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SCIENCE NEWS MAGAZINE
SOCIETY FOR SCIENCE & THE PUBLIC
APRIL 15, 2017

Bad Luck and Cancer

Dinosaurs' New Family Tree

Another Dark Matter Mystery

Moon Formation Puzzle

Microbes at War

Bacteria have long used CRISPR to defeat invaders

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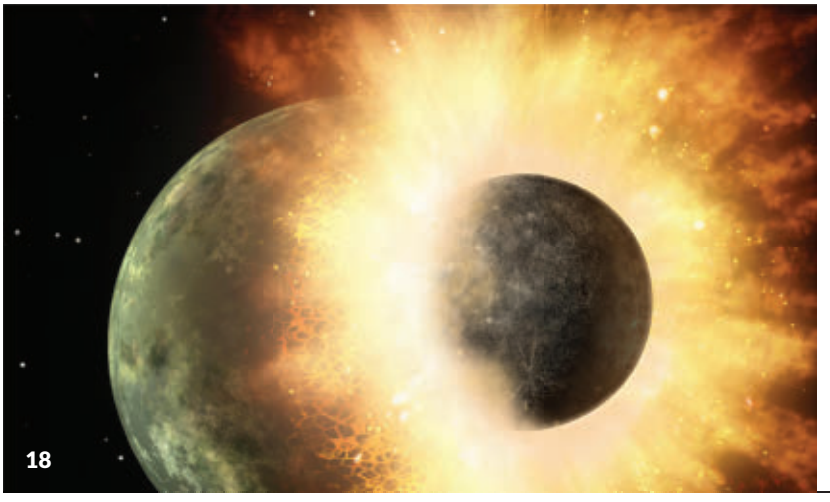
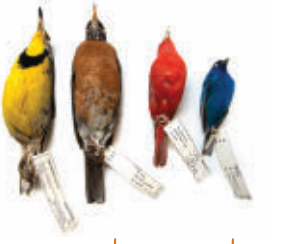


18

Features

News

8



28

Departments

COVER Bacteria and archaea armed with CRISPR systems have been at war with viruses for eons. *Davide Bonazzi*

CLOCKWISE FROM TOP: JPL-CALTECH/NASA; THE FIELD MUSEUM; J. O'NEIL

If there are curious young minds, science will survive

One evening last month at the National Building Museum in Washington, D.C., 40 high school seniors dressed in formal wear and nibbling hors d'oeuvres showed off their scientific research to a crowd of more than 500 people. Positioned at their posters, the students enthusiastically described their efforts to improve quadcopter flight control, study implicit bias and gender stereotypes, and track space debris, for just a few examples. Before the evening was over, one deserving senior received a $250,000 top prize, and her peers went home with hefty scholarships, too. The students had come to Washington as finalists for the 2017 Regeneron Science Talent Search, a program of Society for Science & the Public, which publishes *Science News*. It was their big night — and a night I look forward to every year.

In many ways, attending the Science Talent Search gala is like going to the poster session at a scientific meeting. Anybody eager can dive in and find out something new. There are questions to ask about methodology, results and applications. Certain themes emerge: Cancer treatment and machine learning appeared a few times each this year. But in other ways the event is unusual. Rarely does such glamour accompany scientific sessions. Science Talent Search finalists are treated like stars, with standing ovations, a balloon drop and media attention more often reserved for athletes or rock bands. Here, there's no doubt that the science kids are cool.

The event is inspiring because these teens offer hope that the future is bright for science. We live in challenging times. There's much talk about public distrust of science. Climate change, evolution and vaccine safety face unfounded assaults. Issues of irreproducibility and statistical malfeasance in science are hard to escape. Federal funding for basic research and development could be waning (see our budget proposal story on Page 15). Yet despite all of this, deeply curious young people are still asking interesting questions about the world. They want to know how to face science's big challenges, and they want to participate in basic discovery. I went home from the gala convinced that there will always be scientists. (And scientists who value solid science journalism. Apoorv Khandelwal, of Sammamish, Wash., who studied water desalination for his Science Talent Search project, told me he is a big fan of *Science News*.)

And I have good news for the Science Talent Search finalists and young scientists everywhere: There will also always be questions to ask. The stories in *Science News* show again and again that science is an unending search. Future scientists will no doubt still debate the details of the moon's formation, a puzzle that is far from settled (Page 18). The eons-old war between bacteria and phages will rage on, producing fresh fodder for investigation (Page 22), and CRISPR gene editing will need more and more refinement (Page 16).

Even problems thought to be settled are likely to return, such as questions about the dinosaur family tree (Page 7) and what's to blame for the majority of cancer mutations (Page 6). Scientists may not always be celebrated by everyone, but the rewards that come with pursuing knowledge and the thrill of discovery will probably endure. — *Elizabeth Quill, Acting Editor in Chief*

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Phone: (202) 785-2255
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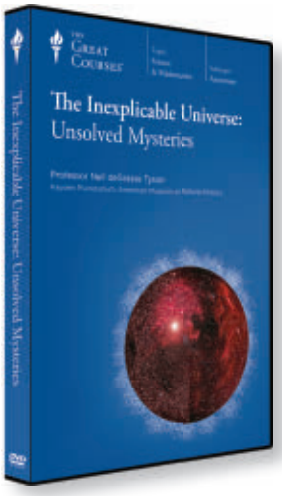

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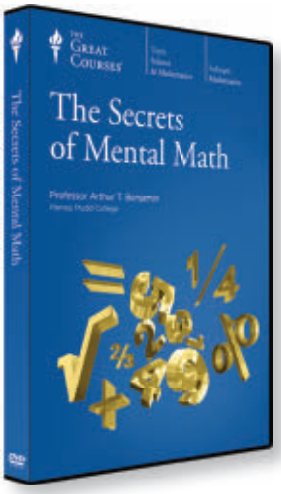

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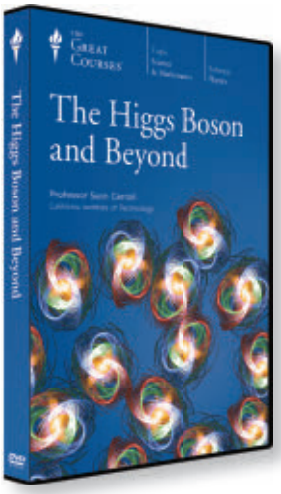

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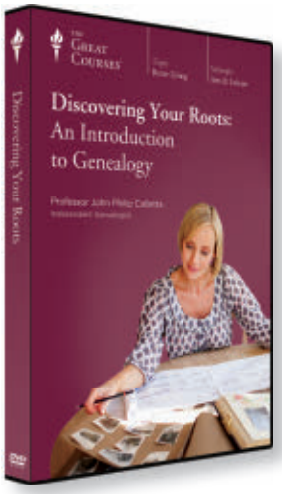

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Excerpt from the April 15, 1967 issue of *Science News*

50 YEARS AGO

Next in birth control

The pill is a sledgehammer approach to contraception.... A second-generation of [drugs] is being designed to do the job without upsetting a woman's normal cycle of ovulation and menstruation.... A contraceptive administered to the man can be given only for a short time without actually affecting the development of sperm ... and, therefore, is not being considered for actual clinical use.

UPDATE: Contraceptives have come a long way since 1967. Women can choose low-dose pills, hormonal rings, implants and intrauterine devices — effective methods that can be less disruptive to normal menstrual cycles. Men have far fewer options, but that may eventually change. A long-acting gel injected into 16 adult male rhesus monkeys' reproductive tracts completely prevented pregnancy in their partners over one to two breeding periods. The gel works like a vasectomy but is less invasive and can be reversed more easily, researchers report February 7 in *Basic and Clinical Andrology*.

A polka dot frog glows under ultraviolet light. The first known fluorescent amphibian, the frog gets its glow from compounds called hyloins not previously found in nature.

IT'S ALIVE

Twilight of the fluorescent frogs

Could fluorescence matter to a frog? Carlos Taboada wondered. They don't have bedroom black lights, but their glow may still be about the night moves.

Taboada's question is new to herpetology. No one had shown fluorescence in amphibians, or in any land vertebrate except parrots, until he and colleagues recently tested South American polka dot tree frogs. Under white light, male and female *Hypsiboas punctatus* frogs have translucent skin speckled with dark dots. But when the researchers spotlighted the frogs with an ultraviolet

FOR DAILY USE

All mosquito repellents are not equal

Mosquitoes can carry serious diseases, including Zika, West Nile and yellow fever. In a test of 11 types of mosquito repellents, spray-ons with DEET or a refined tree extract called oil of lemon eucalyptus were most likely to ward off the insects, scientists report online February 16 in the *Journal of Insect Science*.

In the study, a volunteer sat in a wind tunnel as her attractive scent — and repelling chemicals — were pulled toward a cage of *Aedes aegypti* mosquitoes. After 15 minutes, the researchers determined the portion of mosquitoes that had moved closest to the volunteer-end of the cage.

The OFF! Clip-On repellent, which puffs out a vapor of metofluthrin, killed every mosquito in the cage, probably because the bloodsuckers got a high dose in the enclosed space. Other deterrents — bracelets with geraniol oil, a dragonfly-buzzing sound machine and a citronella candle — had little effect, says study coauthor Immo Hansen, an insect physiologist at New Mexico State University in Las Cruces. — *Elizabeth S. Eaton*

Treatment (1 meter from cage)	Active ingredient	Average attraction rate (percent)
None (control)	N/A	89
OFF! Clip-On fogger	Metofluthrin (31%)	27
Cutter Lemon Eucalyptus spray	Oil of lemon eucalyptus (30%)	30
Ben's Tick & Insect Repellent spray	DEET (98%)	34
Kids Herbal Armor spray	Soybean and citronella oils	60
Repel Sportsmen Max Formula spray	DEET (40%)	69
Avon Skin-So-Soft Bug Guard Plus Picaridin spray	Picaridin (10%)	79

These repellents were not significantly different from the no-repellent control: bracelets (Mosquito-NO!, Invisaband, Mosquitavert), Cutter Citro Guard candle and Personal Sonic Mosquito Repeller.

CLOCKWISE FROM TOP: C. TABOADA *ET AL/PNAS* 2017; YULETO/ISTOCKPHOTO; NODEROG/ISTOCKPHOTO

flashlight, the animals glowed blue-green. The intensity of the glow was "shocking," says Taboada of the Museo Argentino de Ciencias Naturales "Bernardino Rivadavia" in Buenos Aires.

And it is true fluorescence. Compounds in the frogs' skin and lymph absorb the energy of shorter UV wavelengths and release it in longer wavelengths, the researchers report online March 13 in *Proceedings of the National Academy of Sciences*. But why bother, without a black bulb? Based on what he knows about a related tree frog's vision, Taboada suggests that faint nocturnal light is enough to make the frogs more visible to their own kind. When twilight or moonlight reflects from their skin, the fluorescence accounts for 18 to 30 percent of light emanating from the frog, the researchers calculate.

Polka dot frogs, common in the Amazon Basin, have plenty to see in the tangled greenery where they breed. Males stake out multilevel territories in vast floating tangles of water hyacinths and other aquatic plants. When a territory holder spots a poaching male, frog grappling and wrestling ensues. Taboada can identify a distinctive short treble bleat "like the cry of a baby," he says, indicating a frog fight.

Males discovering a female give a different call, which Taboada could not be coaxed to imitate over Skype. The polka dot frogs' courtship is "complex and beautiful," he says. For instance, a male has two kinds of secretion glands on the head and throat. During an embrace, he nudges and presses his alluring throat close to a female's nose. If she breaks off the encounter, he goes back to clambering in rough figure eights among his hyacinths, patrolling for perhaps the blue-green ghost of another chance. — *Susan Milius*

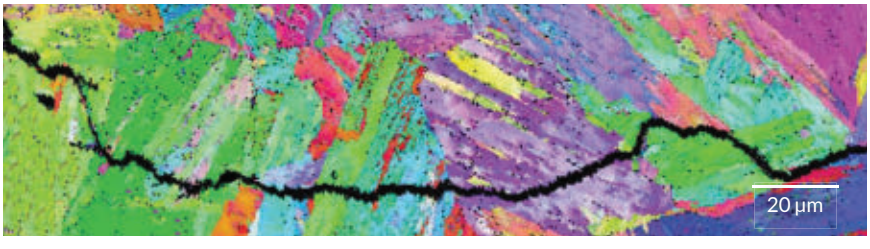
TEASER

Bone-inspired steel cracks less under pressure

The heavy-duty material used to build bridges and sculpt skyscrapers could learn a few tricks from humble bones.

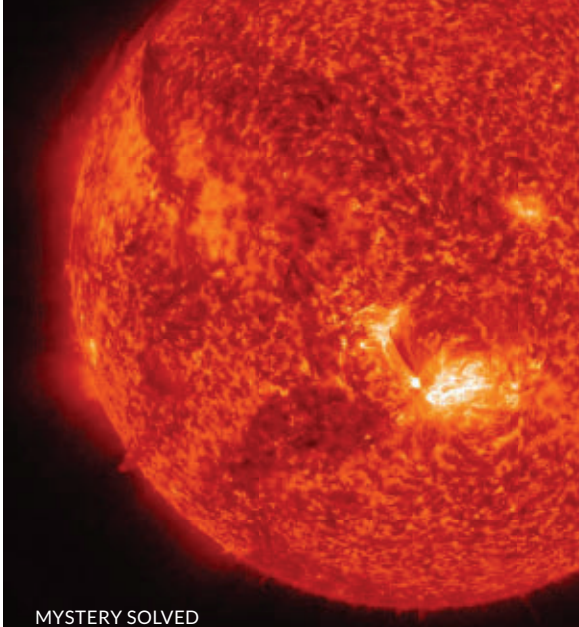
Steel's weakness is its tendency to develop microscopic cracks that eventually make the material fracture. Repeated cycles of stress — daily rush hour traffic passing over a bridge, for example — nurture these cracks, which often aren't apparent until the steel collapses. Bones, however, have a complex inner structure that helps them deal with stress. This structure differs depending on the scale, with tiny vertically aligned fibers building up into larger cylinders.

To mimic this variability, researchers fabricated steel with thin, alternating nanoscale layers of different crystal structures, some of which were just unstable enough to morph a bit under stress. That complicated microstructure prevented cracks from spreading in a straight line, slowing their take-over and preventing the material from collapsing, the scientists report in the March 10 *Science*. This experimental steel requires much more testing before it can be used in construction, says study coauthor C. Cem Tasan, a materials scientist at MIT. But the principles could be applied to other mixed-composition metals, too. — *Laurel Hamers*



A new type of steel mimics bone to make the metal more resistant to failure. Colors represent different crystal structures that force cracks to spread in a jagged pattern, slowing collapse.

FROM TOP: SDO/NASA; M. KOYAMA *ET AL*/*SCIENCE* 2017



MYSTERY SOLVED

A slowdown at the sun's surface explained

Never underestimate the power of a little sunlight.

Light particles, or photons, emitted from the sun's surface could explain a long-standing solar mystery — why the sun's outermost layers rotate more slowly than its core.

Because the sun isn't a solid ball, regions at different depths or latitudes rotate at different rates. For decades, scientists have wondered why the outer 5 percent of the sun revolves slower than inner regions. In the Feb. 3 *Physical Review Letters*, researchers from Brazil and the United States report that photons released from the sun's skin may be tapping the brakes.

Using data from NASA's Solar Dynamics Observatory satellite, scientists measured the rotation in the sun's limb, or outer edge. In a tiny external sliver of the slower outer region, the rotation rate drops by 2 percent — a result that could be explained by photons carrying angular momentum away from the sun, slowing it down bit by bit. Angular momentum is a property of a rotating body that keeps an object spinning unless another force acts on it, as happens when a spinning ice skater gradually comes to a stop due to friction. Over time, that surface drag could have caused the full outer 5 percent of the sun to lag behind, the scientists say. — *Emily Conover*

GENES & CELLS

DNA errors play big role in cancer

Most tumor-linked mutations tied to cell division, study says

BY TINA HESMAN SAEY

Researchers have identified new enemies in the war on cancer: ones that are already inside cells and that no one can avoid.

