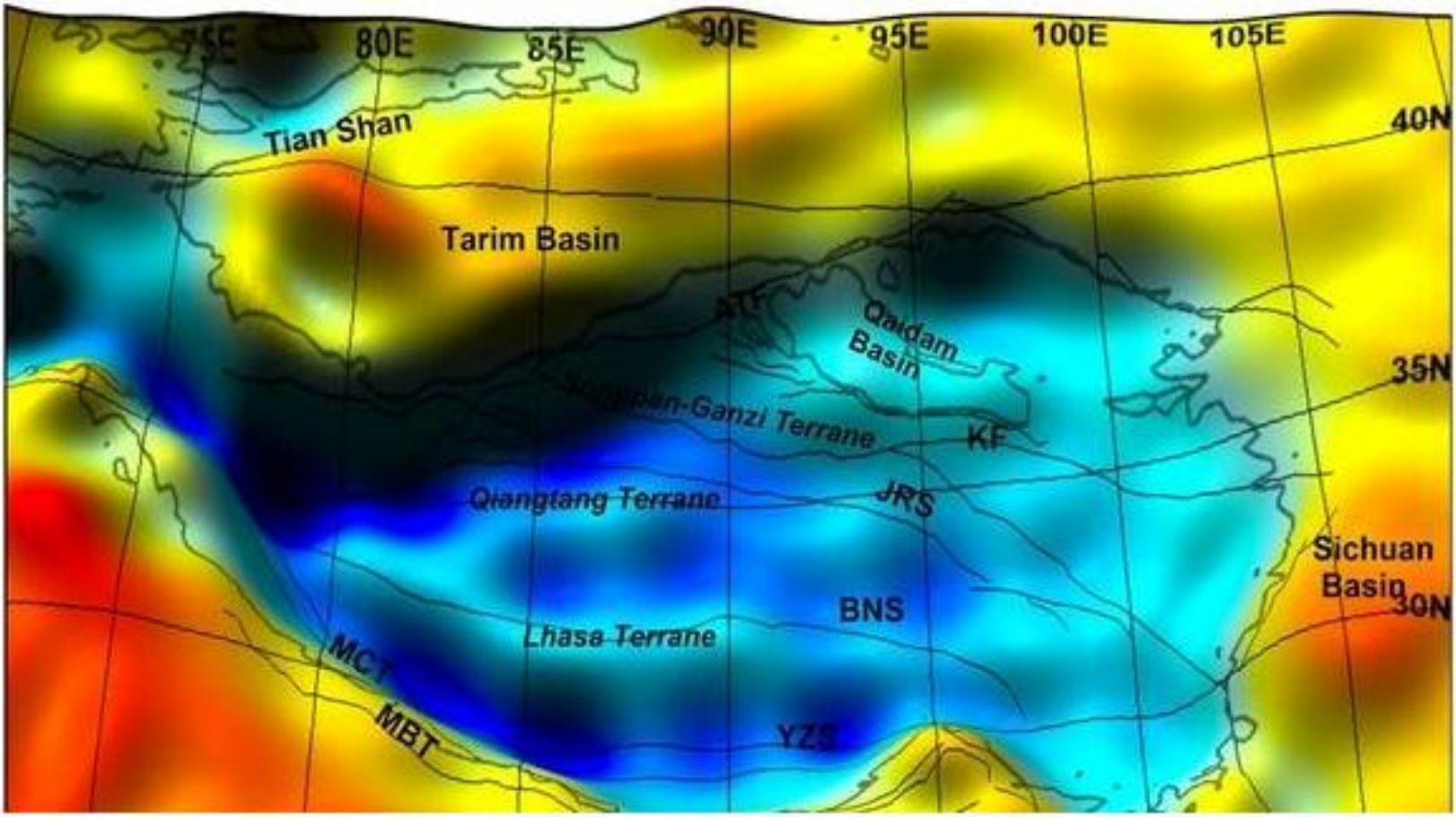
ditions. By taking a page from the current record holder of the highest experimentally-recorded melting point, a mixture of the three elements hafnium, tantalum, and carbon, the team figured that they could find an even better atomical arrangement to make a more heat-resistant substance. After analyzing the record-holder's quantum mechanical properties, the team probed other compounds that might have the same but possibly stronger heat-resistant capabilities. And they found such a substance — or more accurately, they found an optimal arrangement — made of the following elements: hafnium, nitrogen, and carbon. While nitrogen and carbon are common and abundant on our planet, the lesser-known element hafnium — the shiny, silver metal that was discovered in 1923 — is the 45th most abundant element in Earth's crust. "It's not common enough to make cars out of it, but common enough for specialized aerospace applications," van de Walle told us. "It's 100 times cheaper than gold." If their powerful computational approach checks out, this substance would shatter the current world record by 360F. "Melting point is a really difficult prediction problem compared to what has been done before," co-author Axel van de Walle said in a press release. "For the modeling community, I think that's what is special about this." The team and their other collaborators have secured the resources to begin making the substance — the next step in the process. They hope to make something within the next year or so, van de Walle told Tech Insider. And its applications could be endless — from heat shields on hypersonic vehicles to coatings for jet engines. This type of work in general could contribute to a new class of high-performance materials, though it's not clear whether the compound itself will be a useful material, according to a press release. But as for now, it won't get us set on a journey to the sun. But we can still dream.■ This article originally appeared on Tech Insider. By Julia Calderone.

**Boston, USA**

## Millennia-Old Viruses Were Resurrected for Use in Gene Therapy



Scientists have successfully reconstructed a virus thousands of years after it became extinct, a development they believe could herald a new step in treating genetic diseases such as cystic fibrosis and muscular dystrophy. By creating an evolutionary history of adeno-associated viruses (AAVs), which infect humans and primates but do not cause disease, researchers from Harvard Medical School were able to construct Anc80, an ancestral virus which they believe to be between 2,000 and 200,000 years old. A study published in the journal Cell Reports reports that the researchers utilised the ancient virus as a vector—a harmless biological vehicle used to transfer genetic material to a target cell—to safely treat liver, muscle and retina conditions in mice. Reproductive material was removed from the viruses, as gene therapy is used to target specific deficiencies and does not require the viruses to reproduce. The researchers did not encounter any toxic side-effects, though they caution that further tests will be required. Luk Vandenberghe, director of the Grousbeck Gene Therapy Center at Harvard, says that the study could provide a first step towards the creation of fully synthetic viral vectors which could be used to treat genetic disorders. Many of the viruses currently used as vectors in the field of gene therapy are modified forms of viruses which humans have encountered before, which means that the body's immune system can attack the viruses, rendering the therapy useless. "Historically, viruses or modified viruses have been the most effective way to do gene therapy, to transfer genes into cells, be-




cause we're banking on the innate properties of viruses," says Vandenberghe. "We actually believe our work is a first step [towards synthetic vectors] because we have generated a synthetic virus, something that is not currently present in nature." Gene therapy, where genes are used to combat or prevent diseases caused by genetic mutations, is showing great promise for treating a range of diseases. Earlier this month, trials of a form of gene therapy for cystic fibrosis, where sufferers breathed in healthy genes through a ventilator, showed promise in stabilising and in some cases improving the damaged lungs of patients. Cystic fibrosis affects an estimated 70,000 to 100,000 people worldwide, and the life expectancy for sufferers ranges from 15 to 40 years. A recent study by the Swiss Federal Institute of Technology and Harvard Medical School also found that gene therapy could be used to treat hereditary deafness in children, after viral vectors were successfully used to transfer healthy genes into the ears of deaf mice. Viral vectors have also been successful in clinical human trials for gene therapies to treat haemophilia, a bleeding disorder where blood fails to clot properly, with the therapies found to improve symptoms for up to four years in patients. The simple structure of viruses, which consist of a strand of DNA or RNA surrounded by a protective protein coat, means they are ideal for infiltrating the immune system and delivering healthy genes to a target area. Vandenberghe hopes that the technique pioneered in this study will hold promise for treating many diseases using once-extinct viruses as vectors for transferring genes. "Gene therapy is an entirely novel class of drugs and theoretically, it actually has the potential of addressing almost any disease under the sun," he says. ■ By Conor Gaffey.

