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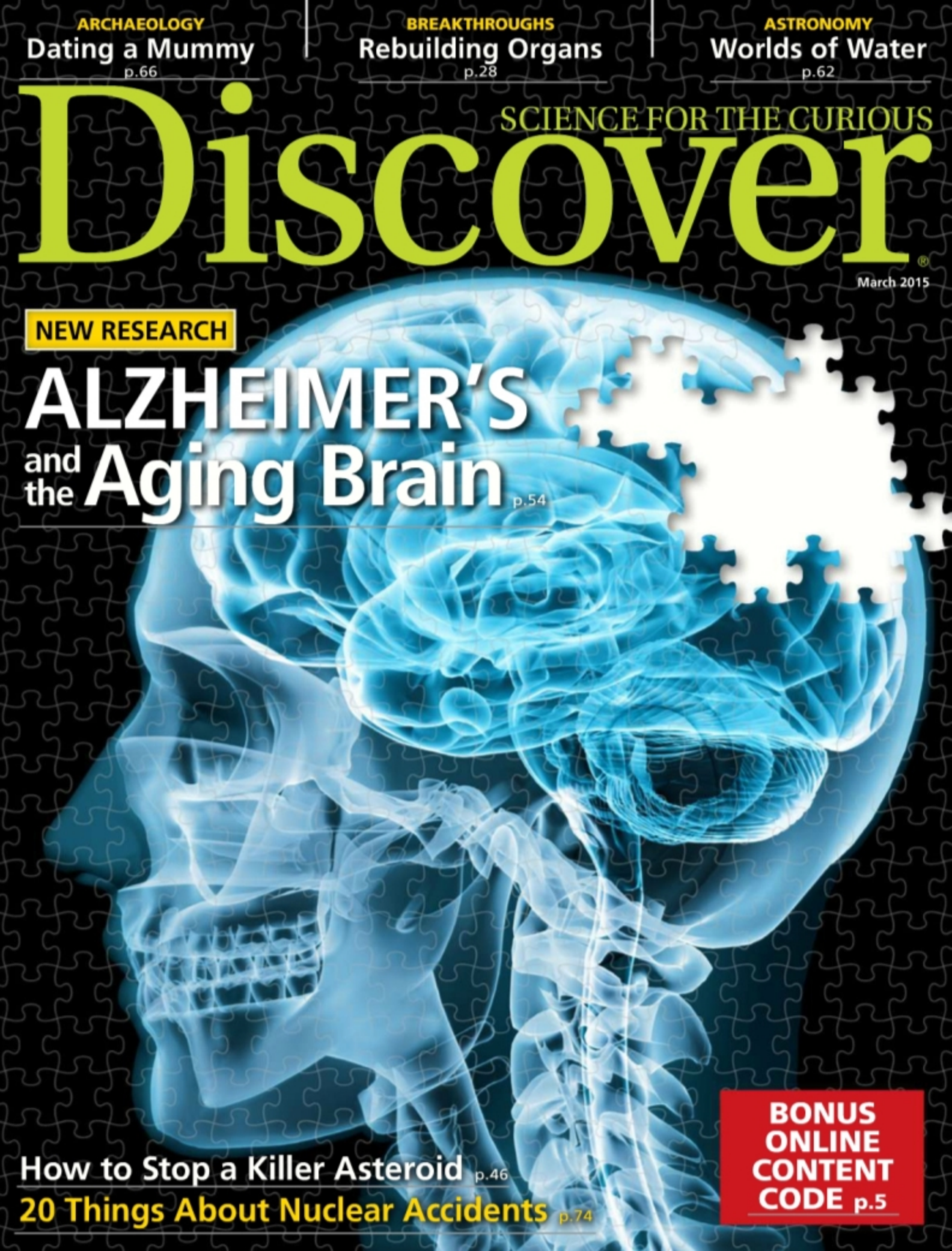
SCIENCE FOR THE CURIOUS

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March 2015

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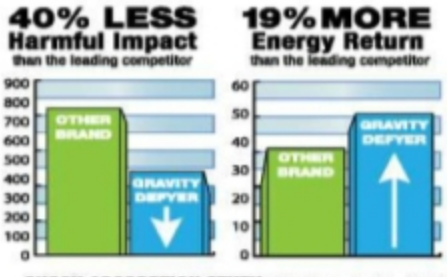
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Jurassic Ark

Resurrecting dinosaurs might be the stuff of fantasy, but a father-son team of biologists entrenched in the world of reconstructing ancient DNA says we could one day bring back other extinct species. But should we? BY VIRGINIA GEWIN

MARCOS CHIN

ON THE COVER *Illustration by Dan Bishop/Discover; Digital Storm/Shutterstock; Milagli/Shutterstock*

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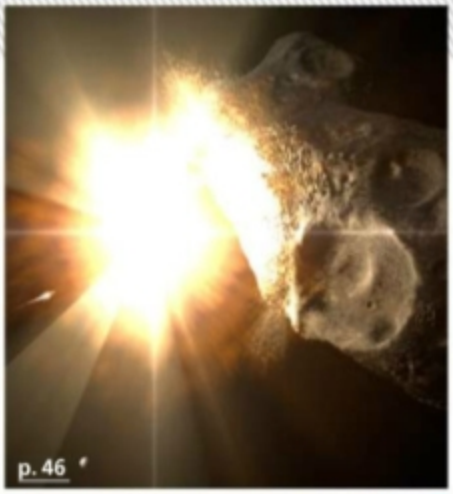
If a giant space rock were hurtling toward Earth, how could we stop it? This question might seem like a tired doomsday movie trope, but it's a scenario that is all too real to physicist John Remo — and his research could help save us all. BY STEVE NADIS

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Cracking the Alzheimer's Code

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Nuclear Accidents

From shrunken bird brains to radioactive reindeer meat, nuclear disasters are devastating. But some species benefit from the aftermath. BY KRISTEN POPE

Editor's Note

Humble Origins



Of ancient tombs, Tinkertoys and theories to be tested.

From an early age, I've been fascinated with archaeology and ancient civilizations, Egypt in particular. By a great stroke of luck, I had a chance to travel to Cairo as a college student and spent a happy week immersed amid ruins and relics. I was awestruck not so much by the size of the tombs, but by the evident complexity of the burial rituals of the ancient Egyptians. How long did it take this culture to develop their customs, to perfect the mix of ingredients and procedures that would underpin their funerary practices?

A lot longer than previously thought, as you'll see in this issue's Origin Story (page 66), a new column that will explore various aspects of human history (and pre-history), as well as the development of ancient cultures.

If you could visit any period of human history or development, which would you visit, and why? Email me at editorial@discovermagazine.com and tell me. You might see your answer on this page in a future issue. Speaking of which …

NEXT ISSUE: *A century ago, Albert Einstein unveiled his general theory of relativity. Has science finally come up with the tests that could prove it wrong? Find out in this special section of our April edition. See you then!*

Stephen C. George, **EDITOR IN CHIEF**

YOUR REPLY

In our December issue, I asked readers to tell me about their favorite educational toys from childhood. Bill Shockley, a fellow Erector set enthusiast, wrote back to remind me of another classic construction toy:

Not especially scientific, but a great first step toward building things, Tinkertoys were almost like an early IQ test, making sticks of various lengths fit properly into hubs to build cars and trucks and buildings. More than one stick got broken trying to force fit it, but that experience made working with the Erector set much easier. Years later, I won first place in the Indiana Regional Science Fair and was awarded a National Science Foundation fellowship. And it all started with Tinkertoys.