Random mistakes made as stem cells divide are responsible for about two-thirds of the mutations in cancer cells, researchers from Johns Hopkins University report in the March 24 *Science*. Environment and lifestyle factors, such as smoking, contribute 29 percent of cancer mutations, and 5 percent are inherited.

That finding challenges the common wisdom that cancer is the product of heredity and the environment. "There's a third cause and this cause of mutations is a major cause," says cancer geneticist Bert Vogelstein. Knowing that the enemy will strike from within even when people protect themselves against external threats indicates that early cancer detection and treatment deserve even more attention than they get, Vogelstein says.

Vogelstein and biomathematician Cristian Tomasetti proposed in 2015 that random mutations are why some organs are more prone to cancer than others. For instance, stem cells are constantly renewing the intestinal lining of the colon, which develops tumors more often than the brain, where cell division is uncommon. That analysis was controversial. It didn't include common cancers such as breast and prostate. Factoring them in might change the results, some scientists said. And because the researchers looked only at the United States, critics charged that the finding might not hold up when considering places where different environmental factors affect cancer development.

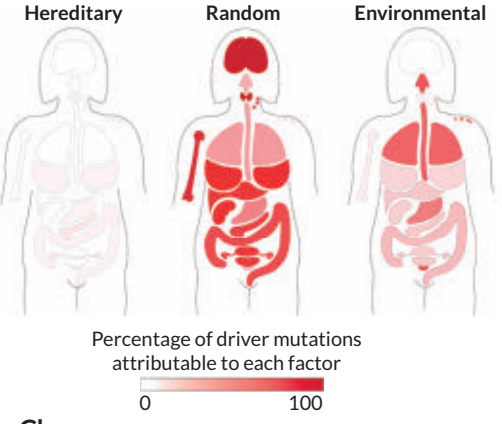
Vogelstein, Tomasetti and colleague Lu Li have now examined data from 69 countries for 17 types of cancer, including breast and prostate. Again, the team found a strong link between cancer and tissues with lots of dividing stem cells. The team used DNA data and epidemiological studies to calculate the proportions of mutations in cancer cells caused by heredity or environmental factors. Remaining mutations were attributed to errors — including typos, gene insertions and deletions, and gene rearrangements — that happen when cells divide.

Usually cancer results after a cell accumulates many mutations. Some people will have accumulated a variety of cancer-associated mutations but won't get cancer until some final insult goads the cell into becoming malignant. For some tumors, all mutations may be the result of cell division mistakes. Other malignancies may spring up as a result of different combinations of heritable, environmental and random mutations. Lung cancer and other tumor types that are strongly associated with environmentally caused mutations could be eluded by avoiding the carcinogen, even when most of the mutations that spur cancer growth arise from random mistakes, Tomasetti says.

Tomasetti, Vogelstein and Li are the first to rigorously estimate the contribution of environment, heredity and DNA-copying errors to cancer, says biostatistician Giovanni Parmigiani of the Harvard T.H. Chan School of Public Health. "They are venturing into new territory," he says. "Perhaps the estimates will improve in the future, but theirs seems like a very solid starting point."

Now that it has been pointed out, the relationship between dividing cells and cancer seems obvious, says biological physicist Bartlomiej Waclaw of the University of Edinburgh. "I don't think that the existence of this correlation is surprising," he says. "What's surprising is that it's not stronger."

Some tissues develop cancers more or less often than others with a similar number of cell divisions. Learning how those tissues avoid cancer could lead to new ways to prevent tumors, Waclaw says.



Chance cancer For many organs, more of the mutations that lead to cancer come from random mistakes in DNA made when cells divide (center) than from inherited or environmental factors, researchers calculate.

Other researchers say the Hopkins scientists are guilty of faulty reasoning. "They are assuming that just because tissues which have high stem cell turnover also have high cancer rates, that one is causing the other," says Anne McTiernan of the Fred Hutchinson Cancer Research Center in Seattle. "They've added data from other countries but haven't gotten away from this biased thinking."

Tomasetti and colleagues based their calculations on data from Cancer Research UK that suggest that 42 percent of cancer cases are preventable, meaning people could avoid a risk factor or take positive steps to lower risks. But those estimates may not be accurate, says McTiernan. "In reality, it's very difficult to measure environmental exposures, so our estimates of preventability are likely very underestimated."

To attribute so many cancer mutations to chance seems to negate public health messages, Waclaw says. Some people who spend a lot of time trying to prevent cancer may find the results disturbing. In fact, Tomasetti and Vogelstein stress that their findings are compatible with prevention recommendations. Avoiding smoking, tanning beds, obesity and other known carcinogens can prevent the environmental mutations that combine with inherited and random mutations to tip cells into cancer. Without those final straws, tumors may be averted or greatly delayed. ■

C. TOMASETTI *ET AL*/*SCIENCE* 2017

Dinosaur family tree gets a makeover

New proposal would radically alter century-old groupings

BY RACHEL EHRENBERG

The standard dinosaur family tree may soon be just a relic.

After examining over 400 anatomical traits, scientists have proposed a radical reshuffling of the major dinosaur groups. The rewrite, reported in the March 23 *Nature*, upsets century-old ideas about dinosaur evolution. It lends support to the accepted idea that the earliest dinosaurs were smallish, two-legged creatures. But contrary to current thinking, the tree suggests that these early dinos had grasping hands and were omnivores.

"This is a novel proposal and a really interesting hypothesis," says Randall Irmis, a paleontologist at the University of Utah in Salt Lake City. Irmis, who was not involved with the work, says it's "a possibility" that the new family tree reflects actual relationships. But, he says, "It goes against our ideas of the general relationships of dinosaurs. It's certainly going to generate a lot of discussion."

The accepted tree of dinosaur relationships has three dominant branches. One branch leads to the "bird-hipped" ornithischians, which include the plant-eating duckbills, stegosaurs and *Triceratops* and its bony-frilled kin. (Despite some pelvic similarities, birds are not part of this group.) Another branch contains the "reptile-hipped" saurischians, which are further divided into two groups: the plant-eating sauropods (typically four-legged, like *Brontosaurus*) and the meat-eating theropods (typically two-legged, like *Tyrannosaurus rex* and birds).

This split between the bird-hipped and reptile-hipped dinos was first proposed in 1887 by British paleontologist Harry Seeley, who had noticed the two strikingly different kinds of pelvic anatomy.

The new tree yields four groups atop two main branches. The bird-hipped ornithischians, which used to live on their own lone branch, now share a main branch with the reptile-hipped theropods like *T. rex*. This placement underscores questions about the bird-hipped dinos, an oddball group with murky origins; they appear late in the dinosaur fossil record and then are everywhere. Some scientists have suggested that these dinos evolved from similarly herbivorous sauropods. But by placing the bird-hipped dinos next to theropods, the new tree hints that the late-to-the-party vegetarians could have evolved from meat-eating theropods.

Sauropods are no longer next to the theropods but now sit on a branch with the meat-eating herrerasaurids. Herrerasaurids are a confusing group of creatures that some scientists think belong near the other meat eaters, while others say herrerasaurids are not true dinosaurs.

The new view came about when researchers led by Matthew Baron, a paleontologist at the University of Cambridge and the Natural History Museum in London, decided to do a wholesale examination of dinosaur anatomy with fresh eyes. Using a mix of fossils, photographs of fossils and descriptions from the scientific literature, the team surveyed the anatomy of over 70 different dinosaurs and close non-dino relatives, examining 457 anatomical features. The presence, absence and types of features, which include the shape of a hole on the snout, a cheekbone ridge and braincase anatomy, were fed into a computer program, generating a family tree that groups animals that share specialized features.

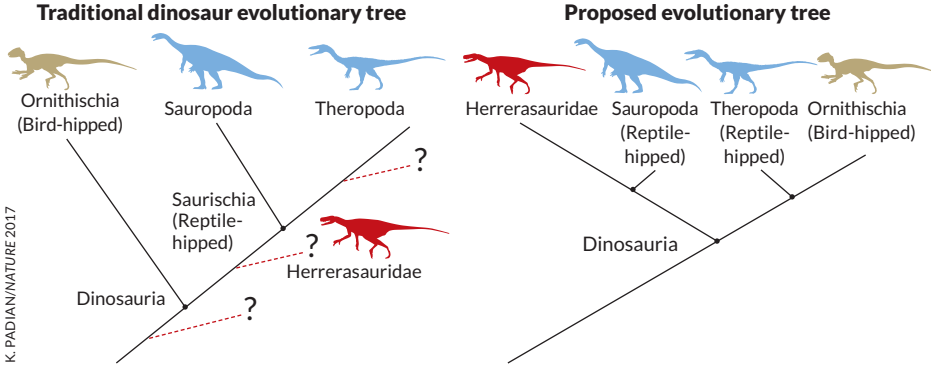
In this new interpretation, many of the earliest dinosaurs have grasping hands and a mix of meat-eating and plant-eating teeth. If the earliest dinos were really omnivores, the evolution of specialized diets — vegetarians and meat eaters — each happened twice in the dinosaur lineage.

When the researchers saw the results, "We were very surprised — and cautious," Baron says. "It's a big change that flies in the face of 130 years of thinking."

The arrangement of the new tree stuck even when the team fiddled with the descriptions of various features, Baron says. The close relationship between the plant-eating ornithischians and the meat-eating theropods, for example, isn't based on one or two distinctive traits but on 21 small details.

"The lesson is that dinosaur groups aren't characterized by radical new inventions," says paleontologist Kevin Padian of the University of California, Berkeley. "The relationships are read in the minutiae, not big horns and frills." That said, Padian, whose assessment of the work also appears in *Nature*, isn't certain that the tree reflects reality. Such trees are constructed based on how scientists interpret particular anatomical features, decisions that will surely be quibbled with. "These guys have done their homework," Padian says, "and now everyone's going to have to roll up their sleeves and start checking their work." ■

Relative rethink Scientists have long divided dinosaurs into two main groups, the bird-hipped and the reptile-hipped (left). A new analysis breaks up the reptile-hipped lineage and suggests the bird-hipped group shares recent ancestors with theropods (right). Scientists had been unsure where to put the two-legged, meat-eating herrerasaurids.



K. PADIAN/*NATURE* 2017

Rocks from an outcrop in northeastern Canada may have formed from material dating back more than 4.2 billion years. That's older than the oldest known rocks on Earth today.

EARTH & ENVIRONMENT

Rocks retain bits of Earth's early crust

Full-blown plate tectonics had late start, geochemical data hint

BY THOMAS SUMNER

Not all of the newborn Earth's surface has been lost to time. Transformed bits of this rocky material remain embedded in the hearts of continents, new research suggests. These remnants hint that full-fledged plate tectonics, the movements of large plates of Earth's outer shell, began relatively late in the planet's history, geochemists report in the March 17 *Science*.

These revelations come from ancient continental rock in Canada that preserves geochemical traces of the even older, 4.2-billion-year-old rock from which it formed. "For the first time, we can say something about what kind of rock was a precursor to the first continental crust," says study coauthor Jonathan O'Neil of the University of Ottawa.

Earth began as a molten ball around 4.54 billion years ago, and over the next tens of millions of years, its surface cooled and solidified. Almost all of Earth's early rocky surface has been destroyed and recycled by geologic processes such as plate tectonics. The oldest known unaltered bits of the planet aren't rocks but tiny zircon crystals formed nearly 4.4 billion years ago. The oldest actual rocks date back to only about 4 billion years. "We're missing a lot of Earth's history," O'Neil says.

The new results fill in some of that history. In northeastern Canada, along the eastern shore of the Hudson Bay, O'Neil and Richard Carlson of the Carnegie Institution for Science in Washington, D.C., discovered 2.7-billion-year-old continental rocks that hinted at something much older. The rocks contain an unusually large abundance of an isotope of neodymium that formed only during the first few hundred million years of Earth's history. To have so much of this neodymium, the rocks must have formed from material that was first created more than 4.2 billion years ago, the researchers calculate. That's far older than the oldest rocks ever studied.

Based on the Canadian rocks' composition, the researchers think the precursor material was similar to the crust that underlies modern oceans. The finding

BODY & BRAIN

Scratching is catching in mice

Brain areas vital to rodents' contagious itching identified

BY SUSAN MILIUS

Catch sight of someone scratching and out of nowhere comes an itch, too. Now, it turns out mice suffer the same strange phenomenon.

Tests with mice that watched itchy neighbors, or even just videos of scratching mice, provide the first clear evidence of contagious scratching spreading mouse to mouse, says neuroscientist Zhou-Feng Chen of Washington University School of Medicine in St. Louis. The quirk opens new possibilities for exploring the neuroscience behind the spread of contagious behaviors.

For the ghostly itch, experiments trace scratching to a peptide called GRP and areas of the mouse brain better known for keeping the beat of circadian rhythms, Chen and colleagues found. They report the results in the March 10 *Science*.

During the research, "there were lots of surprises," Chen says. One was that mice, nocturnal animals that mostly sniff and whisker-brush their way through the dark, would be sensitive to the sight of others scratching. Yet Chen had his own irresistible itch to test the idea.

Researchers housed mice that didn't scratch any more than normal within sight of mice that flicked and thumped their paws frequently at itchy skin. Videos recorded instances of normal mice looking at an itch-prone mouse mid-scratch and, shortly after, scratching themselves. In comparison, mice with not-very-itchy neighbors looked at those neighbors at about the same frequency but rarely scratched immediately afterward.

Videos of scratching mice produced the same result: More audience itching and scratching followed a film of a mouse with itchy skin than one of a mouse poking about on other rodent business.

Next, researchers looked at the nervous system. Brains of mice recently struck by contagious urges to scratch showed heightened activity in several spots, including, surprisingly, a pair of nerve cell clusters called the suprachiasmatic nuclei, or SCN.

Other tests linked the contagious itching with GRP, previously identified as transmitting itch information in the spinal cord. Mice didn't succumb to contagious itching if they had no working genes for producing GRP or the molecule that detects it. Yet these mice still scratched when researchers irritated their skin. Also, in normal mice, GRP injected into the SCN brain regions brought on scratching without the sight of an itchy neighbor, but a dose of saline solution to the same spots failed to do so.

J. O'NEIL

affirms previous studies that suggested that the first continental crust arose from the partial melting of oceanic crust.

But unlike modern oceanic crust, which typically lingers for less than 200 million years before getting recycled by plate tectonics, the precursor crust survived for over a billion years before being reworked into continental crust 2.7 billion years ago. Plate tectonics during the precursor crust's life span must have therefore been nonexistent, sluggish or limited to certain regions, O'Neil says.

"If you ask five geologists the simple question of when did plate tectonics start, you'll have answers from 4.3 billion years ago to 1 billion years ago," he says. The new finding seems to rule out the idea that full-blown, global plate tectonics began early in Earth's history.

The new work sheds light on the processes that set the scene for Earth's subsequent evolution and habitability, says geologist Tony Kemp of the University of Western Australia in Crawley. Other vestiges of early crust may lurk undiscovered elsewhere, he says. "It will be intriguing to see how this [research] unfolds." ■

Dermatologist Gil Yosipovitch, who studies itching at the University of Miami in Florida, wonders how the mouse study might apply to people. So far, brain imaging from his own work has not turned up evidence for an SCN role in human contagious itching, he says.

SCN is better known as a circadian timekeeper, responding to light cues. It's unclear how the nerve cell clusters might orchestrate behavior based on seeing a scratching mouse, "a very specific and rich visual stimulus," says psychologist and neuroscientist Henning Holle of the University of Hull in England. Other work suggests different brain regions are involved in contagious itching in people.

Tracking down the mechanisms behind the phenomenon is more than an intriguing puzzle, Yosipovitch says. People troubled with persistent itching are often unusually susceptible to contagious scratching, and new ideas for easing their misery would be welcome. ■

HUMANS & SOCIETY

Herders helped shape Silk Road

Seasonal migrations played key role in establishing trade route

BY BRUCE BOWER

Nomadic herders took the ancient Silk Road to new heights.

Starting at least 4,000 years ago, Central Asian herders migrated from highland pastures in summer to lowland areas in winter (*SN: 5/3/14, p. 15*). Over roughly the next 2,000 years, those routes through mountainous regions eventually became a key part of the Silk Road, an ancient trade and travel network stretching from China to Europe, says a team led by anthropologist Michael Frachetti of Washington University in St. Louis.