### Seoul, KOREAL

## Weird Rock Beneath Tibetan Plateau

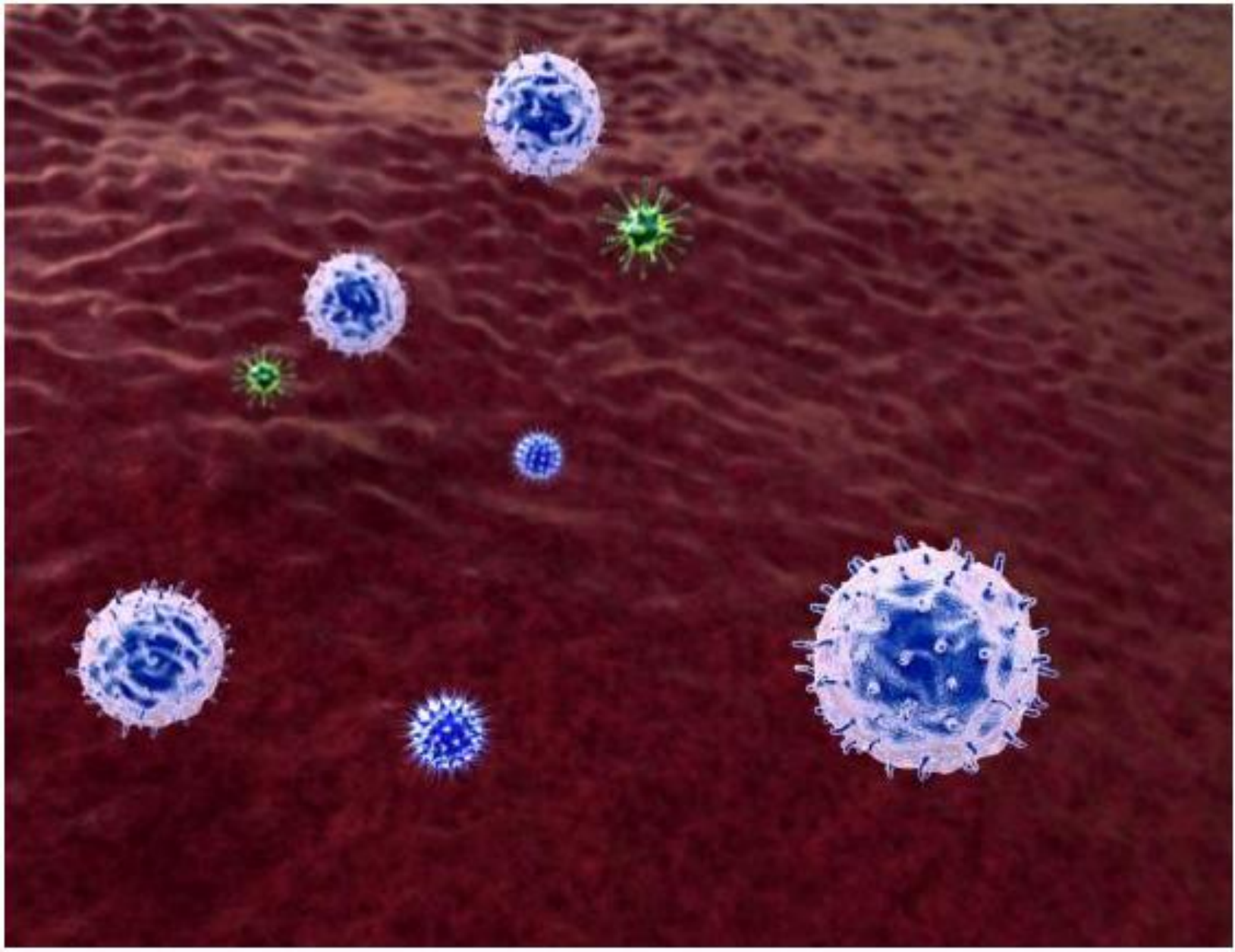
Satellite measurements have provided a new view of the Moho under the Tibetan Plateau, where the Indian plate is violently butting into and diving beneath the Eurasian plate. The Moho is the layer at the deepest edge of Earth's light crust, before the mantle's dense, flowing, soft rock. Below continents, the Moho is usually found about 21 miles (35 km) down from the surface. But at the Tibetan Plateau, where the crust is particularly thick, the Moho is found 40 miles (65 km) down; at the western part of the plateau, it dives as far as 50.9 miles (82 km) deep. The new data also shows that the Moho under the plateau is not a flat layer, but is rucked into a series of bumps

and troughs, like a kicked-up rug. "It could be said that the Moho topography holds the geohistory of the region like the formation of folded mountains," study researcher Young Hong Shin of the Korea Institute of Geosciences and Mineral Resource told Live Science. Shin and his team used eyes in the sky to delve into the Moho's secrets. Scientists tried to drill down to the Moho from the seafloor, where the crust is thinnest, in a project dubbed "Project Mohole" between 1958 and 1966.]The effort unfortunately failed, though it did sample the second layer of the Earth's crust for the first time, according to the National Academies of Science. More recently, the International Ocean Discovery Program (IODP) has declared its intentions to try to reach the Moho again with the Japanese research vessel "Chikyu." However, maintenance issues with the vessel mean that seafloor drilling with the ship will not resume until 2016, according to the IODP. Fortunately, satellites can give scientists a good view of deep structures. The researchers have used two satellite missions: NASA's Gravity Recovery and Climate Experiment, or GRACE, and the European Space Agency's Gravity field and steady-state Ocean Circulation Explorer, or GOCE. With these satellites, researchers were able to detect small changes in the force of gravity caused by the Earth's topography and varying density. Based on these gravity measurements, the team then created a virtual model of the Moho under the Tibetan Plateau. They found that the pressure of the Indian plate pressing into the Eurasian plate buckles the crust, forcing it to climb up (creating the Himalaya mountains) or dive down (becoming the base of the thick Tibetan Plateau). This pattern matches records made by GPS devices that measure the movement of the Earth in the region, Shin said. The Himalayan region is famously the site of seismic activity, such as the magnitude-7.8 earthquakethat struck Nepal in April 2015. The new research won't lend itself to anything as straightforward as earthquake predictions, Shin said. What it can do, he said, is reveal the deformities of the crust, helping to elucidate how the plate collision works. The mechanisms don't just affect earthquake hazards, but also the long-term building of mountains and basins. "In the near future, we'll submit an improved model covering up to [the] upper crust," Shin said. That model should provide something of a backdrop of the region's tectonics, helping to describe the stage upon which earthquakes are set, he said. The researchers reported their findings in the journal Scientific Reports. ■ This article originally appeared on Live Science. By Stephanie Pappas.