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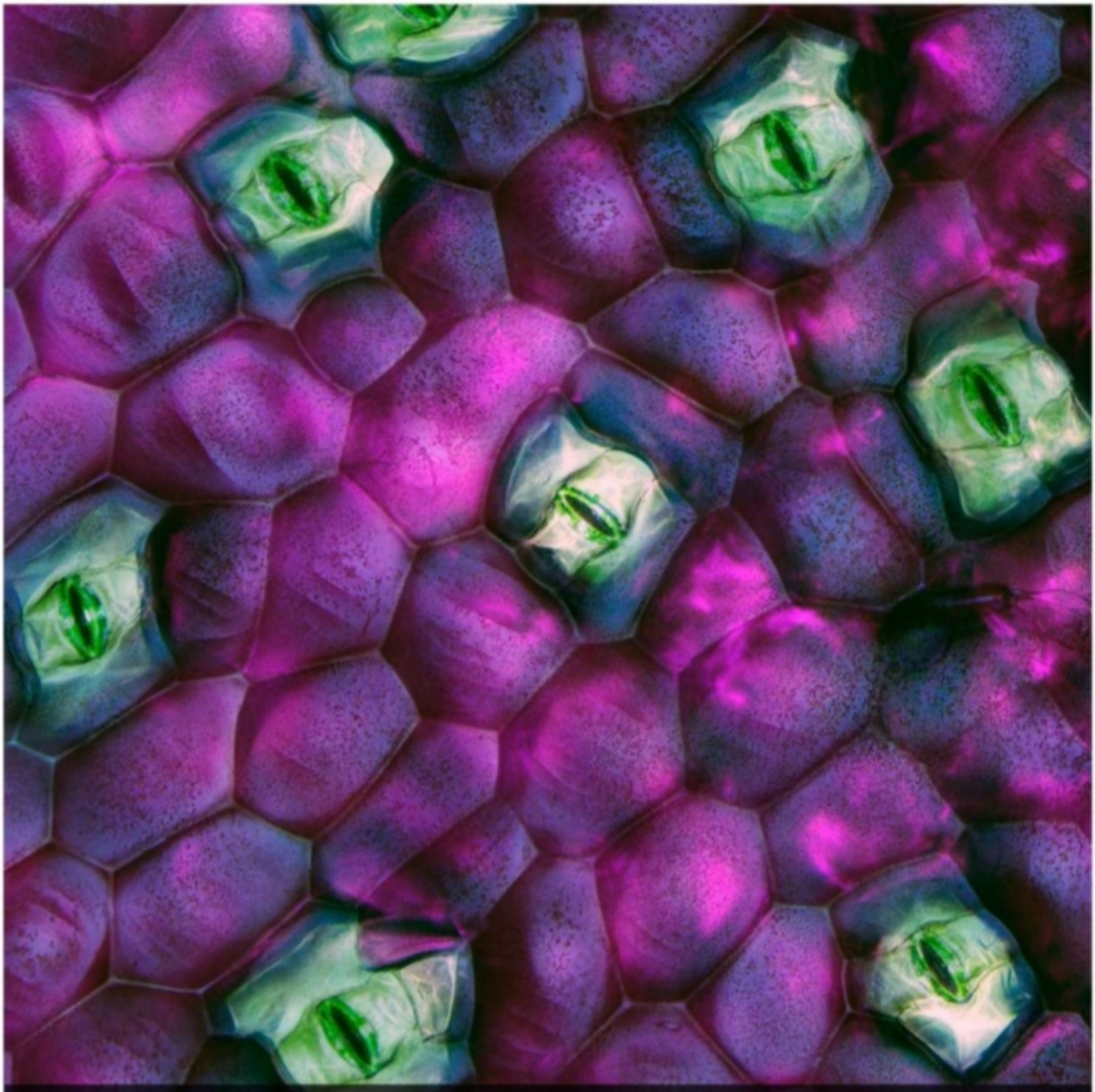
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WILLIAM ZUBACK/DISCOVER

THE CRUX

The Latest Science News & Notes



MANY MOUTHS TO FEED

Mouthlike structures called stomata stand out in this microscopic view of a wandering Jew leaf, or *Tradescantia zebrina*. These tiny pores, magnified 40 times, release oxygen and absorb carbon dioxide to sustain photosynthesis while also regulating moisture. The naturally vivid green of the stomata, contrasting with the purple leaf cells, caught the eyes of judges at the 2014 Nikon Small World contest for microscopic photography, who honored it as an image of distinction. — ERNIE MASTROIANNI; PHOTO BY JERZY GUBERNATOR

INSIDE A SCORPION'S DESERT HAVEN

Biologists use molten metal and 3-D modeling to uncover how large-clawed scorpions build homes in a harsh climate.

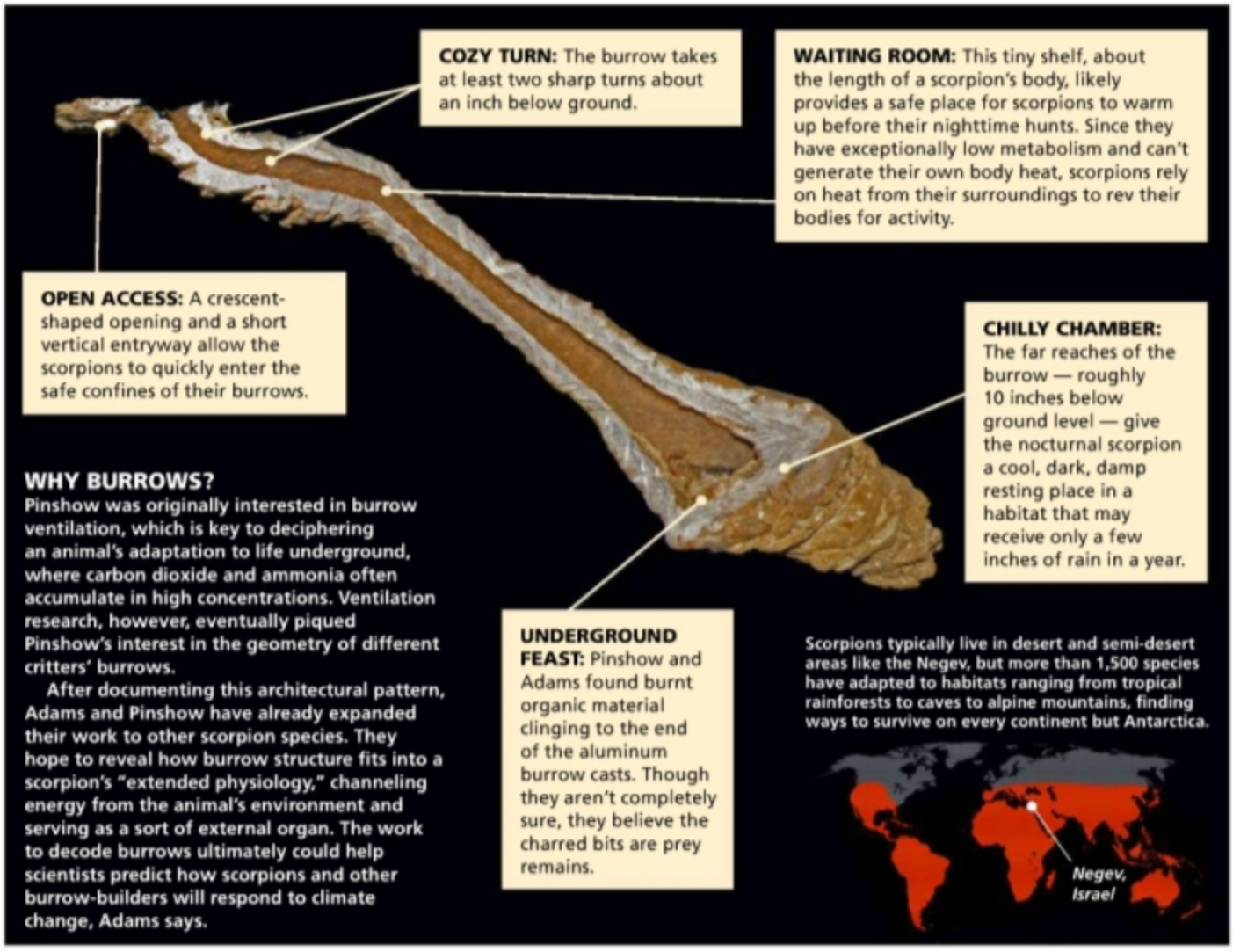


The large-clawed scorpion, *Scorpio maurus palmatus*.