This finding underscores the important contribution of herders, interacting with lowland farmers and early city dwellers, to the Silk Road and overland trade, the team concludes in the March 9 *Nature*. Extensive Silk Road pathways ran across Asia by about 2,200 years ago.

Contrary to the traditional view of nomadic groups as barbarians, the new paper supports a growing conviction among researchers that mobile herders contributed to the rise of early states and civilizations, says Yale University archaeologist William Honeychurch.

Frachetti agrees. In a mountainous part of Central Asia without cities — an area stretching from western China to Afghanistan and Pakistan — highland routes made it possible for travelers from many lowland centers to journey across the continent. Contacts among highland herders and lowland populations eventually resulted in cradles of civilization in China and elsewhere, Frachetti suspects. "Silk Road highland networks were formed by pastoralists interacting with other groups in a lengthy process that was not a construction project and involved no planning," he says.

Herders forged high-altitude routes that may have become part of the Silk Road. This ancient inn sits near a possible route in Kyrgyzstan.

M. FRACHETTI

Because travel routes out of the mountains varied from year to year depending on productive grasslands, herders didn't always beat clear-cut paths. But Frachetti suspects that, like recent nomads, ancient herders built stone structures and other landmarks that served as travel guides and provided directions to outsiders venturing through the area.

Using satellite imagery and geographic mapping software, Frachetti's group created 500 computer simulations of nomadic herders' seasonal descent routes from highland locations situated 750 to 4,000 meters above sea level. These simulations represented 500 years of seasonal treks from highland to lowland camps.

Simulations favored routes with the best pasture from one year to the next, based on modern measures of vegetation and climate fluctuation. Those measures are similar to what's known about conditions in Central Asia several thousand years ago, Frachetti says.

His team mathematically folded all 500 simulations into a cumulative route. A small number of descent paths that frequently popped up in individual simulations largely shaped the proposed route, Frachetti says. That route intersected with 192 of 258 Silk Road archaeological sites at high altitudes, after allowing for a leeway of two kilometers from the simulated route. The team reasoned that, since simulated routes often ran through grassy areas, travelers' inns and other structures were probably built nearby.

Nomads' contributions to the Silk Road need to be explored further by looking for more highland sites that map onto the simulated travel routes, Honeychurch says. Herders trekked in certain directions for many reasons, not just to find pastures and water, he cautions. ■

ATOM & COSMOS

Distant galaxies may lack dark matter

Star velocities defy expectations based on standard theory

BY ASHLEY YEAGER

Very distant galaxies have surprisingly little dark matter, the invisible stuff thought to make up the bulk of matter in the universe, new observations suggest.

Stars in the outer regions of some far-off galaxies move more slowly than stars closer to the center, indicating a lack of dark matter, astronomer Reinhard Genzel and colleagues report in the March 16 *Nature*. If confirmed, the result could lead astronomers to reconsider the role dark matter played in early galaxy evolution and might also offer clues to how nearby elliptical galaxies evolved.

In contrast with these distant galaxies, stars orbiting on the outskirts of the Milky Way and other, nearby spiral galaxies move too fast for their velocities to result only from the gravity of gas and stars closer to the galactic center. If visible galactic matter is embedded in a cloud of invisible dark matter, though, gravity from the invisible matter can explain the high stellar velocities. Using stars' orbital velocities in nearby galaxies as a reference, astronomers expected that stars in galaxies farther away would behave similarly. "Turns out that is not the case," says study coauthor Stijn Wuyts of the University of Bath in England.

The plot of stars' velocities relative to their distances from a galaxy's center is called a galactic rotation curve. In the new paper and others posted online at arXiv.org, the team presents rotation curves measured with the Very Large Telescope in Chile for more than 100 distant galaxies, some seen as they were just a few billion years after the Big Bang, which occurred 13.8 billion years ago.

When the velocities of stars diminish as the stars get farther from their galactic centers, that rotation curve is said to fall off with distance. "The data provide a strong indication that falling curves are common in this population of early galaxies," says Genzel, of the Max Planck Institute for Extraterrestrial Physics in Garching, Germany.

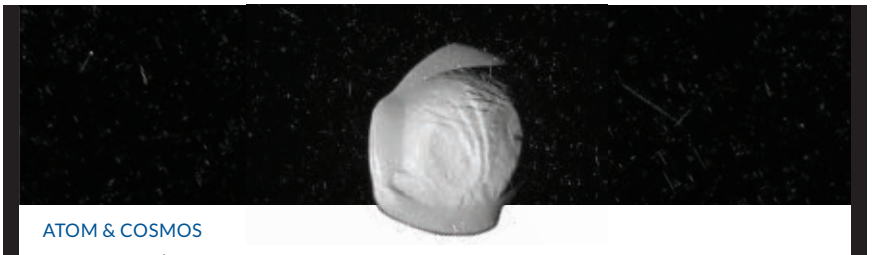
In the papers, the authors provide several plausible explanations for the falling rotation curves, but it's not clear which is correct, says UCLA astronomer Alice Shapley, who was not involved in the research. The results "reveal that we don't fully understand all of the details of how [galactic] disks form in the early universe."

Genzel and colleagues suggest that the rotation curves fall off because turbulent streams of gas bring more and more material into inner regions of these distant galaxies. The gas piles up there, while dark matter is left on the outskirts. Explosions of stars and winds flowing from black holes might also drag dark matter away from the inner regions of the galaxy. Or dark matter may be distributed on a scale of hundreds of thousands of light-years, while the gas and stars in these early galaxies are interacting on a scale of only tens of thousands of light-years, Genzel says, so astronomers detect the gas but not the dark matter.

"Dark matter must be there," he says. "Without it, there are no galaxies and no 'us,' so we need to understand its nature and distribution to explain what we see in the universe."

Current models of galaxy formation suggest that dark matter and ordinary matter intermixed in the early universe, so dark matter should tug on ordinary matter, resulting in rotation curves that are flat — not falling — for galaxies at the distance Genzel and colleagues observed. "We need to understand which physics is required to make simulations match the observations," Shapley says.

Genzel notes that the way the gas and stars move in the distant galaxies is similar to the way gas and stars move in elliptical galaxies nearby. So, he suggests, the clumpy, irregular distant galaxies the team studied may be progenitors of elliptical galaxies in the local universe. ■



JPL-CALTECH/NASA, SSI

ATOM & COSMOS

Saturn's moon Pan looks like ravioli

Saturn serves up the closest thing to space pasta, the latest images from NASA's Cassini probe, released March 9, show.

On March 7, the spacecraft snapped a series of portraits (one shown above) of Pan, Saturn's small moon that orbits within a 325-kilometer-wide gap in one of the planet's rings. Taken at a distance of 24,572 kilometers from the moon, these are the closest images of Pan to date.

The close-ups could help refine astronomers' understanding of the moon's geology. Pan has a distinctive ridge along its equator, which had prompted astronomers to liken the moon to a flying saucer. But in the new images, Pan's ridge isn't uniform. Its unevenness creates an overall shape that more closely resembles a ravioli or a wrinkly walnut.

Still, the ridge's distinctness is "what is so spectacular and eye-opening in these images," says imaging team leader Carolyn Porco of the Space Science Institute in Boulder, Colo. The shape supports the idea that the ridge is made of material from Saturn's rings that continued to rain down on Pan's equator after the moon formed. — *Helen Thompson*

MATTER & ENERGY

Superfluid behaves like black holes

Frictionless form of helium appears to follow odd 'area law'

BY EMILY CONOVER

Black holes and superfluids make for strange bedfellows: One is famous for being so dense that light can't escape, and the other is a bizarre liquid that flows without friction. But new computer simulations confirm that superfluid helium follows an unusual rule known from black holes — one with mysterious significance for physics.

Scientists demonstrated that entropy, a measure of the information contained in a system, behaves in a counterintuitive way in superfluid helium. Entropy grows at the same rate as the surface area of the superfluid helium, instead of its volume — mimicking how the entropy of a black hole grows as it gobbles up matter and expands. It's the first time the phenomenon, known as the "area law," has been demonstrated in simulations of a naturally occurring state of matter, physicists reported March 14. The result was also described March 13 in *Nature Physics*.

"If you double the size of a box, you expect to be able to double the amount of information in that box," said physicist Christopher Herdman of the University of Waterloo in Canada. But that's not the case for black holes. Progress toward a theory that unifies quantum mechanics and general relativity, a still thorny problem, has convinced many physicists that black holes instead follow the area law.

To demonstrate the law in a superfluid, Herdman and colleagues created a computer simulation of helium. The isotope they studied, helium-4, is the same stuff that keeps birthday balloons aloft, and it becomes a superfluid at temperatures below about 2 kelvins (–271° Celsius).

In the simulation, the researchers kept track of the helium atoms' entanglement — quantum linkages that intertwine particles. Within the superfluid, scientists selected an imaginary sphere of the material and studied the entanglement between atoms inside the sphere and those outside of it. That entanglement gives rise to a type of entropy in the superfluid. As the researchers increased the size of that sphere, the entropy of entanglement increased as well. The rate of increase matched that of the sphere's increase in surface area, which grows more slowly than its volume.

The superfluid sphere is analogous to a black hole's event horizon, the region of no return surrounding the black hole, within which light can't escape. In black holes, particles on one side of the event horizon can be entangled with those on the other side, creating entanglement entropy in a similar way.

"I think it's a fascinating result," said physicist Joe Serene of Georgetown University in Washington, D.C. But, to advance from simulations to a measurement of entanglement entropy in real-life helium would probably be difficult. "It remains to be clear how much they can actually get out of real experimental systems," Serene said.

This area law has outsize importance in physics. The realization that a black hole's entropy is proportional to its surface area led to the holographic principle, the idea that the information within a region of space might be completely reproduced on its surface (*SN Online: 9/8/14*). Scientists hope this concept could lead to a full theory of quantum gravity, uniting the physics of the very small with large-scale gravity.

What's more, some scientists now believe that the very structure of spacetime might be the result of quantum entanglement (*SN: 10/17/15, p. 28*), an idea that also grew out of the area law.

"Entanglement entropy is a concept that is successful across many different areas of physics," said physicist Markus Greiner of Harvard University. "The big problem is no one knows how to measure that in ... real-world systems." ■

MEETING NOTES

Single-atom magnets store data

The tiniest electronic gadgets have nothing on a new data-storage device. Each bit is encoded using a single atom, although scientists have stored only two bits of data so far.

Physicist Fabian Natterer of the École Polytechnique Fédérale de Lausanne in Switzerland and colleagues used holmium atoms deposited on a magnesium oxide surface. Each atom's magnetic field was the 1 or 0 of a bit, depending on whether its north pole was pointing up or down, Natterer reported March 16.

To switch a bit from 0 to 1, the scientists flipped an atom's magnetic orientation. To read data, the team measured the current running through an atom, which depends on the magnetic field's orientation. Current hard drives need 10,000 atoms or more to store a bit. — *Emily Conover*

Life's start tied to dividing drops

In Earth's primordial soup, chemical droplets may have paved the way for the first cells. Shape-shifting droplets split, grow and split again in new computer simulations. The result indicates that chemical blobs can replicate, one of life's basic properties, a team of physicists in Germany reported March 16.

In a liquid, droplets of particular chemicals can separate out. Such globs typically stay spherical, growing as they merge with other drops.

But if additional droplet material is continuously produced in reactions, chemicals will accumulate on either end of a droplet, causing it to elongate, the simulations show. At the same time, waste products are eliminated from the middle, causing the droplet to pinch in and split. The resulting droplets would then grow and split again to create a new generation. The process requires an energy source to get reactions going. — *Emily Conover*

GENES & CELLS

Gene offers clues to grasses' success

Cellular cooperation allows for more efficient photosynthesis

BY LAUREL HAMERS

Grasses have top-notch border control to conserve water in their leaves. Now, scientists have identified a genetic switch that makes them such masters at taking in carbon dioxide without losing water. The find might eventually lead to more drought-resistant crop plants, the team reports in the March 17 *Science*.

Adjustable pores called stomata on leaves help plants take in CO_2 while minimizing water loss. Like eye pupils responding to sunlight, stomata open and close in response to changing light, humidity and temperature. Grass stomata can open wider and respond more quickly than pores in other plants, helping grasses to photosynthesize more efficiently.

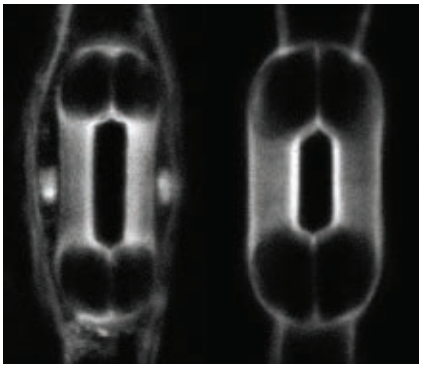
This ability may help explain why grasses grow in so many places, says Brent Helliker, a plant ecologist at the University of Pennsylvania who wasn't part of the study. For instance, grasses are particularly well equipped to deal with the rapidly changing weather and strong winds that can hit plains and prairies.

In most plant stomata, two kidney bean–shaped cells, one on each side of the pore, swell or deflate like balloons to control the size of the opening. But in grass, each of these cells is shaped like a dumbbell. And each dumbbell is linked to two other cells called subsidiary cells.

Scientists have long suspected that grasses' subsidiary cells might give the dumbbells, known as guard cells, an assist by making it easier for them to open and close. But that's been hard to test.

When a stoma opens, "it's elbowing its way into the neighbor cells," says study coauthor Dominique Bergmann, a biologist at Stanford University. "If the neighbors don't want to move, you're stuck." But subsidiary cells have some squish. As guard cells inflate, their neighboring subsidiary cells deflate.

Bergmann and colleagues mutated a gene called *MUTE* in purple false brome (*Brachypodium distachyon*) so that the grass didn't make the MUTE protein. Without MUTE, plants didn't make subsidiary cells and were less efficient than usual at opening and closing stomata.



A grass stoma has two dumbbell-shaped "guard cells" that inflate and deflate to adjust the pore's size. Subsidiary cells (absent from the mutant stoma, right) give a helping hand.

The *MUTE* gene is not unique to grasses, Bergmann says. But in other plants, the gene provides instructions to help make guard cells, not subsidiary cells. At some point in grasses' evolution, the gene took on a function that differs from the rest of the plant kingdom.

The work confirms that subsidiary and guard cells work together to make grass stomata more responsive, but more research is needed to understand how subsidiary cells lend a hand. "It would be really nice to show that there's actually an exchange of ions between the two cell types," says Michael Blatt, a plant physiologist at the University of Glasgow in Scotland. Sharing ions could incentivize water to flow from one cell type to the other, controlling which one is more inflated.

More responsive stomata may have helped grasses survive during periods when Earth's climate was warm and dry. "Grasses got lucky," says study coauthor Michael Raissig, also at Stanford. As Earth's climate continues to change, Raissig says, these genetic innovations might be exploited to help other plants make it through, too. ■

LIFE & EVOLUTION

Brainpower aids guppy mate choice

But the mental boost comes with downsides, study finds

BY SUSAN MILIUS

When choosing more attractive guys, girl guppies with larger brains have an advantage over their smaller-brained counterparts. But there's a cost to such brainpower, and that might help explain one of the persistent mysteries of sex appeal.

One sex often shows a strong preference for some trait in the other, whether it's a longer fish fin or a more elaborate song and dance. Yet after millions of years, there's still variety in many animals' color, size, shape or song, says evolutionary biologist Alberto Corral-López of Stockholm University. Somehow generations of mate choice have failed to make the opposite sex entirely fabulous.

Mate choice could require a certain amount of brainpower, with animals weighing the appeal of suitors and choosing among them, Corral-López and colleagues propose March 22 in *Science Advances*. Previous work suggests a smaller brain dims guppies' mental abilities, and the researchers wondered how brain size might affect the choice of mate.

To test the idea, researchers used female guppies bred for either a larger or smaller brain. Guppy brains are tiny to begin with, but after five generations of breeding, the brain sizes in the study differed by around 14 percent, within the range of what biologists find in the wild.

