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SOCIETY FOR SCIENCE & THE PUBLIC
DECEMBER 12, 2015

DNA Sketch-Artist

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ScienceNews

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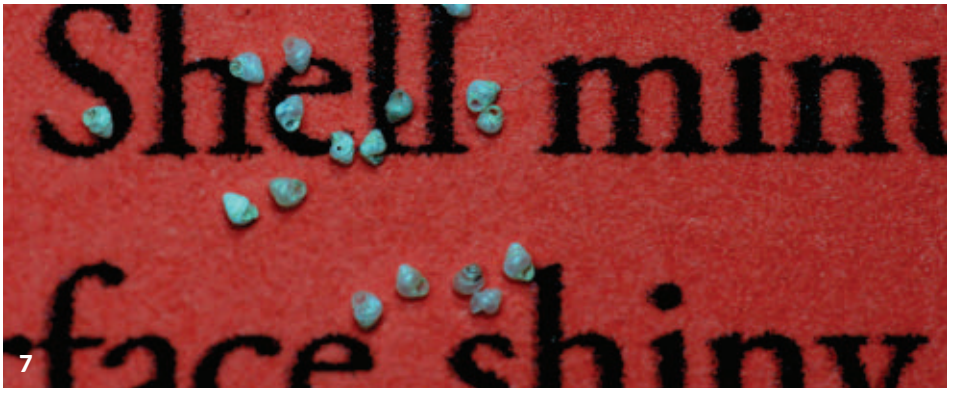
Features

News



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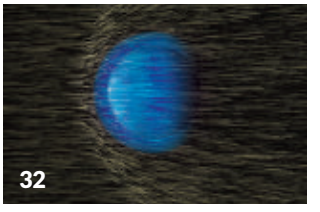

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Departments

COVER Scientists may not be able to control gene drives once the tools are let out of the box. *Michael Morgenstern*

CLOCKWISE FROM TOP: E. OTWELL; NASA SCIENTIFIC VISUALIZATION STUDIO, MAVEN SCIENCE TEAM; M. SCHILTHUIZEN/NATURALIS BIODIVERSITY CENTER

Scientists consider new genetic power and its impacts

This is the moment geneticists have been waiting for. It's also the one they've been worrying about.

Since the 1970s, scientists have pondered the power of genetic engineering to edit and rewrite the instruction book of life. Such technology has already demonstrated much power, if not the full potential initially envisioned. But now that's changing, Tina Hesman Saey reports on Page 16. CRISPR/Cas 9, a gene-editing system plucked from bacteria and developed just in the last few years, appears to be making many of the dreams of early genetic engineers not only possible, but also fairly fast and easy to attain.

Some of those dreams involve editing the genes not just of an individual but of an entire population to prevent disease, battle invasive species or protect crops. These tasks would involve what scientists call gene drives, edited genes that would incorporate themselves into an assemblage of cells, or mosquitoes, or fish, or weeds. Thanks to CRISPR, scientists' plans for effective use of gene drives suddenly look feasible.

Not content to follow the 50–50 rule of Mendelian inheritance, gene drives propel their altered versions of genes into the next and subsequent generations of an organism. Based on natural "selfish" gene elements, these gene drives can spread an engineered change throughout a population in a relatively short time. In this way, mosquitoes may be made unable to carry the malaria parasite, or the problematic Asian carp may be tweaked so it could no longer survive in the Great Lakes.

Being good scientists, most gene-drive researchers want to pause and think about the implications of such powerful technology in a logical, reasoned way. Gene drives could alter the environment in unexpected ways. Eradicating an entire species would have ecological consequences. Such caution is commendable, even if it comes ahead of the technology. There are still, after all, hurdles to overcome. CRISPR is not always as specific in its targets as some reports suggest, for example. Biology is complicated. Nevertheless, the scientists are wise to consider, in a methodical way, both the power and peril of changing the biological world. —*Eva Emerson, Editor in Chief*

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Excerpt from the December 4, 1965, issue of *Science News Letter*

50 YEARS AGO

Past, modern man linked

Neanderthal man may have built structures, indicating that he was far more advanced than formerly believed and implying that he may have evolved into Cromagnon man. Evidence uncovered at the Molodova site in the Ukraine ... is a circle of mammoth animal bones. Directly above this site are similar bone circles dating from ... when man had already made his appearance. Post holes ... indicate that modern or Cromagnon man would cover a large area ... with one single structure.... It is logical to assume that [Neanderthals] also built structures.

UPDATE: Archaeological evidence suggests that Neandertals used tools, but what happened to them is still debated. In one theory, Neandertals were a separate species that sometimes bred with modern humans outside of Africa, leaving behind a genetic trace before going extinct by 30,000 years ago. Others say that Neandertals were an archaic population of *Homo sapiens* that was absorbed into modern populations and lives on in human DNA.

In nine species of howler monkey, researchers found an inverse relationship between testes size and size of the hyoid bone, part of the vocal tract.

THE SCIENCE LIFE

Deep roars, small sperm stores

Just after dawn, barbershop quartets of male howler monkeys echo over the canopy of Mexico's forests. Jake Dunn remembers them well from his early fieldwork in Veracruz. "Most people who don't know what they're listening to assume it's a jaguar," says Dunn, a primatologist at the University of Cambridge.

The calls serve as a warning to male competitors and an alluring pickup line for females. While studying primates in Mexico, Dunn heard drastic differences between resident howler monkeys. He and his colleagues decided to pin down

SAY WHAT?

Superpuff \SOO-per-puf\ n.

Superpuffs (one illustrated) are extra fluffy planets that formed far from their star and subsequently wandered in closer, a new study suggests.

A gassy planet, close to its star, with a puzzlingly small mass.

Not to be confused with a generic breakfast cereal, superpuffs are fluffy planets snuggled up to their suns. A superpuff develops its inflated persona by forming far from its star and then wandering inward, astronomers Eve Lee and Eugene Chiang of the University of California, Berkeley suggest online November 1 at arXiv.org. Starting out in the outskirts of a fledgling planetary system, the researchers say, would mean more cold gas is available to stick to a rocky core.

Superpuffs are quite large for their mass. They typically weigh a few times as much as Earth but stretch up to 10 times as wide. That's about as large as Jupiter but roughly one one-hundredth of its mass. These puffy worlds are the opposite of the rocky heavyweights known as super-Earths (*SN: 4/18/15, p. 17*), which have surprisingly little gas and live a bit farther out than where superpuffs end up. Unlike superpuffs, super-Earths probably stay where they form, Lee and Chiang suggest, but begin to form later, after much of the gas swirling around their young sun has dissipated.

— Christopher Crockett

Watch a howler roar at **bit.ly/SN_howler**

the origin and evolution of this well-known variation among species.

After reading a 1949 paper that classified howlers based on a vocal tract bone called the hyoid, Dunn paired up with Lauren Halenar of the American Museum of Natural History in New York City, who was studying the hyoid's role in howler biology.

Scouring collections at museums and zoos in the United States and Europe, the team used laser scanners to create 3-D models of hyoids from nine howler species. The work required a lot of digging through cupboards for skeletons. "Some of these specimens are hundreds of years old," says Dunn, who recalls imagining "the early naturalists hunting these animals and bringing back the collections."

Real pay dirt came from the National Museums of Scotland, which had preserved the remains of two howlers that had died of natural causes in zoos. CT and MRI scans of the two specimens provided a rare peek at the howler vocal system's layout.

Dunn thinks the container-like hyoid functions as a resonating chamber for calls. "It's a bit like when you blow over the top of a bottle," he says. Based on acoustic measurements, the team found species with larger hyoids roar at lower frequencies. Their findings appear in the Nov. 2 *Current Biology*.

Howler species with bigger hyoids have smaller testes and live in harem-style social groups (*SN Online: 10/22/15*). In this less-crowded playing field, reproductive success depends heavily on luring females rather than producing plenty of sperm to compete with sperm from other males living in the group. Harem species invest energy in vocals over testicles. Bigger hyoid bones give males deeper calls, fooling females, rivals and unsuspecting humans into thinking they are more fearsome, virile animals.
— Helen Thompson

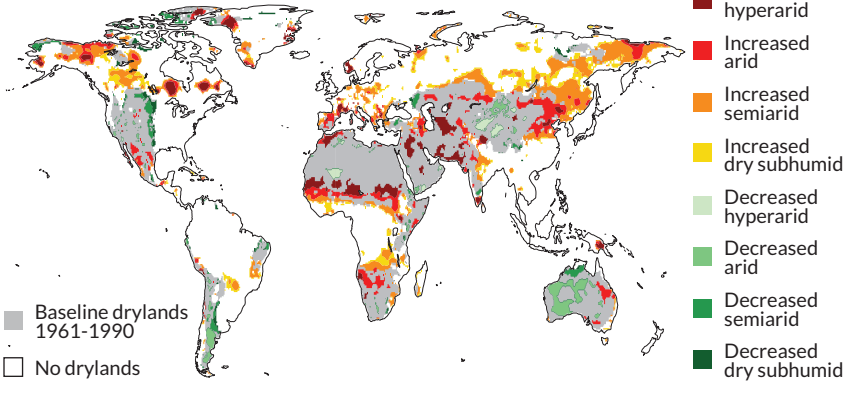
SCIENCE STATS

Parched parts of Earth expanding

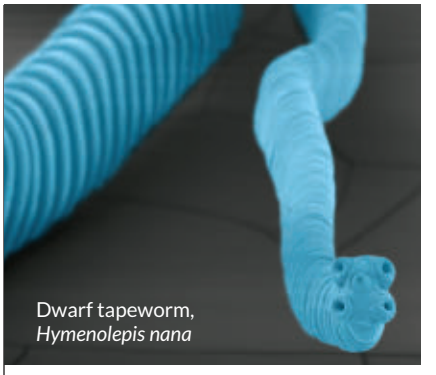
Arid, hardscrabble landscapes could cover up to 56 percent of Earth's land surface by 2100, a new study finds. Today, drylands make up about 40 percent of the planet's land surface.

The expansion of drylands — fragile regions where vegetation is sparse and soil is fairly infertile — will predominantly occur in developing countries, according to new climate simulations published October 26 in *Nature Climate Change*. These countries are also where much of the world's population growth is expected. More humans will mean a greater need for food and farming, which could further degrade and expand dryland environments, say Jianping Huang of Lanzhou University in China and colleagues. *— Chris Samoray*

Change in drylands by 2100



FROM TOP: COURTESY OF PETER OLSON/NATURAL HISTORY MUSEUM LONDON; J. HUANG *ET AL*/*NATURE CLIMATE CHANGE* 2015


Dwarf tapeworm, *Hymenolepis nana*

HOW BIZARRE

Parasite gives man cancer

Tapeworms can kick parasitism up a notch to become cancer, a case in Colombia shows.

A 41-year-old man in Medellín went to the doctor complaining of fever, cough, fatigue and weight loss that had lasted several months. Scans revealed tumors in his lungs, liver, adrenal glands, lymph nodes and elsewhere. The disease looked like cancer, but puzzled doctors: The small cells in the growths weren't human cancer cells.

DNA analysis revealed a shock: The cancer cells came from dwarf tapeworms (*Hymenolepis nana*), pathologist Atis Muehlenbachs of the U.S. Centers for Disease Control and Prevention and colleagues report in the Nov. 5 *New England Journal of Medicine*. Contagious cancers affect dogs, Tasmanian devils and clams (*SN: 5/16/15, p. 14*), but this is the first time researchers have seen a person get cancer cells from a parasite.

HIV infection had weakened the man's immune system, letting tapeworm stem cells grow unchecked, the researchers speculate. Mutations then turned the stem cells into cancer. The case raises concerns that people with weakened immune systems may be in danger of contracting similar tapeworm cancers. Says Muehlenbachs, "This is a rare disease," but "we don't know how rare." *— Tina Hesman Saey*

MATH & TECHNOLOGY

New algorithm cracks graph problem

Computer science advance helps identify identical networks

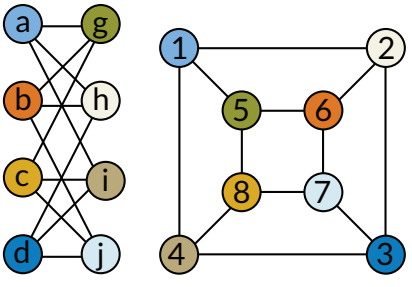
BY ANDREW GRANT

A puzzle that has long flummoxed computers and the scientists who program them has suddenly become far more manageable.

A new algorithm efficiently solves the graph isomorphism problem, computer scientist László Babai announced November 10 at a Combinatorics and Theoretical Computer Science seminar at the University of Chicago. The problem requires determining whether two separate sets of interconnected points, known as graphs, are linked in the same way even if the graphs look very different. In practice, existing algorithms can do the job in reasonable time, but it was possible that extremely complex graphs would make the problem intractable. Not anymore.

"My first thought was that this was a joke. I checked the month to make sure it wasn't April," says Ryan Williams, a Stanford University computer scientist. "It's a huge jump in our understanding of the problem." He says the discovery is potentially the most important theoretical computer science advance in more than a decade.

Babai's algorithm still needs to be vetted, but his expertise gives colleagues confidence in the result: He was grappling with the problem even before he made it the topic of his 1984 doctoral thesis. While the problem may seem abstract, it's a prominent example of a strange class of puzzles that computers have trouble solving despite being able to quickly verify a solution if one is provided. The result could also reverberate beyond computer science, such as allowing chemists to determine whether complex molecules have the same bonding structure.



Same but different Despite the differing shapes, these two graphs are isomorphic. Each circle on one graph corresponds to a circle on the second graph and connects to the same other circles. Corresponding nodes are shown in the same color.

In math terminology, "graph" is a fancy word for a network, the kind of diagram that depicts, for instance, a web of friends on Facebook or the spread of a disease. Each point, or node, is like a ping-pong ball that connects to one or more balls with string. With such a setup, it's easy to make two initially identical graphs look very different by shifting the balls around. The graph isomorphism problem requires a computer to examine two graphs that may look very different and determine whether all the balls share the same connections. Graphs that do are isomorphic.

> The discovery is potentially the most important computer science advance in more than a decade.

Computers generally have little trouble determining if graphs are isomorphic. But for even the best algorithms, there is a worst-case scenario in which the solving time grows nearly exponentially as the number of nodes increases.

Babai claims that he has developed an algorithm that evaluates even the trickiest graphs in what's called quasipolynomial time, which computer scientists consider reasonable. "We weren't even close to quasipolynomial," Williams says. The solving time still increases along with the number of nodes, but it does so much more gradually.

Babai declined an interview, saying he wants to confirm that his results survive several rounds of grilling from colleagues. It's unusual for a mathematician to announce such a major result before submitting a written proof, says Neil Immerman, a theoretical computer scientist at the University of Massachusetts Amherst. But "Babai is very smart and reliable and one of the top world experts on the graph isomorphism problem," Immerman says. "So I am sure that he has proved what he has announced."

Jeremy Kun, a theoretical computer scientist at the University of Illinois at Chicago, warns that "it's going to take a while for everyone to sort through the details." But he came away impressed after attending the packed seminar. "Most of the proof seems like very, very hard work rather than a flash of insight," he says.

The advance could help researchers sort out a big mystery regarding whether every problem that can be easily verified can also be easily solved (*SN Online: 9/9/10*). Until Babai's result, computers could quickly check if a solution showing that two graphs are isomorphic is correct but couldn't necessarily solve the problem from scratch efficiently.

Some easily checkable problems are also quickly solvable; they belong to a category called P, for polynomial time. Others are classified as NP-complete (NP stands for nondeterministic polynomial time) and are the hardest to crack. The traveling salesman problem (*SN Online: 2/20/12*), which tries to determine the optimal route to visit a set of locations, is an NP-complete puzzle. Graph isomorphism falls in between.