Scorpions may call to mind snapping pincers and a poisonous sting, but these ancient arthropods are far from invincible. To survive in harsh environments and evade predators like lizards and owls, many scorpions spend most of their time hunkered in their underground burrows.

To learn more about the scorpion's retreat, physiological ecologist Berry Pinshow of Israel's Ben-Gurion University of the Negev focused on *Scorpio maurus palmatus*, or large-clawed scorpion, which is common in Israel. He teamed up with behavioral ecologist Amanda Adams to capture some 30 scorpions and map out their homes.

By pouring molten aluminum into the burrows and creating 3-D images of the resulting casts, the pair was surprised to find a consistent shape with sharp curves. The pattern suggests this scorpion species has evolved a simple yet highly functional blueprint for a life-sustaining burrow. —JOSIE GARTHWAITE



WHY BURROWS?

Pinshow was originally interested in burrow ventilation, which is key to deciphering an animal's adaptation to life underground, where carbon dioxide and ammonia often accumulate in high concentrations. Ventilation research, however, eventually piqued Pinshow's interest in the geometry of different critters' burrows.

After documenting this architectural pattern, Adams and Pinshow have already expanded their work to other scorpion species. They hope to reveal how burrow structure fits into a scorpion's "extended physiology," channeling energy from the animal's environment and serving as a sort of external organ. The work to decode burrows ultimately could help scientists predict how scorpions and other burrow-builders will respond to climate change, Adams says.

Scorpions typically live in desert and semi-desert areas like the Negev, but more than 1,500 species have adapted to habitats ranging from tropical rainforests to caves to alpine mountains, finding ways to survive on every continent but Antarctica.

FROM TOP: STUART SUMMERFIELD; BERRY PINSHOW; ALISON MACKEY/DISCOVER

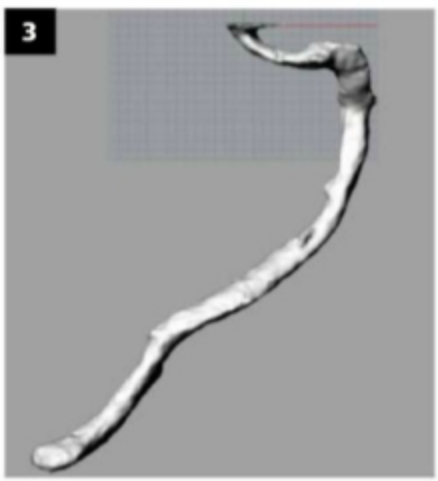
HOW THEY DID IT

Casting burrows with molten aluminum can be a dangerous process. It begins with heating aluminum in a miniature gas-powered smelter to temperatures upward of 1,200 degrees Fahrenheit **[1]**. Next, researchers pour the molten aluminum into the burrow and let it solidify and cool for about 20 minutes. They then use a hand trowel to dig out the cast **[2]**, which is more robust than traditional plaster casts, and carefully document the site. The result is a sturdy block of metal displaying the burrow's intricate architecture.

Back at the lab, Pinshow's team scans each cast to create a 3-D digital model **[3]**. The scanner sweeps laser beams over the aluminum cast while cameras capture the laser beams' location to give a precise measurement of the cast. The 3-D model can then serve as a comparison for other burrows.







CLOCKWISE FROM TOP RIGHT: WILLIAM STUTZ/BIOGLOW (3); AMANDA ADAMS; STUART SUMMERFIELD; BERRY PINSHOW

Leafy Lighting

Illuminate your life with this natural night light.



LIGHTS ON LIGHTS OFF

Mary, Mary, quite contrary, how does your garden glow? Missouri-based molecular biologist Alexander Krichevsky knows. He's engineered light-generating plants reminiscent of the foliage in the film *Avatar*.

Most bioluminescent organisms, including fireflies, get their glow from a chemical reaction between the enzyme luciferase and a molecule called luciferin. Scientists have tried to re-create the effect in plants before: In the 1980s, researchers added a firefly's luciferase gene into tobacco plant cells. But the plants grown from those cells didn't produce luciferin and needed an external spritz of it in liquid form just to give off a weak, temporary glow.

In 2010, borrowing genes from marine bacteria, Krichevsky engineered tobacco plant DNA to include both luciferase and luciferin-producing proteins for a prototype that eventually became his glowing Starlight Avatar plant.

Krichevsky has amped up the seedless plant's brightness in subsequent iterations. Throughout its three-month life span, the plant now emits a green glow that's about as luminous as a glow-in-the-dark stick-on star.

Want one? Krichevsky's company, Bioglow, sold the first batch at auction last year for an average price of $300 per plant, but he says the next round, coming soon on the Bioglow website (bioglowtech.com), will go for a more affordable $30 per plant. – LEAH SHAFFER



Unlike glowing plants of the past, the Starlight Avatar can sustain a soft glow on its own for its entire three-month life span.

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THE CRUX

Sight, Seen

New treatment improves vision in those with an inherited eye disease.



Robert Koenekoop tests a child's eyesight at the McGill University Health Center in Montreal.

A new oral drug can improve vision in people with a specific form of blindness, researchers announced in July.

A team led by pediatric ophthalmologist Robert Koenekoop at McGill University gave the medication to 14 patients with Leber congenital amaurosis, an inherited disease that causes retinal degeneration leading to blindness. Ten of the patients, both children and adults, saw their visual field expand, and six experienced improved visual acuity, according to the team's study, published in *The Lancet*.

"This is very exciting; we could possibly provide treatment for these disorders that until very recently were considered untreatable," says Janine Mendola, a McGill neuroscientist involved in the study. – CONNOR WALTERS

INBOX

Expansion Explanation

In November, "20 Things You Didn't Know About … Galaxies" threw one reader for a loop.

Two sentences contradicted each other. The first said, "Due to the expansion of the universe, all other galaxies are receding from our own." But on the same page, I read, "In about 4 billion years, the Milky Way will merge with the Andromeda galaxy." This makes me feel a bit like I am in the twilight zone.

Bruce Carleton *Henniker, N.H.*

Good catch, Bruce. The phrase "all other galaxies" should have been "most other galaxies." Writer Katherine Kornei explains: "Expansion of the universe should cause all galaxies to recede from one another, but there are certainly cases (such as Andromeda) in which local gravitational forces are strong enough to cause galaxies to approach one another, instead of receding."

DANIEL HÉON/MCGILL UNIVERSITY HEALTH CENTER

Ape Escape

Some chimpanzee social behaviors seem strangely familiar.





Biologist Julie Rushmore studies chimps in Uganda.

We often hear about diseases that jump from animals to humans. But as human contact with wildlife becomes more frequent and people continue to encroach on habitat, wild animals are being exposed to human pathogens more than ever. For the great ape, whose populations are already endangered, diseases such as measles can have a devastating effect.

To help wildlife officials with vaccine efforts and management of epidemics, ecologist Julie Rushmore of the University of Georgia studies social behavior among great apes in Uganda. By applying social network analysis — the mathematical theory behind Facebook that explains how different individuals are connected — Rushmore found that high-ranking mothers and their juveniles (as well as high-ranking males) were most likely to transmit diseases to other chimps because everyone in the community wants to be with them. Knowing which chimp is most at risk makes ape vaccination campaigns more successful because it minimizes the number of individual immunizations necessary to prevent an epidemic.

During her observations, though, Rushmore saw firsthand some of the other unwanted side effects that can accompany ape popularity.



Rushmore analyzes the contact patterns of chimpanzees in the Kanyawara community of Uganda's Kibale National Park to learn how diseases travel.

IN HER OWN WORDS

One day I followed an adult female chimpanzee that has five kids. That's a lot for a chimp! An adult male in the community attempted to sneak her and her family away so that he would have exclusive access to mate with her. But the female seemed incredibly resistant to the idea of leaving the community.

While the female stalled, her children were eager to hang out with the high-ranking male. Her young son watched his every action and followed him continually. After a while, they all went to the periphery of the community's range. For two hours, everyone ate and played together. Then suddenly, the female was nowhere to be found.