### San Diego, USA

## Blood Cancer Drug Reaches Cells Hiding in Bone Marrow

A new drug aimed at dormant cancer stem cells that hide in the hypoxic zones of bone marrow, where most drugs can't reach, is currently entering 5 Phase II clinical trials after it was shown to make blood cancer treatment more effective. Researchers in a Phase I clinical trial, the results of which are published in The Lancet Haematology, found that the drug vismodegib was effective against three types of blood cancer -- refractory or resistant myeloid leukemia, myelodysplastic syndrome and myelofibrosis. Vismodegib inhibits the Hedgehog signaling pathway, which is essential to both vertebrate embryonic development and has been implicated in the development of some cancers. The drug, trade name Erivedge, is already approved in the U.S. and Europe for treatment of metastatic or locally advanced basal cell carcinoma. "Our hope is that this drug will enable more effective treatment to begin earlier and that with earlier intervention, we can alter the course of disease and remove the need for, or improve the chances of success with, bone marrow transplantation," said Dr. Catriona Jamieson, chief of the Division of Regenerative Medicine in the School of Medicine at the University of California San Diego, in a press release. "It's all about reducing the burden of disease by intervening early." Preclinical research showed the drug could "coax" dormant cancer stem cells in hypoxic zones to begin differentiating and enter the bloodstream, where they can be attacked by the chemotherapy and the immune system. In the study, researchers treated 47 adults with blood and marrow cancers with with the drug in 28-day cycles. Treatment cycles were continued with escalating doses until a participant experi-

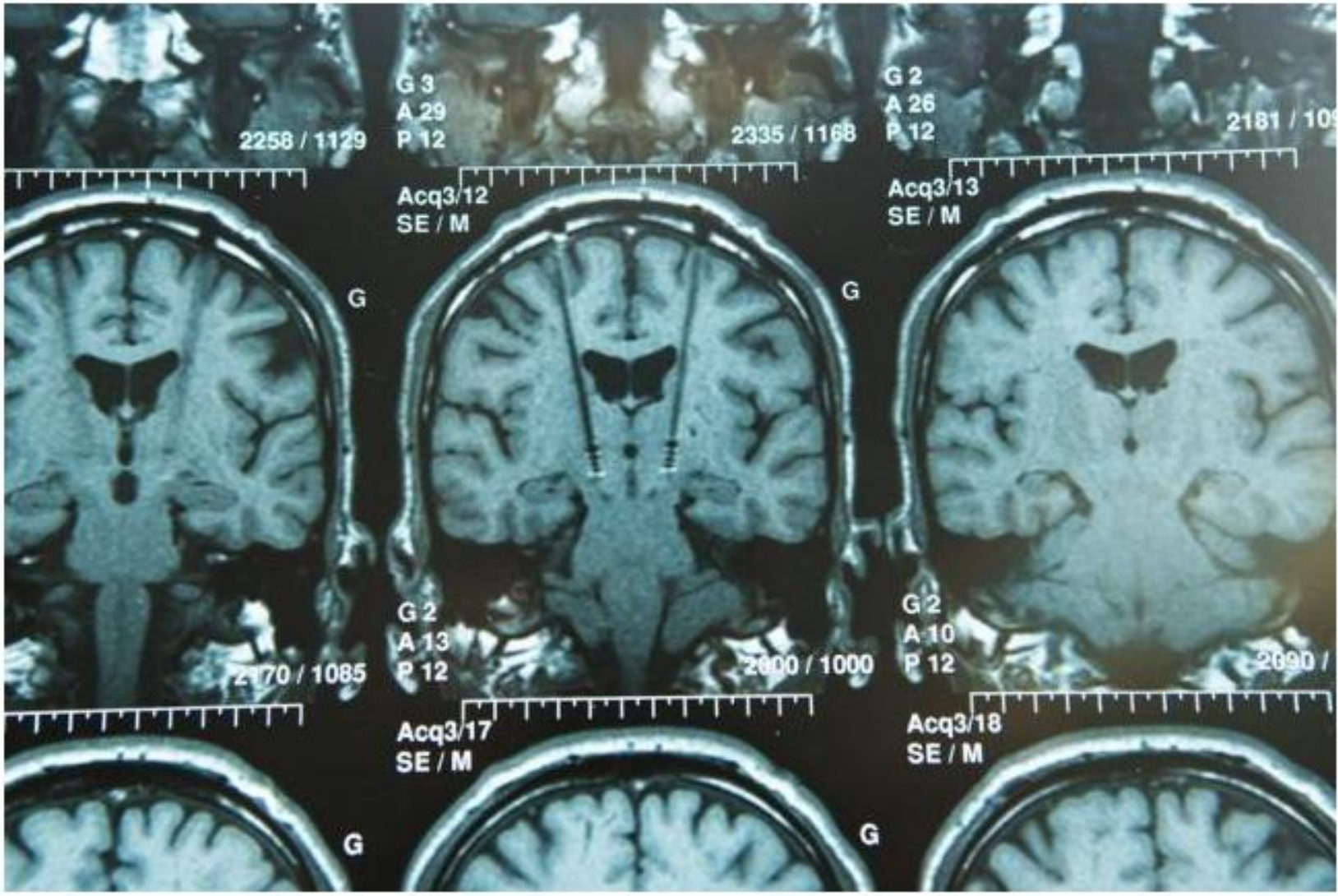


enced adverse effects with no improvement in their condition. The participants who did not have adverse reactions or serious side effects continued to receive treatment cycles of the drug. Serious adverse effects were seen in only 3 of the participants, though 60 percent of the group experienced treatment-related problems. Nearly half the people in the study saw positive clinical activity as a result of treatment with vismedogib, the researchers said, and 5 Phase II clinical trials are being scheduled for the drug for use with blood cancer. "This drug gets that unwanted house guests to leave and never come back," Jamieson said. "It's a significant step forward in treating people with refractory or resistant myeloid leukemia, myelodysplastic syndrome and myelofibrosis. It's a bonus that the drug can be administered as easily as an aspirin, in a single, daily oral tablet." ■ By Stephen Feller.

### Philadelphia, USA

## Deep Brain Stimulation Fails to Improve Depression Symptoms

The results of the first large-scale clinical trial using deep brain stimulation, or DBS, to treat depression failed to show a significant improvement in symptoms. DBS has previously been shown in smaller studies to be effective for depression and obsessive-compulsive disorder, and has been shown to be highly effective in treating Parkinson's disease, essential tremor, and other neurologic conditions. DBS therapy requires doctors to drill a small hole in the skull and insert an electrode into the brain. The electrode delivers electrical impulses designed to block neural impulses from the specific part of the brain that is thought to be the source of the symptoms. Researchers enrolled 30 patients with treatment-resistant




depression in the sham-controlled study, with some receiving impulses and some receiving "sham" placebo treatment for 16 weeks. Improvement in symptoms was measured by the Montgomery–Åsberg Depression Rating Scale, a series of 10 questions used to numerically measure responders' symptom levels. The group that received actual treatment had a 20 percent response rate to treatment on the scale, while the sham group had a 14 percent response rate. "While initial open-label trials of DBS at the ventral capsule/ventral striatum target were promising, the results of this first controlled trial were negative," said Dr. Darin Dougherty, director of neurotherapeutics at Massachusetts General Hospital, in a press release. "Alternative study designs will have to be considered as we conduct future clinical trials in this critical area." Despite a 20 to 26 percent response rate from patients who received actual treatment over the course of 12, 18 and 24 month followups, the researchers said DBS treatment for depression needs at least to be rethought based on the negligible difference between patients who received electrical impulses and those who did not. "This study raises serious questions about the advisability of continuing to stimulate these reward regions in the manner employed in this study," said Dr. John Krystal, Editor of Biological Psychiatry. "It is critical to understand that this study is not a universal indictment of DBS as a strategy for depression. It may turn out that stimulating other brain regions or stimulating these regions in different ways could provide important benefit." ■ By Stephen Feller.