Each female was offered a choice between a colorful male with orange spots and a bigger tail versus a drab male of about the same weight but without much glory behind. The male fish were installed in compartments at either end of a tank, and females swam back and forth, forced to remember and mentally compare one suitor with his rival.

Females with larger brains showed a preference overall for the more colorful male. Smaller-brained females showed

M. RAISSIG AND D. BERGMANN

no preference. (The difference did not come from differences in color vision, Corral-López says. The researchers checked the eye genes of the fish and tested their ability to distinguish colors.)

Interest in flashy-looking males may not be just a fashion choice. Orange colors come from pigments in food; brighter males may be healthier foragers with better genes, likely to sire prime offspring. Corral-López also tested females that had not been bred for brain size, and these fish preferred the colorful males, too.

But big-brained females did not beat their compatriots in all tests. Smaller-brained guppies tended to grow faster when they were young and to have better immune systems and more offspring.

Thus, circumstances might tip the balance toward or against braininess, the researchers say. Having more babies might be more useful than a discriminating brain, for instance, when food is plentiful and most males manage a decent orange. Such changes in fortune might help explain how variety in appearance persists despite strong mating preferences, Corral-López and colleagues argue. Sometimes flashier males win the females, but sometimes drab is just fine.

Molly Cummings of the University of Texas at Austin, who studies fish brains and sexual selection, calls the work "exciting." Checking the fish's vision was especially important, she says. The results show that females were not "simple slaves to their sensory system."

The new paper, of course, tracked lab animals, and there's little data on what differences in brain size mean in the wild, says evolutionary biologist Kimberly Hughes of Florida State University in Tallahassee. The new study suggests it's certainly worth looking at what girl guppies do naturally, she says. ■

LIFE & EVOLUTION

King snake's strength is in its squeeze

How the constrictor coils may matter more than muscle size

BY ELIZABETH S. EATON

It's not the size of a snake's muscles that matters, but how it uses them. King snakes can defeat larger snakes in a wrestling match to the death because of how king snakes coil around their prey, scientists report in the March 15 *Journal of Experimental Biology*.

King snakes wrap around their food and squeeze with about twice as much pressure as rat snakes do, says David Penning, a functional morphologist at Missouri Southern State University in Joplin. Penning, along with colleague Brad Moon of the University of Louisiana at Lafayette, measured the constriction capabilities of almost 200 snakes. "King snakes are just little brutes," says Penning.

King snakes, which are common in North American forests and grasslands, are constrictor snakes that "wrestle for a living," Penning says. They eat lizards, amphibians, rodents and birds, squeezing hard enough to stop their prey's heart (*SN: 8/22/15, p. 4*). In addition, about a quarter of the king snake diet is other snakes. King snakes can easily attack and eat pit vipers because they're immune to the venom, but it has been unclear what gives king snakes the edge when they take on larger constrictors, such as rat snakes. "That's not how nature goes," Penning says, because predators are usually larger than their prey.

King snakes, though, can eat snakes up to 35 percent larger than themselves. One of the largest king snake conquests on record, from 1893, is of a 5-foot-3-inch rat snake consumed by a 4-foot-6-inch king snake, Penning says.

"David Penning is really one of the first researchers that has been looking at the anatomy, physiology and function of these snakes" to understand how king snakes manage to outpower rat snakes, says Anthony Herrel. Herrel is a functional morphologist and evolutionary biologist at the French National Museum of Natural History in Paris.

To determine what makes these snakes kings, Penning and Moon compared king snakes' muscle size, ability to escape attack and the strength of their squeeze with those of rat snakes. In one test, the researchers shook dead rodents enticingly in front of the snakes to goad them into striking and squeezing. Sensors on the rodents recorded the pressure of the squeeze.

The king snakes constricted with an average pressure of about 20 kilopascals, stronger than the pumping pressure of a human heart. Rat snakes in the same tests applied only about 10 kilopascals of pressure.

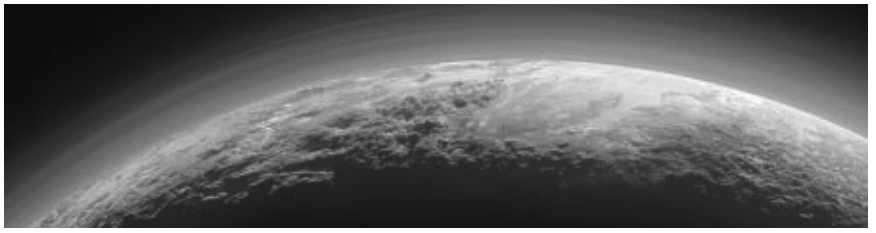
But the king snakes weren't bigger body builders. Controlling for body size, the two kinds of snakes "had the exact same quantity of muscle," Penning says.

The king snakes' more powerful constriction is probably due to how they use their muscles, not how much muscle they have, the researchers conclude. The majority of king snakes observed in the study wrapped around their food like a spring in what Penning calls the "curly fry pattern." Rat snakes didn't always coil in the same way and often ended up looking like a "weird pile of spaghetti," he says.

Penning plans to study how other factors influence constriction as well, such as how long the king snakes can squeeze, how hungry they are and the temperature of their environment. ■

D. PENNING

King snakes coil around mice tightly enough to stop the heart. A new study looks at how the snakes overcome much bigger prey.



Pluto's atmosphere is divided into about 20 layers, as seen in this New Horizons image. That haze affects surface features, including Pluto's red patches, a new study suggests.

ATOM & COSMOS

Haze may explain Pluto's red spots

Atmosphere's collapse darkens surface, researchers report

BY ASHLEY YEAGER

Pluto may get its smattering of red spots from the fallout of its hazy blue skies.

Haze particles from the dwarf planet's atmosphere settle onto all of Pluto's surfaces. But some regions may become redder and darker than others because parts of the atmosphere collapse, exposing those spots to more surface-darkening radiation from space, researchers reported March 22 at the Lunar and Planetary Science Conference in The Woodlands, Texas.

"The atmospheric haze on Pluto was a spectacular surprise," says NASA New Horizons mission scientist Andrew Cheng, a physicist at Johns Hopkins University. When the New Horizons spacecraft flew past Pluto in 2015, scientists weren't expecting to see haze reaching at least 200 kilometers above the dwarf planet's surface; nor were they expecting to see the haze divided into about 20 delicate and distinct layers.

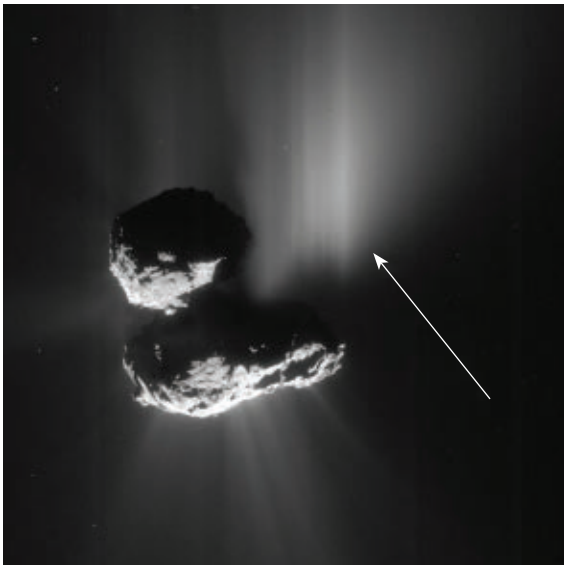
These discoveries led researchers to suspect that the layers formed as a result of weak winds blowing across Pluto's surface and over its mountains. Cheng and colleagues describe how the winds would shape the haze layers in a paper accepted in *Icarus* and posted online February 24 at arXiv.org. The team also explains how the atmosphere may affect the color of the dwarf planet's surface features.

"Haze particles continually fall out onto the surface and rapidly build up," Cheng says. This process should effectively "paint" the entire surface a uniform color. But Pluto isn't a single color. It has strikingly bright and dark terrains. The contrast forms because portions of the atmosphere periodically collapse, with air freezing and falling onto the surface, Cheng and colleagues suggest.

When a section of the atmosphere collapses, parts of the surface are exposed directly to radiation from space, which would darken the surface particles there, Cheng explains. The richness of the reds, the team says, cannot be explained without some kind of collapse of the atmosphere, which eventually redevelops.

Observations from NASA's Kepler spacecraft support the idea that Pluto's atmosphere collapses. In fact, as Pluto moves away from the sun, most if not all of its atmosphere may collapse onto the surface, Carey Lisse, also of Hopkins, reported at the conference.

Exactly how much of Pluto's atmosphere freezes out during its year, which lasts for 248 Earth years, isn't clear. But that is being monitored, says Timothy Dowling, an atmospheric scientist at the University of Louisville in Kentucky who was not involved in the new work. Pluto, he notes, won't complete the first lap that humans have watched it make around the sun until 2178. ■



ATOM & COSMOS

Pass by sun didn't reshape comet 67P

Recent surface changes haven't radically altered comet 67P/Churyumov–Gerasimenko's appearance, suggesting the comet has had roughly the same look for decades — or longer.

Images from the Rosetta spacecraft show what happened to 67P as it passed by the sun in 2015. Cliffs collapsed, ripplelike features about 100 meters across appeared and disappeared, dust eroded and boulders moved — probably due to changes in sunlight exposure, researchers report March 21 in *Science*.

Another research group reports March 21 in *Nature Astronomy* that a single landslide ejected up to a million kilograms of material into space (arrow points to the debris).

But after these changes, 67P still retains its rubber duck–like look. 67P probably acquired this shape and major features during previous passes by the sun, perhaps as far back as 1840 or earlier, the authors of the paper in *Science* say. — *Ashley Yeager*

FROM TOP: SWRI, JHUAPL, NASA; NAVCAM/ROSETTA/ESA (CC BY-SA IGO 3.0)

Budget proposal would slash science

President's fiscal 2018 plan calls for deep cuts at EPA, NIH, DOE

Huge cuts in federal science spending could be in store if President Donald Trump's vision for fiscal year 2018 becomes reality.

Trump's $1.15 trillion budget proposal, released March 16, calls for a $54 billion increase in defense spending, offset by an equally big reduction in nondefense activities. Among the big losers are the Environmental Protection Agency, which could see its budget shrink by 31 percent compared with 2017, and the National Institutes of Health, which faces an 18 percent spending slash. The Department of Energy's Office of Science could lose about 17 percent of its funding, while DOE's Advanced Research Projects Agency-Energy, or ARPA-E — which supports research on promising energy technologies — faces elimination.

The budget blueprint doesn't even mention the National Science Foundation, a major source of federal funding for basic research. NSF is currently operating on a $7.5 billion budget. Full breakdowns aren't available for most departments, so there's no information on what's to come for such programs as the National Institute of Standards and Technology, the U.S. Fish and Wildlife Service and the Defense Advanced Research Projects Agency, or DARPA. More details for these and other agencies not mentioned may be included in a full budget proposal that the White House expects to release in May.

The White House's budget outline is already raising alarm in the scientific community. "Major national goals are served by these investments in science and technology," says Matt Hourihan, director of the R&D Budget and Policy Program at the American Association for the Advancement of Science in Washington, D.C. The proposed cuts, he says, "would set back our scientific leadership and would set back our technologies."

The president's budget will ultimately go to Congress. Last year, Congress failed to reach agreements on fiscal 2017 spending; the government has been operating under a continuing resolution that has largely kept agencies funded at their 2016 levels. That resolution ends April 28. But if the House and Senate can find common ground for fiscal 2018, which begins October 1, they are likely to be kinder to science than Trump was, Hourihan predicts. "Overall, Congress tends to find ways to support science and technology."

Leland Cogliani, a lobbying consultant with Lewis-Burke Associates LLC in Washington, D.C., who specializes in DOE policy, agrees. "There's a lot of angst and concern and worry about these proposed cuts to federal agencies as a whole," he says. "My discussions with appropriators is that this budget is dead on arrival."

Trump's budget would devastate the EPA, dropping its budget from $8.2 billion to just $5.7 billion, and shedding about 3,200 of roughly 15,000 employees.

The budget plan would slash $5.8 billion from the $31.7 billion the NIH currently receives. Supporters of biomedical research call the proposal "disastrous" and say that deep cuts will topple the United States from its position as the world leader of such research. "We're not going to be No. 1 anymore. We're going to slide down to the bottom of the pile," says Jennifer Zeitzer, director of legislative relations at the Federation of American Societies for Experimental Biology.

DOE faces a 5.6 percent cut in Trump's proposal, dropping it from $29.7 billion to $28 billion. The cut "falls disproportionately on the basic research and applied energy programs," Cogliani says.

NASA would not be hit as hard as some agencies. Its proposed funding for fiscal 2018 is $19.1 billion — down 2 percent from 2017 before accounting for inflation. On March 21, after the budget plan was released, President Trump signed a bill authorizing NASA to receive $19.5 billion for fiscal 2017.

"NASA's top-line budget for 2018 is favorable," says planetary scientist Alan Stern of the Southwest Research Institute in Boulder, Colo. "I bet there are many agency heads who would trade numbers with NASA in a heartbeat." But NASA's Office of Education, with an estimated cost of $115 million, would be eliminated.

It's not clear how the Centers for Disease Control and Prevention would fare; the proposal mentions no funding total. The budget does propose a new Federal Emergency Response Fund to respond to outbreaks such as Zika, but doesn't say how much money would be budgeted or which agencies would get it.

As for the Food and Drug Administration, user fees that companies pay to the FDA to review medical products would increase to "over $2 billion in 2018," about double 2017 levels. The budget request glossed over the main source of FDA dollars, money appropriated by Congress, which was nearly $2.72 billion for 2017. Without naming a number for appropriated funds, the fates of many FDA programs, including food safety, remain in the dark. — *Laurel Hamers, Meghan Rosen, Tina Hesman Saey, Thomas Sumner, Erin Wayman, Ashley Yeager*

Funding outlook The chart below shows the president's proposed fiscal year 2018 budgets for select agencies in billions of dollars. Numbers are not adjusted for inflation, which is predicted to be 2 percent in 2018. SOURCE: OFFICE OF MANAGEMENT AND BUDGET 2017

Agency	2017 (continuing resolution)	2018 (president's request)	Change (2017 to 2018)
NASA	19.5*	19.1	–2%
NIH	31.7	25.9	–18%
EPA	8.2	5.7	–31%
DOE Office of Science	5.3	4.4**	–17%

**Amount authorized in bill signed March 21, 2017*
***Estimate based on reported $900 million cut*

GENES & CELLS

Human embryo editing yields results

Lab studies are beginning to work out CRISPR/Cas9's kinks

BY TINA HESMAN SAEY

Scientists have long sought a strategy for curing genetic diseases, but — with just a few notable exceptions — have succeeded only in their dreams. Now, though, researchers in China and Texas have taken a step toward making the fantasies a reality for all inherited diseases.

Using the gene-editing tool known as CRISPR/Cas9, the researchers have successfully edited disease-causing mutations out of viable human embryos. Other Chinese groups had previously reported editing human embryos that could not develop into a baby because they carried extra chromosomes, but this is the first report involving viable embryos (*SN Online: 4/8/16; SN Online: 4/23/15*).

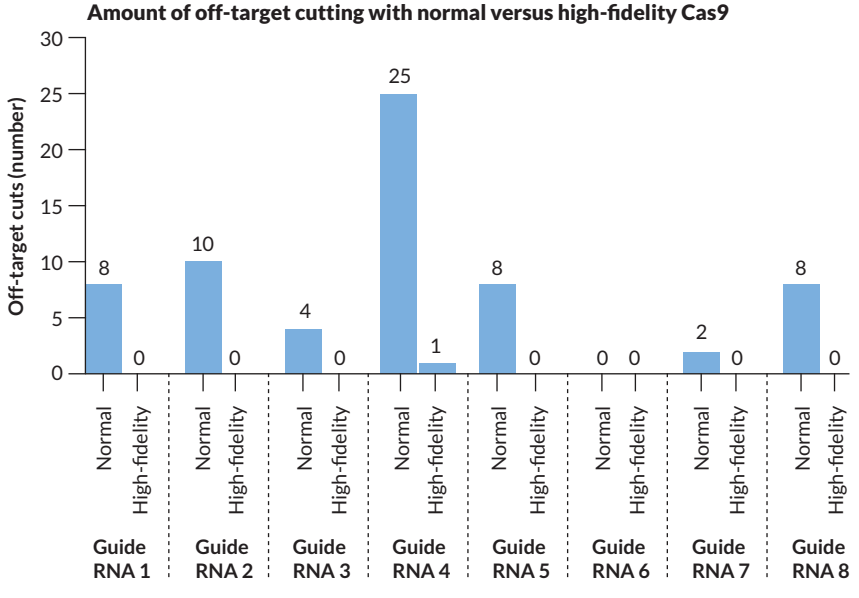
In the new work, reported March 1 in *Molecular Genetics and Genomics*, Jianqiao Liu of Guangzhou Medical University in China and colleagues used embryos with a normal number of chromosomes. The embryos were created using eggs and sperm left over from in vitro fertilization treatments. In theory, the embryos could develop into a baby if implanted into a woman's uterus.