Her kids began running back through the forest, screaming loudly. The male followed, displaying aggressively — banging on trees and making loud vocalizations. Eventually, the male gave up and left. Once he was gone, the mom reappeared, the kids stopped screaming and the family traveled back to the central area. Several hours later, the same male found them there and attacked the female. Then it started all over again. Eventually they reached a feeding patch and spent the day there.

At day's end, several other families arrived at the feeding patch, and everyone started traveling back to the central area together. While the high-ranking male was walking back with everyone, the female slipped away with her kids without anyone noticing. They were quick and quiet. In the distance, I could hear the male crying out. I suspect he realized she'd sneaked away again. — AS TOLD TO ROBYN BRAUN



The interactions between adult and juvenile chimps can often resemble human behaviors.

CLOCKWISE FROM TOP LEFT: REBECCA STUMPF/UNIVERSITY OF ILLINOIS; JULIE RUSHMORE/UNIVERSITY OF GEORGIA; STUMPF; RUSHMORE

If You Can't Beat 'Em, Eat 'Em

An innovative community of biologists picks away at invasive species one meal at a time.

At the University of Notre Dame Environmental Research Center's (UNDERC) field station in Michigan's remote Upper Peninsula, more than a dozen doctoral students went beyond the bounds of academia to combat invasive plants and animals. The group spent their days collecting data for their dissertations, helping point to strategies to keep exotic species in check. But evenings at the Michigan field station saw the team experimenting with another approach to controlling invasives — eating them.

"I've always thought real biologists shouldn't be afraid to eat their study organisms," says Andrew Deines, who spent a few weeks during the past few summers at the field station wading through rivers and wetlands with his gastronomically intrepid colleagues.

Invasivorism at the center began as a fun outreach project in 2011, and it simultaneously caught fire as a national culinary trend. From backwater juke joints to fine Manhattan eateries, invasivore dishes bring awareness of an ecological problem to the table.

The invasivore biologists have graduated and dispersed to other research labs, but their zest for "eating our enemies," as Deines puts it, lives on. Here are just a few of the dishes Deines, now a postdoctoral associate at the Michigan State University Center for Systems Integration and Sustainability, and some of his fellow biologists cooked up to take a bite out of this invasive problem. — BRIAN BARTH



Cajun-Style Rusty Crawfish

Ashley Baldridge, research ecologist, NOAA Great Lakes Environmental Research Laboratory

Crawfish is one invasive that's easy to picture as a normal cuisine, since it's already a common Southern dish and is related to popular crustaceans like lobsters. Rusty crawfish are native to the Ohio River basin, "but they've become a nasty invader elsewhere," plaguing areas in the Upper Midwest, especially in Wisconsin and Michigan, Baldridge says. It was a potluck favorite at the field station, where the team caught crawfish with minnow traps in order to dissect them back in the lab, although more than a few were diverted to the kitchen while en route.

Chinese Mysterysnail Fettuccine

Matthew Barnes, assistant professor, natural resources management department, Texas Tech University

"I put on my snorkel and fins and in 20 minutes had a bag full of them," Barnes says of the golf ball-size snails that are scattered in lakes and rivers across North America. Though the story of how the snails spread across the U.S. is still a mystery, Barnes is certain of their palatability. To cut the mud flavor, he feeds them cornmeal for 24 hours before sautéing them in garlic and oil and serving over pasta.







Deep-Fried Invasive Earthworms

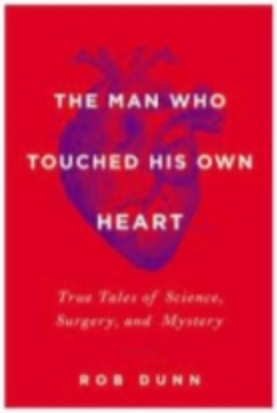
David Costello, assistant professor, biological sciences department, Kent State University

After the last ice age, earthworms inched their way from the frozen grounds of the northern United States and Canada down south, Costello says, and they've yet to inch their way back. These detritivores consume the litterfall of dead leaves and twigs, altering nutrient cycles and exposing the soil to erosion. Though earthworms might be garden heroes, they're surprisingly detrimental to forest ecosystems. As for their taste, "even though they're gritty," Costello says, they're "not too bad."

For those interested in experimenting, the UNDERC researchers created a web portal for sharing recipes (and stories) in the pursuit of eating edible invasives. Log on at Invasivore.org to learn more. You can even post the location of your catch on the interactive map.

ILLUSTRATION BY **ANGELA LAU**

BOOKS

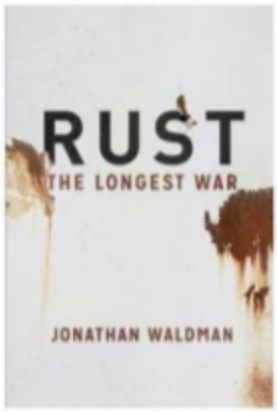


THE MAN WHO TOUCHED HIS OWN HEART

By Rob Dunn

Our hearts are one of our biggest weaknesses; the organ is implicated in 1 out of every 3 adult deaths. Biologist Dunn burrows deep into the valves and ventricles, looking at what makes our hearts tick and what can keep them ticking longer, including pacemakers, angioplasty and transplants. He covers science, symbolism and superstition surrounding the heart, from mummification in ancient Egypt to Leonardo da Vinci's exploratory dissections and the medical advances of the Atomic Age. Dunn paints a detailed picture of the myriad ways our hearts can break and the men and women brave enough to try putting them back together.

— BRENDA POPPY

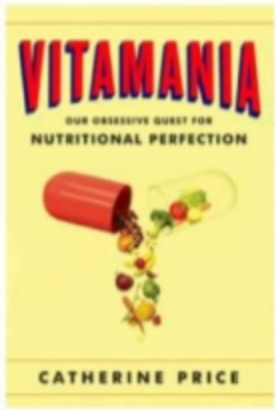


RUST

By Jonathan Waldman

It never sleeps, as Neil Young noted: Rust is too busy wrecking our world. The relentless, destructive process has downed planes, sunk ships, crashed cars, dissolved priceless artifacts and committed countless other crimes of corrosion. Waldman uses our long war with the iron oxide as a loose frame, focusing more on the people crusading against the electrochemical reaction than on the science they marshal to fight it. Some of his musings, such as facial hair preferences among engineers, wander well off-topic. But anecdotes about "Can School," for those bent on building a better soda can, and a robotic "pig" that inspects Alaskan pipelines for rust offer fascinating insights into our endless battle with the dreaded four-letter word.

— GEMMA TARLACH



VITAMANIA

By Catherine Price

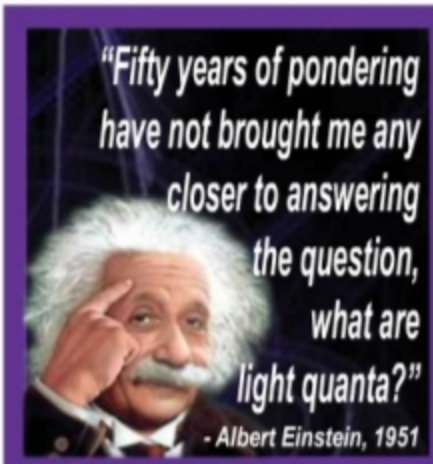
"Both individually and as a society," writes journalist Price, "we have been seduced by a word." That word is *vitamin*, and Price chronicles our love affair with it in riveting detail, from its first appearance in 1912 to its recent co-opting by junk food marketers and snake oil peddlers. What's amazing is how little we know about how vitamins actually work in our bodies, and how much of them we really need. Price doesn't solve these mysteries — no one has, at least not yet — but her investigation, full of scurvy-ridden sailors, questionable nutritional supplements and solid science, is both entertaining and enlightening. — GT

DID YOU KNOW?