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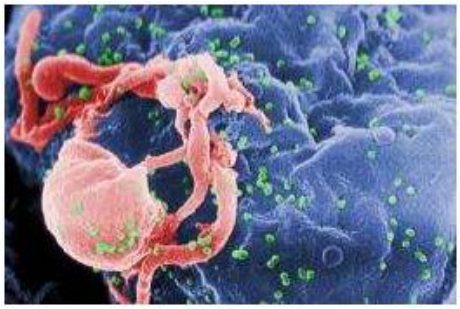
MEDICINE, UK

## HIV Grows Despite Treatment

During treatment for HIV the virus hides in blood cells that are responsible for the patient's immune response. The virus does this by inserting its own genetic information into the DNA of the blood cells, called CD4 T lymphocytes. The study by the University's Institute of Infection and Global Health measured the levels of integrated HIV in the CD4 cells of patients undergoing uninterrupted treatment for up to 14 years, and compared patients receiving treatment for different lengths of time. The researchers discovered that the amount of HIV found to be integrated in the CD4 cells was undiminished from year 1 to year 14. The research demonstrates that whenever a CD4 cell multiplies to produce more cells, it copies itself and also copies the HIV genes. This process - a sort of silent HIV replication - means the virus does not need to copy itself, produce new virus particles, and infect new CD4 cells - but is automatically incorporated at the birth of the cell. Anti-retroviral therapy is given to HIV patients to stop the production of new virus which prevents the infection and death of CD4 T-lymphocytes and the progression of the disease to full-blown AIDS. Advances in anti-



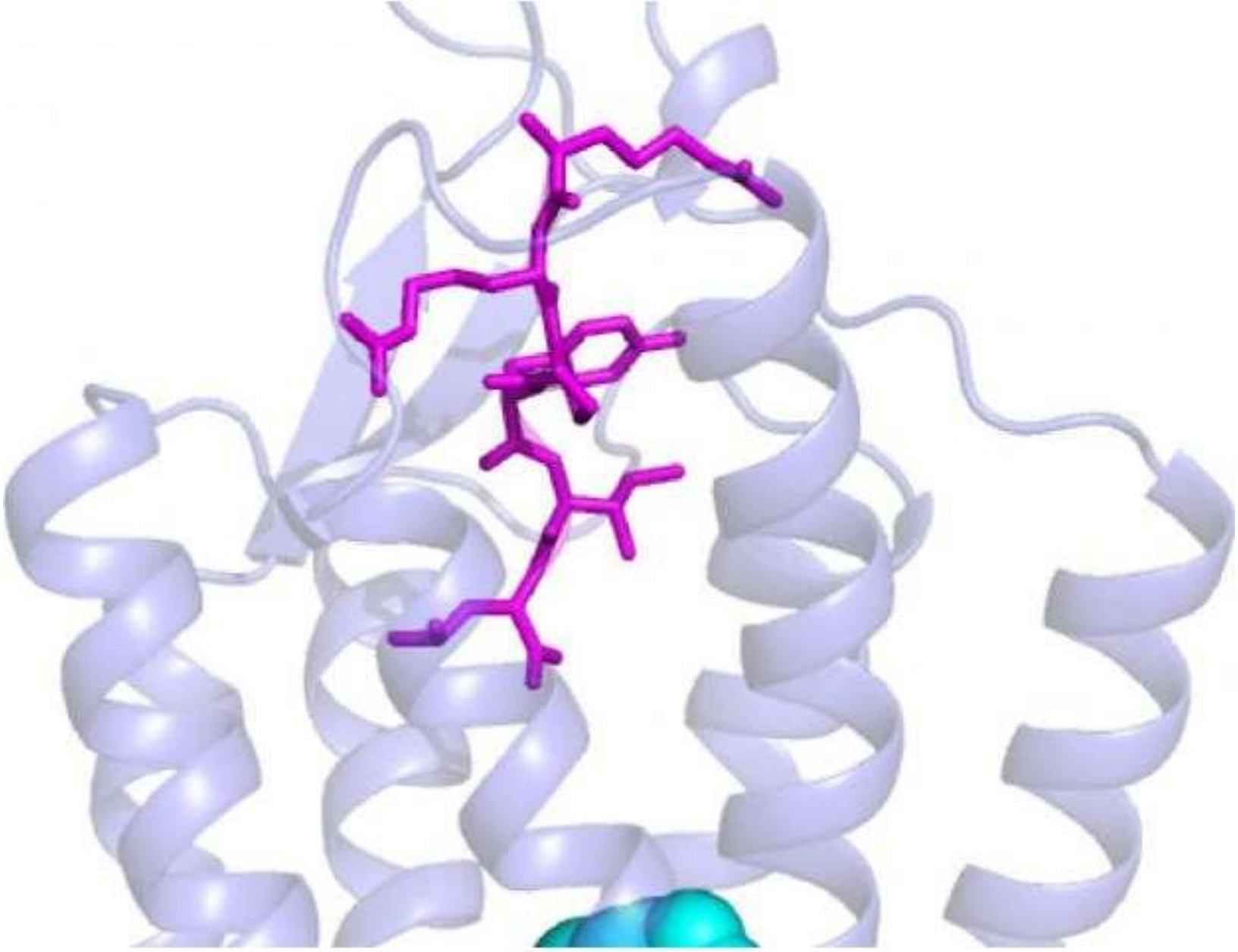
retroviral therapy over the last 30 years mean that most patients can have their virus suppressed to almost undetectable levels and live a long and healthy life. It had been thought that after many years of successful treatment, the body would naturally purge itself of the virus. Professor Anna Maria Geretti, who led the study, said: "This research shows that sadly, the HIV virus has found yet another way to escape our treatments. "We always knew HIV is difficult to suppress completely and that it hides inside CD4 cells, but we always hoped that as the body gradually renews its CD4 cells that the hidden HIV would die out. We were surprised to find that the levels of HIV integrated in the CD4 cells didn't reduce over the 14-year period. "The good news is that we did not see any worsening over time, but the bad news is that these findings really cast doubt over whether HIV can be 'cured' by increasing immune cell responses against it - a strategy that now looks like it will eventually fail."

**From EBioMedicine, 2015**

BIOLOGY, USA

## Secrets of Hormone Receptors

Many hormones and neurotransmitters work by binding to receptors on a cell's exterior surface. This activates receptors causing them to twist, turn and spark chemical reactions inside cells. NIH scientists used atomic level images to show how the neuropeptide hormone neurotensin might activate its receptors. Their description is the first of its kind for a neuropeptide-binding G protein-coupled receptor (GPCR), a class of receptors involved in a wide range of disorders and the target of many drugs. "G protein-coupled receptors are found throughout the body. Knowing how they work should help scientists devise better treatments," said Reinhard Grisshammer, Ph.D., an investigator at the NIH's National Institute of Neurological Disorders and Stroke (NINDS) and the senior author of the study published in *Nature Communications*. Neurotensin is thought to be involved in Parkinson's disease, schizophrenia, temperature regulation, pain, and cancer cell growth. Previously, Dr. Grisshammer and his colleagues showed how neurotensin binds to the part of its receptor located on a cell's surface. In this study, they demonstrated how binding changes the structure of the rest of the receptor, which



passes through a cell's membrane and into its interior. There neurotensin receptors activate G proteins, a group of molecules inside cells that controls a series of chemical chain reactions. For these experiments, scientists shot X-rays at crystallized neurotensin receptor molecules. Making crystals of receptors that activate G proteins is difficult. In most studies, scientists have investigated inactive receptors. "The receptor we crystallized is very close to the active form found in nature," said Dr. Grisshammer. "We may have the first picture of a peptide-binding G protein-coupled receptor just before it engages with the G protein." To achieve their results, the scientists made multiple genetic modifications to a less active version of the neurotensin receptor they had used before. Experiments performed in test tubes showed that mixing the receptor with neurotensin sparked the G protein reactions for which the scientists were looking. When the scientists looked at the structure of the new crystals, they discovered how binding of neurotensin to the receptor caused critical parts of the receptor located below a cell's surface to change shape. In particular, they saw that a region in the middle of the receptor dropped like a draw bridge to link the neurotensin binding site to parts of the receptor found inside cells that are important for G protein activation. The scientists concluded that this change may prepare the receptor for activating G proteins. "For years scientists have made educated guesses about how peptide receptors work. Now we may finally know," said Dr. Grisshammer. His lab plans to continue its work in order to

fully understand how neurotensin and other G protein-coupled receptors translate messages delivered by neuropeptides into reactions inside cells.