Williams says that Babai's discovery could improve mathematicians' understanding of the boundary zone between P and NP-complete, a region that includes problems such as factoring large integers, which plays an important role in Internet security. ■

E. OTWELL

GENES & CELLS

Gene editing helps baby battle cancer

T cells get tweaked to target leukemia but not harm the patient

BY TINA HESMAN SAEY

Molecular scalpels that slice genes helped push a 1-year-old girl's leukemia into remission, doctors announced November 5 at a news briefing.

A medical team at the Great Ormond Street Hospital in London treated the girl, named Layla, with immune cells altered by one type of the molecular instruments known as TALENs. It's the first time TALENs have been successfully used to treat a person.

A kind of gene-editing tool, TALENs (transcription activator-like effector nucleases) are pairs of proteins engineered to latch on to DNA at specific sites and then cut it.

In Layla's case, researchers used TALENs to engineer immune cells that can seek out and destroy cancer cells without harming the patient. The immune cells are called chimeric antigen receptor T cells, or CAR T cells. T cells help the body distinguish itself from invaders, such as bacteria or viruses, and attack the foreign cells.

Layla had a blood cancer called acute lymphoblastic leukemia. Her bone marrow made too many immature immune cells called B cells. B cells are studded with a protein known as CD19. To treat her cancer, doctors tried an experimental treatment using CAR T cells engineered to carry an antibody that targets and kills any cell that makes CD19.

In some previous cases, doctors have taken T cells from a patient's own blood and inserted the tracking antibody to create CAR T cells.

That strategy was not an option for Layla. She'd had treatment to kill the cancer, and her bone marrow had been replaced in a transplant. Researchers were unsuccessful in making CAR T cells from Layla's bone marrow donor.

Using T cells from yet another donor would not have worked: Those immune cells would recognize Layla's body as a foreign entity and attack; likewise, Layla's immune system would see the donated cells as invaders and repel them.

Layla's medical team, including Waseem Qasim of University College London, had a way to get around both problems. The team had previously made an experimental batch of "universal" CAR T cells that could be used for any patient.

Qasim and colleagues had used TALENs to disable a protein that allows T cells to distinguish between a person's own cells and invaders. Cutting out the protein means the T cells "can no longer recognize anything as foreign," says Mark Osborn, a molecular biologist at the University of Minnesota Medical School in Minneapolis. That modification lets donor CAR T cells attack cells carrying CD19, but leaves the rest of the patient's cells alone.

The team still had to find a way to stop a patient's body from rejecting the engineered cells. So Qasim and colleagues used a different pair of TALENs to remove a protein called CD52 from the CAR T cells. Getting rid of CD52 makes the cells invisible to a recipient's immune system. It was a clever trick, Osborn says, because doctors could then give a patient an antibody drug called alemtuzumab that would kill the patient's existing T cells, letting the new donor cells grow.

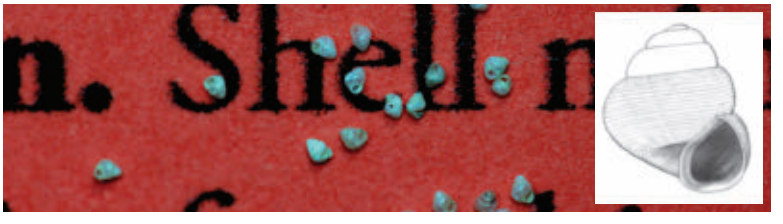
The cells had not yet been tested in clinical trials and researchers had to get special permission to give Layla the experimental treatment. Only one tiny vial containing a milliliter of engineered cells was available, but that was enough.

About a month after Layla got the treatment last summer, her doctors couldn't find any leukemia. Her bone marrow was 90 percent cells from her donated marrow, 7 percent cells from the CAR T cell treatment and 3 percent of her own bone marrow. Because Layla had some of her own marrow, it means her cancer wasn't cleared by the transplant alone. The engineered T cells helped kill the leukemia.

Since then, Layla has had another bone marrow transplant and is free of leukemia. Qasim says he's waiting until she has been cancer-free for at least a year until he'll consider the therapy "curative." ■

LIFE & EVOLUTION

World's smallest snail record broken again



M. SCHILTHUIZEN/NATURALIS BIODIVERSITY CENTER

Tiny, meet tiniest. The record for the world's smallest known snail has been broken just over a month after its announcement. The latest champ: a new species a full 0.3 millimeters smaller.

The new winner is a mere pinhead of a gastropod named *Acmella nana* (shown in false color above, with snails lying on top of the journal article that describes them). Found in Borneo, the snail grows a shell 0.5 to 0.6 millimeters in diameter, researchers report November 2 in *ZooKeys*.

Its white shell has "some nice spiral lines," but otherwise it's not the most spectacular looking of Malaysian snails, says codescriber Menno Schilthuizen of Naturalis Biodiversity Center and Leiden University in the Netherlands.

The previous record holder for smallest snail was *Angustopila dominikae* from China, described September 28. — *Susan Milius*

GENES & CELLS

Gene catalog will improve diagnosis

New dataset can help identify mutations that cause disease

BY TINA HESMAN SAEY

A new catalog of human genes reveals that people have many different ways to build proteins. This listing can help doctors sort through mutations to see which ones cause diseases — and which don't.

An international group of researchers banded together to compile the catalog, an inventory of the exome — the small portion of the genome that produces proteins — of 60,706 adults from different populations around the world. Researchers in the Exome Aggregation Consortium, known as ExAC, report the findings online October 30 at bioRxiv.org.

"This is one of the most useful resources ever created for medical testing for genetic disorders," says Heidi Rehm, a clinical lab director at Harvard Medical School who is not an ExAC member.

A journal reviewing the work for publication prohibits the ExAC researchers from speaking with journalists about the manuscript posted on bioRxiv.org, one researcher involved in the project told *Science News*. The work has yet to be peer-reviewed, and researchers are not allowed to "publicize" their findings before they are vetted. Other scientists who have viewed the manuscript and commented on bioRxiv.org have pointed out a few minor flaws, including broken links and formatting errors. But no one has yet criticized the data or analysis.

"This work is both technically very impressive ... and will be a fantastic mine of information to explore over the next years, and also hugely useful in clinical genetics settings," says Gilean McVean, a statistical geneticist at the University of Oxford. Looking at just the protein-coding parts of the genome is a good start for trying to tie specific genetic changes to disorders, he adds, "but we will need the full spectrum of the whole genome to ultimately make sense of what causes disease."

The ExAC researchers found more than 7.4 million genetic variants, letters in the DNA instructions for building proteins that differ from one person to another, among the people who donated DNA to the project. On average, people had one genetic variant for every eight base pairs, the information-carrying chemicals that make up DNA.

Those variants aren't spread evenly among genes. The team found 3,230 genes that are almost devoid of any variants that are likely to be harmful. These genes are probably important for human development and survival, Rehm says. Such genes, when mutated, may cause severe genetic disease or stop an embryo from developing so that no living person would carry mutations in those genes.

For other genes, "lightning does strike several times in the same spot," says Tuuli Lappalainen, a geneticist at the New York Genome Center and Columbia University. About 43 percent of new mutations in a child that are not also present in the parents turned out to be variants carried by other people in the ExAC database. So doctors who just look for new mutations to explain a child's genetic disease could mistake these types of mutations for disease-causing ones even though they may be harmless.

The exome project may help medical geneticists avoid making similar mistakes due to not knowing how rare variants are. The data revealed that some variants are not as uncommon as researchers had believed. For instance, some variants rarely show up in some populations, but are relatively common in others. Finns are a good example: Finland had a small founding population, so some mutations are found in Finns more frequently than in other Europeans.

An average participant had about 53 variants previously classified as disease-causing. But, on average, 41 of those mutations are found relatively frequently in at least one population, where they do not cause disease, the data show.

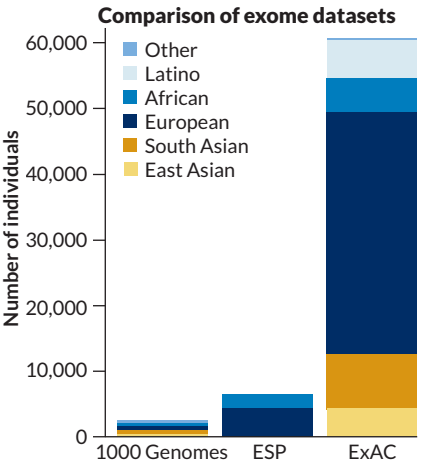
The ExAC team discovered an example of such a false accusation when it investigated 192 variants that had previously been implicated in disease. These variants were rarely found in people in the limited datasets researchers could access before. But the ExAC data show that many of those variants are found in more than 1 percent of healthy South Asians or Latinos, indicating that these variants are probably not the culprits. The misleading mutations include a variant thought to cause a liver disease, known as North American Indian childhood cirrhosis, when kids inherit two copies of the variant. That variant was found in 226 Latin Americans, including four people who had two copies of the gene but didn't have the liver disease.

Researchers outside the ExAC team have had access to the data for over a year, but have agreed not to publish large-scale findings until after the ExAC team reports its analysis in a journal. Lappalainen says she expects ExAC's official debut to be accompanied by multiple companion papers, followed by researchers using the data in other types of studies. Those studies may guide doctors toward better diagnosis of diseases and may suggest treatments.

Already, thousands of patients may need to have their cases reevaluated in light of the new data, Rehm says. ■

Data deluge The Exome Aggregation Consortium (ExAC) has compiled genetic information from 60,706 individuals. That's nearly 10 times as many people, and from more diverse backgrounds, than previous efforts such as the Exome Sequencing Project (ESP) and the 1000 Genomes project.

SOURCE: EXAC/BIORXIV.ORG 2015



BODY & BRAIN

Enlarged hearts found in obese kids

MRI scans reveal signs of cardiac disease in young children

BY LAURA BEIL

Obese children as young as 8 years old may experience worrisome changes to their hearts, according to data presented November 10.

In a small study involving 20 obese children, 40 percent had enlarged hearts, a sign that the organ is under strain. The study is one of the few to use MRI to get a close look at cardiac muscle, said Linyuan Jing of Geisinger Health System in Danville, Pa. Her team's data add to a number of studies suggesting that children who are overweight or obese could be setting themselves up for lifelong cardiac problems (*SN Online: 5/21/12*).

The prevalence of childhood obesity in the United States has leveled off in recent years, but is still high: Over a third of kids and adolescents are overweight or obese.

Youth may not protect the heart from obesity-related problems. The Bogalusa Heart Study found that some overweight preschool children had elevated cholesterol levels. After following the kids for an average of 28 years, researchers reported last year in the *Journal of the American College of Cardiology* that kids with a high body mass index and high blood pressure were more likely to have left ventricular hypertrophy (an unhealthy thickening of heart muscle) as adults.

Such data have raised concerns that heart enlargement begins in childhood. But it's been hard to get clear images of obese children's hearts, Jing said.

In the new study, Jing and colleagues evaluated MRIs of 20 obese kids ages 8 to 18 and compared them with 20 healthy-weight peers. The obese kids were more likely to have enlarged hearts: The mass of the left ventricle, the heart's most muscular pumping chamber, was 27 percent higher on average, and the heart muscle was 12 percent thicker, even after taking age into account.

40 percent
Fraction of obese kids studied who had enlarged hearts

"This adds to the data trail saying childhood obesity can have consequences right during childhood," said Sarah deFerranti, director of the preventive cardiology program at Boston Children's Hospital.

In adults, an enlarged heart is associated with premature death. In children, the significance is still under study. "We don't know if it's reversible," Jing said. ■

BODY & BRAIN

Small steps bring big health benefits

Eating at home, light exercise can reduce some disease risks

BY LAURA BEIL

Simple changes like regularly getting up from your chair, eating an extra homemade meal or two and running errands on foot might substantially reduce your future risk of disease. Several new studies suggest that such small lifestyle adjustments can have big health payoffs, even for people with diabetes.

Public health officials recommend 30 minutes of moderate exercise most days of the week. Yet only one in three U.S. adults gets that much, according to the U.S. Department of Health and Human Services. One reason may be that 30 minutes of brisk walking or cycling "sets the bar too high" for some and they get discouraged, said Bronwyn Kingwell of Baker IDI Heart and Diabetes Institute in Melbourne, Australia.

But studies that she and others presented show that health gains can occur from doing much less. In the Australian study, interrupting prolonged bouts of sitting with just three minutes of light walking or simple resistance exercises (like knee lifts) each half hour lowered mean blood pressure. With light walking, for instance, systolic blood pressure dropped from 130 millimeters of mercury to 120. Mean diastolic pressure fell from 82 to 76. The study, presented November 9, was conducted in 24 inactive adults with type 2 diabetes.

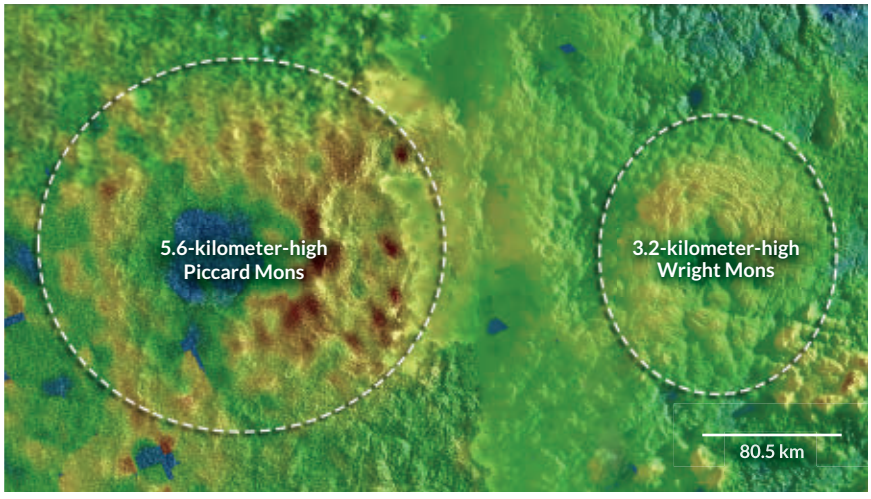
"The magnitude of the benefit was as much as it is with some antihypertensive drugs," Kingwell said. While the findings don't deny the importance of getting more exercise, "this is something you can do at your desk," she said. Previous studies have found similar results in people who do not have diabetes.

Other work by Canadian researchers, presented November 8, found that adults who moved from a neighborhood with low walkability — where every errand involves a car — to one with nearby shops and schools experienced on average a 54 percent lower risk of high blood pressure. The scientists adjusted for other known influences on health, including age, weight and income.

Researchers from the Moriguchi City Health Examination Center in Osaka, Japan, presented data on November 8 from a study of 5,900 commuters. Compared with drivers, those who took public transportation to work had a lower incidence of high blood pressure and diabetes and were less likely to be overweight.

Small differences in eating habits may also matter. Consuming more meals at home was associated with a lower risk of type 2 diabetes, researchers at Harvard T.H. Chan School of Public Health reported November 8. The study, based on data from 58,000 women and 41,000 men, found that people who ate 11 to 14 homemade meals a week had a 13 percent lower risk of developing type 2 diabetes than those who ate out more. Eating at home was also associated with lower weight gain over time.

While the study didn't examine mechanisms, Harvard's Geng Zong speculated that eating out could encourage consumption of sugary drinks. Zong also emphasized the need for portion control, no matter where the food is eaten. ■



Topographical maps of Pluto, created from the latest data from the New Horizons mission, have revealed two possible ice volcanoes, the first of their kind in the outer solar system. Red and yellow colors on the map indicate higher elevations, red the highest.

ATOM & COSMOS

Pluto continues to deliver surprises

Spinning moons, possible ice volcanoes found on dwarf planet

BY CHRISTOPHER CROCKETT

At this point, the only thing unsurprising about Pluto is that it continues to offer up surprises.

A wide variety of landscapes, ongoing surface transformations and a family of wildly spinning moons were among the curiosities reported by the New Horizons mission team November 9.