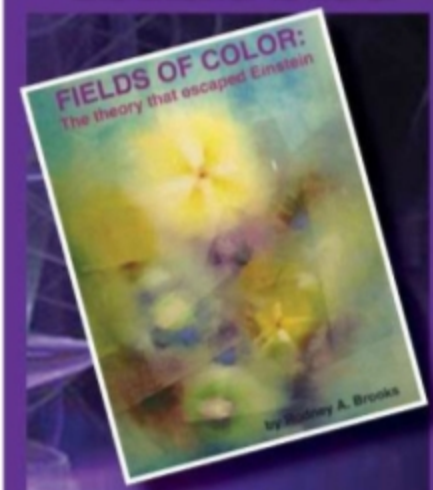
It's the enemy of caves, disrupting ecosystems, skewing food webs and ruining stalactite and stalagmite formations. It's … lint? The hairs, skin cells, fibers and dust sloughed off by human tourists all add up with nowhere to go in windless caves. At Carlsbad Caverns in New Mexico, volunteer cleanups have removed 443.5 pounds of lint from the cave system since 1986.



GRETCHEN BAKER/NATIONAL PARK SERVICE



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Starting next year, you can put the balloonists of old to shame by traveling via helium-filled balloon 100,000 feet up, to the top of the atmosphere (as seen in these renderings). Simply hand over $75,000 to Tucson, Ariz.-based World View, and let the 4.5-ton 19-by-12-by-9-foot luxury passenger capsule whisk you away. The five- to six-hour flight includes light refreshments, a bar and an in-capsule lavatory for its eight passengers and crew. Testing, which falls under the purview of the FAA Office of Commercial Space, is already underway and on schedule for commercial flights in 2016. – DAVIDE SHER AND BILL ANDREWS



RENDERINGS: WORLD VIEW (2)

Out of the Woods

An Amazonian tribe seeks help for a deadly problem.

In June, an isolated tribe known to semi-permanently reside in Peru emerged from the forest on the neighboring Envira River in Brazil to make contact with the outside world. Such contact happens surprisingly often, but it is usually brief. "This is unique in that they've chosen to stay," says Chris Fagan, director of the nongovernmental group Upper Amazon Conservancy.

Reportedly under threat from illegal loggers, a few dozen tribespeople remain near the village where they first emerged. They are under the supervision of FUNAI, Brazil's agency for Indian affairs. During many past contact events, members of the isolated groups died after encountering modern diseases for the first time. But experts hope the group that emerged in June will fare better because members have stayed long enough to receive medical care. There's still concern that other members of the group's tribe may have remained in the forest, vulnerable to disease and unreachable by medical personnel.

"The worst-case scenario is that some people get sick and go back to the original tribe," says University of Missouri anthropologist Robert Walker, who studies Amazonian populations. "That's the huge worry."

Walker, who studies satellite imagery of the rainforest for evidence of isolated villages, says four or five such nomadic hunter-gatherer groups live in the Envira River watershed, though he estimates between 50 and 100 isolated indigenous groups live in Greater Amazonia.



These normally self-isolated tribespeople sought help from the established Ash Anika community to handle threatening outsiders.

These groups often make fleeting contact to steal tools from frontier towns, but most, he says, remain isolated out of fear. "Some of these folks' ancestors have been massacred," he says. "They were contacted, violently, in the past."

Now, with illegal loggers and drug smugglers invading land reserves established to protect the tribespeople's way of life, these isolated groups are feeling pressured out of their homes. And although activist groups and government anthropologists train locals to temporarily leave the area when isolated tribes arrive as a way to prevent the spread of disease, lack of official protocols, consistent enforcement and regular compensation for villagers often make it an ineffective solution.

These tribespeople "have a right to continue their lifestyle as long as they want to," Fagan says. "There are [land] reserves set up to allow them to do that, and [those reserves are] failing."

—ANDREW CURRY

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Europan Life

Jupiter's watery moon might just prove hospitable.



Is there life on Europa, a frigid icy moon of Jupiter? *Discover* asked that question nearly 13 years ago — and looked to the sea ice in Barrow, Alaska, for an answer ("Like Alaska, like Europa," May 2002).

Glaciologist Hajo Eicken and his team were studying the survival strategies of microorganisms in Europa-like environments. They found that microbes thrive, even in the depths of winter, in a briny liquid beneath the ice. The microbes most likely feed on sediments and on long chains of sugars they produce called extracellular polymeric substances. It wasn't a definite yes to life on Europa, but it was a strong maybe.

Since then, we've learned even more about life in hostile locations, but we still don't have a clear-cut yes or no. In a 2006 paper, oceanographer Karen Junge, along with Eicken, showed that bacteria can remain active in environments as cold as minus 320 degrees Fahrenheit, though whether that activity is life-sustaining is unknown. That resiliency might hold up on Europa, where surface temperatures can reach minus 370 degrees.

In 2011, geophysicist Britney Schmidt determined that liquid water exists just beneath Europa's surface. "Before, we only expected to find fluid under a hundred or hundreds of kilometers of ice," Eicken says. "But now, potentially, it's under just a few kilometers of ice." And where there's water, there could be life. – BRENDA POPPY



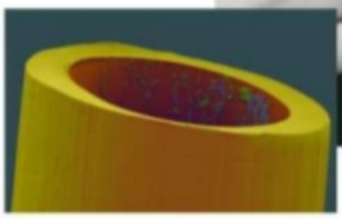
For more on the search for life on watery worlds, including Europa, see this month's Out There on page 62.

OPPOSITE FROM TOP: UIG/PHOTOTAKE; DENNIS KUNKEL MICROSCOPY INC./PHOTOTAKE; COURTESY OF QUENTIN STAFFORD-FRASER. THIS PAGE: NASA/JPL-CALTECH/SETI INSTITUTE

Cleaning Up Catheters

A hospital is a place of healing, but sometimes patients acquire new medical problems during their stays, such as catheter-related bloodstream infections. To prevent these potentially deadly infections, hospitals traditionally use the blood-thinning drug heparin to block germ-attracting blood clots from forming inside catheters. But a Henry Ford Health System study found that cleaning catheters with an antibiotic combination of gentamicin and citrate, instead of heparin, lowered mortality rates a whopping 68 percent. If widely implemented, this simple procedure could save thousands of lives each year. – LACY SCHLEY





Catheters (above) have a valid medical purpose, but without proper treatment, the inner surface can become infected with harmful pathogens, such as the fungus *Candida albicans* (left).

DID YOU KNOW? **In 1991, University of Cambridge computer scientists invented the first webcam, and its broadcast became one of the most popular sites on the early Internet. What did it show? The break room coffee pot — so the scientists could determine whether it was worth the trip to fill up.**



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Forging New Elements

How long can scientists keep finding new pure units of matter?

BY **ADAM HADHAZY**



Take a look around: Every single thing you see is made up of elements in the periodic table. Ever since scientists first cobbled together these catalogs of nature's building blocks in the 19th century, they have wondered if there was any end to the elements and their variants, called isotopes. It's a profound question at the heart of the physical universe.

Nowadays, we have 118 elements on the books, distinguished by the number of protons in their nuclei. About two dozen of these elements, however, do not occur in nature. Over the years, physicists have conjured new, short-lived and typically supersized elements (as defined by their atomic number, or proton count) by smashing atomic nuclei together in particle accelerators. Hordes of interesting isotopes also have emerged from these colliders.

Each new record-setting "superheavy" element tacked on to the periodic table gives us insight into natural laws and their limits. Meanwhile, isotopes — variants of an element with different numbers of neutrons in their nuclei — can have distinct properties that make them scientifically and industrially

Each new record-setting "superheavy" element tacked on to the periodic table gives us insight into natural laws and their limits.

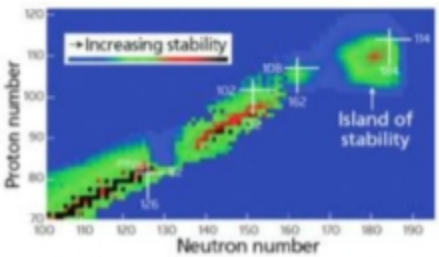
valuable. For example, the most frequently used isotope for medical imaging is an isotope of technetium, the first element ever artificially synthesized in 1937. And many smoke detectors contain an isotope of americium, a man-made, radioactive superheavy element originally forged in 1944.

Scientists are eager to keep filling out the periodic table. One big reason: the hope of reaching the conjectured "island of stability." There, "magic numbers" — as normally dour physicists call them — of protons and neutrons should play together nicely, making for a more stable nucleus.