**From Nat Commun, 2015**

## MEDICINE, GERMANY

## Sugar Antigen Lost Its Resistance

Immunotherapy using monoclonal antibodies is a promising treatment strategy, and it might now be within reach: American scientists have successfully prepared an oligosaccharide enterobacterial antigen for which a monoclonal antibody has been developed. The study is published in the journal *Angewandte Chemie*. Monoclonal antibodies are indispensable as diagnostic tools in biomedical applications and are increasingly used in therapy. As Enterobacteriaceae, a large family of gram-negative pathogens with as prominent members as Escherichia coli, Salmonella, or Klebsiella, can develop resistance against multiple antibiotics and can thus cause severe infections with high mortality, the development of monoclonal antibodies for a new therapeutic approach is required. Geert-Jan Boons at the University of Georgia and his group, in collaboration with MedImmune, USA, chose the enterobacterial common antigen (ECA), an oligosaccharide, as a target antigen because it is expressed by all members of this bacterial family. The hope was that a monoclonal antibody recognizing ECA would recognize the pathogens in general and thus provide the basis for vaccines or immunotherapy. The authors explain: "Although ECA can be isolated from natural sources, chemical synthesis offers a much more attractive approach for obtaining such compounds. It allows the installation of reactive linkers for controlled conjugation of oligosaccarides to carrier proteins." However, before conjugation and evaluation of ECA, the Boons group, which dedicates its research to carbohydrate sciences, had to meet the extraordinary task of synthesizing the challenging molecule. It contains highly functionalized monosaccharides, the glycosidic linkages were difficult to install, and the central monosaccharide formed internal linkages rather than undergoing glycosidic linking. Finally, they succeeded with two hexasaccharides and two trisaccharides as synthetic variants of ECA. After conjugation to bovine serum albumin, which is a widely used carrier protein, natural antisera effectively bound to the variants and especially to the central trisaccharide unit, the synthesized epitope for which the monoclonal antibody was then successfully developed as well. As multiresistant bacteria pose the threat of incurable infections, the development of monoclonal antibodies as a potential new therapeutic approach against pathogenic bacteria is highly significant. Boons and Wang and their colleagues have laid the basis by identifying and preparing the immunogenic target.

**From Angewandte Chemie, 2015**

## REVOLUTION, BRAZIL

## Ancient Reptiles Attacked with Giant Fangs

Ancient mammal-like reptiles that once grazed across the globe may have possessed many of the fighting tactics seen in modern herbivores, including head butting and attacks with giant fangs, researchers say. A number of these extinct beasts

also possessed complex, molarlike teeth on the roofs of their mouths, scientists added. Before the rise of the dinosaurs, the most successful vertebrates on land were the ancestors of mammals — animals known as primitive therapsids that are sometimes called mammal-like reptiles. These ancient creatures included the anomodonts, which were the most abundant tetrapods, or four-legged animals, of the Permian period, which occurred about 250 million to 300 million years ago, right before the age of dinosaurs. The new finding comes from an analysis of two such bizarre anomodonts, both the size of large dogs: Tiarajudens eccentricus and Anomocephalus africanus. Vertebrate paleontologist Juan Carlos Cisneros at the Federal University of Piauí in Teresina, Brazil, and his colleagues recently discovered Tiarajudens eccentricus, an odd saber-toothed anomodont that once dined on leaves and stems amidst the dunes, ponds and streams of ancient Brazil. Although saber teeth might ordinarily conjure images of fearsome extinct predators, a number of modern herbivores possess these dagger teeth as well, such as the musk deer, water deer and muntjacs native to Asia. The giant fangs of Tiarajudensmay have played many different roles. Among males, the saber teeth may have been used during fights against rivals "for territory, resources and females," Cisneros told Live Science. "The sabers could also be used against potential predators that existed in the middle Permian, such as dinocephalians and therocephalians. Tiarajudens could deter predator attacks by displaying the canines, or indeed fight back with them. Modern deer also fight back predators in this way." Dinocephalians were the first really large tetrapods to walk on land, reaching lengths of about 11.5 feet (3.5 meters); the group included herbivores that practiced head-butting combat, much like stags and rams, Cisneros noted. In their new analysis of anomodonts and dinocephalians, the researchers noted that combat strategies typical of modern herbivores likely evolved more than 250 million years ago, back when Earth's first complex groups of land herbivores emerged. "We now know that as soon as the herbivores became more diverse in the middle Permian, they began to employ these

forms of combat," Cisneros said. In addition, in their new analysis, the scientists also discovered how anomodonts may have used strange, molarlike teeth on the roofs of their mouths to eat — unusually shaped lower jaws had molars that could fit together with those on the palate for an efficient chew. The researchers compared 260-million-year-old fossils of T. eccentricus with those of Anomocephalus africanus, which lived at least 265 million years ago in what is now South Africa. Scientists had previously seen large teeth on the palates of T. eccentricus, but the lower jaws they had of this species lacked teeth, so the researchers could not say for sure how the upper and lower teeth worked together. The lower jaws of A. africanus revealed how anomodonts might have eaten with their odd teeth. "These species chew by using the jaws and the roof of their mouths," Cisneros said. "Obviously, the rows of teeth in the palate had some space in between, otherwise the animals would bite their tongues!" By Charles Q. Choi. Original article on Live Science.

**From Open Sci, 2015**

BASE

MEDICINE, USA

## First Self-injectable HIV Antibody May Prevent Virus Transmission

The first self-injectable HIV antibody, PRO 140, has a 98 percent success rate in reducing the virus in HIV patients' blood, according to results released Tuesday from a Phase 2b clinical trial of the drug. PRO 140 works by blocking the HIV co-receptor CCR5 on T-cells, protecting healthy cells from viral infection. One dose a week has been shown to effectively reduce viral loads by nearly 100 fold, according to a news release. In a monotherapy study, researchers found that some HIV patients who used PRO 140 had a completely suppressed viral load, meaning they saw the amount of HIV in their blood eliminated, for about 11 months. The transmission rate for HIV drops to nearly zero if a patient's viral load is completely suppressed. HIV, or human immunodeficiency virus, destroys T cells, a type of white blood cell vital to fighting infection. Individuals with compromised immune systems are then vulnerable to other infections, diseases and complications — the final stage of HIV infection is AIDS. According to a news release, the drug could be available commercially in 2017, pending positive results from an upcoming Phase 3 trial. The Food and Drug Administration has designated PRO 140 as a "fast-track" product candidate. The drug has undergone seven clinical trials.

**From FoxNews.com, 2015**

MICROBIOLOGY, FRENCH

## Bacteria That Prevent Type 1 Diabetes

Our bodies have ten times more microbes than human cells. This set of bacteria is called microbiota. In some instances, bacteria known as pathogens can cause infectious diseases. However, these micro-organisms can also protect us from certain diseases. Researchers from Inserm, Paris Descartes University and the CNRS (French National Centre for Scientific Research), in collaboration with teams from China and Sweden, have recently shown how microbiota protects against the development of type 1 diabetes in mice. This research is published in the *Immunity* journal. To combat pathogens, the immune system has developed various mechanisms to detect, fight and even destroy micro-organisms that are harmful to the body. This includes antimicrobial peptides and natural proteins that destroy pathogenic bacteria by disrupting their cellular membrane. Not only are they produced by immune cells, they are also produced by cells whose functions are not immune-related. A research team coordinated by Julien Diana, an Inserm Research Fellow at Inserm Unit 1151 "Institut Necker-Enfant Malades" [Necker Institute for Sick Children] (Inserm/ CNRS/