"Pluto is like a graduate course in planetary science," mission leader Alan Stern said at a news briefing. "It's going to take the larger planetary science community many years to digest all this."

The New Horizons spacecraft (*SN: 6/27/15, p. 16*), which buzzed the dwarf planet on July 14, has so far sent back only about 20 percent of the data it acquired from the Pluto system. Every new nugget continues a story that's pretty familiar by now: Pluto is weird.

Terrains both new and old sit side-by-side on Pluto's surface. Some heavily cratered regions are about 4 billion years old, about as old as Pluto itself. Others appear to have been laid down in the last 10 million years, judging by the lack of craters.

Dramatic landscapes are coming into focus as images streaming in over the last couple of months have let researchers create topographical maps. One 320-kilometer-long crack informally dubbed Virgil Fossa features walls roughly 4 kilometers high, about twice the depth of the Grand Canyon.

Two mountains look strangely similar to shield volcanoes on Earth. But on Pluto, the volcanoes would spew ice. "There's nothing like this seen in the outer solar system," says planetary scientist Oliver White of NASA Ames Research Center in Moffett Field, Calif. The mountains aren't definitely volcanoes, but scientists aren't sure what else to call them.

Pluto's atmosphere is much colder and more compact than researchers thought, which implies that it's escaping into space at a much lower rate than predicted. Calculations before the encounter suggested that the planetwide ice level has dropped by nearly 1 kilometer over Pluto's lifetime as the ice sublimated into the atmosphere and drifted into space. But at the current escape rate, Pluto would have knocked only about 15 centimeters off its icy crust. "It's dangerous to go from a snapshot to 4.5 billion years," cautions Leslie Young, a planetary scientist at the Southwest Research Institute in Boulder, Colo. "But we're scientists — that's what we do."

Whirling far above Pluto, four tiny satellites — Nix, Hydra, Kerberos and Styx — are also behaving unexpectedly (*SN: 11/28/15, p. 14*). Pluto's gravity should have slammed on the brakes and slowed down their spins. But the rapidly twirling moons seem to be unfazed. Hydra, the outermost moon, whips around its axis about 89 times during each loop around Pluto and Charon, Pluto's largest moon. Nix, meanwhile, appears to be flipped nearly upside down; the other three tiny moons might be spinning on their sides. "This is unprecedented," says planetary scientist Mark Showalter of the SETI Institute in Mountain View, Calif.

Lots more data are yet to come. If the first 20 percent is any indication, Pluto is probably not done surprising researchers. "Pluto and its system of satellites really outsmarted us," Stern says. "I think it's fair to say that New Horizons gets an A for exploration ... but we get an F for predictive ability." ■

MEETING NOTE

Impact from a space rock may have helped shape Pluto's heart

Pluto's got a roughly 4-billion-year-old case of heartbreak. The left ventricle of the dwarf planet's famous heart-shaped feature might owe its existence to a run-in with a big space rock, planetary scientist Paul Schenk reported November 10.

The region, informally called Sputnik Planum, is an 825-kilometer-wide, 4-kilometer-deep basin, said Schenk, of the Lunar and Planetary Institute in Houston. And except for some erosion to the south, the basin is roughly circular, which is typical for other impact craters in the solar system. If an interplanetary interloper is at fault, it would have smashed into Pluto at least 4 billion years ago. "It's difficult to explain by other mechanisms," Schenk said. — *Christopher Crockett*

SWRI, JHU-APL, NASA

See how Pluto's moons spin at **bit.ly/SN_PlutoMoons**

ATOM & COSMOS

Moon might have formed in 2 stages

Chemicals missing from lunar rocks may be under crust

BY CHRISTOPHER CROCKETT

Rocks on Earth and the moon are nearly identical — except when they're not. New simulations may be close to figuring out why lunar samples are in many ways chemically identical to counterparts on Earth, yet missing a few key ingredients.

Easily vaporized elements, called volatiles, are largely missing from moon rocks but might be sequestered in the lunar interior. This core is hidden beneath a crust that accumulated in a second phase of moon formation, planetary scientist Robin Canup reported November 11.

Volatiles such as sodium and zinc were long assumed to have been blasted away in Earth's collision with a Mars-sized planet that formed the moon roughly 4.5 billion years ago. "People made this assertion for decades," said Canup, of the Southwest Research Institute in Boulder, Colo. "But it doesn't work very well."

Even in the disk of molten and vaporized rock that hung out after the impact, temperatures weren't high enough to launch volatiles away from Earth, Canup said. The atoms must have stayed local but somehow avoided the moon.

"We are in a strange situation where some things match perfectly and some things do not match," says planetary scientist Sébastien Charnoz of the Institute of Earth Physics of Paris. "So you have to find a strange scenario to explain it all."

Canup and colleagues ran computer simulations that tracked how Earth's temporary ring evolved over time. Material in the outer part of the ring, still packed with volatiles, was far enough away to not be strongly affected by Earth's gravity. That material quickly cooled and condensed into a ball roughly half as massive as the moon.

The inner part of the ring is more complicated. A molten river of rock encircled the planet, sandwiched between layers of gas. The liquid ring would have spread while the gas — where the volatiles ended up — stayed put. "This is a key idea," Charnoz says. "You have a physical mechanism to separate the two things."

As the liquid disk spread away from Earth, the outer edges cooled and formed volatile-depleted pebbles, which were snagged by the protomoon's gravity. Drawing from the molten ring, the moon slathered itself in a crust devoid of the elements that are still missing today.

By the time the rest of the disk cooled enough for gas and liquid to mingle, the moon had drifted too far from Earth to harvest the remaining pieces, Canup says.

Some evidence supports the idea that volatiles are hiding in the moon, she says. A few rocks dredged up from deep within the moon by Apollo missions have traces of a highly volatile molecule: water. ■

ATOM & COSMOS

Martian moon headed for breakdown

Gravity from Red Planet causing Phobos to stretch and crack

BY CHRISTOPHER CROCKETT

Mars' moon Phobos is stressed and starting to crack under pressure. A network of grooves encircling the moon are early signs that the Red Planet's gravity is splintering Phobos, Terry Hurford reported November 10.

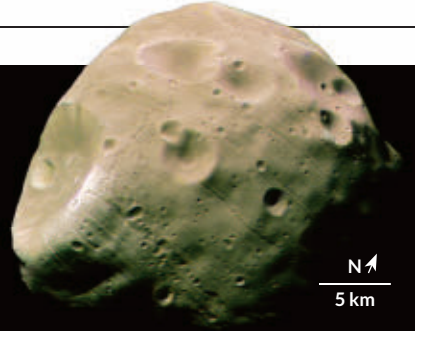
Phobos, unlike its sibling satellite Deimos, is slowly spiraling toward Mars. "As [Phobos] gets closer ... it gets pulled out into a football shape," says Hurford, a planetary scientist at the NASA Goddard Space Flight Center in Greenbelt, Md. "The changing shape causes stresses that we think form the grooves." Sometime in the next 50 million years, the stress will become too much and the moon will break apart.

The grooves were first seen by the Viking landers in 1976, and some researchers proposed stress fractures as a cause. But scientists also thought Phobos was a monolithic chunk of rock, making it hard to crack. If Phobos is instead a loose conglomeration of rubble encased in a rocky crust (*SN: 6/5/10, p. 11*), as Hurford assumes in his computer simulations, Mars' gravity could deform the moon and form the cracks seen today.

"It all fits together pretty well," says Alan Harris, a planetary scientist at the Space Science Institute in Boulder, Colo. Harris is one of the scientists who proposed in 1977 that the grooves were Mars' fault. Stress can't explain every fissure, however; some grooves aren't lined up the way stretch marks from Mars' gravity should be, he notes. "The sticky wicket continues to be these other grooves."

A rain of debris from meteorites probably created those misfit grooves, suggested Michael Nayak, a graduate student at the University of California, Santa Cruz, in a separate presentation. Nayak ran computer simulations that showed that some rocks blown off the moon's surface stay in orbit around Phobos for a while. The debris eventually falls back on Phobos and can form grooves that resemble the anomalous trenches.

Harris agrees that the two hypotheses together offer a tidy explanation for the Phobos fissures. While scientists generally like to keep explanations simple, he says, "every now and then, nature doesn't have a simple cause." ■



Grooves etched across Mars' moon Phobos, seen in this 2004 photo from the Mars Express orbiter, are caused by a mix of stress fractures and impact debris, new studies suggest.

ESA, DLR, FU BERLIN (CC BY-SA 3.0 IGO)

BODY & BRAIN

Brain's GPS cells map time, distance

Neurons that monitor location have many jobs, rat study find

BY LAURA SANDERS

Specialized cells that make up the brain's GPS system have an expanding job description. In addition to mapping locations, these cells can keep track of distance and time, too, scientists report in the Nov. 4 *Neuron*.

Those specialized cells, called grid cells, were thought to have a very specific job, says neuroscientist Loren Frank of the University of California, San Francisco. But, he says, the new study says, "not so fast, everybody."

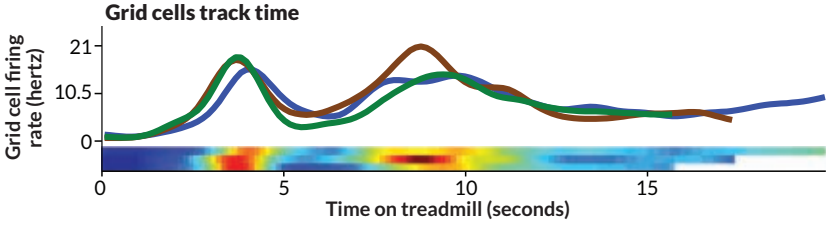
The growing to-do list of grid cells shows that the brain's navigational system is surprisingly flexible.

The discovery of grid cells, found in a part of the brain called the entorhinal cortex, was recognized with the Nobel Prize last year (*SN Online: 10/6/14*). These brain cells fire off regular signals as animals move around in space, helping to form an internal map of the environment. Neuroscientist Howard Eichenbaum of Boston University and colleagues wondered what those cells do when an animal stays put. By training rats to run on a treadmill, the researchers had a way to study grid cells as time and distance marched forward, but location remained the same.

Unlike recently discovered "speed cells" (*SN: 8/8/15, p. 8*), these grid cells don't change their firing rates to correspond to changes in the rats' swiftness, the team found. Instead, these cells stay tuned to distance or time, or both.

Most of these grid cells fired off bursts of messages at particular distances or times, electrodes implanted into the rats' brains revealed. During a 16-second run, for instance, a time-detecting grid cell might become active at second 5, and then again at second 10. Similarly, a distance-marking grid cell might fire every time the rat ran 200 centimeters. Those responses stayed the same even when the scientists varied the speed of

Keeping time A grid cell fires off signals at particular times as a rat runs on a treadmill. The cell behaved similarly as the rat ran at slow (blue), moderate (brown) and fast (green) speeds.



EARTH & ENVIRONMENT

Origin of Earth's water questioned

Deuterium levels in mantle suggest comets not the source

BY THOMAS SUMNER

Molecules entombed inside pristine magmas suggest that Earth's water came from soggy dust, not icy comets.

The relative abundance of a heavier version of hydrogen called deuterium serves as a fingerprint of where in the solar system a reservoir of H_2O originated (*SN: 5/16/15, p. 18*). Previous work hunting for the source of Earth's water measured deuterium in seawater, but that's a tainted metric, researchers report in the Nov. 13 *Science*. Aboveground processes such as hydrogen atoms leaking into space can hike deuterium concentrations in the planet's surface water (*SN: 9/5/15, p. 8*).

The researchers found that deuterium levels in water trapped inside molten rock and unaltered since the planet's early days are significantly lower than those in seawater. The lower deuterium fingerprint for Earth's primordial water hints that the world's wetness resulted from water-soaked dust grains present during the planet's assembly, the researchers conclude.

"Water came in during Earth's formation and has been around ever since," says study coauthor Lydia Hallis, a planetary scientist at the University of Glasgow. "It wasn't added later."

Not all experts agree with this conclusion. But if it holds up, it would cast doubt on previously proposed water sources such as a fortuitous bombardment of icy space rocks around 4.5 billion to 3.8 billion years ago, says study coauthor Karen Meech. "If you need exotic mechanisms to get water to Earth, then just being in a habitable zone doesn't mean you have all the ingredients for life," says Meech, a planetary scientist at the University of Hawaii in Honolulu.

At colder temperatures, deuterium forms a more stable bond with oxygen than hydrogen does. So water enriched in deuterium is a sign that the H_2O formed in the solar system's chillier regions, such as the outer areas where comets originate. Water low in deuterium is more likely to come from the warmer, inner solar system.

Uncovering which region supplied Earth's water requires collecting H_2O molecules left over from the planet's deep past. Volcanoes occasionally spit out water-containing molten rock from the deep mantle, providing an accessible record of Earth's original composition.

The team had a few false starts. Hawaiian lavas were contaminated with water from a nearby aquifer. Lava samples from Icelandic and Canadian volcanoes, however, seemed largely unperturbed by processes that alter deuterium levels. Within the lavas were small bits of glass encased inside a mineral called olivine. This glass serves as an

B. KRAUS *ET AL*/*NEURON* 2015

the treadmill. About 40 percent of grid cells detected both time and distance.

This recurring rhythmicity for both time and distance echoes the way that grid cells map locations. "It's not clear why they have this kind of cycle, but it's really the same thing the grid cells would do in space, where they fire as the animal passes through a series of locations," Eichenbaum says.

When a rat is on a treadmill, visual landmarks and locations in space no longer matter, and the grid cells switch gears accordingly, Eichenbaum says. "The important part to the animals is how far they ran and how long it took, and that seems to be what the cells are tracking."

The results show how adaptable the brain is, Frank says. "The major, important point is that the brain reconfigures itself," he says. "Even these things that look like they'd be crystalline and rigid can be reconfigured or reappropriated for other things when those other things matter." ■

undisturbed time capsule preserving the molten rock's original composition.

Analyzing the hydrogen atoms trapped inside the glass revealed deuterium levels as low as 122 parts per million, roughly 22 percent less than the 156 ppm found in seawater. This scarcity doesn't match the large deuterium abundances found in ice-laden comets, Hallis says. Earth's water instead probably originated from a warmer part of the early solar system. Water molecules could have stuck onto dust grains floating in the gas cloud that birthed the sun and planets. As Earth assembled, this waterlogged dust created a wet planet right from the start, Hallis and colleagues propose.

Although cosmic dust may have provided some of Earth's water, it couldn't have provided all of it, contends cosmochemist Conel Alexander of the Carnegie Institution for Science in Washington, D.C. As the planet formed, Earth's raw materials would have heated up and dried out, he says, requiring an extra delivery of water. ■

HUMANS & SOCIETY

Bees sweetened early farmers' lives

Chemical traces on pottery point to broad use of wax, honey

BY BRUCE BOWER

Here's the latest buzz on ancient farmers in Southwest Asia and Europe — they were big into honeybees.

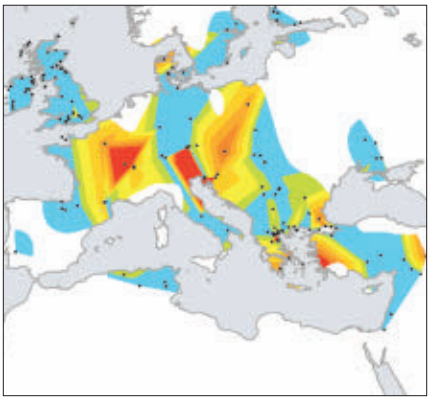
Farmers spreading west across that wide swath of territory acquired beeswax and probably consumed honey around 9,000 to 5,000 years ago, say biogeochemist Mélanie Roffet-Salque of the University of Bristol in England and colleagues. Fragments of organic material clinging to pottery from early farming sites display a chemical signature typical of beeswax, the group reports in the Nov. 12 *Nature*.