Researchers in Sweden and England are also conducting gene-editing experiments on viable human embryos (*SN: 10/29/16, p. 15*), but those groups have not yet reported results.

Human germline editing wasn't realistic until CRISPR/Cas9 and other new gene editors came along, says R. Alta Charo, a bioethicist at the University of Wisconsin Law School in Madison. "We've now gotten to the point where it's possible to imagine a day when it would be safe enough" to be feasible. Charo was among the experts on a National Academies of Sciences and Medicine panel that in February issued an assessment of human gene editing. Altering human embryos, eggs, sperm or the cells that produce eggs and sperm would be permissible, provided there were no other alternatives and the experiments met other strict criteria, the panel concluded (*SN: 3/18/17, p. 7*).

Still, technical hurdles remain before CRISPR/Cas9 can cross into widespread use in treating patients.

Better aim Snipping the wrong bit of DNA is a potential problem for gene editing. In recent experiments, researchers modified the Cas9 enzyme in a CRISPR/Cas9 system to create a high-fidelity version that reduced off-target cutting. SOURCE: B. KLEINSTIVER *ET AL/NATURE* 2016



CRISPR/Cas9 comes in two parts: a DNA-cutting enzyme called Cas9, and a "guide RNA" that directs Cas9 to cut at a specified location in DNA (see Page 22). Guide RNAs work a little like a GPS system, says David Edgell, a molecular biologist at Western University in London, Ontario. Given precise coordinates or a truly unique address, a good GPS should take you to the right place every time.

Scientists design guide RNAs so that they will carry Cas9 to only one stretch of about 20 bases (the information-carrying subunits of DNA) out of the entire 6 billion base pairs that make up the human genetic instruction book, or genome. But most 20-base locations in the human genome aren't particularly distinctive. They are like Starbucks coffee shops: There are a lot of them and they are often similar enough that a GPS might get confused about which one you want to go to, says Edgell. Similarly, guide RNAs sometimes direct Cas9 to cut alternative, or "off-target," sites that are a base or two different from the intended destination. Off-target cutting is a problem because such edits might damage or change genes in unexpected ways.

"It's a major issue for sure," says Bruce Korf, a geneticist at the University of Alabama at Birmingham and president of the American College of Medical Genetics and Genomics Foundation. Doctors trying to correct one genetic defect in a patient want to be sure they aren't accidentally introducing another.

But CRISPR/Cas9's propensity to cut undesired sites may be exaggerated, says Alasdair MacKenzie, a molecular biologist at the University of Aberdeen in Scotland. In experiments with mice, MacKenzie and colleagues limited how much Cas9 was produced in cells and made sure the enzyme didn't stick around after it made an edit. No off-target cuts were detected in any of the mice resulting from successfully edited embryos, MacKenzie and colleagues reported in November in *Neuropeptides*.

Other researchers have experimented with assembling the Cas9 and guide RNAs outside of the cell and then

putting the preassembled protein-RNA complex into cells. That's the strategy the Chinese researchers took in the new human embryo–editing study. No off-target cuts were detected in that study either, although only one edited embryo was closely examined.

Other researchers have been tinkering with the genetic scissors to produce high-fidelity versions of Cas9 that are far less likely to cut at off-target sites in the first place.

When a guide RNA leads Cas9 to a site that isn't a perfect match, the enzyme can latch onto DNA's phosphate backbone and stabilize itself enough to make a cut, says Benjamin Kleinstiver, a biochemist in J. Keith Joung's lab at Harvard Medical School. By tweaking Cas9, Kleinstiver and colleagues essentially eliminated the enzyme's ability to hold on at off-target sites, without greatly harming its on-target cutting ability.

Regular versions of Cas9 cut between two and 25 off-target sites for seven guide RNAs the researchers tested. But the high-fidelity Cas9 worked nearly flawlessly for those guides. For instance, high-fidelity Cas9 reduced off-target cutting from 25 sites to just one for one of the guide RNAs, the researchers reported in January 2016 in *Nature*. That single stray snip, however, could be a problem if the technology were to be used in patients.

A group led by CRISPR/Cas9 pioneer Feng Zhang of the Broad Institute of MIT and Harvard tinkered with different parts of the Cas9 enzyme. That team also produced a cutter that rarely cleaved DNA at off-target sites, the team reported last year in *Science*.

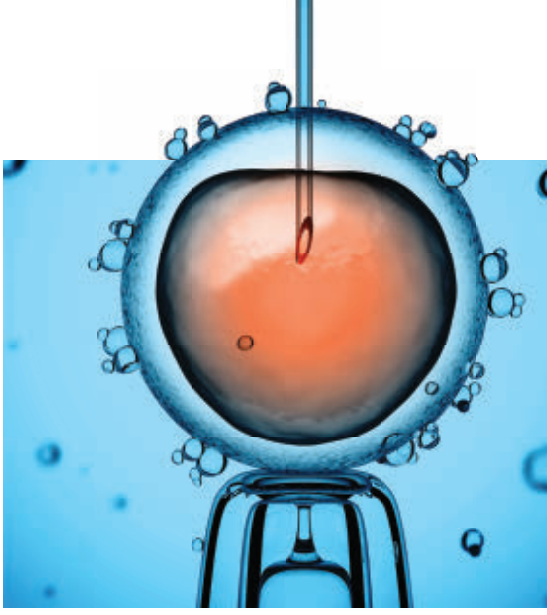
Another problem for gene editing has been that it is good at disabling, or "knocking out," genes that are causing a problem but not at replacing genes that have gone bad. Knocking out a gene is easy because all Cas9 has to do is cut the DNA. Cells generally respond by gluing the cut ends back together. But, like pieces of a broken vase, they rarely fit perfectly again. Small flaws introduced in the regluing can cause the problem gene to produce nonfunctional proteins. Knocking out genes may help fight Huntington's disease and other genetic disorders caused by single, rogue versions of genes.

Many genetic diseases, such as cystic fibrosis or Tay-Sachs, are caused when people inherit two mutated, nonfunctional copies of the same gene. Knocking those genes out won't help. Instead, researchers need to insert undamaged versions of the genes to restore health. Inserting a gene starts with cutting the DNA, but instead of gluing the cut ends together, cells use a matching piece of DNA as a template to repair the damage.

In the new human embryo work, Liu and colleagues, including Wei-Hua Wang of the Houston Fertility Institute in Texas, first tested this type of repair on embryos with an extra set of chromosomes. Efficiency was low; about 10 to 20 percent of embryos contained the desired edits. Researchers had previously argued that extra chromosomes could interfere with the editing process, so Liu's group also made embryos with the normal two copies of each chromosome (one from the father and one from the mother). Sperm from men that have genetic diseases common in China were used to fertilize eggs. In one experiment, Liu's group made 10 embryos, two of which carried a mutation in the *G6PD* gene. Mutations in that gene can lead to a type of anemia.

Then the team injected Cas9 protein already leashed to its guide RNA, along with a separate piece of DNA that embryos could use as a template for repairing the mutant gene. *G6PD* mutations were repaired in both embryos. Since both of the two embryos had the repair, the researchers say they achieved 100 percent efficiency. But one embryo was a mosaic: It carried the fix in some but not all of its cells. Another experiment to repair mutations in the *HBB* gene, linked to blood disorders, worked with 50 percent efficiency, but with some other technical glitches.

Scientists don't know whether editing just some cells in an embryo will be enough to cure genetic diseases. For that



Researchers in China and Texas have used CRISPR/Cas9 to repair disease-causing mutations in viable human embryos.

reason, some researchers think it may be necessary to step back from embryos to edit the precursor cells that produce eggs and sperm, says Harvard University geneticist George Church. Precursor cells can produce many copies of themselves, so some could be tested to ensure that proper edits have been made with no off-target mutations. Properly edited cells would then be coaxed into forming sperm or eggs in lab dishes. Researchers have already succeeded in making viable sperm and eggs from reprogrammed mouse stem cells (*SN: 11/12/16, p. 6*). Precursors of human sperm and eggs have also been grown in lab dishes (*SN Online: 12/24/14*), but researchers have yet to report making viable human embryos from such cells.

The technology to reliably and safely edit human germline cells will probably require several more years of development, researchers say.

Germline editing — as altering embryos, eggs and sperm or their precursors is known — probably won't be the first way CRISPR/Cas9 is used to tackle genetic diseases. Doctors are already planning experiments to edit genes in body cells of patients. Those experiments come with fewer ethical questions but have their own hurdles, researchers say.

"We still have a few years to go," says MacKenzie, "but I've never been so hopeful as I am now of the capacity of this technology to change people's lives." ■

KOYA79/ISTOCKPHOTO

How Earth Got its MOON

Standard formation tale may need a rewrite

By Thomas Sumner

The moon's origin story does not add up. Most scientists think that the moon formed in the earliest days of the solar system, around 4.5 billion years ago, when a Mars-sized protoplanet called Theia whacked into the young Earth. The collision sent debris from both worlds hurling into orbit, where the rubble eventually mingled and combined to form the moon.

If that happened, scientists expect that Theia's contribution would give the moon a different composition from Earth's. Yet studies of lunar rocks show that Earth and its moon are compositionally identical. That fact throws a wrench into the planet-on-planet impact narrative.

Researchers have been exploring other scenarios. Maybe the Theia impact never happened (there's no direct evidence that the budding planet ever existed). Instead of a single colossal collision, scientists have proposed that a string of impacts created miniature moons largely from terrestrial material. Those mini moons merged over time to form one big moon.

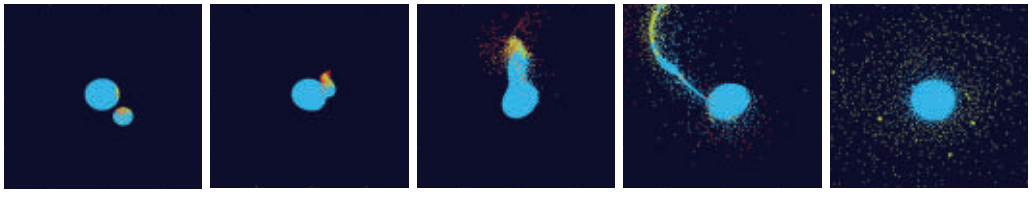
"Multiple impacts just make more sense," says planetary scientist Raluca Rufu of the Weizmann Institute of Science in Rehovot, Israel. "You don't need this one special impactor to form the moon."

But Theia shouldn't be left on the cutting room floor just yet. Earth and Theia were built largely from the same kind of material, new research suggests, and so had similar compositions. There is no sign of "other" material on the moon, this perspective holds, because nothing about Theia was different.

"I'm absolutely on the fence between these two opposing ideas," says UCLA cosmochemist Edward Young. Determining which story is correct is going to take more research. But the answer will offer profound insights into the evolution of the early solar system, Young says.

Mother of the moon

The moon is an oddball. Most of the solar system's moons are way out among the gas giant planets. The only other terrestrial



A collision of early Earth and a smaller protoplanet called Theia hurled debris from both into space, many scientists think. In this simulation, red particles escaped the system, yellow formed the moon, blue fell to Earth.

FROM TOP: NASA; R. CANUP/SWRI

planet with orbiting satellites is Mars. Its moons, Phobos and Deimos, are small, and the prevailing explanation says they were probably asteroids captured by the Red Planet's gravity. Earth's moon is too big for that scenario. If the moon had come in from elsewhere, asteroid-like, it would probably have crashed into Earth or pulled off into space. An alternate explanation dating from the 1800s suggested that moon-forming material flew off of a fast-spinning young Earth like children tossed from an out-of-control merry-go-round. That idea fell out of favor, though, when scientists calculated that the spin speeds required were impossibly fast.

In the mid-1970s, planetary scientists proposed the giant-impact hypothesis and the mysterious planet-sized impactor (named Theia in 2000 for the Greek deity who was mother of the moon goddess Selene). The notion made sense given that the early solar system was like a game of cosmic billiards, with giant space rocks frequently colliding.

A 2001 study of lunar rocks collected during the Apollo missions cast doubt on the giant-impact hypothesis. The research showed that the Earth and moon had surprising similarities. To determine a rock's origin, scientists measure the relative abundance of oxygen isotopes, which act something like fingerprints at a crime scene. Rocks from Earth and its moon, the scientists found, had seemingly identical mixes of oxygen isotopes. That didn't make sense if much of the moon's material came from Theia, not Earth. Using impact simulations, Rufu and colleagues recently estimated that the chance of a Theia collision yielding an Earthlike lunar composition is very slim.

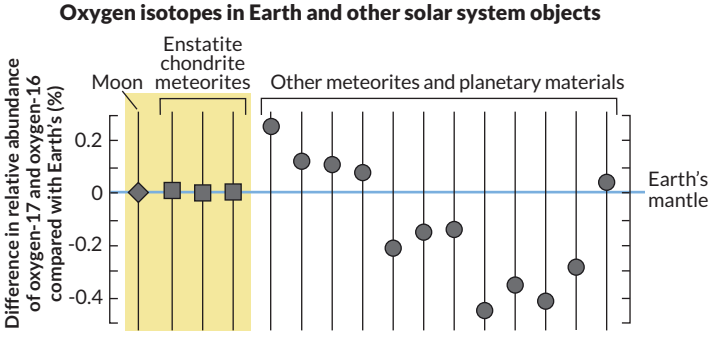
Studies of other elements in Apollo rocks, such as titanium and zirconium, also suggest that the Earth and moon originated from the same material. Young and colleagues recently repeated the oxygen isotope measurements with the latest techniques, hunting for even the slightest difference between Earth and the moon. In January 2016, the team published the results in *Science*. "We measured the oxygen to the highest precision available," Young says, "and, gosh, the Earth and moon still look identical."

Some scientists have built simulations of a giant Theia impact that fashion a moon made mostly from terrestrial material. But the scenarios struggle to match the modern positions and movements of the Earth-moon system.

It's time to think outside the giant-impact box, some scientists argue. Not one but many impacts contributed to the moon's formation, Rufu and colleagues proposed January 9 in *Nature Geoscience*. The moon, they say, has an Earthlike composition because most of the material flung into orbit from these impacts came from Earth.

Mini-moon merger

The multi-impact hypothesis was first put forward in 1989, though scientists at the time didn't have the computer power to run the simulations that could support it. Rufu and colleagues recently revisited the proposal with computer simulations of multiple impactors, each about a hundredth to a tenth of Earth's mass, smacking into the early Earth.



Perfect match The mix of oxygen isotopes inside lunar material and meteorites called enstatite chondrites (shaded yellow) is surprisingly similar to that of Earth rocks (blue line). Other solar system materials have largely different isotopic mixes. SOURCE: N. DAUPHAS/*NATURE* 2017

Any impactors that were direct hits would have transferred lots of energy into the Earth, excavating terrestrial material into space. Debris from each impact combined over centuries to form a small moon, the simulations show. As more impacts rocked Earth over tens of millions of years, more moons formed. Gravity pulled the moons together, combining them. Over roughly 100 million years, according to this scenario, around 20 mini moons ultimately merged to form one mighty moon (*SN Online: 1/9/17*).

The multimoon explanation yields the right lunar mix in simulations roughly 20 percent of the time, better than the 1 to 2 percent for the giant-impact hypothesis, the researchers note. "The biggest takeaway is that you cannot explain everything with one shot," Rufu says.