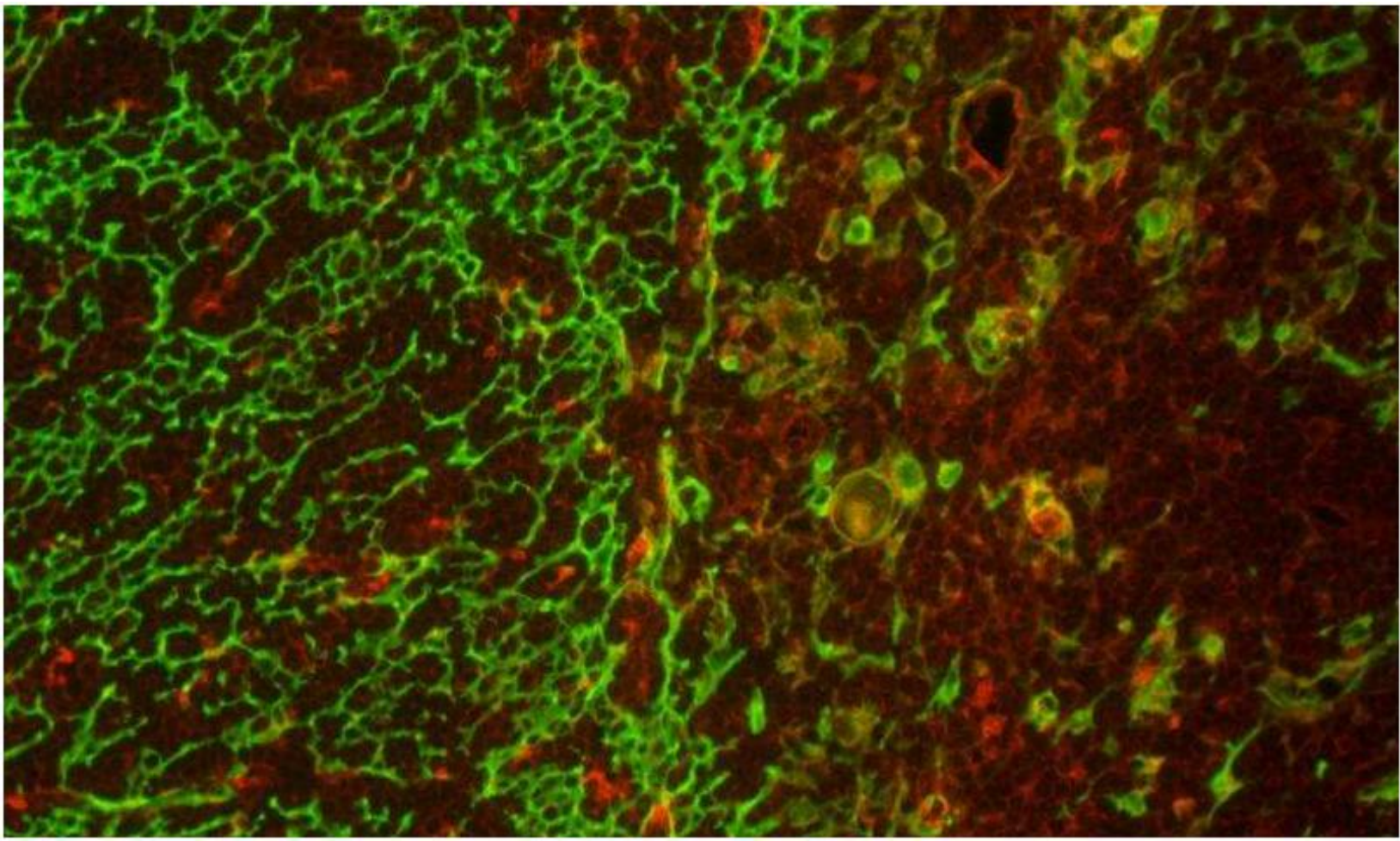
Université Paris Descartes), is focussing on a category of antimicrobial peptides, i.e. cathelicidins. Apart from their protective function, these peptides have also exhibited immunoregulatory abilities against several autoimmune diseases. As such, scientists hypothesise that cathelicidins may be involved in the control of type 1 diabetes, an autoimmune disease where certain cells in the immune system attack beta cells in the pancreas which secrete insulin. Firstly, they observed that beta pancreatic cells in healthy mice produce cathelicidins and that, interestingly, this production is impaired in diabetic mice. To test this hypothesis, they injected diabetic mice with cathelicidins where production was defective. "Injecting cathelicidins inhibits the development of pancreatic inflammation and, as such, suppresses the development of autoimmune diabetes in these mice" states Julien Diana. Given that the production of cathelicidins is controlled by short-chain fatty acids produced by gut bacteria, Julien Diana's team are studying the possibility that this may by the cause of the cathelicidin deficiency associated with diabetes. Indeed, researchers have observed that diabetic mice have a lower level of short-chain fatty acids than that found in healthy mice. By transferring part of the gut bacteria from healthy to diabetic mice, they are re-establishing a normal level of cathelicidin. Meanwhile, the transfer of microorganisms reduces the occurrence of diabetes. For the authors, "this research is further evidence of the undeniable role microbiota plays in autoimmune diseases, particularly in controlling the development of autoimmune diabetes". Preliminary data, as well as scientific literature, suggest that a similar mechanism may exist in humans, paving the way for new therapies against autoimmune diabetes.

**From Immunity, 2015**

## BIOLOGY, USA

## How Aging Cripples the Immune System?

Scientists from the Florida campus of The Scripps Research



Institute (TSRI) have shown how aging cripples the production of new immune cells, decreasing the immune system's response to vaccines and putting the elderly at risk of infection. The study goes on to show that antioxidants in the diet slow this damaging process. The research, published August 6 in the journal *Cell Reports*, focused on an organ called the thymus, which produces T lymphocytes, critical immune cells that must be continuously replenished to respond to new infections. "The thymus begins to atrophy rapidly in very early adulthood, simultaneously losing its function," said TSRI Professor Howard Petrie. "This new study shows for the first time a mechanism for the long-suspected connection between normal immune function and antioxidants." Scientists have been hampered in their efforts to develop specific immune therapies for the elderly by a lack of knowledge of the underlying mechanisms of this process. To explore these mechanisms, Dr. Petrie and his team developed a computational approach for analyzing the activity of genes in two major thymic cell types — stromal cells and lymphoid cells — in mouse tissues, which are similar to human tissues in terms of function and age-related atrophy. The team found that stromal cells were specifically deficient in an antioxidant enzyme called catalase, which resulted in elevated levels of the reactive oxygen by-products of metabolism and, subsequently, accelerated metabolic damage. To confirm the central role of catalase, the scientists increased levels of this enzyme in genetically altered animal models, resulting in preservation of thymus size for a much longer period. In addition, animals that were given two common dietary antioxidants, including vitamin C, were also protected from the effects of aging on the thymus. Taken together, the findings provide support for the "free-radical theory" of aging, which proposes that reactive oxygen species such as hydrogen peroxide, produced during normal metabolism, cause cellular damage that contributes to aging and age-related diseases. While other studies have suggested that sex hormones, particularly androgens such as testosterone, play a major role in the aging process, it fails to answer the key question—why does the thymus atrophy so much more rapidly than other body tissues? "There's no question that the thymus is remarkably responsive to androgens," Dr. Petrie noted, "but our study shows that the fundamental mechanism of aging in the thymus, namely accumulated metabolic damage, is the same as in other body tissues. However, the process is accelerated in the thymus by a deficiency in the essential protective effects of catalase, which is found at higher levels in almost all other body tissues."

**From Cell Reports, 2015**

# Stop wasting foods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# Map Shows Where the Most Endangered Animals in the World

**By Matthew Speiser**


Close to half of all living species on the Earth could disappear by the end of this century, and several recent studies suggest humans will be the cause. Keeping that in mind, the folks at Signature African Safaris put together a map using data from the World Wildlife Fund (WWF) to show where in the world the most endangered animal species are located. The dark red regions denote the areas where the critically endangered animals reside, while the lighter shaded regions signify animals living in that area that are endangered. The box at the bottom right is a map key. ■ By Matthew Speiser. From the Business Insider.