The new study is the largest analysis of chemical residues on pottery to date and the first to document the widespread use of bee products among ancient farmers, says bioarchaeologist Oliver Craig of the University of York in England.

It's still unclear how early farmers acquired beeswax and presumably honey, Roffet-Salque says. "We have shown that these farmers were exploiting bee products, but we cannot really tell if it was a result of honey hunting or beekeeping."

People probably didn't control honeybees to a large-enough extent to domesticate the insects until "well after" 4,000 years ago, says Greger Larson, a bioarchaeologist at the University of Oxford.

Waxy spread A map of Europe, West Asia and North Africa shows early farming and herding sites (dots) that had pottery analyzed in a new study. Colors denote proportion of beeswax residues relative to all residues on vessels.



M. ROFFET-SALQUE *ET AL*/*NATURE* 2015

Remains of a large, 3,000-year-old beekeeping facility have been found in Israel (*SN: 9/27/08, p. 11*). Depictions of small-scale beekeeping in ancient Egypt date to as early as 4,400 years ago, Larson says.

Evidence of honey hunting spans an even broader time period. Rock art in Spain that may be as old as 10,000 years portrays two men climbing a rope ladder with sacks to collect honey and honeycombs from a wild hive. Present-day hunter-gatherers in warm regions collect honey from wild hives, often making fires to smoke out bees and avoid getting stung, a team reported last year in the *Journal of Human Evolution*.

Roffet-Salque's group analyzed over 6,400 pottery vessels from 154 farming sites. The most abundant evidence of beeswax appeared on pottery shards from the Balkan Peninsula, including Greece and the Aegean Islands. Of 1,915 pottery pieces found there dating to 7,800 to 5,000 years ago, about two dozen yielded beeswax residue.

Evidence of beeswax also turned up on a 7,000- to 6,000-year-old pottery fragment from an Algerian site. This is the first evidence of honeybee exploitation by ancient North African animal herders.

Two vessels from a farming site in eastern Turkey contained the oldest confirmed beeswax remains, dating back some 8,500 years.

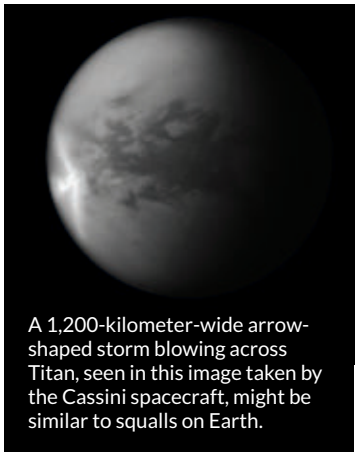
Early farmers and herders may have used honey in cooking, leaving behind beeswax residue on pottery, the researchers say. Vessels may have also been used to boil down wax honeycombs so wax could be used for ritual, medical or other purposes. A 6,500-year-old human jaw from Slovenia in southern Central Europe contains a tooth with a beeswax filling. ■

ATOM & COSMOS

Mighty winds fuel megastorms on Titan

OXON HILL, MD. — Beneath the orange haze of Saturn's moon Titan, methane rains from the sky and pools in lakes — and might even burst forth from massive storm squalls like those seen on Earth.

Titan has garden-variety thunderstorms that bring a bit of rain, then disappear. Now, the Cassini orbiter has seen phenomena that can't be explained by these run-of-the-mill storms: cloud outbursts, liquid-carved channels and dark regions "reminiscent of rain falling on a parking lot," planetary scientist Scot Rafkin reported November 11 at a meeting of the American Astronomical Society's Division for Planetary Sciences.



A 1,200-kilometer-wide arrow-shaped storm blowing across Titan, seen in this image taken by the Cassini spacecraft, might be similar to squalls on Earth.

Using computer simulations of cloud systems, Rafkin found that with a bit of wind shear, Titan could produce giant, long-lasting storm systems. On Titan, though, these storms would be beefed up: The squalls would last for longer than 24 hours and travel for more than 1,000 kilometers while dumping a couple of meters' worth of methane from clouds three times as high as their counterparts on Earth.

Such storms would cause massive flooding on Earth as well as on Titan. "It's more than enough to carve the river channels and fluvial features we see on the surface," says Rafkin, of the Southwest Research Institute in Boulder, Colo. — *Christopher Crockett*

BODY & BRAIN

Football linemen's cardiac risks rise over a season

ORLANDO, FLA. — Blocking and tackling may not be the riskiest thing that linemen face on the football field. Blood pressure and cardiac function of college football linemen worsened over the course of a season, researchers reported November 10 at the American Heart Association's annual scientific sessions. The study adds to evidence that these players suffer more risk of heart disease than any other members of the team.

Since a controversial study in the 1990s reported that linemen have triple the risk of death from cardiovascular disease compared with other players, researchers have paid particular attention to the health consequences of playing football. Linemen are usually the largest members of a team, and they're getting bigger, now averaging more than 300 pounds — a heart disease risk factor in itself. A 2013 study led by Stanford researchers found that even after taking body size into account, linemen were more likely to have an unhealthy enlargement of cardiac muscle.

Most studies have been snapshots in time without follow-up. For the new research, doctors at Massachusetts General Hospital in Boston analyzed the cardiac health of 87 college freshman athletes at the beginning of the football season and again after the last game. While no player had high blood pressure at the beginning of the season, nine of 30 linemen did by the end of the season. Four of 57 players in other positions ended the season with high blood pressure.

Cardiac function also suffered in linemen. They were more likely to experience a thickening in the wall of the left ventricle, the heart's main pumping chamber, and a decrease in its function.

The long-term effects of the cardiac changes are still under investigation, said study researcher Jeffrey Lin, now at Columbia University Medical Center. — *Laura Beil*

ATOM & COSMOS

Nearby Earth-sized planet spotted

The nearest Earth-sized planet beyond the solar system is at most 39 light-years away.

That's the distance to GJ 1132b, a newly discovered rocky planet about 1.2 times as large as Earth that orbits a small, dim star in the constellation Vela. The planet is almost certainly too hot to support life, but it is about 90 light-years nearer to us than the next-closest known Earth-sized planets. The discovery could herald the era of probing the atmospheres of nearby small worlds for signs of life. GJ 1132b is "arguably the most important planet ever found outside the solar system," astronomer Drake Deming of the University of Maryland in College Park writes in a review that accompanies the study in the Nov. 12 *Nature*.

The MEarth-South Observatory, eight automated, 40-centimeter telescopes in Chile, spotted the shadow of GJ 1132b as it crossed in front of its star once every 1.6 days. The researchers claim that the Hubble Space Telescope could determine the composition of the planet's atmosphere by measuring the starlight that passes through it. — *Andrew Grant*

LIFE & EVOLUTION

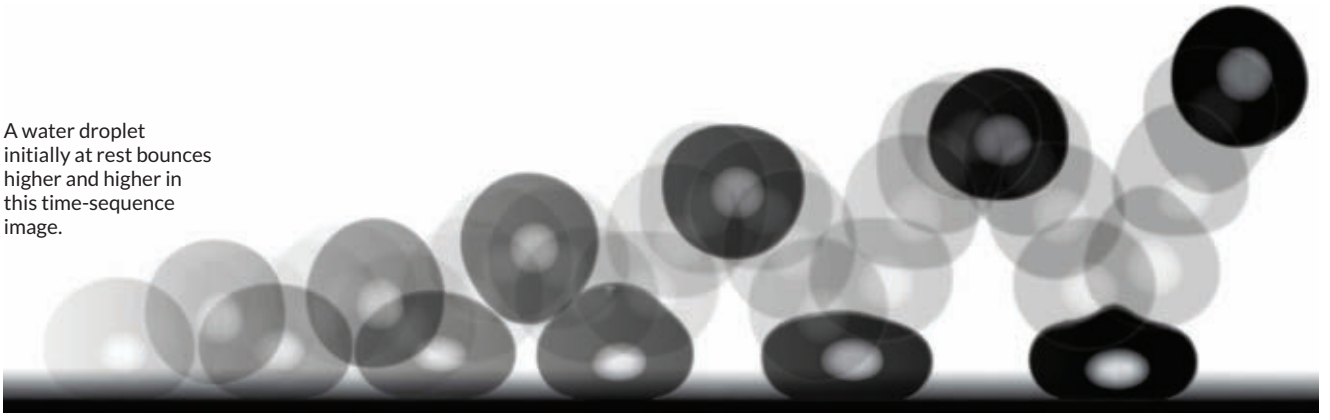
Ancient gardeners saved the gourd

Humans may have saved pumpkins, squashes and gourds from an Ice Age extinction, researchers say online November 16 in the *Proceedings of the National Academy of Sciences*. Genetic analysis of 91 ancient and modern gourds (*Cucurbita* sp.) suggests that people began cultivating the plants nearly 10,000 years ago.

Wild gourds are very bitter, so the team tested genomes from 46 modern mammals for a gene related to tasting bitterness. Smaller mammals had more copies of this gene, suggesting that ancient small mammals probably rejected the fruit, while megafauna like mastodons helped spread early *Cucurbita* seeds.

When the big animals died out, gourds lost a seed disperser. Without humans to fill the role, some favorite fall fruits might not be around today. — *Chris Samoray*

JPL-CALTECH/NASA, SPACE SCIENCE INSTITUTE



A water droplet initially at rest bounces higher and higher in this time-sequence image.

MATTER & ENERGY

Water droplets spontaneously bounce, sans trampoline

When in a tough spot, some water droplets bounce their way to freedom.

Initially stationary droplets on an extremely water-repellent surface such as etched aluminum bounce as if on a trampoline, researchers at ETH Zurich reveal in the Nov. 5 *Nature*. The scientists suspect that speedy molecules of water vapor stuck between the droplet and the surface exert enough pressure to launch the droplet skyward.

The phenomenon occurs only if the surrounding air pressure is about a hundredth of that at sea level. Still, studying the interaction of water with various materials could lead to better water-repellent and deicing surfaces.
— Andrew Grant

BODY & BRAIN

Blood-brain barrier jiggled loose to deliver medicine

In its job protecting the brain from would-be invaders, the blood-brain barrier also blocks medicines from reaching the brain. But on November 5, ultrasound zaps shook loose that tight barrier in a woman who has a brain tumor, potentially granting entry to a chemotherapy drug. The technique, which relies on tiny bubbles set jiggling by ultrasound beams, has shown promise in animals (*SN: 9/27/08, p. 20*). But this is the first time it has been tried on a person, says neurosurgeon Todd Mainprize of Sunnybrook Health Sciences Centre in Toronto, who led the procedure.

Mainprize and colleagues injected microbubbles, a chemotherapy drug and an imaging agent that could be visualized by a scanner into the woman's blood. Then, targeted ultrasound beams passed through her brain, where they made the microbubbles in her blood vessels contract and expand. This jostling temporarily opened the blood-brain barrier, allowing the imaging agent — and presumably the drug — to enter the brain tissue near her tumor, Mainprize reported in a November 10 news briefing.

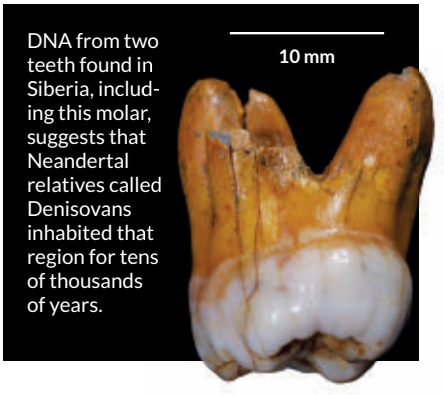
The unpublished results are preliminary; the researchers don't know how much of the drug made it into the tumor, or how the patient will fare long-term. Mainprize and colleagues plan to perform the procedure on other patients to test whether it is safe and feasible. If so, the method might ultimately be used to deliver medicine to treat a wide range of brain maladies, such as tumors and Alzheimer's disease. *— Laura Sanders*

HUMANS & SOCIETY

DNA puts Neandertal relatives in Siberia for 60,000 years

Mysterious Neandertal relatives known as Denisovans may have hung out in southern Siberia for 60,000 years or so.

Until now, Denisovans were known only by DNA from a finger bone found in Siberia's Denisova Cave in 2008. Susanna Sawyer of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, and colleagues have now extracted DNA from two Denisovan teeth found in the same cave.



DNA from two teeth found in Siberia, including this molar, suggests that Neandertal relatives called Denisovans inhabited that region for tens of thousands of years.

The finger and one of the teeth had many more modifications in their mitochondrial DNA than corresponding DNA from the other tooth. To have accumulated that many changes, Denisovans must have lived in the area for 60,000 years, the scientists report online November 16 in the *Proceedings of the National Academy of Sciences*. The two younger finds date to about 50,000 years ago, suggesting the other tooth is 110,000 years old.

Nuclear DNA comparisons show that all three specimens from Denisova Cave belonged to a common population distinct from Neandertals and modern humans (*SN: 8/25/12, p. 22*). *— Bruce Bower*

BODY & BRAIN

Study brews up more evidence for coffee's health benefits

The benefits of drinking coffee continue to filter in.

An analysis of over 200,000 medical professionals followed for up to 28 years finds that drinking up to five cups of coffee a day is associated with reduced risk of dying early from heart and brain diseases as well as from suicide.

The results were adjusted for factors like smoking, weight and diet. Benefits were more pronounced for those who had never smoked, an international research team reports online November 16 in *Circulation*.

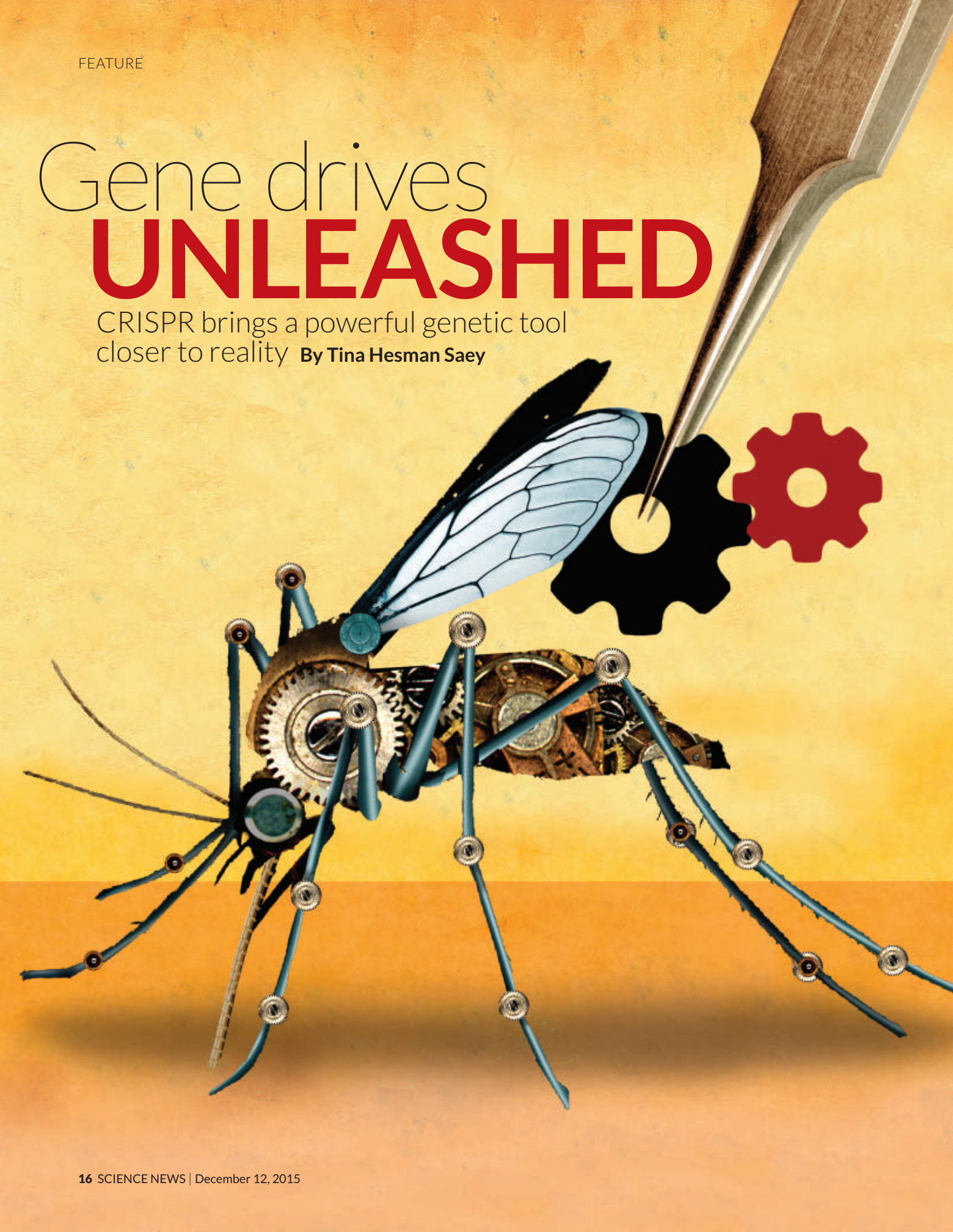
Both caffeinated and decaf java had positive effects, leading the researchers to speculate that coffee's potency as a health elixir stems from chemical compounds in the bean such as chlorogenic acids (*SN: 10/3/15, p. 16*).
— Teresa Shipley Feldhausen

FROM TOP: T. M. SCHUTZIUS, G. GRAEBER, D. POULIKAKOS; BENCE VIOLA

Watch water droplets bounce at **bit.ly/SN_droplet**

Gene drives UNLEASHED

CRISPR brings a powerful genetic tool closer to reality **By Tina Hesman Saey**



Genies are said to have the power to grant three wishes. But genies recently released from laboratory flasks promise to fulfill nearly any wish a biologist can dream up.