Planetary scientist Robin Canup finds the scenario convincing. "To me, this appears to be a real contender alongside the one big impactor hypothesis," says Canup, of the Southwest Research Institute in Boulder, Colo.

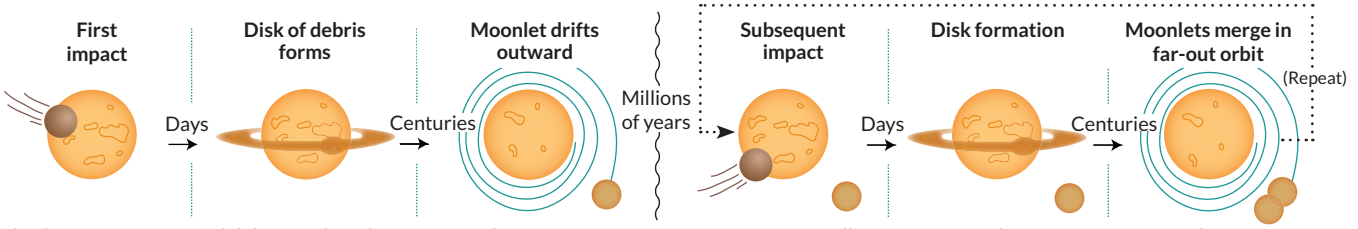
Don't discount Theia

But the Theia hypothesis has recently found fresh support. The odds of Theia resembling Earth's composition enough to yield an Earthlike moon may be a lot higher than originally thought, new chemical analyses suggest. Most of the material that makes up Earth came from the same source as a type of meteorite called enstatite chondrites, planetary scientist Nicolas Dauphas of the University of Chicago reported January 26 in *Nature*.

The rock-evaporating smack of the proposed large protoplanet Theia into the young Earth would have sent plenty of terrestrial material into orbit, eventually coalescing into the moon.

FROM TOP: T. TIBBITTS, JPL-CALTECH/NASA

Making moons The multi-impact hypothesis says several small hits sent terrestrial materials into orbit that eventually formed our large moon.



The first impact spawned debris circling the young Earth. Over centuries, the material pulled together into one mini moon.

Over tens of millions of years and many impacts, around 20 moonlets orbiting around Earth merged to form one large moon.

Just as with oxygen, the isotopic mix of various other elements in Earth's rocks serves as a fingerprint of the rocks' origins. Some of these elements are iron-lovers, such as ruthenium, which quickly sink toward Earth's iron-rich core (*SN: 8/6/16, p. 22*). Any ruthenium found close to Earth's surface, in the mantle, probably arrived late in Earth's development. Iron-indifferent elements like calcium and titanium don't sink to the core; they stay in the mantle. Their isotopes record what went into Earth's assembly over a much longer period of time. By looking at the iron-lovers and iron-indifferent elements together, Dauphas created a timeline of what types of space rocks added to Earth's mass and when.

A mix of different rocks, including some resembling enstatite chondrite meteorites, supplied the first 60 percent of Earth's mass, Dauphas says. The remaining balance came almost exclusively from the meteorites' precursors. In total, around three-quarters of Earth's mass came from the same material as enstatite chondrites, Dauphas estimates. If Theia formed at around the same distance from the sun as Earth, then it primarily formed from the same material, and consequently had a similar isotopic composition. So if the moon formed largely from Theia, it makes sense that lunar rocks would have a similar composition to Earth, too.

"Most of the problem is solved, in my opinion, if you admit that the great impactor's material was no different than that of the [early] Earth," says cosmochemist Marc Javoy at the Institute of Earth Physics of Paris. "It's the simplest hypothesis" and would mean that the material gobbled up by budding planets in the inner solar system was fairly uniform in composition, offering insight into the arrangement of material that built the solar system.

The notion that Earth is made from the same material as enstatite chondrites "doesn't make many people happy," says geochemist Richard Carlson of the Carnegie Institution for Science in Washington, D.C. The isotopes in Earth's mantle and the meteorites may match, but the relative abundance of the elements themselves do not, Carlson wrote in a commentary in the Jan. 26 *Nature*. An additional step in the process is needed to explain this compositional mismatch, he says, such as some of the element silicon getting stashed away in Earth's core.

"What we have now are a lot of new ideas, and now we need to test them," says Sarah Stewart, a planetary scientist at the University of California, Davis.

One recently proposed test for the moon's formation is based on temperature, though it seems to be consistent with both origin stories. A new study comparing the moon's chemistry with glass forged by a nuclear blast suggests that temperatures during or just after the moon's inception reached a sizzling 1400° Celsius. That means any plausible moon-forming scenario must involve such high temperatures, researchers reported February 8 in *Science Advances*.

High heat causes rocks to leach light isotopes of zinc. The green-tinged glass forged in the heat of the 1945 Trinity nuclear test in New Mexico lack light isotopes of zinc, says study coauthor and geologist James Day of the Scripps Institution of Oceanography in La Jolla, Calif. The same goes for lunar rocks. Such high temperatures during or just after the moon's formation fit with the giant-impact hypothesis, he says. But Rufu calculates that her multi-impact hypothesis also yields high enough temperatures.

So maybe temperature can't resolve the debate, but probing the composition of Earth and the moon's deep interiors could prove the mini-moon explanation right, says Rufu. Without a single giant collision, the interiors of the two worlds may not have been well mixed, she predicts. Dauphas says that measuring the compositions of other planets could lend credence to his Earthlike Theia proposal. Mercury and Venus would also have formed largely from the same kind of material as Earth and therefore also have Earthlike compositions, he says. Future studies of the solar system's inhabitants could confirm or rule out these predictions, but that will require a new chapter of exploration. ■

Isotopes in green-tinted glass forged during the first nuclear bomb test suggest that the moon had a hot beginning.

Rocks similar to enstatite chondrites may have been a common source material for Earth, the protoplanet Theia and the moon.

Explore more

■ Richard W. Carlson. "Earth's building blocks." *Nature*. January 26, 2017.

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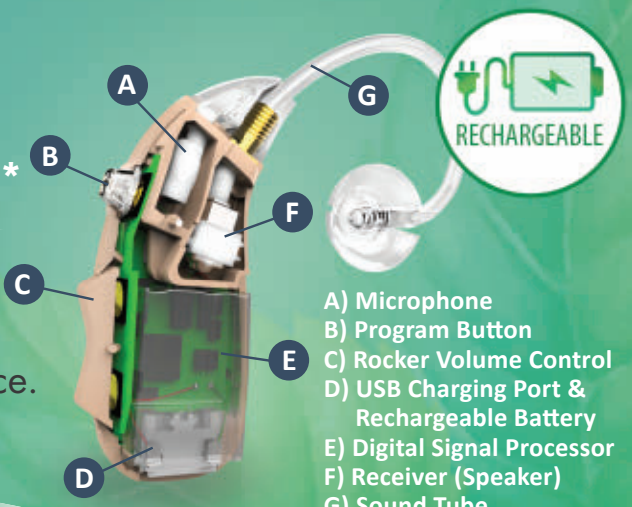

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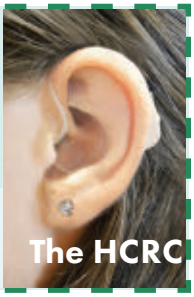

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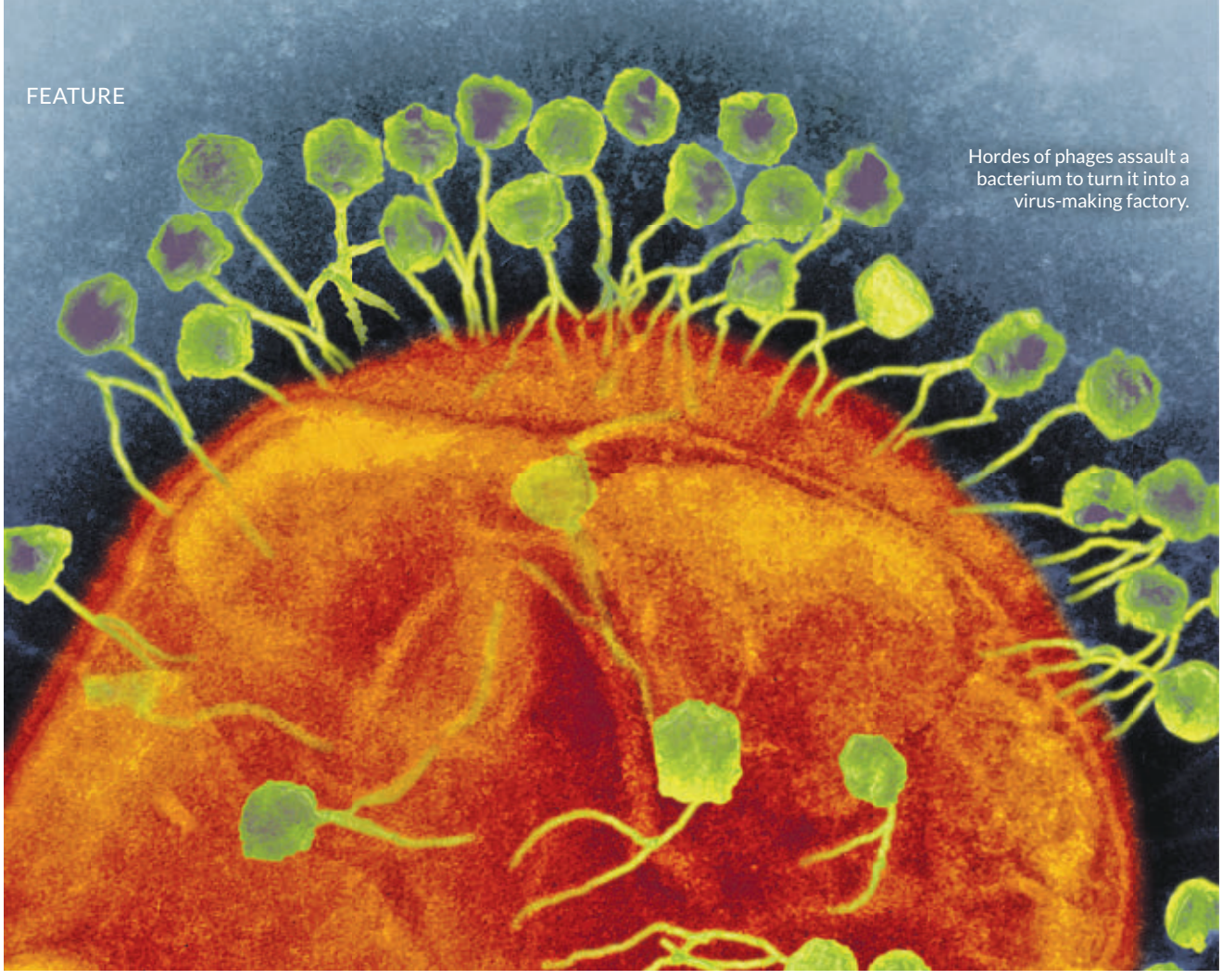


Hordes of phages assault a bacterium to turn it into a virus-making factory.

AMI IMAGES/SCIENCE SOURCE

The Original CRISPR

Before becoming a famous tool, the gene editor was a weapon in an unending microscopic war

By Rosie Mestel

It is the dazzling star of the biotech world: a powerful new tool that can deftly and precisely alter the structure of DNA. It promises cures for diseases, sturdier crops, malaria-resistant mosquitoes and more. Frenzy over the technique — known as CRISPR/Cas9 — is in full swing. Every week, new CRISPR findings are unfurled in scientific journals. In the courts, universities fight over patents. The media report on the breakthroughs as well as the ethics of this game changer almost daily.

But there is a less sequins-and-glitter side to CRISPR that's just as alluring to anyone thirsty to understand the natural world. The biology behind CRISPR technology comes from a battle that has been raging for eons, out of sight and yet all around us (and on us, and in us).

The CRISPR editing tool has its origins in microbes — bacteria and archaea that live in obscene numbers everywhere from undersea vents to the snot in the human nose. For billions of years, these single-celled organisms have been at odds with the viruses — known as phages — that attack them, invaders so plentiful that a single drop of seawater can hold 10 million. And natural CRISPR systems (there are many) play a big part in this tussle. They act as gatekeepers, essentially cataloging viruses that get into cells. If a virus shows up again, the cell — and its offspring — can recognize and destroy it. Studying this system will teach biologists much about ecology, disease and the overall workings of life on Earth.

But moving from the simple, textbook story into real life is messy. In the few years since the defensive function of CRISPR systems was first appreciated, microbiologists have busied themselves collecting samples, conducting experiments and crunching reams of DNA data to try to understand what the systems do. From that has come much elegant physiology, a mass of complexity, surprises aplenty — and more than a little mystery.

Spoiled yogurt

The biology is complicated, and its basic nuts and bolts took some figuring out. There are two parts to CRISPR/Cas systems: the CRISPR bit and the Cas bit. The CRISPR bit — or "clustered regularly interspaced short palindromic repeats" — was stumbled on in the late 1980s and 1990s. Scientists then slowly pieced the story together by studying microbes that thrive in animals' guts and in salt marshes, that cause the plague and that are used to make delicious yogurt and cheese.

None of the scientists knew what they were dealing with at first. They saw stretches of DNA with a characteristic pattern: short lengths of repeated sequence separated by other DNA sequences now known as spacers. Each spacer was unique. Because the roster of spacers could differ from one cell to the next in a given microbe species, an early realization was that these differences could be useful for forensic "typing" — investigators could tell whether food poisoning cases were linked, or if someone had stolen a company's yogurt starter culture.

But curious findings piled up. Some of those spacers, it turned out, matched the DNA of phages. In a flurry of reports in 2005, scientists showed, to name one example, that strains of the lactic acid bacterium *Streptococcus thermophilus* contained spacers that matched genetic material of phages known to infect *Streptococcus*. And the more spacers a strain had, the more resistant it was to attack by phages.

This began to look a lot like learned or adaptive immunity, akin to our own antibody system: After exposure to a specific threat, your immune system remembers and you are thereafter resistant to that threat. In a classic experiment published in *Science* in 2007, researchers at the food company Danisco showed it was so. They could see new spacers added when a phage infected a culture of *S. thermophilus*. Afterward, the bacterium was immune to the phage. They could artificially engineer a phage spacer into the CRISPR DNA and see resistance emerge; when they took the spacer away, immunity was lost.

This was handy intel for an industry that could find whole vats of yogurt-making bacteria wiped out by phage infestations. It was an exciting time scientifically and commercially, says Rodolphe Barrangou of North Carolina State University in Raleigh, who did a lot of the Danisco work. "It was not just discovering a cool system, but also uncovering a powerful phage-resistance technology for the dairy industry," he says.

The second part of the CRISPR/Cas system is the Cas bit: a set of genes located near the cluster of CRISPR spacers. The DNA sequences of these genes strongly suggested that they carried instructions for proteins that interact with DNA or RNA in some fashion — sticking to it, cutting it, copying it, unraveling it. When researchers inactivated one Cas gene or another, they saw immunity falter. Clearly, the two bits of the system — CRISPR and Cas — were a team.

It took many more experiments to get to today's basic model of how CRISPR/Cas systems fight phages — and not just phages. Other types of foreign DNA can get into microbes, including circular rings called plasmids that shuttle from cell to cell and DNA pieces called transposable elements, which jump around within genomes. CRISPRs can fend off these intruders, as well as keep a microbe's genome in tidy order.

The process works like this: A virus injects its genetic material into the cell. Sensing this danger, the cell selects a little strip of that genetic material and adds it to the spacers in the CRISPR cluster. This step, known as immunization or adaptation, creates a list of encounters a cell has had with viruses, plasmids or other foreign bits of DNA over time — neatly lined up in reverse chronological order, newest to oldest.