This should afford new superheavy atoms much longer lifetimes than their rapidly decaying neighbors on the periodic table. Superheavy nuclei, by their fundamentally unstable and synthetic nature, behave in different and unpredictable ways compared with the nuclei of naturally occurring elements, so no one's sure just where the island will be. But researchers think we're close.

Annoyingly, though, we might first hit a wall when it comes to creating new elements beyond the 92 natural and 26 synthetic elements that currently exist. That's because today's atom-smashing methods are near their theoretical and technological limits.

"We think we have a path forward to element 120," says Dawn Shaughnessy, a chemist and project leader of the heavy element program at Lawrence Livermore National Laboratory.



The white crosses show combinations of protons and neutrons that form stable isotopes among the heaviest elements. Researchers hope an "island of stability" awaits them at high numbers.

TOP: AGSANDREWSHUTTERSTOCK. BOTTOM: YURI OGANESSIAN

Whether we can get beyond 120 is anyone's guess, she says.

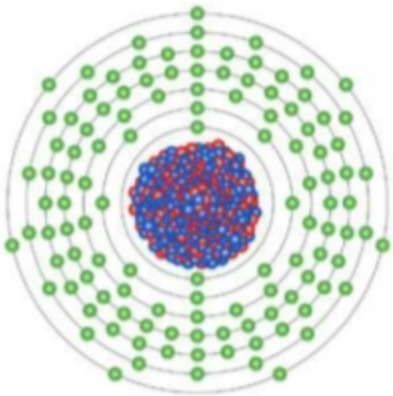
To keep the periodic table party going, in the coming decade, labs will be revving up next-generation atomic colliders to crank out exotic elements and probe how nature itself produces all the elements of the universe. "When you make heavier and heavier elements, you make elements with very different chemical properties," says Walt Loveland, a professor of chemistry at Oregon State University. "That can inform us how atomic structure works."

Pushing nature's envelope could also shed light on the ultimate origins of matter in the Big Bang and stellar furnaces, how particles self-organize into discrete elements and more. "We're trying to answer the fundamental question, 'Where does matter end?'" says Shaughnessy.

NEW ELEMENTS ON THE BLOCK

Manufacturing elements is straightforward, but not easy. Electric and magnetic fields accelerate beams of lighter elements smack-dab into a heavier target element. Building bigger elements is basic math: beam element protons plus target element protons. The vast majority of the time, the colliding beam bounces off the target, but occasionally they fuse into a new, sought-after element.

The resulting superheavy element, along with various smaller particles, then careens into silicon detectors surrounding the target. The detectors distinguish the nuclei based upon the energies of the detected particles.



This diagram of element 117, the most recently discovered member of the periodic table, shows its 117 protons (red) and 117 electrons (green). Shown here is the most stable isotope of the element, ununseptium-294, with 177 neutrons (blue).

The most recent elemental advance came last year when nuclear scientists at the Helmholtz Center for Heavy Ion Research in Germany bombarded a lump of 97-proton berkelium with a beam of 20-proton calcium ions. The result was a few atoms of the 117-proton element, which still awaits a formal name. (So does element 118, discovered in 2002.)

Like most superheavy elements, 117 proved unstable, lasting only a fraction of a second before splitting apart into lighter elements. But one of its initial breakdown products was a never-before-seen isotope, lawrencium-266 (meaning lawrencium, element number 103, with 163 neutrons). It lasted 11 hours — an eternity in the superheavy realm. That exciting find hints that the island of stability is coming into view.



This particle storage ring at the Helmholtz Center for Heavy Ion Research in Germany helped scientists forge element 117. Such giant facilities are the only means of finding new elements.

TOP: SPLISCIENCE SOURCE. BOTTOM: J. MAIGGS/HELMHOLTZ CENTER FOR HEAVY ION RESEARCH

FORGING ONWARD

To push on to element 120 and the predicted island, researchers will make use of the Super Heavy Element Factory (SHE-Factory) in Dubna, Russia, which should begin knocking nuclear heads together in 2016. Like today's colliders, it will use magnetic fields to smash beams of lighter elements into heavier target elements.

But to create new superheavies, SHE-Factory and other facilities are exploring new, more powerful beams and state-of-the-art particle detectors. From the start, SHE-Factory will unleash beams with 20 times the intensity of today's best accelerators.

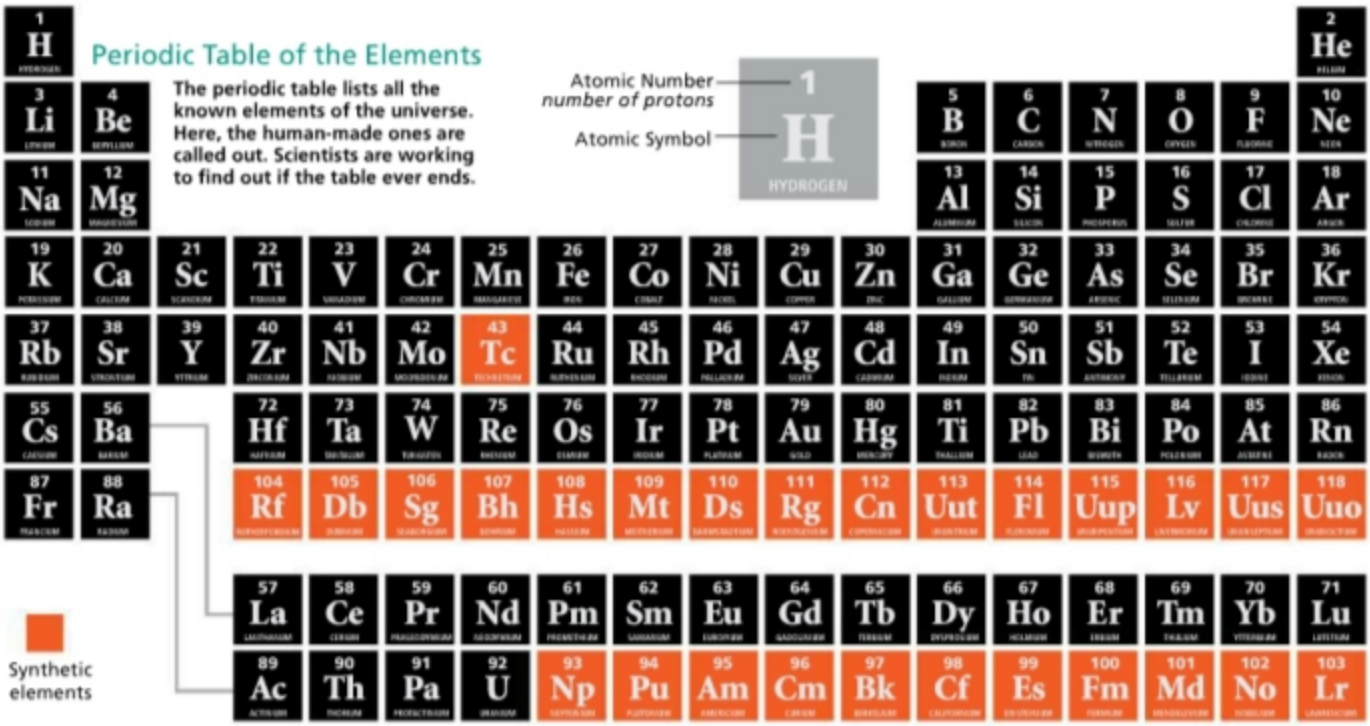
The facility will also rely on new ultrasensitive instruments capable of spotting easily missed particles that continuously check data for superheavy element generation for months on end. Patience is key in the superheavy world because the vast majority of collisions in the reactor produce unwanted nuclei, and a vanishing few, if any, are superheavy elements.

In 2012, when Japanese researchers successfully produced an atom of element 113, they had been running the experiment for 553 days over a period of more than nine years. "The problem is when you're looking for one atom, you may have to wait a long, long time," says Loveland.

"SHE-Factory will allow experiments with a sensitivity of approximately 100 times higher than what we have today," says Yuri Oganessian, scientific leader of the Flerov Laboratory of Nuclear Reactions at the Joint Institute for Nuclear Research in Dubna. "It will increase our chances of synthesizing 119, 120 and heavier elements."