End the scourge of insect-borne diseases? Check. Inoculate endangered amphibians against killer fungi? Yes. Pluck invasive species from environments where they don't belong? As you wish.

These genies aren't magical; they are research tools known as gene drives — clever bits of engineered DNA designed to propel themselves into the DNA of a pesky or troubled organism. A gene drive is a targeted contagion intended to spread within species, forever altering the offspring.

Gene drive enthusiasts say these genies could wipe out malaria, saving more than half a million lives each year. Invasive species, herbicide-resistant weeds and pesticide-resistant bugs could be driven out of existence. Animals that carry harmful viruses could be immunized with ease.

Scientists have sought the power of gene drives for decades. But only with the emergence of a genetic tool called CRISPR/Cas9 — the bottle opener that unleashed the genie — has gene drive technology offered the prospect of providing a speedy means to end some of the world's greatest health and ecological scourges.

"Everything is possible with CRISPR," says geneticist Hugo Bellen. "I'm not kidding."

But genes designed to spread through populations and alter ecosystems could have unforeseen consequences. Researchers have designed ways to keep gene drives confined in the lab, but no such safety nets exist for gene drives released into the wild. A technology to eradicate entire species, even when those species are pests, raises ethical and regulatory issues that scientific and government agencies are just beginning to consider.

As yet, no CRISPR gene drive has been released in the wild — few have even been built. There are plenty of technical hurdles to overcome. But there is enough awareness of the peril accompanying the promise that researchers and philanthropic organizations interested in the technology recently asked the U.S. National Academy of Sciences to weigh in on gene drives. The academy's report won't be issued until next year, but that hasn't stopped the debate — or gene drive science — from moving forward.

Rule breakers

Gene drives aren't naked DNA floating around the air and water. They are molecular tools that scientists engineer into an organism's DNA. While biologists have long imagined building gene drives, it was the arrival of CRISPR that transformed imagination into application.

CRISPR (an acronym for "clustered regularly interspaced short palindromic repeats") refers to bits of viral DNA that bacteria have incorporated into their own genomes. With assistance from the enzyme known as Cas9, CRISPRs help bacteria defend themselves against viruses.

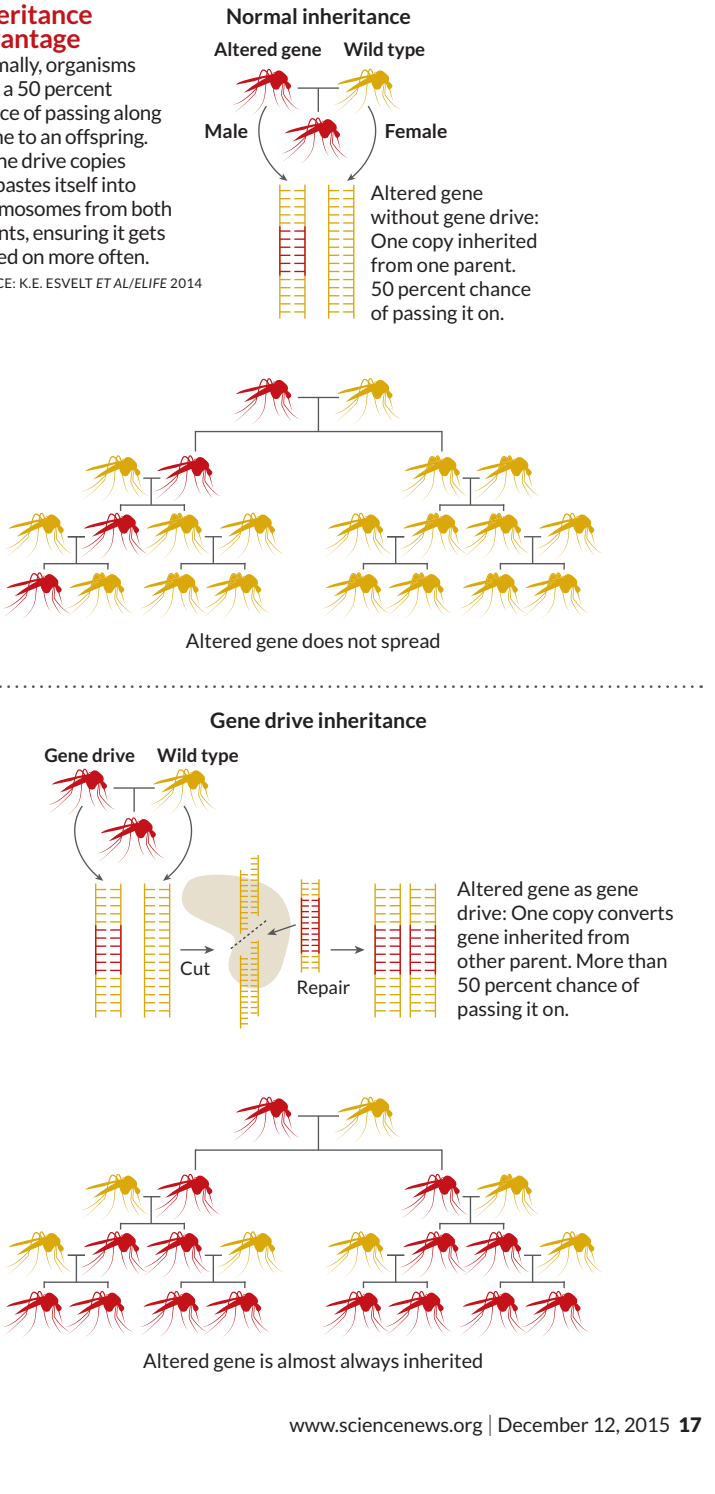
"Everything is possible with CRISPR. I'm not kidding."

HUGO BELLEN

Inheritance advantage

Normally, organisms have a 50 percent chance of passing along a gene to an offspring. A gene drive copies and pastes itself into chromosomes from both parents, ensuring it gets passed on more often.

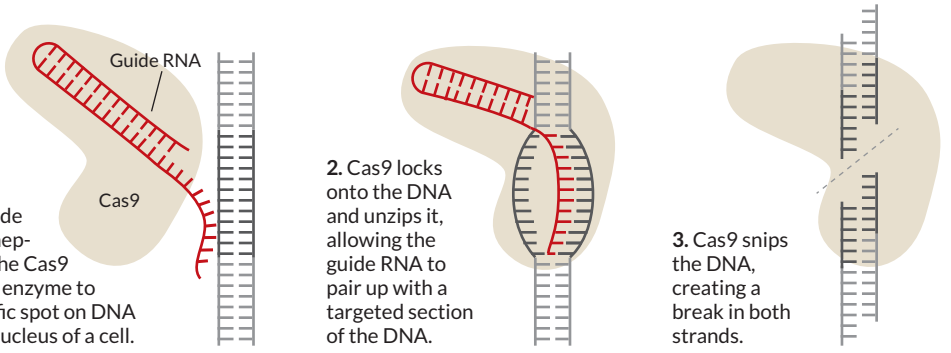
SOURCE: K.E. ESVELT *ET AL*/*ELIFE* 2014



OPPOSITE PAGE: MICHAEL MORGENSTERN; THIS PAGE: E. OTWELL AND M. TELFER

Drive chain reaction

Gene drives became much easier to build with CRISPR/Cas9. These new drives insert genes that produce the components of the system: a cutting enzyme and an RNA to guide it to the proper cutting site. When an organism mates, the drives convert the mate's DNA to a gene drive as well, setting off a chain reaction that will continue in perpetuity.



1. A guide RNA shepherds the Cas9 cutting enzyme to a specific spot on DNA in the nucleus of a cell.

2. Cas9 locks onto the DNA and unzips it, allowing the guide RNA to pair up with a targeted section of the DNA.

3. Cas9 snips the DNA, creating a break in both strands.

In 2012, researchers announced that they had modified the CRISPR system into a gene-editing tool for cutting and pasting nearly any gene into any organism. Since then, CRISPR gene editing has taken biology by storm. It has become so widespread and easy that even third-graders are using it in science class, says CRISPR cocreator Jennifer Doudna of the University of California, Berkeley.

Already, researchers have used CRISPR/Cas9 to edit genes in human cells grown in lab dishes, monkeys (*SN: 3/8/14, p. 7*), dogs (*SN: 11/28/15, p. 16*), mice and pigs (*SN: 11/14/15, p. 6*), yeast, fruit flies, the worm *Caenorhabditis elegans*, zebrafish, tobacco and rice.

"I do CRISPR every day," says Bellen, of Baylor College of Medicine in Houston. All around him, scientists are engineering fruit flies, nematode worms and mice using the bacteria-derived tool. "It's one of those very rare events when a technology revolutionizes how you do science."

Usually, molecular biology techniques are specific to one organism, so CRISPR's flexibility in editing genes from such a wide array of organisms is extremely attractive for researchers, says Anthony James, a molecular biologist at the University of California, Irvine.

If they can nimbly edit any gene in any organism, scientists ought to be able to design a gene drive for that species as well. That could mean that invasive species such as Australia's pesky cane toads and other organisms that scientists haven't been able to manipulate genetically could now become gene drive targets with CRISPR.

Editing made easier Gene-editing tools are improving. The CRISPR/Cas9 system is easier to program and faster to produce than other gene editors in use.

SOURCE: MARK OSBORN/UNIV. OF MINNESOTA

Platform	Year developed	First used in live animals	Time to do an experiment
Zinc finger nucleases	1996	2002	Months/year
TALENs	2010–2011	2011	Week(s)
CRISPR/Cas9	2012	2012–2013	Days

Gene drives are just the latest attempt at biological control systems. In the past, biologists have introduced natural enemy species to control pests. For instance, a fungus has been used to tamp down gypsy moth incursions in the northeastern United States. Gene drives aren't much different, says gene drive pioneer Austin Burt, an evolutionary geneticist at Imperial College London. "But instead of releasing a whole species, you're releasing a gene."

Burt has made a career studying "selfish genetic elements," parasitic pieces of DNA or RNA that exist only to propagate themselves. They go by other names, such as jumping genes, transposable elements, biased gene converters or meiotic drivers. Selfish elements live in a wide variety of organisms (including humans), and have devised a variety of methods for getting themselves passed on. What they have in common is the ability to circumvent the normal rules of inheritance, first described by Gregor Mendel in the 1860s.

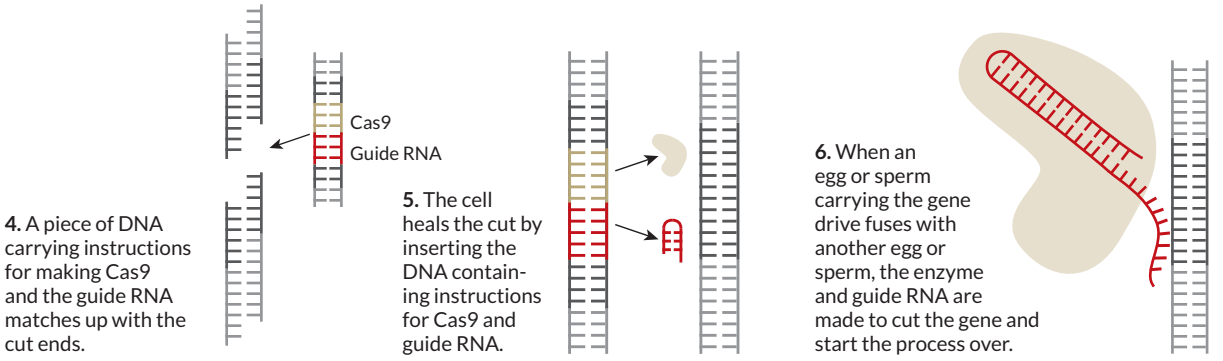
Under Mendelian rules, a gene has a 50-50 shot at being passed from a parent to an offspring. Selfish elements don't play by those rules. They manipulate the system to get inherited by more than 50 percent of offspring, even if it means harming the organism.

Engines of change

In 2003, Burt proposed harnessing some of these selfish entities for the greater good. He envisioned inserting a selfish element into a particular gene, creating a gene drive, which would change the inheritance rules to make sure that the drive would get passed on to a majority of a creature's progeny.

Burt's notion was to domesticate a microbial family of selfish elements called homing endonuclease genes. Those genes make endonucleases — DNA-cutting enzymes that target one spot in an organism's entire genetic catalog, or genome. Like molecular scissors, the enzyme snips the

E. OTWELL AND M. TELFER



target DNA if it doesn't already have the selfish element. Next, a copy of the homing endonuclease gene with its surrounding DNA inserts itself into the gap as the cell heals the breach. Once inserted into one chromosome, the gene snips and pastes itself into the matching chromosome inherited from the other parent. So when the organism mates and divides its genetic material, both chromosomes will carry the editing machinery. In the fertilized egg, this cut-and-paste machinery would also convert the mate's DNA. This repetitive editing allows the selfish element to drive itself into nearly every organism in a population. Gene drives could speed through a population like wildfire blazing across grasslands.

This approach has special appeal for weakening the disease-carrying dexterity of mosquitoes. A gene drive carried by 1 percent of mosquitoes in a population can be inherited so efficiently that in about 20 generations, 99 percent of all the mosquitoes will carry it, Burt calculates.

Burt's math probably isn't far from what might happen if a gene drive were released in the wild. "This has happened in nature," says Nora Besansky, who studies malaria-carrying mosquitoes. A selfish element called the P element invaded the DNA of *Drosophila melanogaster* fruit flies in the 1950s, and "in less than 50 years, spread itself worldwide, across oceans, without any human intervention," says Besansky, of the University of Notre Dame.