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# γ-Aminobutyric Acid-Mediated Neurotransmission Inhibition in the Pontine Reticular Formation: A Potential Mechanism of Propofol Anesthesia

Mary K. Pathak, Senzhu Bao, Fred Wang

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# γ-Aminobutyric Acid-Mediated Neurotransmission Inhibition in the Pontine Reticular Formation: A Potential Mechanism of Propofol Anesthesia

Mary K. Pathak,* Senzhu Bao,† Fred Wang *,Δ

**Study for underlying anesthetic mechanisms is the key point of general anesthesia. Propofol is a representative of general anesthetics. Many general anesthetics are thought to produce a loss of wakefulness, in part, by enhancing *γ*-aminobutyric acid (GABA) neurotransmission. However, GABAergic neurotransmission in the pontine reticular formation promotes wakefulness. We hypothesized that propofol inhibited GABA current and promoted long-term potentiation (LTP) of pontine tissue, which might be the underlying mechanism of propofol anesthesia. In our pre-study investigation, propofol enhanced GABA current in the thalamic neuron and showed as a characteristic of burst discharge, but burst inhibition was observed in the pontine neuron. Hence, the hypothesis of the GABAergic neurotransmission inhibition in the pontine reticular formation might be the mechanistic base of propofol anesthesia, and given an experimental basis of the theory of central nervous inhibition in general anesthesia.■**

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**Keywords:** GABA – Pon – Propofol - Consciousness

BIG ADVANCE has being made in exploring the pharmacological mechanisms of general anesthesia since the first case reported anesthetized with ether in 1846, but the precise recognition of the mechanism is still unclear because of the complexity of the nervous system. Approximately 160 million patients underwent general anesthesia every year in the world, and the mortality associated with general anesthesia was near one per ten thousands (1), and the incidence of related complications including recognition dysfunction and hypomnesis was up to 30 per cent (2). These high incidences of complications and mortality are attributed to inadequate knowledge of the potential mechanisms of general anesthesia (3). As thus it is one of the challenges for clarifying the underlying mechanisms of general anesthetics to anesthetic professionals.

To date, several theories produced on the pharmacological mechanisms of general anesthetics, such as activation or inhibition of the ion channels, receptor regulation of neuron synapse, involvement of neurotransmitter receptors and the balancing regulation of excitatory and inhibitory networks of the nervous system (3). Each theory has its own basis, but it alone cannot explain the complexity of the general anesthesia in whole. Therefore, there have potentially pivotal implications in identifying the mechanisms of general anesthetics' neurobehavioral effectiveness.

## Hypothesis

Components of the anesthetized state include unconsciousness, immobility, sedation, amnesia and analgesia (4), and the unconscious state is produced through enhancing GABAergic neurotransmission by the general anesthetics (5). This gives a hint that the activation of the GABAergic nervous network plays an essential role in the anesthetizing effectiveness of general anesthesia. Besides, this also is the base of the theory of central inhibition of general anesthesia (6). The ascending reticular activating system (ARAS) plays a key role in wakefulness, in which the pontine reticular formation is the major part functioning through GABAergic neurotransmission. Interestingly, however, the recognition of the conception of the pontine reticular formation's role in wakefulness by activating the GABAergic network (7) is contrasting with the knowledge of the general anesthetics, which reaches unconsciousness by enhancing GABAergic neurotransmission. As thus we hypothesized that the general anesthetics produced loss of consciousness by inhibiting GABAergic neurotransmission of the pontine reticular formation. Therefore, it would provide an experimentally novel basis for the effect of general anesthetics if the detailed role for GABAergic neurotransmission of pontine reticular formation was clarified during general anesthesia.

So far, general anesthetic was mainly divided into two kinds of, i.e. intravenous and inhalable anesthetics, and propofol is the representative of intravenous general anesthetic. Previous study has showed that propofol produced unconsciousness through regulating GABAergic neurotransmission of hypothalamic sleeping pathways (5). Meanwhile, mutative research discovered that propofol and sevoflurane displayed the nerve-inhibiting effect via different binding sites on neuron, but this originally separated inhibition was integrated by affecting the activity of GABA receptor (8). Moreover, different anesthetics produce similar anesthetic effectiveness showed that a common pathway might exist. Exploring and verifying such potentially common binding sites has a clinically important implication. Above mentioned common functioning pathway theory was consistent with our presumption whether the GABAergic neurotransmission in pontine reticular formation functioning as the molecular basis of wakefulness was inhibited or not during propofol anesthesia, and it played the role of information integration in general anesthesia or not are yet to be guaranteed in the further studies.

To verify the role for GABAergic neurotransmission inhibition in the pontine reticular formation during general anesthesia, a pre-study investigation was performed. We recorded the whole-cell GABA current of hippocampal neuron, nucleusdorsomedialthalamus neuron and pontine neuron with voltage patch clamp during propofol incubation, and found that propofol played a significant role in enhancing GABA current in nucleusdorsomedialthalamus neuron, and minor effect on hippocampal neuron, but all two kinds of neuron displayed a characteristic of burst discharge. However, burst inhibition was observed in pontine neuron after propofol treatment (see Fig. 1). These results were consistent with previous reports regarding the role

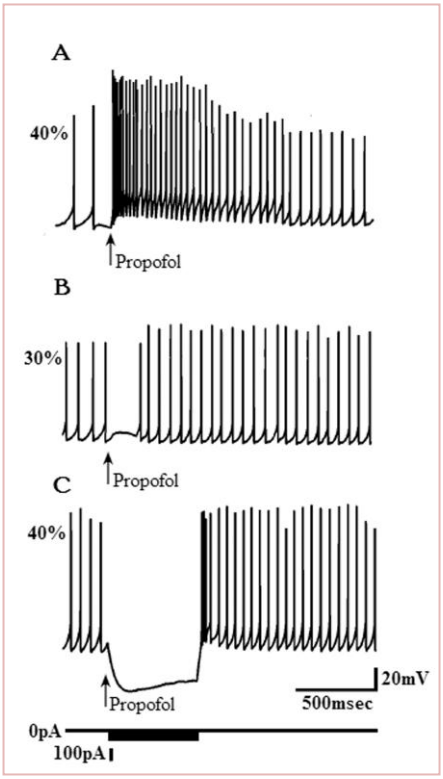


**Figure 1. Effect of propofol on GABAergic current in different neurons.**

The whole-cell GABA current of hippocampal neuron, nucleus dorsomedial thalamus neuron and pontine neuron with voltage patch clamp were recorded during propofol incubation. Propofol played a significant role in enhancing GABA current in nucleus dorsomedial thalamus neuron (Panel A), and minor effect on hippocampal neuron (Panel B), but all two kinds of neuron displayed a characteristic of burst discharge. However, burst inhibition was observed in pontine neuron after propofol treatment (Panel C).

for propofol in hypothalamus and hippocampus (5, 9). Based on this observation, a standardized current curve of pontine tissue section stimulated with GABA was built up (data were not shown), and then incubated with propofol for measuring the long-term depression (LTD) as the symbol of central inhibition during general anesthesia (10), which was for investigating the potential relationship between GABA inhibition and LTD. We found that propofol significantly inhibited pontine GABA current, but increased LTD (see Fig. 2). As thus we hypothesized that GABA-mediated neurotransmission inhibition in pontine reticular formation played a crucial role in the loss of consciousness during propopfol anesthesia.