PUTTING NEUTRONS TO WORK

For scientists to reach the island of stability, they'll have to take advantage of neutrons as well as protons. These subatomic particles are bound together in the atomic



nucleus by the strong force, one of the four fundamental forces of nature (along with gravity, electromagnetism and the weak force). More neutrons can promote stability by upping the strong-force interactions among the particles packed like sardines in a superheavy nucleus, which would otherwise repel each other.

"We are not yet to the center of the island of stability because we are too neutron-deficient," says Shaughnessy. But by adding neutrons into the nucleus, it might be possible to increase their lifetimes.

Boosting neutron numbers will be the purview of Michigan's $730 million Facility for Rare Isotope Beams (FRIB), which broke ground last March. FRIB will unleash neutron-rich beams at both conventional and unconventional elemental targets, making longer-lasting, neutron-loaded superheavies.

FRIB's beams will consist of large, yet common, atoms, like uranium-238, accelerated to half the speed of light. The targets in this case are smaller atoms, which shatter the larger particles upon collision. The resulting atomic shards will be carefully separated on the fly, using electromagnetic fields and other tricks to corral and store the radioactive, neutron-dense isotopes of interest that emerge from the collision.

After it opens in 2022, FRIB should also spawn about 1,000 new isotopes and useful quantities of 3,500 known isotopes — which together make up 80 percent of all the isotopes thought possible between hydrogen and uranium. "If scientists want an isotope, FRIB would be a good place to get it," says Brad Sherrill, chief scientist at FRIB.

Among the most desired isotopes will be those of elements heavier than iron, including gold and silver. Theory holds that supernovas, the explosive deaths of giant stars, forge these heavy elements. Yet our finest supercomputer models of supernovas fail to produce the right mix of gold, silver and numerous other familiar metals. "The elements in people's jewelry? We don't know where those came from," says Sherrill. FRIB will produce the short-lived precursors to such elements in quantity, and the results could solve that astrophysical mystery.

More down to Earth, FRIB could also unveil new radioactive isotopes for zapping cancer. These isotopes could have chemistries that favor binding to delivery agents, thus packing potent, tumor-directed punches. Another benefit could be helping scientists at work on innovative nuclear power plants better understand the exotic new neutron-laden materials they might be working with, resulting in more efficient and less wasteful reactors.

Overall, the coming crop of new superheavy elements and novel isotopes looks set to revamp our understanding of nature at the atomic level. "In nuclear physics, there are many frontiers," says Sherrill. "This is a story where we don't know the ending."

Adam Hadhazy *is a freelance science writer based in New Jersey.*

ALISON MACKEY/DISCOVER



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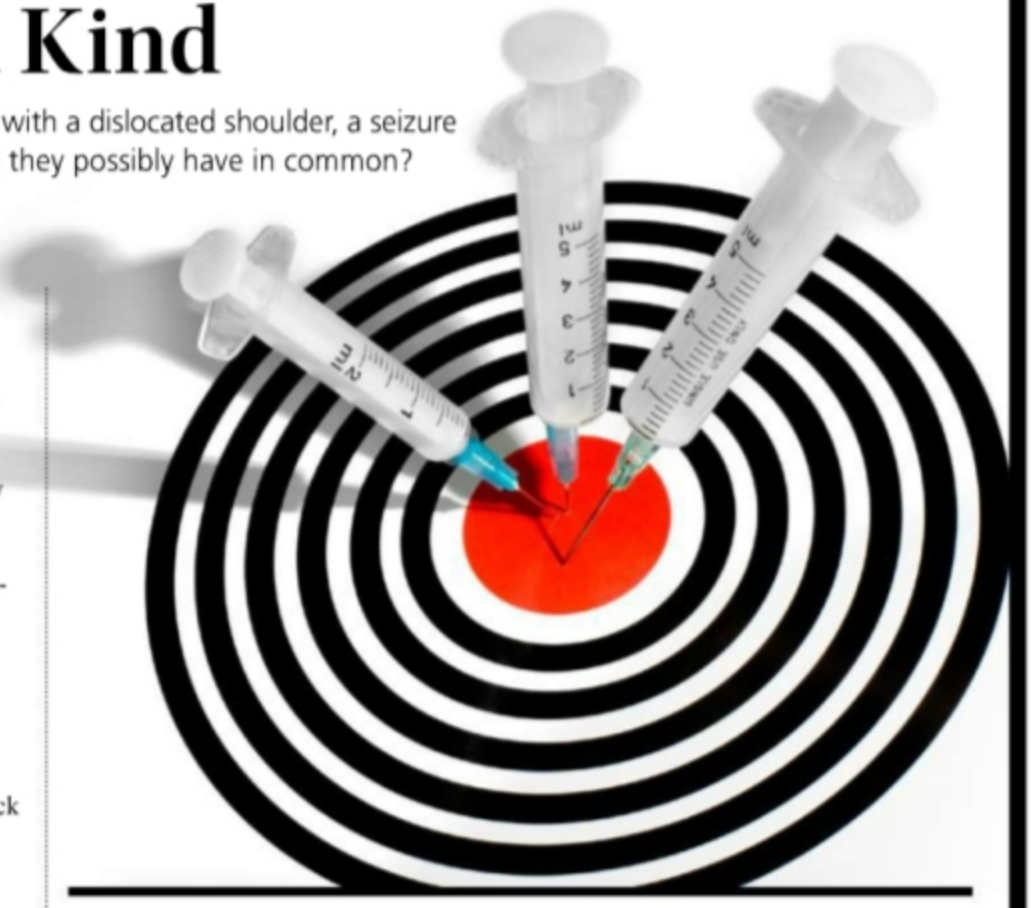
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Three of a Kind

A trio of patients land in the ER with a dislocated shoulder, a seizure and a heart attack. What could they possibly have in common?

BY **TONY DAJER**



In retrospect, you can't believe you missed it: three different days, the same diagnosis. They pop back into your head: the kid hanging off the chair, left arm askew; the three-piece-suit-and-briefcase guy, head jerking like a man with runaway Tourette's; the 30-something Latino clutching his chest.

The kid showed up on a busting-at-the-seams Friday night.

"Doc, it kills. Oh gawd, it kills," he wailed, cradling his left arm. The 20-something had a junior camp counselor look to go with his Long Island accent.

Obvious shoulder dislocation. Quick discharge. I grabbed him ahead of three other patients.

"Doc, you're the best!" he cried. "How do I fix this? The shoulder keeps slipping out and dislocating. If only that drug addict hadn't kicked me in the ambulance."

"You were a medic?"

"That junkie ended my career. Destroyed my rotator cuff."

Clucking in sympathy, I eased his shirt off. A surgical scar bisected his left shoulder — likely a rotator cuff repair. Then I spotted the needle marks inside his elbow creases. He caught my surprise.

"The IV team at Methodist, doc." He shook his head. "Last week they tried again and again to get some meds in and get my shoulder back in."

A cell phone appeared in his right palm. "My brother is an anesthesiologist in Las Vegas. I'm sure he'd be happy to consult with you on my care."

"Work with me and we can do this without medications," I assured him. "We'll have you out of here in a minute."

"I'm with you, doc." He jumped on the stretcher. Galvanized by my own persuasiveness, I began manipulating his arm to reduce the dislocation.

"Ow. You're almost there, doc. Keep pulling. I can take it," he groaned.

■■■

The second case — the businessman — rushed in, trailing a worried nurse. "Sudden worst headache ever," she cried. "Head keeps pulling to the side. Could be a seizure!"

For a moment, I wondered, *Then why is he still clutching his briefcase?*

He yelled, "God, it hurts, doc! My head!"

His head jerked to the right, slowly came back, then whipped again. Was this a focal seizure? A brain hemorrhage can trigger headache and rhythmic contractions by provoking a patch of brain to fire to the body part it controls.

The only other clue was a scuba diving trip six weeks earlier. Was this a late symptom of the bends? Either way, it looked bad.

"Sir, we're going to need a CT scan right away," I told him.