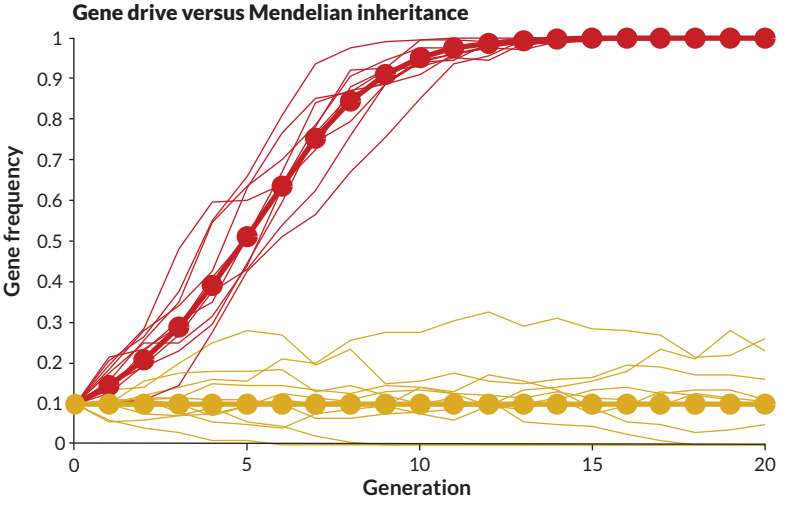
Humans might be able to direct gene drives to kill only female mosquitoes (the ones that bite and spread disease), or render the insects incapable of carrying malaria, dengue or other diseases.

To put his gene theory into practice, all Burt and his colleagues had to do was reengineer a homing endonuclease to cut a certain spot in a mosquito's genome. Not so easy, says synthetic biologist Kevin Esvelt of Harvard Medical School. "It's one of the hardest problems in protein engineering."

It took years, but in 2011, Burt and colleagues announced in *Nature* that they had created a homing endonuclease that could find and cut a gene in mosquitoes. That experiment showed that building a gene drive in mosquitoes is possible. But gene drives that will get rid of mosquitoes or hinder their ability to transmit malaria are in the works *(SN Online: 11/23/15)*.

In addition to homing endonucleases, scientists have been tinkering with two artificial protein systems as programmable gene-editing tools. Those tools, called zinc finger nucleases and TALENs (short for transcription activator-like effector nucleases), link a cutting enzyme to a protein that binds DNA in specific spots. Those molecules have enabled scientists to make precision edits to a menagerie of genomes (see story, Page 7). But the proteins "are a burden to make," says Bellen. Working with them is "just too painful and too slow," he says. "If it's not fast and efficient, it's not good technology."

CRISPR provides the speed. Like earlier technologies, the part of the CRISPR system that snips



Kicking into high gear Computer simulations predict that a gene drive inherited by 75 percent of progeny (red lines) starting at 10 percent of the population could be passed to all individuals within a few generations. A gene that follows normal 50-50 rules of inheritance (yellow lines) would not overtake the population.
SOURCE: M. VELA/NORTH CAROLINA STATE UNIV.

M. TELFER

Golden touch
A gene drive turned normal fruit flies (A) into yellow flies (B). The gene drive didn't work perfectly, however. In one fly (C), the gene drive worked only in cells on the left side of the body.

DNA is a protein (the Cas9 enzyme). But unlike other systems, CRISPR pairs the enzyme scissors with pieces of RNA that guide it to the gene researchers want to cut. When the RNA finds a match on the information-carrying units of DNA, called bases, the Cas9 enzyme cleaves the DNA.

RNA is very easy to program. Researchers just need to select the DNA segment they want to cut and synthesize an RNA molecule that matches. The process takes days, as opposed to weeks or months for other technologies.

Researchers have wholeheartedly embraced CRISPR and used the technology to easily manipulate the genomes of many organisms in ways that would have taken years to achieve, if ever. "It's not oh, maybe someday," Doudna says. "It's now."

Fast forward

Harvard's Esvelt was among the first to recognize that CRISPR is essentially an ultraflexible homing endonuclease that could easily be turned into a gene drive. He and colleagues laid out some of the possible uses for CRISPR gene drives in July 2014 in *eLife*.

At the time, no one had reported creating a gene drive using CRISPR. That soon changed. In January, Esvelt and colleagues reported online at bioRxiv.org that they had made a gene drive in yeast. In March, researchers from the University of California, San Diego reported online in *Science* that they had created a gene drive in fruit flies.

Those researchers, biologists Valentino Gantz and Ethan Bier, were looking for a way to easily make mutations in *Drosophila* fruit flies. Gantz focused on the yellow gene, which affects a fly's color. He devised a piece of DNA carrying the gene that produces the Cas9 protein along with DNA that produces guide RNAs, which direct the drive to cut and plunk itself in the yellow gene, breaking it.

A broken yellow gene jaundices the flies, which are normally tan with dark stripes. The yellow gene is on the X chromosome. Female flies, which have two copies of the X chromosome, can inherit one copy of the broken yellow gene and retain their normal coloring. Two copies turns them golden. But males have only one X chromosome, and therefore just one copy of the gene, so any disruption will turn them yellow.

When an altered X chromosome is passed down to female offspring, Gantz reasoned, the gene drive should convert the normal X from the other parent into one with a broken yellow gene. Every female would be yellow.

"I figured this was beautiful on paper, but the odds of it really happening were pretty long," Bier says. As it turns out, says Gantz, "it worked the first time."

When the researchers bred female flies containing the yellow gene drive to normal males, 95 to 100 percent of both male and female progeny were yellow. If the drive hadn't worked, and normal Mendelian inheritance rules were in effect, only 50 percent of male and no female offspring would be yellow.

The system wasn't perfect. In 4 percent of cases, female flies were born with patches of normal cells and patches of yellow cells. One female was only half yellow. Clearly, some X chromosomes managed to outrun the drive. Still, the system worked with remarkable efficiency.

Gantz and Bier didn't call their invention a gene drive. They named it the "mutagenic chain reaction." By any name, it was the first time researchers had deployed a CRISPR gene drive in a multicelled organism.

What gene drives could do:

- Immunize animals that carry human disease
- Control insect-borne diseases
- Spread pest-specific pesticides and herbicides
- Reduce populations of rodents and other pests
- Control invasive species
- Aid threatened species

SOURCE: K.E. ESVELT *ET AL*/ *ELIFE* 2014

Release and crash

If others can achieve the kind of efficiency that Gantz and Bier did, researchers could make a giant leap in wiping out insect-borne diseases. Theoretically, even one gene-drive–engineered organism could crash an entire population.

That possibility terrified some people when they learned about the yellow fruit fly experiment. If a gene-drive–containing organism were to escape from the lab and start breeding with its wild counterparts, it could irrevocably alter the wild population. Maybe even wipe it out.

In July, 27 scientists (Gantz and Bier among them) issued guidelines in *Science* for working with gene drives in the laboratory. The researchers want to keep their gene-drive experimental insects and other animals contained to protect wild populations, but also safeguard the potential

V.M. GANTZ AND E. BIER/*SCIENCE* 2015

Can gene drives win public approval?

Whether gene drives will ever make it out of the lab is a big question. Researchers still don't know how gene drives will behave in the wild, whether the public will accept them or what regulatory hoops they will have to jump through.

Ecologist Ron Thresher got a sense of how the public might react to gene drives when he described his plan to use genetic engineering to rid the Australian waterways of invasive European carp, a voracious fish that can turn a crystal-clear stream into "a disgusting mudhole." Thresher, with Australia's Commonwealth Scientific and Industrial Research Organization in Hobart, Tasmania, has a genetic trick to do it.

When he talked about his idea with environmentalists, ecologists, aboriginal groups and Boy Scout troops, every group asked the same question: What if one of your carp got loose in Europe?

"We could say with hands to heart that [for our system] nothing would happen," Thresher says. But with a gene drive, a single smuggled fish could theoretically wipe out the entire carp population of Europe.

Even with public support, government approval won't come easy unless rules change. The whole point of a gene drive is to disperse in the wild, but government regulations are designed to keep genetic engineering out of wild organisms, says Zach Adelman, a molecular biologist at Virginia Tech in Blacksburg. "There is no regulatory pathway that can deal with something that, by definition, can't be contained."

It's not even clear which government agency would have jurisdiction over gene drives, Kenneth Oye of MIT and colleagues wrote in a commentary last year in *Science*. U.S. Food and Drug Administration regulations require that genetic modifications to animals be safe and effective for the engineered critters. Gene drives designed to wipe out invasive species might be effective, but they certainly would not be "safe" from the target species' point of view. Then there's the Department of Agriculture and the Environmental Protection Agency, which have overlapping regulations on the use of toxic substances, pest control and animal and plant health.

Gene drives spreading through wild populations would not respect international boundaries, so they might run afoul of international treaties, such as the Cartagena Protocol on Biosafety that governs cross-border movement of genetically engineered organisms. Nations that release gene drives could also be accused of violating the United Nations Biological Weapons Convention if gene-drive–carrying organisms cause harm to native species in another country.

Gene drives may make getting rid of disease and pests easy, but resolving questions surrounding their use will be anything but. — *Tina Hesman Saey*

humanitarian benefits of the technology.

"What's it going to do to public trust if we accidentally release a gene drive into the wild?" Esvelt asks. He fears an accidental breach could damage malaria eradication and other much-needed public health measures.

The guidelines may help researchers avoid creating an accidental gene drive, but they don't apply to gene drives that would actually be used in the wild, says molecular biologist Zach Adelman of Virginia Tech in Blacksburg. The whole purpose of a gene drive is to spread. Exactly how its spread will affect ecosystems isn't known. Some people speculate that rapidly removing an invasive species could shock that system and have unknown costs. Even getting rid of disease-carrying mosquitoes might have consequences: Bats, birds and other critters that eat insects could lose a valuable food supply.

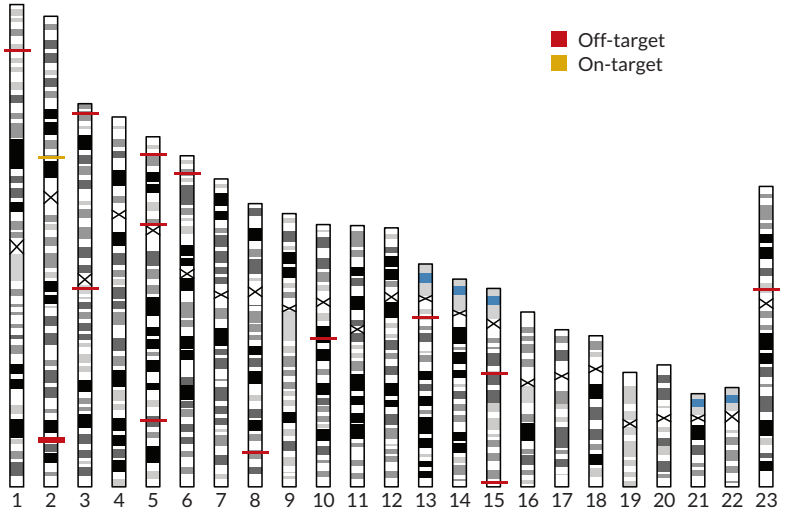
Scientists are also unclear whether gene drives could spread to closely related species. For *Anopheles* mosquitoes, many of which carry malaria, the answer could be yes, Besansky says.

Eight species known as the *Anopheles gambiae* complex of mosquitoes in Africa became separate species less than 5 million years ago, and they sometimes still interbreed, producing fertile hybrids. Gene drives might pass from one species to another through this interbreeding. But given that all but a couple of those species can carry malaria, spillover from one species into another might actually be desirable, Besansky says.

Still, many people are uncomfortable with the idea of gene drives that have the potential to eradicate entire species. Some researchers, including James of UC Irvine, prefer an approach that would prevent mosquitoes from spreading disease without reducing their numbers.

In 2012, James and colleagues reported that they had engineered *Anopheles stephensi* mosquitoes with genes that produce antibodies against malaria parasites. The antibodies prevented *Plasmodium falciparum* parasites from making sporozoites, the stage of the malaria life cycle that is infectious to humans. No sporozoites means the mosquitoes can't pass the parasite on to humans.

CRISPR target specificity



Misplaced scissors
CRISPR/Cas9 doesn't always cut where it is supposed to. In one experiment with human cells, a guide RNA should have led the Cas9 enzyme only to a gene on chromosome 2 (yellow bar), but it also directed the enzyme to many off-target sites (red) on several other chromosomes.

With Gantz and Bier, James created a CRISPR gene drive to speed the spread of the antimalaria antibodies in mosquito populations. The team reported its work online November 23 in the *Proceedings of the National Academy of Sciences (SN Online: 11/23/15)*. Getting the gene drive into the mosquitoes proved tricky; only two males out of more than 25,000 that were screened carried the drive. But once the drive was in the insects, males passed it to progeny with about 99 percent efficiency. Females, however, passed it to their offspring only slightly more often than Mendelian rules would suggest.

While this gene drive will not work in the wild because of the problems with female inheritance, James expects that gene-drive–carrying mosquitoes resistant to malaria will help form a front line against the disease. Any wild mosquitoes entering a zone made disease-free with a gene drive would quickly be assimilated.

Miles from reality

All of the benefits and drawbacks to gene drives are "just so hypothetical right now," says Allison Snow, a plant population ecologist at Ohio State University. She doubts, for instance, the suggestion that weeds could be gene-drive engineered to eliminate herbicide resistance.

"These early predictions are rosy," she says, and it is far too soon to say what will happen if such engineered weeds are ever released.

There is still time to work out the uncertainties, says Virginia Tech's Adelman. "People are jumping the gun thinking these are going to be released any day now. It's going to be years and years," he says. Scientists have a number of technical hurdles to overcome.

One of the biggest barriers to making gene drives of any kind is getting them into the organism. That is harder in mosquitoes than it is in fruit flies or other lab animals.

Genetically engineering mosquitoes that will pass along a gene requires access to the organism's eggs. At less than a millimeter long and a quarter of a millimeter wide, a mosquito egg doesn't give researchers much room for error. Few labs have perfected the technique, James says.

When creating the antimalaria antibody gene drive, the researchers had to inject Cas9, guide RNAs and bits of DNA containing the gene drive into the egg. Cas9 appears to be toxic to mosquitoes, so the team also included a separate piece of RNA to dampen the amount of Cas9 produced. That reduced the toxicity of the enzyme, but also squelched initial insertion of the gene drive.

Ensuring the gene drive goes where it is supposed to is turning out to be tricky as well.

Just as some human guides give better tours than others, some guide RNAs are better than others at shepherding Cas9 to the proper spot. Guide RNAs targeting five different *Aedes aegypti* mosquito genes varied in efficiency from 24 to 90 percent, Adelman and colleagues reported in March in the P*roceedings of the National Academy of Sciences*.

In experiments with human cells, Shengdar Tsai of Massachusetts General Hospital and Harvard Medical School found that some guide RNAs nearly always lead Cas9 to the correct cutting site. Other guides take the enzyme to more than 150 "off-target" sites, Tsai and colleagues reported in the February *Nature Biotechnology*.

Another problem is that researchers know little about the biology of most disease-carrying critters, pests and invasive species, Burt says. That makes it hard to know which gene or genes to disrupt to sterilize or otherwise incapacitate a pest.

Even with these obstacles, CRISPR technology is moving so fast that human reaction times may not be enough to cork the bottle before the genie escapes. Scientists are scrambling to learn how to keep the genie under control, so that "make a wish" won't turn into "be careful what you wish for." ■

Explore more

■ K.E. Esvelt *et al*. "Emerging technology: Concerning RNA-guided gene drives for the alteration of wild populations." *eLife*. July 17, 2014.