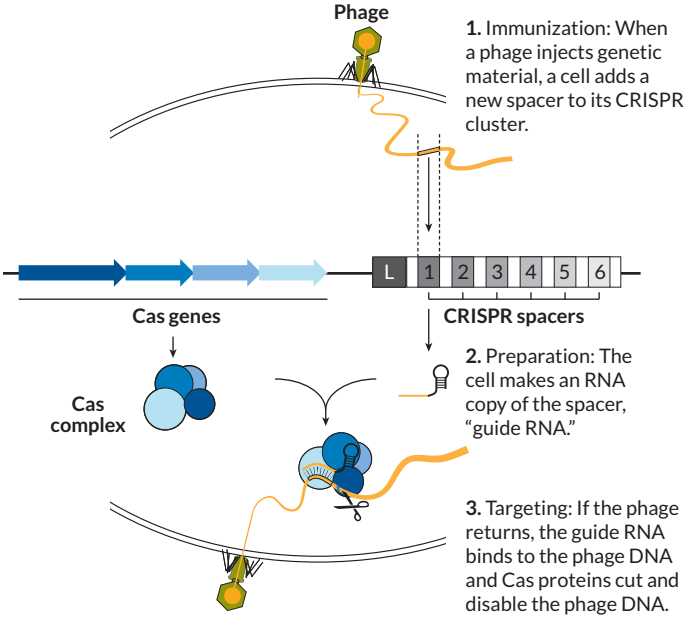
Older spacers eventually get shed, but a CRISPR cluster can grow to be long — the record holder to date is 587 spacers in *Haliangium ochraceum*, a salt-loving microbe isolated from a piece of seaweed. "It's like looking at the last 600 shots you had in your arm," says Barrangou. "Think about that."

New spacer in place, the microbe is now immunized. Later comes targeting. If that same phage enters the cell again, it's recognized. The cell has made RNA copies of the relevant spacer, which bind to the matching spot on the genome of the invading phage. That "guide RNA" leads Cas proteins to target and snip the phage DNA, defanging the intruder.

Researchers now know there are a confetti-storm of different CRISPR systems, and the list continues to grow. Some are simple — such as the CRISPR/Cas9 system that's been adapted for gene editing in more complex creatures (see Page 16) — and some are elaborate, with many protein workhorses deployed to get the job done.

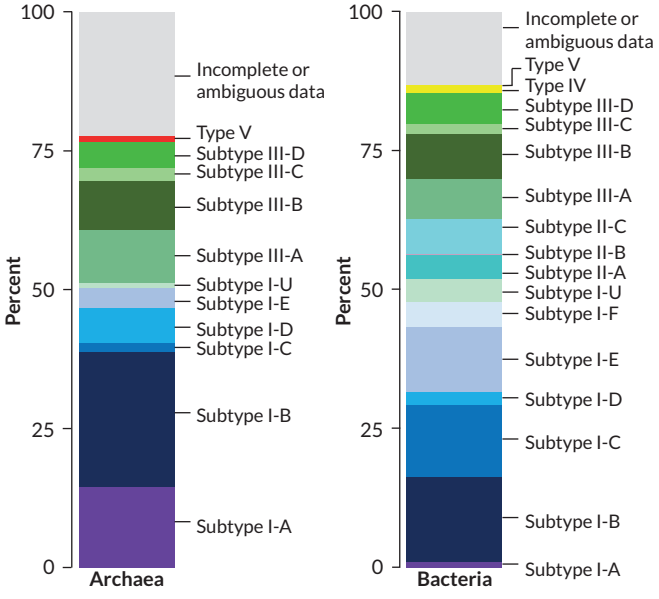
Those who are sleuthing the evolution of CRISPR systems are deciphering a complex story. The part of the CRISPR tool-

Close encounters Bacteria use CRISPR/Cas as a form of immunity or self-defense against invaders. A bacterium builds a library of genetic material from past invaders so that, if the same invader attacks again, the bacterium and its offspring can disable it.



L. MARRAFFINI/*NATURE* 2015, ADAPTED BY J. HIRSHFELD

All stripes of CRISPR Scientists have divided the array of known CRISPR systems into five types and 16 subtypes based on DNA sequence data. The distribution of types differs in archaea and bacteria.



box involved in immunity (adding spacers after phages inject their genetic material) seems to have originated from a specific type of transposable element called a casposon. But the part responsible for targeting has multiple origins — in some cases, it's another type of transposable element. In others, it's a mystery.

The downsides

Given the power of CRISPR systems to ward off foes, one might think every respectable microbe out there in the soils, vents, lakes, guts and nostrils of this planet would have one. Not so.

Numbers are far from certain, partly because science hasn't come close to identifying all the world's microbes, let alone probe them all for CRISPRs. But the scads of microbial genetic data accrued so far throw up interesting trends.

Tallies suggest that CRISPR systems are far more prevalent in known archaea than in known bacteria — such systems exist in roughly 90 percent of archaea and about 35 percent of bacteria, says Eugene Koonin, a computational evolutionary biologist at the National Institutes of Health in Bethesda, Md. Archaea and bacteria, though both small and single-celled, are on opposite sides of the tree of life.

Perhaps more significantly, Koonin says, almost all the known microbes that live in superhot environments have CRISPRs. His group's math models suggest that CRISPR systems are most useful when microbes encounter a big enough variety of viruses to make adaptive memory worth having. But if there's too much variety, and viruses are changing very fast, CRISPRs don't really help — because you'd never see the same virus again. The superhot ecosystems, he says, seem to have a stable amount of phage diversity that's not too high or low.

And CRISPR systems have downsides. Just as people can develop autoimmune reactions against their own bodies, bacteria and archaea can accidentally make CRISPR spacers from bits of their own DNA — and risk chewing up their own genetic material. Researchers have seen this happen. "No immunity comes without a cost," says Rotem Sorek, a microbial genomicist at the Weizmann Institute of Science in Rehovot, Israel.

But mistakes are rare, and Sorek and his colleagues recently figured out why in the microbe they study. The researchers reported in *Nature* in 2015 that CRISPR spacers are created from linear bits of DNA — and phage DNA is linear when it enters cells. The bacterial chromosome is protected because of its circular form. Should it break and become linear for a spell, such as when it's being replicated, it contains signals that ward off the Cas proteins.

There are other negatives to CRISPR systems. It's not always a bonus to keep out phages and other invaders, which can sometimes bring in useful things. *Escherichia coli* O157:H7, of food poisoning fame, can make humans sick because of toxin genes it harbors that were brought in by a phage, to name just one of myriad examples. Even CRISPR systems themselves are spread around the microbial kingdom via phages, plasmids or transposable elements.

For microbes that lack CRISPR systems, there are many other ways to repel foreign DNA — as much as 10 percent of a microbial genome may be devoted to hawkish warfare, and new defense systems are still being uncovered.

Countermeasures

The war between bacteria and phages is two-sided, of course. Just as a microbe wants to keep doors shut to protect its genetic integrity and escape destruction, the phage wants in.

And so the phage fights back against CRISPRs. It genetically morphs into forms that CRISPRs no longer recognize. Or it designs bespoke artillery. Microbiologist Joe Bondy-Denomy, now at the University of California, San Francisco, happened upon such customized weapons as a grad student in the lab of molecular microbiologist Alan Davidson at the University of Toronto. The team knew that the bacterium *Pseudomonas aeruginosa*, which lives in soil and water and can cause dangerous infections, has a vigorous CRISPR system. Yet some phages didn't seem fazed by it.

That's because those phages have small proteins that will bind to and interfere with this or that part of the CRISPR machinery, such as the Cas enzyme that cuts phage DNA. The binding disables the CRISPR system, the researchers reported in 2015 in *Nature*. Bondy-Denomy and others have since found anti-CRISPR genes in other phages and other kinds of interloping DNA. The genes are so common, Davidson says, that he wonders how many CRISPR systems are truly active.

In an especially bizarre twist, microbiologist Kimberley Seed of the University of California, Berkeley found a phage that carries its own CRISPR system and uses it to fight back against the cholera bacterium it invades, she and colleagues

K.S. MAKAROVA *ET AL/NAT. REV. MICROBIO.* 2015, ADAPTED BY J. HIRSHFELD

reported in 2013 in *Nature*. It chops up a segment of bacterial DNA that normally inhibits phage infection.

Of course, in this never-ending scuffle one would expect the microbes to again fight back against the phages. "It's something I often get asked: 'Great, the anti-CRISPRs are there, so where are the anti-anti-CRISPRs?'" Bondy-Denomy says. Nobody has found such things yet.

Evolution drivers

It's one thing to study CRISPR systems in well-controlled lab settings, or in just one type of microbe. It's another to understand what all the various CRISPRs do to shape the ecosystem of a bubbling hot spring, human gut, diseased lung or cholera-tainted river. Estimates of CRISPR abundance could drop as more sampling is done, especially of dark horse microbes that researchers know little about.

In a 2016 report in *Nature Communications*, for example, geomicrobiologist Jill Banfield of UC Berkeley and colleagues detected 1,724 microbes in Colorado groundwater that had been treated to boost the abundance of types that are difficult to isolate. CRISPR systems were much rarer in this sample than in databases of better-known microbes.

Tallying CRISPRs is just the start, of course. Microbial communities — including those inside our own guts, where there are plenty of CRISPR systems and phages — are dynamic, not frozen. How do CRISPRs shape the evolution of phages and microbes in the wild? Banfield's and Barrangou's labs teamed up to watch as *S. thermophilus* and phages incubated together in a milk medium for hundreds of days. The team saw bacterial numbers fall as phages invaded; then bacteria acquired spacers against the phage and rallied — and phage numbers fell downward in turn. Then new phage populations sprang up, immune to *S. thermophilus* defenses because of genetic changes. In this way, the researchers reported in 2016 in *mBio*, CRISPRs are "one of the fundamental drivers of phage evolution."

CRISPR systems can be picked up, dropped, then picked up again by bacteria and archaea over time, perhaps as conditions and needs change. The bacterium *Vibrio cholerae* is an example of this dynamism, as Seed and colleagues reported in 2015 in the *Journal of Bacteriology*. The older, classical strains of this medical blight harbored CRISPRs, but these strains went largely extinct in the wild in the 1960s. Strains that cause cholera today do not have CRISPRs.

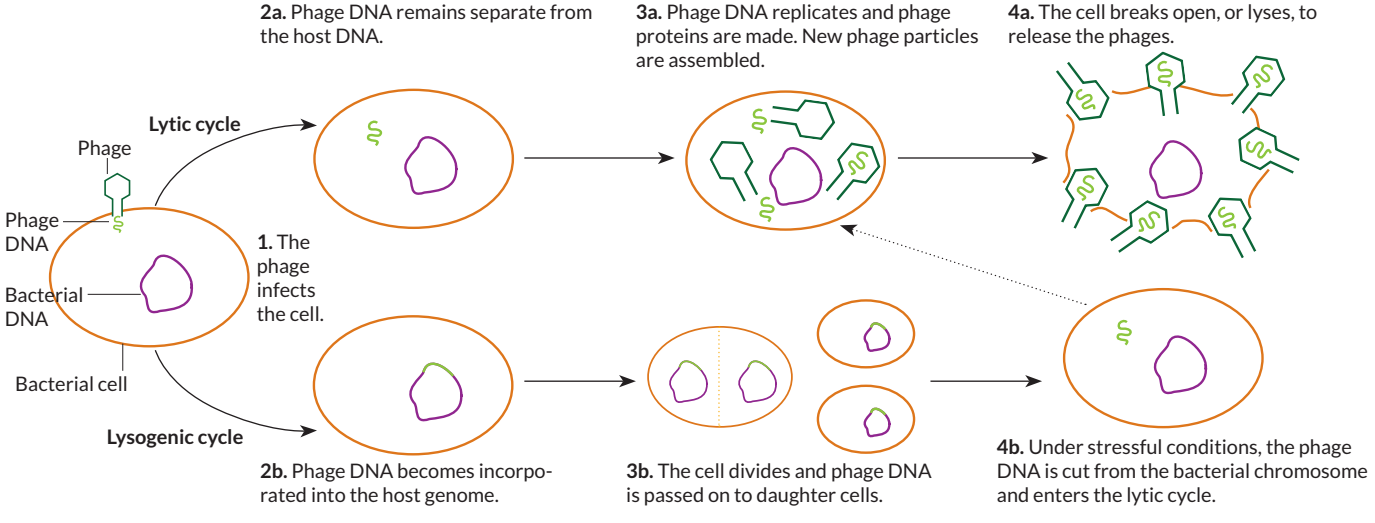
Nobody knows why, Seed says. But scientists stress that it is a mischaracterization to paint the relationship between microbes and phages, plasmids and transposable elements as a simplistic war. Phages don't always wreak havoc; they can slip their genomes quietly into the bacterial chromosome and coexist benignly, getting copied along with the host DNA. Phages, plasmids and transposable elements can confer new, useful traits — sometimes even essential ones. Indeed, such movement of DNA across species and strains is at the heart of how bacteria and archaea evolve.

So it's about finding balance. "If you incorporate too much foreign DNA, you cannot maintain a species," says Luciano Marraffini, a molecular microbiologist at the Rockefeller University in New York City whose work first showed that DNA-cutting was key to CRISPR systems. But you do need to let some DNA in, and it's likely that some CRISPR systems permit this: The system he studies in *Staphylococcus epidermidis*, for example, only goes after phages that are in their cell-killing, or lytic, state, he and colleagues reported in 2014 in *Nature*.

Beyond defense

One thing is very clear about CRISPR systems: They are perplexing in many ways. For a start, the spacers in a microbe

Two roads to travel Phages don't always destroy the microbes they invade. Many have two states: They can co-opt a cell's protein-, RNA- and DNA-making systems to mass produce more of themselves, in what is called the "lytic" cycle, ultimately killing the cell. Or they can insert their genetic material into the host chromosome, to be passively copied each time the cell divides, in the "lysogenic" cycle. That incorporated genetic material can sometimes be useful to the bacterium. SOURCES: RON FEINER *ET AL/NAT. REV. MICROBIOL.* 2015; "THE LYTIC AND LYSOGENIC CYCLES OF BACTERIOPHAGES." BOUNDLESS BIOLOGY, AUGUST 2016. BIT.LY/BOUNDLESS-PHAGE



E. OTWELL

should reflect its own, individual story of the phages it has encountered. So you'd think there would be local pedigrees, that a bacterium sampled in France would have a different spacer cluster from a bacterium sampled in Argentina. This is not what researchers always see.

Take the nasty *P. aeruginosa*. Rachel Whitaker, a microbial population biologist at the University of Illinois at Urbana-Champaign, studies *Pseudomonas* samples collected from people with cystic fibrosis, whose lungs develop chronic infections. She's found no sign that two patients living close to each other carry more-similar *P. aeruginosa* CRISPRs than two patients thousands of miles apart. Yet surely one would expect nearby CRISPRs to be closer matches, because the *Pseudomonas* would have encountered similar phages. "It's very weird," Whitaker says.

Others have seen the same thing in heat-loving bacteria sampled from very distant bubbling hot springs. It's as if scientists don't truly understand how bacteria spread around the world — there could be a strong effect of far-flung passage by air or wind, says Konstantin Severinov, who studies CRISPR systems at Rutgers University in New Brunswick, N.J.

Another weirdness is the differing vigor of CRISPR systems. Some are very active. Molecular biologist Devaki Bhaya of the Carnegie Institution for Science's plant biology department at Stanford University sees clear signs that spacers are frequently added and dropped in the cyanobacteria of Yellowstone's hot springs, for example. But other systems are sluggish, and *E. coli*, that classic workhorse of genetics research, has a respectable-looking CRISPR system — that is switched off.

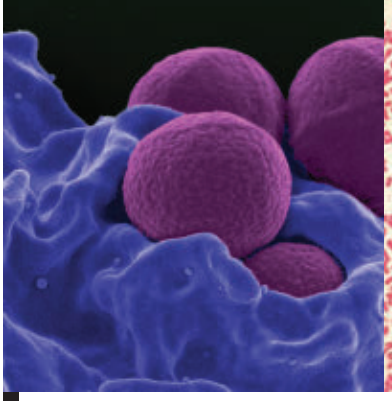
It may have been off for a long time. Some 42,000 years ago, a baby woolly mammoth died in what is now northwestern Siberia. The remains, found in 2007, were so well-preserved that the intestines were intact and *E. coli* DNA could be extracted.

In research published in *Molecular Ecology* in January, Severinov's team found surprising similarities between the spacers in the mammoth-derived *E. coli* CRISPR cluster and those in modern-day *E. coli*. "There was no turnover in all that time," Severinov marvels. If the CRISPR system isn't active, why does *E. coli* bother to keep it?