## Methodology of Testing the Hypothesis

To verify this hypothesis and find novel mechanism of general anesthesia, following procedures should be performed on the basis of the pre-study investigation. First, the induction time of propofol anesthetized cat will be recorded and the GABA level in the pontine reticular formation will be simultaneously measured with microdialysis technique, and their potential relationship will be analyzed. Furthermore, GABA absorbing inhibitor nipecotic acid (NCA) or GABA synthetic inhibitor 3-Mercaptopropionic acid (3-MPA) will be injected into the pontine reticular formation of cat using the intracranial microinjection technique, and then will make following detections: 1) record propofol induction time and respiratory rate, and compare the GABA levels after the two GABA inhibitors administration; 2) compare the difference of resuscitation time after propofol anesthesia and the GABA levels in the pontine reticular formation during the resuscitating period; 3) a polygraphic system can be used to record the cortical electroencephalogram and neck muscle electromyogram as the signals to assess arousal state, and observe the influence of propofol on GABAergic neurotransmission in the pontine reticular formation; 4) the expression of glutamate receptor-interacting protein (GRIP) (11) and transmembrane AMPA receptor regulatory protein γ2 (TARP γ2) (12) will be detected as the symbol of LTD. In addition, GABA current and LTD will be recorded with tissue electrophysiology after incubating pontine tissue section and cultured neuron. After then administered NCA or 3-MPA to observe the effect of propofol on GABA current.

## Concluding Remarks

In conclusion, GABAergic neurotransmission inhibition in the pontine reticular formation might be an underlying mechanism of general anesthesia. This hypothesis should be verified by investigating the relationship among the propofol induction time, pontine GABA level, cortical electroencephalogram and

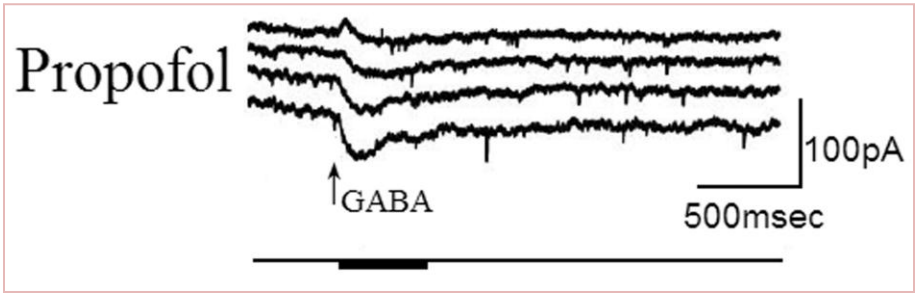


**Figure 2. Effect of propofol on GABAergic current and long-term depression of pontine section.**

Pontine tissue section was incubated with propofol for measuring the long-term depression (LTD). Propofol significantly inhibited pontine GABA current.

neck muscle electromyogram after injection of GABA absorbing inhibitor and synthetic inhibitor into pontine reticular formation through intracranial microinjection in propofol anesthesia. Furthermore, the influence of propofol on GABA level and LTD of pontine tissue section should be explored to unravel the underlying mechanism of propofol anesthesia. To date, given the precise role for GABAergic neurotransmission in the pontine reticular formation during propofol anesthesia, to our knowledge, is unknown, as thus this study possesses the originality.■

## Conflict of Interest

None

## Acknowledgement

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# Amazing Exciting Discoveries in Archaeology

**By Erin Brodwin**

## The Corner of A Lost Civilization

Some 1,000 years ago in the middle of Honduras, a thriving populace once built giant statues, homes, and even a complex network of irrigation channels and reservoirs. The flourishing enclave, uncovered using laser scanning technology by a team of researchers from the University of Houston, was likely part of a network of other dwellings throughout this part of the Honduran rain forest. Together, these sites would have formed an active community that bustled with hundreds of people long before the arrival of European explorers. So far, the researchers have already found evidence of the tips of more than 50 objects, including giant stones possibly used for construction purposes, the head of a large statue resembling a combination of a werewolf and a jaguar, stone seats for ceremonies, and containers that had been intricately etched with the figures of vultures and snakes. They estimate the community was active in sometime between A.D. 1000 and A.D. 1400.

## A Secret Fortress of Genghis Khan

Genghis Khan's Mongolian Empire, the largest of its kind in history, stretched from the Sea of Japan to as far west as Arabia and from Siberia to as far south as India and Iran How did he come to control such a vast domain? A team of archaeologists recently uncovered a clue that may help answer that question: A secret fortress that may have been used to help expand the empire during its westward march toward Europe. The large fortress, located near what was once rich farmland and key parts of the silk trade route, would have played a key role in providing supplies and carrying information to the Mongolian army as they expanded west. Inside the fortress, which measures about the size of three football fields and was likely built in 1212, researchers uncovered a vast array of Chinese pottery, wood fragments, and animal bones.

## The Oldest-Ever-Preserved Beer

Ever wonder what a bottle of 170-year-old beer would smell like? Thanks to the recent discovery of a shipwreck off the coast of Finland, you don't have to keep guessing. A team of researchers uncorked two bottles of the 19th-

century-brew in early March, unleashing powerful odors of cabbage, burnt rubber, over-ripe cheese, and sulfur. When chemists analyzed the bottles' contents, they found the cause of the stench: bacteria that had likely been growing inside the bottles for decades, taking over any malty, beer-like smells they may once have had. Bacteria aside, the beer probably tasted much like the beers we drink today, according to the researchers' chemical analysis of its other ingredients. Both brews were produced with hops but had a bit more of a rose-flavoring compound than we might be used to.

## An Ancient Celtic Prince

Some 2,500 years ago, an ancient prince got a lavish burial in France. His body was recently uncovered inside his chariot, along with pottery and a gold-tipped drinking vessel decorated with intricate images of Bacchus, the Greek god of wine and revelry. The prince is not buried alone, however. The burial site, located a few hours' drive south of Paris, houses many other ancient bodies. Nearby, researchers recently uncovered another grave dating to about 800 BC holding the body of an ancient warrior and his sword and a woman with bronze jewelry, Tia Ghose wrote in a recent post for LiveScience. The tombs build on existing evidence that the Celtic and Mediterranean peoples exchanged goods. Mediterranean merchants were thought to have used Greek pottery frequently as gifts, contributing to the Celts' growing wealth inland.

## A Vast Underground City

Deep in central Turkey in a region successively ruled by Alexander the Great, the Romans, the Byzantine Empire, and the Ottoman Empire, more than a hundred square miles of once-hidden passages snake beneath the ground. The subterranean tunnels link thousands of underground homes and temples. Archaeologists who first discovered the hidden city in 2013 estimate the network once housed up to 200 villages and was most likely occupied until around 5,000 years ago, according to Hurriyet Daily News. This March, a team of archaeologists and engineers began mapping the details of the underground terrain using machinery that sends radar pulses beneath the surface. Once it's mapped completely, the Anatolian government plans to open the area to the public.

## A 250-Year-Old Pretzel


Archaeologists recently unearthed a pretzel that was likely served up sometime around 1765 in the southern German state of Bavaria. It could be the oldest surviving remnant of the doughy snack ever discovered in Europe. Ancient traces of food are tough to find — once they're discarded, edible goods are quickly consumed by small animals and bacteria. But this pretzel was unique because it had been burned. The carbon in the burned remnant preserved it against the forces of time. While digging for other remains in the city of Regensburg, archaeologists also found a handful of blacked rolls and other pretzel bits that suggests they were tossed from a bakery that was once located there, reports the Guardian. Carbon dating suggests the toasty treats were baked sometime between 1700 and 1800.

## A Hoard of Ancient Coins and Jewelry

In the middle of their underground adventure in northern Israel, a group of amateur cavers accidentally discovered a stockpile of ancient coins and jewelry from the time of Alexander the Great. Along with the stash of 2,300-year-old coins and silver rings, bracelets, and earrings, archaeologists who later excavated the site uncovered pottery dating back as far as 6,000 years. Officials from the the Israel Antiquities Authority think people living in the area at the time may have stashed the valuables in the cave during the period of political turmoil that followed Alexander the Great's death in 323 BC. This wouldn't be the first time someone stumbled across a mass treasure trove in the area. In February, amateur divers accidentally discovered a store of 2,000 gold coins off the coast of the ancient harbor city of Caesarea. By Erin Brodwin. The original article from Business Insider.

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