S.Q. TSAI ET AL/NATURE BIOTECHNOLOGY 2015

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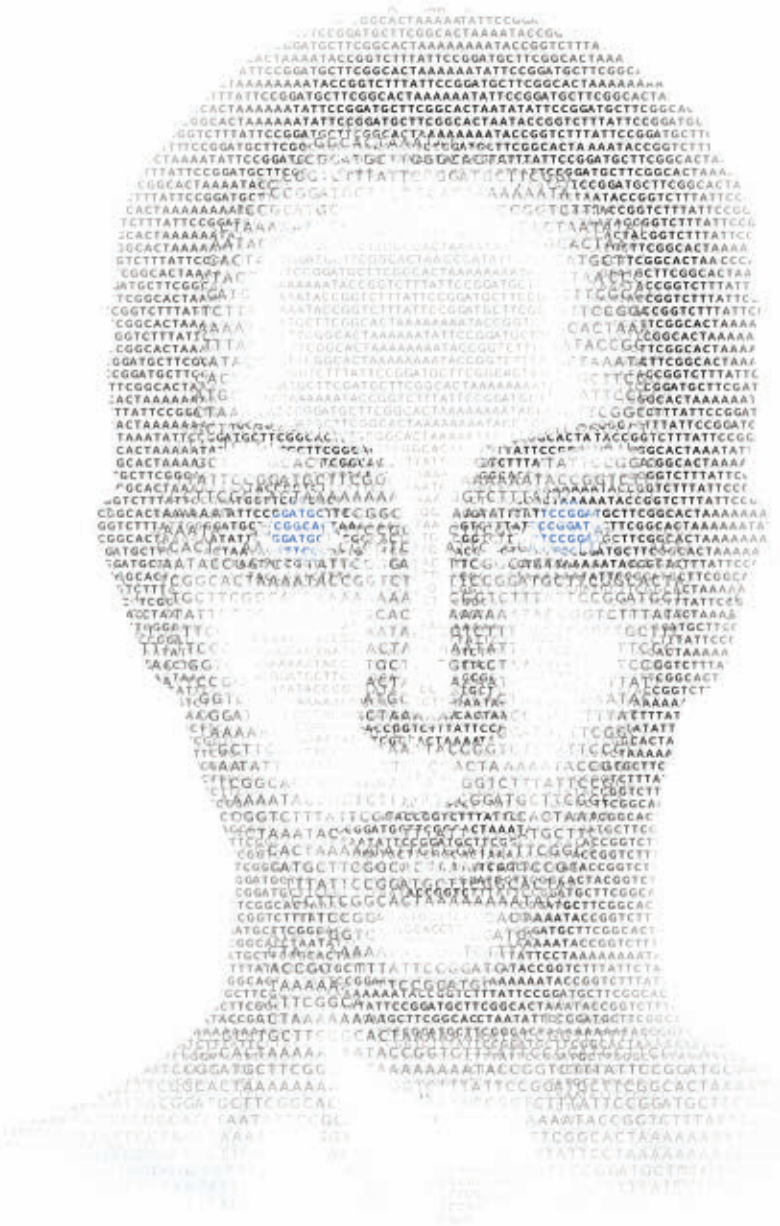


What's in a face?

Appearance-prediction technology is still in its infancy

By Meghan Rosen

Florida police are searching for a man who lurks in the shadows.

For more than two years, he has terrorized at least a dozen women, peeping into windows and slipping into bedrooms to watch them sleep. He has touched several women's feet or hair — some, he has sexually assaulted.

The media dubbed him the "Serial Creeper," and police are desperate to find him. In September, they released a sketch of a dark-haired, dark-eyed Latino man with smooth skin, high cheekbones and a pointed chin. But the sketch wasn't drawn by a police artist based on eyewitness accounts. The Creeper has kept his face covered in every assault, says Kelly Denham, a police officer in Coral Gables, Fla. "He's never been seen."

So local police had to pursue a less-conventional route: They bought a computer-generated image based on the Creeper's DNA.

For $4,500, a company based in Reston, Va., called Parabon NanoLabs analyzed DNA that the Creeper left behind at crime scenes. The analysis zeroed in on genetic clues linked to hair color, eye color, facial features and ancestry. Then, Parabon crafted a digital mash-up of the Creeper's face.

The images Parabon creates don't offer an exact picture of a suspect, says Ellen Greytak, Parabon's bioinformatics director. "We work with law enforcement to give them an idea of who they should be looking for," she says — or which people to cross off the suspect list.

In the last few years, several scientists and companies have ventured into the new world of appearance prediction. It's a hazy place, where the roots of a person's looks hide out in their genetic instruction books. Scientists dig up these roots by linking people's physical features with tiny landmarks in their DNA. If investigators could use DNA to predict nose width, say, or eye size, they might have an easier time tracking down criminals.

Proponents say the technology can do more than give investigators a lead in a case. It could also help put a face to ancient people — long-lost ancestors, or perhaps even Neandertals. Some even imagine giving parents-to-be a glimpse at their unborn child's visage, though that's still a far-off dream.

In truth, the science for conjuring a person's appearance from DNA remains a little skimpy. Facial features may be shaped by hundreds or thousands of genes — each with very tiny effects.

And scientists have only just begun to sort it all out. Hair, eye and skin color, as well as ethnic background, are relatively easy to pin down. But the genetic roots of other traits, such as height and face shape, are scattered throughout people's DNA like dandelion seeds in the wind. It's hard to track down every wispy speck. That's why some researchers think current prediction attempts aren't ready for prime time.

Some attempts rely mostly on genetic information about sex and ancestry (whether a person is male and of European descent, for example) to construct an image of someone's face, says Manfred Kayser, a geneticist at Erasmus University Medical

E. OTWELL

Center in Rotterdam, the Netherlands. And that, he says, "is not much more accurate than using your imagination."

The face of a king

Until recently, the face of one of England's most notorious kings was left to artists' imaginations.

Known for his twisted spine and villainous ways, King Richard III probably had brown hair and dark eyes. Or maybe light hair and blue eyes — portraits painted after his death varied. But now, DNA has given scientists a better picture.

In 2012, more than 500 years after Richard was cut down in battle, archaeologists dug up the monarch's yellowed skeleton under a parking lot in England (*SN: 3/9/13, p. 14*). Analyses of dozens of genetic clues from the DNA in his ancient bones finally offered solid details about Richard's appearance, Kayser and colleagues reported last year in *Nature Communications* (*SN Online: 12/2/14*).

"Quite certainly he had blue eyes," Kayser says. "And it's very likely that he was blond as a kid and either blond or light brown as an adult."

Kayser and colleagues knew what to look for because they and other scientists have tracked down genes controlling hair and eye color. The researchers first had to scan the genetic instruction books of thousands of people.

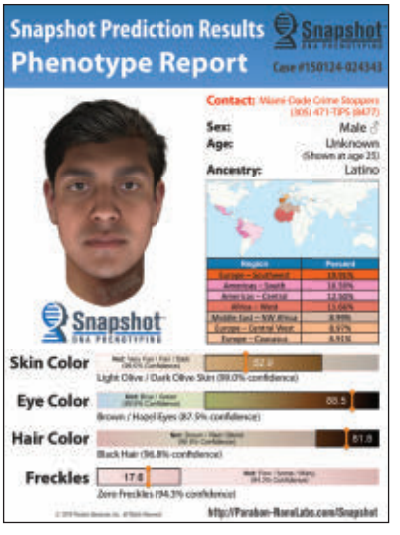
Each person's instruction book, or genome, holds 3 billion chemical base pairs, DNA "letters" that spell out the plans for everything from sex to skin color. Most of those letters don't vary much from person to person. But scientists can use slight changes in the text, one-letter differences called single nucleotide polymorphisms, to predict certain physical features.

Kayser's team can, for example, deduce a person's eye color by looking at just six letters spread out over six genes. To figure out hair color, the researchers focus on 22 letters. For blue or brown eyes, the team's predictions are more than 90 percent accurate. Hair color is almost as good, with accuracies ranging from about 80 to more than 90 percent — pointing out a redhead is the easiest.

The team has used its system, called HIrisPlex, on DNA from King Richard's bones. The system has crime-fighting appeal as well. It can pick out a person's hair and eye color from blood, semen and saliva — even when DNA in the samples has broken down, the researchers reported last year in *Forensic Science International: Genetics*. That's a big deal because forensic DNA can get shabby. If samples sit around too long at crime scenes, DNA can fall to pieces, becoming hard to analyze.

With hair and eye color in hand, Kayser's team has now added skin color to its system, the team reported in September at the International Society for Forensic Genetics meeting in Krakow, Poland. Preliminary results suggest that the skin-color test is about as accurate as the tests for eye and hair color.

Royal features DNA from the bones of King Richard III suggest that the monarch had blue eyes (something close to the shades shown in the top row) and blond or light brown hair (bottom).



A man suspected of several sexual assaults in Florida may be of Latino descent, with black hair and brown or hazel eyes, as in this DNA-based image from Parabon NanoLabs.

Clues about coloring are a good start for estimating appearance, but prediction tools are still rough around the edges. Eye colors other than blue and brown are difficult to predict, and DNA can't distinguish between blond adults and brunet adults who were blond as children, for example.

Still, those traits, along with ancestry, are the easy ones, the low-hanging fruit, says geneticist Peter Visscher of the University of Queensland in Australia. Other features can be much harder for scientists to grab onto. Height and face shape, for example, are still mostly out of reach.

It's complicated

If not for a scoliosis-curved spine, King Richard would have stood about 5 feet, 8 inches tall.

Scientists calculated this number from the length of his thighbone. Using his DNA probably would have gotten them only somewhere in the ballpark.

"For any individual, your best guess might be correct — but it might be off by two or three inches," Visscher says.

When it comes to predicting traits from DNA, two main factors come into play, he says. The first is how much genes, versus environment, influence a certain trait. (For some traits, like body weight, environment plays a big role.) The second is how many genes are involved. If lots of genes affect nose shape, for example, each gene's individual contribution may be tiny and hard to suss out.

The number of genes influencing height could be huge — probably in the thousands, Visscher says. For height more than any other complex trait, scientists have made a Herculean effort. Last year, Visscher and more than 400 colleagues pulled together data from 79 studies that scanned the genomes of more than 250,000 people. The analysis uncovered about 10,000 DNA letters linked to height sprinkled throughout the genome, the researchers reported in *Nature Genetics*.

But even all that information isn't enough for researchers

FROM TOP: T.E. KING *ET AL*/*NAT. COMM.* 2014; PARABON NANOLABS

to pin down a person's height using just his or her DNA. And if scientists can't predict a well-studied trait like height, there's even less hope for other, more obscure traits, like mouth size or distance between the eyes.

In five to 10 years, Visscher says, with more data from more people, scientists might be able to say whether a person is much taller or shorter than average. But now, predicting height from DNA "is not good enough to be particularly helpful," he says. "My guess is that it's probably even worse for facial features."

Show me the data

A person can change the look of his or her face with a little makeup or a new haircut. But the underlying architecture — the length of the nose, the size of the ears — comes mostly from mom and dad.

Scientists know that the blueprints for people's features lie in their genes, Kayser says, but they have "an embryonic understanding of where in the genes." He has been part of recent attempts to flesh out the links between DNA and appearance.

In 2012, Kayser and colleagues used DNA and 2-D or 3-D images of nearly 10,000 participants to pick out five genes that influence face shape. One of those genes, *PAX3*, seems to tweak the bridge of the nose; that gene was also identified by other researchers earlier that year. Those findings are a great start, says Benedikt Hallgrimsson, an evolutionary biologist at the University of Calgary in Canada. But overall, "we still don't know very much about the genetics of the shape of the face."

Last year, researchers tried to ferret out more clues. In a controversial paper published in *PLOS Genetics*, Penn State anthropologist Mark Shriver and colleagues crafted 3-D models of people's faces by tapping into genetic information from 592 participants. That's not nearly enough people to study something so complex, Hallgrimsson says.

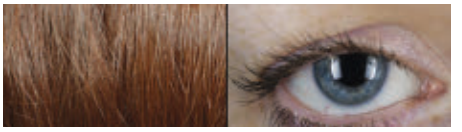
Some of the data Parabon uses in its analyses come from Shriver's collection efforts, but even Shriver isn't convinced that face-predicting technology is ready for the mainstream. Hallgrimsson agrees: "My worry is that they're going into this too soon on too shaky a foundation of science."

Parabon hasn't yet published a study that tests its predictions' accuracy, but several law enforcement agencies have checked it out, says bioinformatics director Greytak. Sometimes agencies give the company a test drive, and send out a few DNA samples before buying the product. The agencies then compare photographs with Parabon's predictions. "We've nailed every single one of those," Greytak says, though the agencies haven't made test results public.

Parabon's predictions consider genetic information about sex, ancestry and facial characteristics from databases that include about 15,000 people. Still, Greytak says, "we need a lot more data. That's the big thing." If you want to capture the variation of human faces, she says, you need to know what a wide variety of faces look like relative to their genetics.

Greytak acknowledges that Parabon's technology can't identify individuals, like a photograph can. But the technology is "absolutely ready from the point of view of exclusion," she says. Investigators can use the images to rule out suspects. So in the search for the Serial Creeper, for example, police could eliminate suspects with red hair and blue eyes.

For the Creeper, who hasn't been linked to a crime since August, the profile gave stumped investigators a new avenue to explore. "We're at a standstill in the investigation — that's why we turned to the Parabon DNA profile," Denham says. "Let's see what we can come up with to try and find this guy." ■

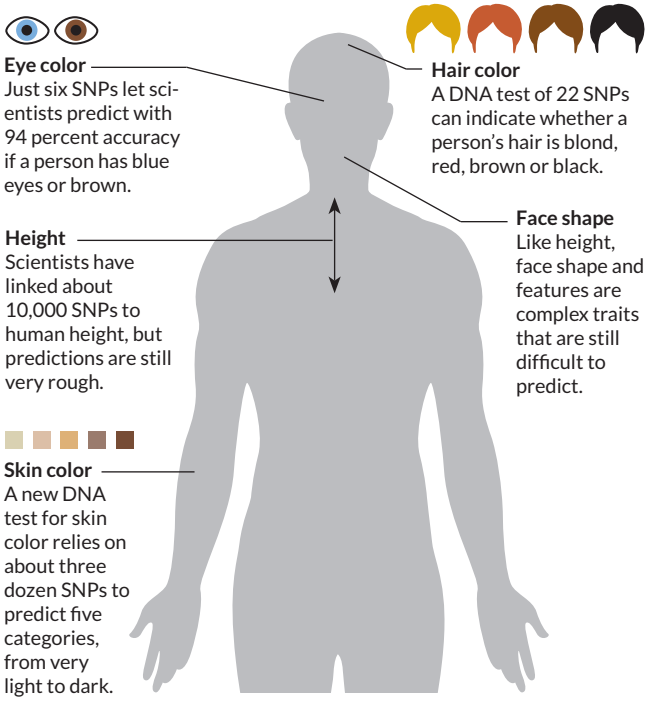


Hair	Dark	Light	
	0.033	0.967	
Black	Brown	Red	Blond
0.007	0.077	0.816	0.1

Eyes	Blue	Intermediate	Brown
	0.965	0.027	0.007

Test case This person's red hair and blue eyes were predicted using the HIrisPlex DNA testing system, which offers probabilities (see numbers) about a person's likely coloring.

Genetic snapshot Tiny differences in a person's DNA, known as single nucleotide polymorphisms, or SNPs, can help predict physical features. Some traits are easier to predict than others.



Explore more

■ Susan Walsh *et al.* "Developmental validation of the HIrisPlex system: DNA-based eye and hair colour prediction for forensic and anthropological usage." *Forensic Science International: Genetics*. March 2014.

FROM TOP: S. WALSH *ET AL*/*FORENSIC SCI. INT. GENET.* 2013; E. OTWELL

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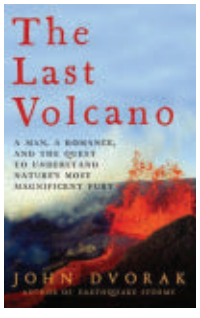
Thomas Jaggar, second from left in this 1917 photo at Kilauea, was one of the 20th century's most influential volcanologists.