That quandary leads neatly to what some researchers refer to as an intellectually "scandalous situation."

In some cases, the genetic sequence of spacers nicely matches phage DNA. But overall, only a fraction (around 1 to 2 percent) of the spacers scientists know about have been matched to a virus or a plasmid. In *E. coli*, the spacers don't match common, classic phages known to infect the bacterium. "Is it the case that there is a huge, unknown amount of viral dark matter in the world?" says Koonin — or are phages evolving superfast? "Or is it something completely different?"

Faced with this conundrum, some researchers strongly suspect — and have evidence — that CRISPR systems may do more than defend; they may have other jobs. Communication, perhaps. Or turning genes on and off.



FROM LEFT: NIAID/FLICKR (CC BY 2.0); Y_TAMBE/WIKIMEDIA COMMONS (CC BY-SA 3.0)

Invaders with benefits

Sometimes there are rewards when foreign DNA gets into a cell. The ability to evade antibiotics and resist heavy metals has been traced to genes from phages, plasmids and transposable elements.

- *Staphylococcus aureus* (top left), *Salmonella typhimurium* and other disease-causing bacteria have become resistant to antibiotic drugs with the help of resistance genes carried in on plasmids, transposable elements and phage DNA. Multiple genes are often transferred together.
- *Escherichia coli* O157:H7 contains Shiga toxins, a gift from phage DNA, among other imported traits that make the bacterium dangerous.
- Strains of *E. coli*, *Pseudomonas aeruginosa* (top right), *Bacillus subtilis* and others are resistant to heavy metals, such as mercury, arsenic and chromium. These bacteria are found in polluted waters and in hospitals, where heavy metals are used as disinfectants. Plasmids and transposable elements often transferred the resistance.
- *Rhizobium leguminosarum* and other rhizobia can pull nitrogen from the air and make it available to plants because of genes on plasmids that the bacteria harbor.

— *Rosie Mestel*

But some microbes' CRISPR sequences *do* make sense, especially if looking at the spacers most recently added, and others may be clues to phages still undiscovered. So even as they scratch their heads about many things CRISPR, scientists are also excited by the stories CRISPR clusters can tell about the viruses and other bits of DNA that bacteria and archaea encounter and that they choose, for whatever reason, to note for the record. What do microbes pay attention to? What do they ignore?

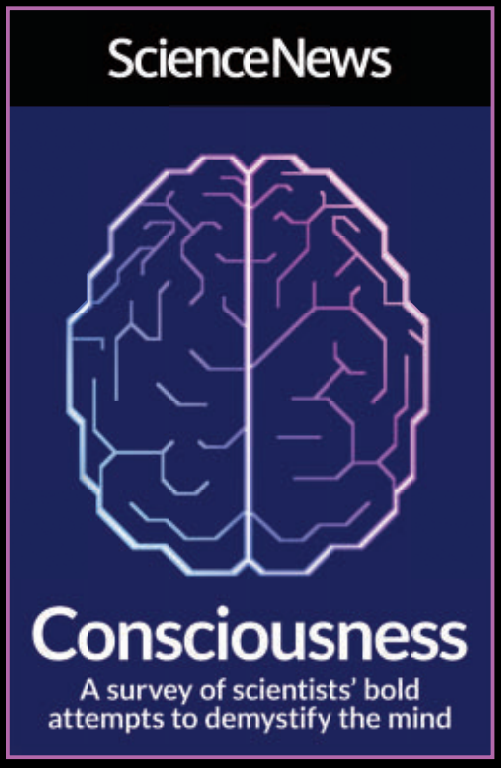
CRISPRs offer a bright new window on such questions and, indeed, already are unearthing novel phages and facts about who infects whom in the microscopic world.

"We can catalog everything that's out there. But we don't really know what matters," says Bondy-Denomy. "CRISPRs can help us understand." ■

Explore more

- Luciano A. Marraffini. "CRISPR-Cas immunity in prokaryotes." *Nature*. October 1, 2015.

Rosie Mestel is a freelance writer based in Los Angeles.



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ScienceNews

A new exhibit at the Field Museum puts seldom-seen collections on display, including these butterflies, to spotlight their role in science.

EXHIBIT

‘Specimens’ goes behind the scenes

Most visitors to a large natural history museum don’t know it, but they are only scratching the surface of the museum’s holdings, even if they check out every exhibition. Most of the scientific treasures are tucked away in collection rooms filled with millions of specimens, which scientists use in their research.

The Field Museum in Chicago, home to Sue, the famous *T. rex*, is displaying some of its secreted goodies in its new exhibit “Specimens: Unlocking the Secrets of Life.” The museum has more than 30 million biological specimens, mummies, minerals, cultural artifacts and other objects in its collections. At any one time, only 0.5 to 1.5 percent of the holdings are on display. For the new exhibit, curators brought out about 5,600 additional items — from preserved deep-sea creatures and fossilized brains to meteorites — to show the diversity of the museum’s hidden collections, says Rusty Russell, director of collections.

“Specimens”
THROUGH JANUARY 8, 2018
THE FIELD MUSEUM | *Chicago*

“Specimens” not only provides access to these items, but it also informs the public about what natural historians do for a living. “Field Museum’s scientists do collections-based research. Without our vast collections, we could not carry out our science,” says William Simpson, head of geological collections and collections manager of fossil vertebrates. “In fact, almost none of our collecting is done for exhibit.”

Visitors wandering the exhibit will notice that all of this collecting has helped shed light on life millions of years ago, as well as stories ripped from today’s headlines.

Remember the Miracle on the Hudson in 2009? Pilot Chesley B. “Sully” Sullenberger safely landed a plane after its engines failed in a bird strike. To identify the birds, a scientist compared the remains recovered from the plane’s engines with tissues from known birds in the museum’s collection, some of which are on display in “Specimens.” The researcher determined that the birds were migratory Canada geese, not year-round Big Apple residents.

Museum collections play central roles in all kinds of identifications, especially for classifying new species. The museum has more than 20,000 holotypes — specimens that researchers have used to define species — in its collections, most of which were identified by museum scientists. The new exhibit features about 10 of these.

One example: dinosaur bones discovered in 1900 in the Colorado Rockies. In his lab, Elmer Riggs, the Field Museum’s first paleontology curator, removed rock covering the bones and realized he had unearthed a dinosaur bigger than *Brontosaurus*, the largest dinosaur known at the time. Riggs named the new dinosaur *Brachiosaurus altithorax*.

Another holotype on display is a skull and jaw of the early mammal *Morganucodon oehleri*, named in 1963, from the early Jurassic Period some 200 million years ago. The fossils show evidence of key evolutionary changes in early mammal history.

Several parts of “Specimens” are more hands-on. Visitors are urged to touch a giant, 160-kilogram clamshell from the Philippines, and they can peruse a drawer full of now-extinct butterflies with silvery-blue wings. Visitors also can sort seashells into different species. An interactive touch screen offers a look at ancient insects trapped in amber a la *Jurassic Park*.

When specimens are collected, researchers often don’t know how they’ll be used in the future. In one recent case, researchers analyzed two Arctic ivory gulls collected in 1896 to show that mercury levels in the ocean are now 45 times higher than a century ago. In another example in the exhibit, rodent and marsupial bones found in owl pellets recovered from Australian caves document wildlife before European settlement. Managers are now using the fossils as a blueprint to re-create ecosystems with species that still live in Australia.

All of these specimens show Field visitors a world they may not have known existed behind museum walls. Other large museums would do well to highlight their hidden bounty, too. — *Howard Wolinsky*

THE FIELD MUSEUM

Teen scientists already changing the world

Forty finalists took home more than $1.8 million in awards at the 2017 Regeneron Science Talent Search

Indrani Das, 17, of Oradell, N.J., won the top award of $250,000 for conducting a three-year study of brain injury that identified a potential major mechanism of neuron death and a possible treatment method.

Aaron Yeiser, 18, of Schwenksville, Pa., received the second place honor and $175,000. Yeiser developed a new numerical method for solving partial differential equations on complicated geometries. His method could lead to better airplanes and possibly better artificial heart pumps.

Arjun Ramani, 18, of West Lafayette, Ind., won the third place award of $150,000. Ramani developed a new mathematical method that could potentially accelerate the process of network evaluation.

Fourth Place: **Byron Xu**, 17, of Sugar Land, Texas, received a $100,000 award. Xu examined marine seismic data — the reflections of sound waves — with the goal of calculating water temperature over wider areas than current techniques allow.

Fifth Place: **Archana Verma**, 17, of Jericho, N.Y., received a $90,000 award for her study of the molecular orbital energy dynamics of dyes, which may someday result in windows that produce solar energy.

Sixth Place: **Laura Pierson**, 17, of Oakland, Calif., received an $80,000 award for her use of theoretical algebra to study the representation theory of mathematically symmetric groups.

Seventh Place: **Prathik Naidu**, 18, of Potomac Falls, Va., received a $70,000 award for his creation of a new machine learning software to study 3-D interactions of the human genome in cancer.

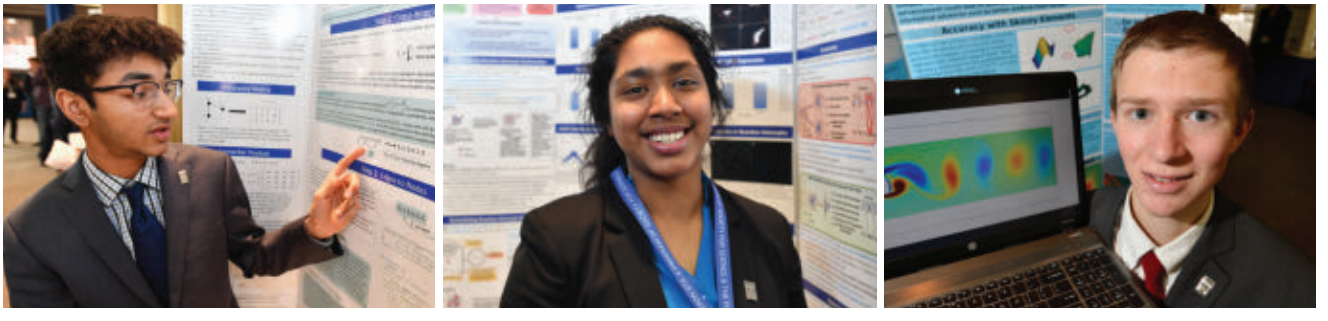
Eighth Place: **Ethan Novek**, 18, of Greenwich, Conn., received a $60,000 award for developing a new carbon capture process powered entirely by abundant low-temperature waste heat.

Ninth Place: **Vrinda Madan**, 17, of Orlando, Fla., received a $50,000 award for her study of 24 potential compounds to treat malaria, in which she found two potential candidates that appear to target the disease-causing organism in a novel way and may warrant further study.

Tenth Place: **Stefan Wan**, 17, of Wellington, Fla., received a $40,000 award for developing a new material that removes phosphate from wastewater and storm runoff and recycles it to enrich farm soil.

The remaining 30 finalists each received $25,000.

These students join the ranks of other Science Talent Search alumni who have gone on to receive more than 100 of the world's most esteemed science and math honors, including the Nobel Prize and the National Medal of Science.



CHRIS AYERS

From left to right: Arjun Ramani developed a new mathematical method to answer questions about networks. Indrani Das studied a possible approach to treating brain cell death caused by injury and disease. Aaron Yeiser developed a new numerical method for solving partial differential equations.

MARCH 4, 2017

Tongue-tied

Frogs can grab large and oddly shaped prey with their tongues, thanks to a combination of soft, squishy tissue and saliva that quickly changes its viscosity, **Susan Milius** reported in "What gives frogs the gift of grab" (*SN: 3/4/17, p. 11*). Watch a high-speed video of frogs nabbing bugs at **bit.ly/SN_frogtongue**

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New normal

People who stay mentally healthy throughout life are exceptions to the rule, a small study suggests. Only 17 percent of study participants experienced no bouts of anxiety, depression or other mental ailments from late childhood to middle age, ***Bruce Bower*** *reported in "Lasting mental health may be unusual"* (SN: 3/4/17, p. 7). Reader **Lou Floyd** found the article disturbing and the research hard to believe. "I have to question any set of characteristics that results in declaring that 80 to 85 percent of a given population is abnormal. A more likely explanation might be that the definitions of the various possible mental maladies are overly broad and lacking in precision," **Floyd** wrote.

That definitions of psychiatric disorders are imprecise will come as no surprise to *Science News* readers (*SN: 12/28/13, p. 29*). "Legitimate or not, psychiatric diagnoses have helped multiple long-term studies identify widespread episodes of emotional problems in Western populations," **Bower** says. "Perhaps these findings will help to destigmatize the experience of emotional difficulties, whether given a diagnostic label or not."

Making waves

If released at the right time, a pair of sound waves known as acoustic-gravity waves could weaken a destructive tsunami and knock its height down by almost 30 percent, ***Emily Conover*** *reported in "How to sap a tsunami's strength"* (SN: 3/4/17, p. 5). **Michael Oman-Reagan** and other readers on Twitter wondered if these large sound waves might have sonarlike effects on ocean critters.

Acoustic-gravity waves occur naturally in the ocean and some studies suggest they may be crucial for marine life, says applied mathematician **Usama Kadri**. Naturally occurring acoustic-gravity waves generate currents that transport nutrients as well as plankton and other microorganisms that are sources of food for larger marine animals, **Kadri** reported in the *Journal of Geophysical Research: Oceans* in 2014.

But it is unclear what impact waves produced by artificial sources may have on marine life. "Since we're interested in the low-frequency end, [the waves] cannot be compared to sonar noise that's in the audible range of marine animals," he says. "Nevertheless, a comprehensive study of the environmental effect is vital."

Neutrons' lease on life

Two experiments — trapping neutrons in a bottle and shooting them in a beam — disagree over the particle's life span, ***Emily Conover*** *reported in "Neutron longevity remains elusive"* (SN: 3/4/17, p. 13). Reader **Kimberly Barden** wondered if the discrepancy scientists have found in measurements between the experiments could be due to relativistic effects: "Since motion slows time, it would make sense if neutrons in motion decay more slowly."

Fast-moving particles will live longer due to special relativity, but the neutrons in beam experiments travel at speeds too slow to account for the discrepancy seen in measurements of the neutron lifetime, **Conover** says. Neutrons in those experiments travel at about 2,000 meters per second, or about 0.0007 percent of the speed of light. "Those speeds would add only a fraction of a billionth of a second to the lifetime," she says. "To account for the nine-second-longer lifetime seen in neutron beam experiments, the neutrons would have to be traveling at more than 10 percent of the speed of light."

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Finding beauty in a mouse wheel of life

This rainbow pinwheel of mouse placentas isn't just an eye-catching image. The differences in color also provide researchers with clues to how a mother's immune system may affect her or her baby's health during pregnancy. The work could lead to earlier diagnosis and treatment of preeclampsia, a common and potentially serious pregnancy complication that can affect blood supply to a fetus.

Suchita Nadkarni, an immunologist at Queen Mary University of London, used a technique called confocal microscopy to snap individual photos of nine developing mouse placentas. The composite image above is one of the winners of the 2017 Wellcome Image Awards, an annual contest for scientific and medical images.

The circular arrangement highlights how neutrophils, a type of white blood cell, affect placental development, Nadkarni says. The first five placentas (clockwise from top) are from mice with intact neutrophils, while the next four are from mice that had the cells removed.

Neutrophils interact with T cells to promote blood vessel formation. Around the edges of the normal placentas, blood vessels (red) are prominent. But the placentas from mice with no neutrophils haven't properly developed blood vessels or other structures. Cell nuclei (blue) and placenta cells called trophoblasts (green) are also shown.

In pregnant women with preeclampsia, blood vessels in the placenta don't appear to develop normally. As a result, a developing baby may not get enough nutrients or oxygen from its mother. Abnormal neutrophils have been connected to preeclampsia, although the exact cause of the disorder remains a mystery. — *Elizabeth S. Eaton*

S. NADKARNI/WILLIAM HARVEY RESEARCH INST./QUEEN MARY UNIV. OF LONDON, WELLCOME IMAGES

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