BOOKSHELF

Geologist sought to demystify volcanoes

Since prehistoric times, erupting volcanoes have been both awesome and mysterious. But these days, they're a good bit less mysterious thanks to Thomas Jaggar. In *The Last Volcano*, geologist John Dvorak captivatingly chronicles the life and times of this vanguard scientist.

Jaggar's research in the late 19th and early 20th centuries forms the foundation of almost every aspect of modern volcanology, Dvorak says. Jaggar foresaw the need for a network of volcano and earthquake observatories. And as the director of such a facility in Hawaii, he was among the first scientists to collect samples of gas spewing from Mauna Loa — samples that are still some of the best ever collected during an eruption there.



The Last Volcano
John Dvorak
PEGASUS BOOKS, $28.95

In a career spanning more than 50 years, Jaggar visited and studied volcanoes in Europe, Central America, Japan and the Pacific. During much of that time, his home base was a cliff overlooking the lava lake inside Hawaii's Kilauea volcano, taking data at the observatory he founded there in 1912 (and where a museum for the public bears his name today).

The Last Volcano is packed with details about Jaggar's personal as well as professional life, many of which are taken from his voluminous writings. Born in Philadelphia and the youngest son of an Episcopal bishop, Jaggar witnessed an eruption of Vesuvius as a teenager — and even hiked down into the peak's smoldering crater — when his family traveled through Europe in 1886. But the biggest influence on the budding geologist came in 1902, when he served on a team of U.S. scientists investigating an eruption of Mount Pelée on the Caribbean island of Martinique. Interviewing survivors of that event, which killed tens of thousands of people, inspired him to study the then-inexplicable behaviors of volcanoes.

Dvorak also shows how Jaggar's pioneering efforts extended beyond volcanology: He was the first scientist to issue a tsunami warning, and he built an amphibious vehicle whose design formed the basis for the DUKW (or "duck") boats used as landing craft by the U.S. military during World War II. — *Sid Perkins*

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SCREENTIME

Searching for fossils from the comfort of home

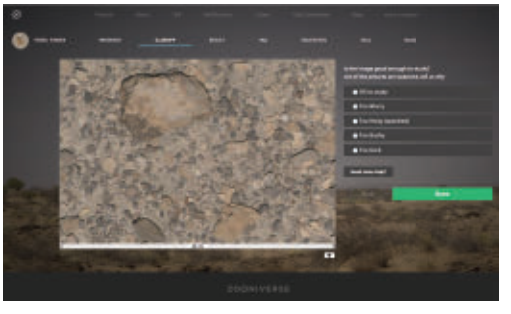
"Armchair anthropologist" takes on new meaning at FossilFinder.org. The citizen science website is seeking volunteers to look for fossils and stone tools and to classify rocks captured in aerial photos of Kenya's Lake Turkana Basin. The basin has been home to important discoveries in human evolution, including many hominid fossils and the earliest known stone tools (*SN: 6/13/15, p. 6*).

Researchers at the University of Bradford in England and the Turkana Basin Institute teamed up to create Fossil Finder. Using radio-controlled helicopters, as well as cameras hung from kites and photographic poles, the team has collected more than 900,000 images from a roughly 4-hectare swath of land. About 46,000 of these photos are online and more are being added regularly, says project coinvestigator Adrian Evans of Bradford.

"The aim is to surpass what could be ordinarily achieved with a more traditional boots-on-the-ground model of exploration," Evans says. With more eyes carefully surveying the area, the team hopes to get a better look at Lake Turkana's past environment.

Using Fossil Finder doesn't require special skill, but it does take some practice. The website lacks a tutorial, but helpful pop-up windows explain what to look for and how to classify various types of rocks, fossils and other objects. The quality of the photos vary: Some have a resolution as high as 0.3 millimeters while others are too blurry to classify. Users have already analyzed over 32,000 images, and have uncovered some neat finds, including an extinct crocodile specimen, hippopotamus teeth and stone tools.

In February, Evans says, the team intends to visit Lake Turkana to investigate these and other promising discoveries. — *Erin Wayman*



At FossilFinder.org, users search for rocks, fossils and stone tools in photos from Kenya's Lake Turkana.

FROM TOP: USGS/WIKIMEDIA COMMONS; FOSSIL FINDER/ZOONIVERSE

Reflections from Maya Ajmera, publisher of *Science News*

In this season of giving, we here at Society for Science & the Public wanted to thank all of you, our members and readers, for supporting us throughout the year. As 2015 draws to a close, I am proud to look back on our accomplishments and to share my thoughts about how the Society is poised to further its critical mission in the coming year.

In September, we launched the *Science News* in High Schools program. Thanks to generous sponsors (including members like you), more than 170,000 students and 10,000 educators in 245 schools from 22 states and the United Kingdom now have access to *Science News*. Many of you also helped fund our teacher guides — 331 supporters donated $35,751. This sponsorship gives schools access to *Science News* at no cost to students, teachers or the school district.

Science News is also going to China. We signed an agreement with the Beijing-based Publishing House Electronics Industry this fall. The publisher will produce four "mooks" (magazine-book hybrids), each a compilation of *Science News* articles on a specific topic from the last four years. The first issue focuses on humans and society and will inform readers about the most fascinating and important advances in anthropology, archaeology and human behavior.

We also have four e-books coming soon through a partnership with Diversion, a publisher based in New York. Our first e-book, due out in spring 2016, will explore the topic of time, from the role of the second law of thermodynamics in fundamental physics to the biological circadian rhythms that govern sleeping, waking and jet lag. Future collections will explore subjects such as consciousness, cosmic mysteries and gravity.

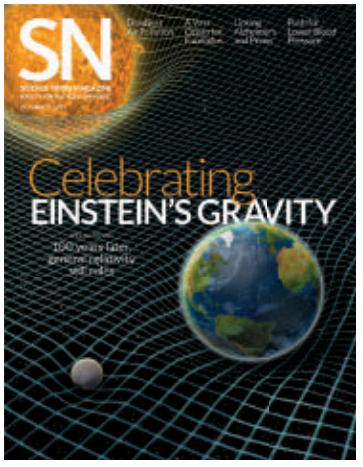
In November, we announced a partnership between CommonLit and our online, award-winning *Science News for Students*. Educator guides with Common Core–aligned questions, discussion topics and paired passage suggestions are now available for select *Science News for Students* articles. The aim is to expose more students to high-quality science news and support literacy development in grades five through 12.

And, of course, we continue to provide the quality science journalism you have come to expect on a wide breadth of scientific topics and research. We are proud to have been recognized this year by the Online News Association, AAAS/Kavli Science Journalism awards and Eddie & Ozzie awards from Folio, among others. Our talented staff of science journalists, editors and designers has an exciting suite of topics planned for the upcoming year, so stay tuned.

In addition, we are:

- Gearing up for the 75th anniversary celebration of the Science Talent Search in March 2016;
- Expanding the SSP Advocate Grant program, which provides stipends to individuals who shepherd disadvantaged students through the science competition application process;
- Building on the successes of Broadcom MASTERS, now sponsored by the Broadcom Foundation through the Society's 100th anniversary in 2021, and the Intel International Science and Engineering Fair to inspire even more students to participate in hands-on research.

As subscribing members, you help us achieve our mission of informing, educating and inspiring the world about science. We thank you and ask you to continue to help spread the good word about the importance of science in our everyday lives — by volunteering at a local science fair, mentoring a student, gifting a *Science News* subscription to a science enthusiast in your life and otherwise sharing your experience and knowledge to help create a more scientifically literate world. Happy holidays from the Society!



OCTOBER 17, 2015

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Grasping gravity

An illustration of an accelerating space rocket in ***Tom Siegfried's*** *essay "Getting a grip on gravity"* (SN: 10/17/15, p. 16)*, explained that a clock at the top of the ship would tick faster than one at the bottom thanks to gravitational time dilation. A few perplexed readers argued that acceleration aboard the rocket ship would be the same for both clocks, so they should tick at the same rate.*

"Once the rocket has reached equilibrium, both clocks are accelerating at the same rate and will run at the same rate," **Bart Bresnik** wrote in an e-mail.

The issue, **Siegfried** says, isn't the equal acceleration of the clocks. It's the direction of the acceleration and how long it takes for a light signal to travel from the bottom clock to the top clock. If the rocket were moving at a constant rate (making it an inertial frame), both clocks would keep the same time. But if the rocket is uniformly accelerating, a light beam traveling in the direction of the acceleration will take longer to reach the top clock than it would have in an inertial frame. Nevertheless the speed of light is always the same, whether in an inertial frame or in an accelerating rocket. Since the distance between the two clocks in an accelerating ship remains the same, but the light takes longer to reach the top, the top clock must tick faster to measure the same speed of light as would be measured in an inertial-frame ship.

Einstein's theory requires gravity to be equivalent to acceleration, so the same principle applies to a tall building in a gravitational field: A clock on the building's top floor will tick faster than a clock on the bottom floor.

Correction

In the article "Elusive acid finally created" (*SN: 10/31/15, p. 11*), hydrogen fluoride was incorrectly referred to as a strong acid. While it can cause serious problems to people exposed to it, hydrogen fluoride is technically classified as a weak acid.

King Solomon's Secret Treasure: FOUND

Ancient beauty trapped in mines for centuries is finally released and available to the public!

King Solomon was one of the wealthiest rulers of the ancient world. His vast empire included hoards of gold, priceless gemstones and rare works of art. For centuries, fortune hunters and historians dedicated their lives to the search for his fabled mines and lost treasure. But as it turns out, those mines hid a prize more beautiful and exotic than any precious metal: chrysocolla.

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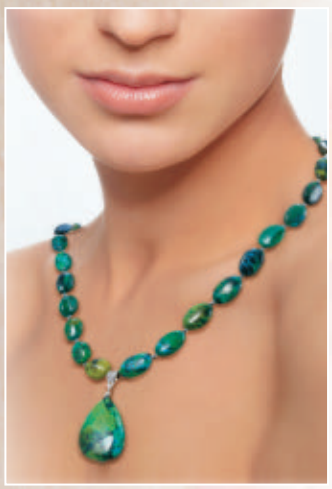

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The solar wind (beige streaks) rips molecules from Mars' atmosphere. Orange lines represent high energies of outgoing ions, blue low.

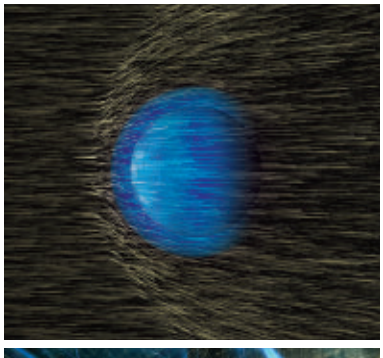
A defenseless Mars is losing its atmosphere

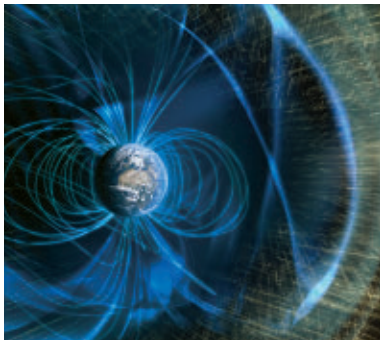
The Martian atmosphere's not what it used to be. Solar winds bombard the planet, taking gas molecules (represented by colored streaks in the image above) with them. New measurements of atmospheric loss by NASA's MAVEN probe should help scientists determine how a planet with rushing water and a temperate climate a few billion years ago transformed into a cold, dry desert.

Atmospheric "loss to space was a significant, if not dominant, process in changing the climate," says MAVEN principal investigator Bruce Jakosky of the University of Colorado Boulder.

The key factor in the atmospheric demise is that unlike Earth, Mars doesn't have a global magnetic field (see illustrations at right). As a result, the planet can't protect itself from particles and plasma streaming from the sun. Mars loses about 100 grams of its atmosphere every second, MAVEN researchers report in the Nov. 6 *Science*.

While the sun steadily erodes Mars' atmosphere, solar flares can take out relatively big chunks. After a flare in March, MAVEN noticed that the number of ions escaping the planet jumped by roughly a factor of 10. Such flares were probably more common and more intense in the past when the sun was younger and feistier, Jakosky notes, and might have sloughed off much of the atmosphere. — *Christopher Crockett*





Magnetic defense Mars (above right) has little magnetic shielding, allowing solar particles to shear off the planet's atmosphere. Earth's global magnetic field (bottom right) provides much more protection.

TOP TWO: NASA SCIENTIFIC VISUALIZATION STUDIO, MAVEN SCIENCE TEAM; BOTTOM: GSFC/NASA

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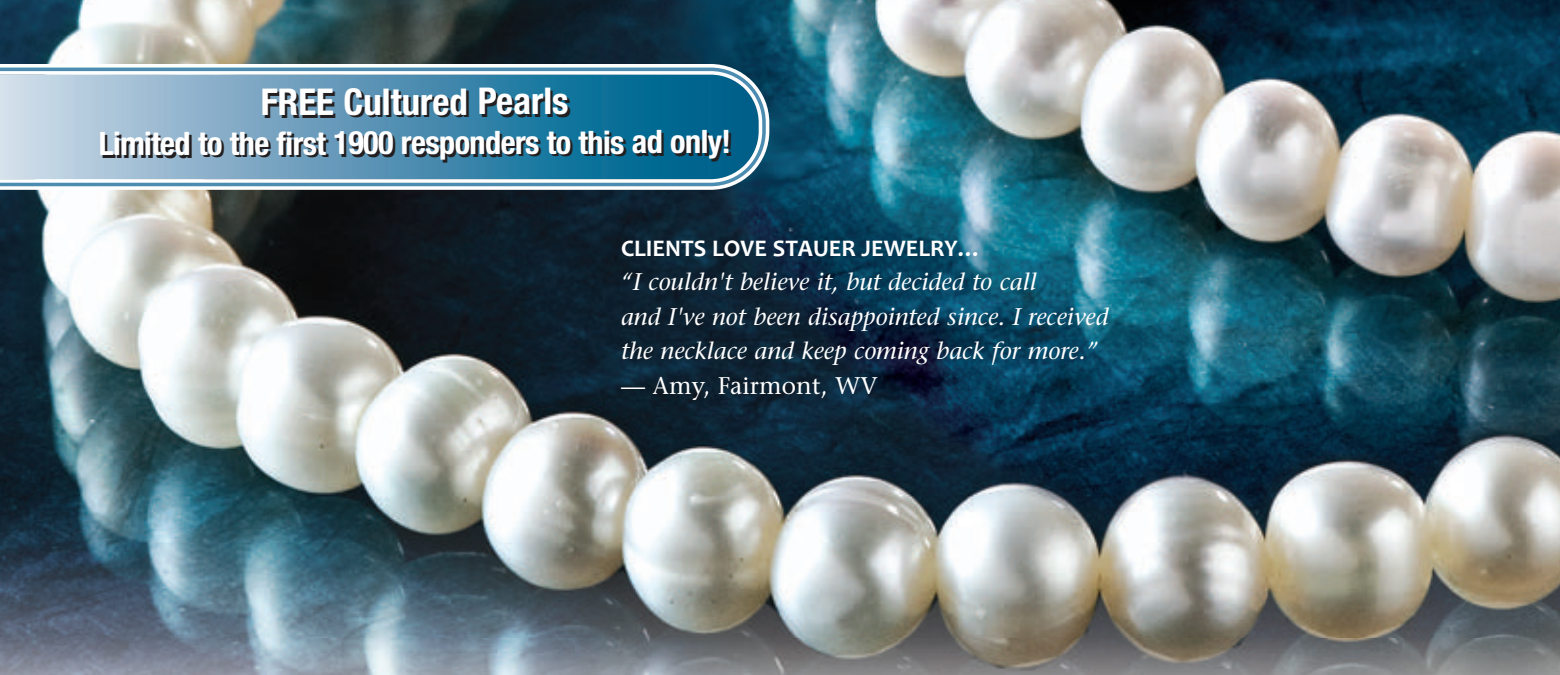

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