Turning to May, my nurse, I said, "Let's load him with Ativan and morphine and get him to CT." Ativan, a cousin of Valium, would stop the focal seizures — if that's what they were — and relax him for the CT scan. The morphine, well, was morphine.

The first doses went in. We waited 10 minutes.

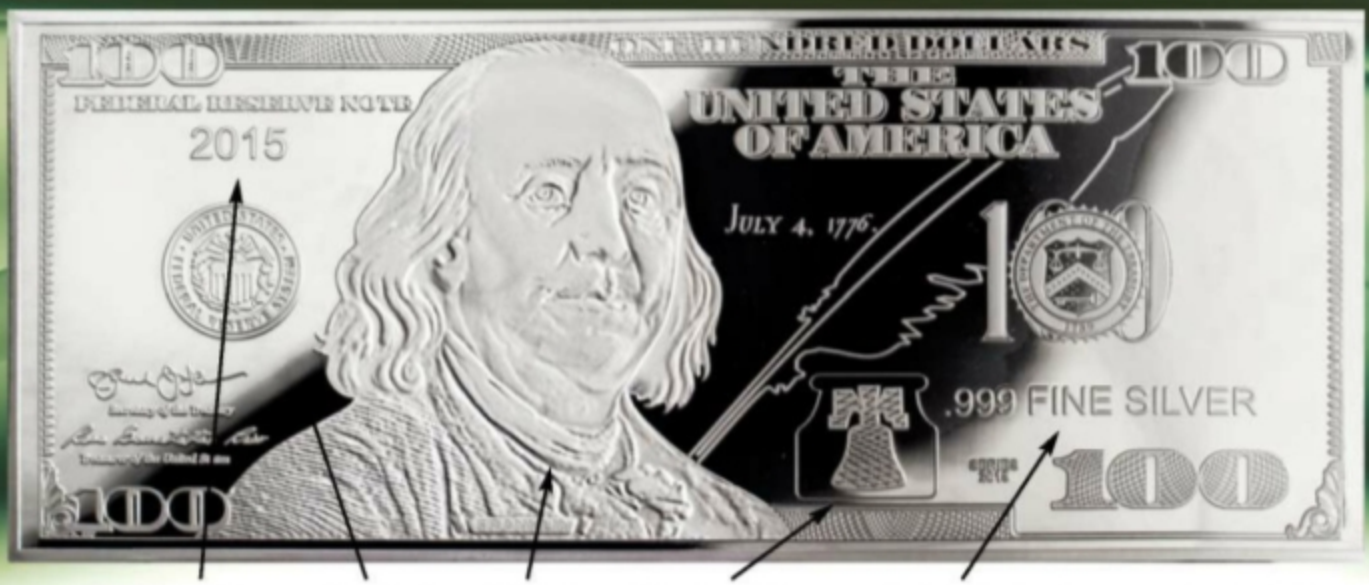
"It pounds, oh it pounds, doc!" he wailed.

"Let's double the morphine and

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Ativan doses," I ordered. May pushed the meds through the IV. The CT scan tech wheeled him off.

■■■

Third case: "A 37-year-old with chest pain. Heart attack two years ago." Brian, my medical student, read off the triage note as we studied the EKG.

"No heart attack now," I concluded. "Go ahead and see him."

Fifteen minutes later, Brian was back. "Thirty-seven-year-old man, MI (myocardial infarction, or heart attack) in Puerto Rico two years ago. Got a right coronary artery stent. Done well since. Two hours ago, he felt crushing substernal chest pain radiating down his left arm. Took nitroglycerin three times without relief. Also complains of shortness of breath and a cold sweat. Pain is still 9 out of 10. No change with position or deep breathing. Father died of a heart attack at 45."

"Wow, that's a perfect story," I remarked. A suspicion took shape. "Does he have his stent card?" Interventional cardiologists always give their patients a wallet card diagraming which coronary arteries they stented.

"I didn't ask," Brian replied.

■■■

Long Island grimaced and tensed as I pulled his arm. "I'm with ya, doc," he grunted.

I kept pulling. The bone seemed to clunk in but then kept slipping out again. The hallways were filling with new patients. "Take a breather," I panted.

The kid's left hand clenched. "I think my arm's turning blue!"

The arm looked OK to me. "I'll be back," I said.

Ten minutes later, one of our anesthesiologists walked in.

"What are you doing here?" I asked.

"Do you have a patient with his arm turning blue?"

"Huh? How do you know?"

"The brother called me from Las Vegas."

Flabbergasted, I thought, *Did he complain? Was I in trouble?* But then I saw an opportunity.

"OK, since you're here, help me sedate him, and we'll pop it in."

He shrugged. "Sure."

A nurse readied knockout doses of narcotics and sedatives. As the drugs went in, the kid's eyes went all dreamy. His muscles relaxed; the shoulder slid back in.

"OK, quick, let's immobilize it," I shouted.

As we slid the arm into a shoulder immobilizer, Long Island started coming around. Then he squirmed. The shoulder slipped out again. I swore.

■■■

The businessman came back from CT.

"I couldn't do it," the tech apologized. "He wouldn't hold still."

This was a nightmare. But what about the scuba diving? I Googled a diving information center and gave them a call. A laid-back, weathered voice came on.

"Neurological complications six weeks out? Wow, that's a new one. Can I have the patient's info?" I filled him in.

"Nothing here," he apologized. "Yes, the bends can cause headaches and seizures, and in extreme cases coma, but not six weeks out." No help.

Another idea: Maybe a contrast CT scan would show something. When dye is injected into the bloodstream, it lights up the cerebral arteries, making it easier to detect a leak.

The businessman's head kept beating time. "Ow, doc. That pain is coming back."

"OK, let's bump up his meds this time," I told May. "We'll get the contrast scan and be done."

May stopped, flicked a hand at the human metronome and gave me the look.

■■■

"Puerto Rico, is that right?" I asked.

"Yes, doctor," the young cardiac patient answered politely. "They said I had a big heart attack."

"Do you happen to have your stent card?" I asked.

"Ah, it's in my wallet, but I left it at home."

Showing him the pink, glossy EKG, I said, "The good news is there is no heart attack."

"Oh, that's good." He worked his palm into the left side of his sternum.

"Then why does it hurt so much?"

"We'll give you another nitro."

"I took the full three at home, doc!"

He grimaced with gusto. Then I asked, "Where were you treated?"

"Puerto Rico. I told you."

"Let's double the morphine and Ativan doses," I ordered. May pushed the meds through the IV.

"San Juan?"

"Huh? Um, yes, Centro Medico."

"Do you have your doctor's phone number?"

Still kneading his chest, he eyed me with a new wariness. "I left my wallet at home, like I told you. Dr. Garcia."

"OK, we'll give him a call," I replied briskly.

He probably figured the Centro Medico switchboard operators didn't speak English (never mind that Garcia is the Puerto Rican version of Smith). What he didn't figure was that I grew up in San Juan.

Two calls did the trick. Brian watched, then ventured, "The story wasn't so perfect after all?"

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The nurse came over. "He wants something for pain. Just so you know, he asks you for nitro, but yelled at me for morphine."

I went back, placed my hands on the stretcher rails and said to my patient, "There is no cardiologist named Dr. Garcia at Centro Medico."

■■■

The shoulder wouldn't go in. Desperate, I called the surgery residents covering orthopedics. "Look, I get *all* my shoulder dislocations in, but this one won't go," I pleaded. "Can you help?"

Long Island surveyed the residents, the anesthesiologist, the nurse and me, and said in an aw-shucks tone, "I'm sorry to be such a bother, you guys." He flashed a winning smile. "I do appreciate what you're doing for me."

The anesthesiologist drew up more morphine and propofol. As he pushed them into the IV, Long Island's face relaxed, yet again, into bliss.

While he was under, a resident reached into Long Island's pocket and fished out his cell phone. Holding it up, he showed everyone. "Last number called is the hospital paging operator. There is no brother in Vegas."

■■■

May didn't have to say anything.

"Sir," I told the businessman, "we need to do a spinal tap. The CT scan was too blurry. It's the only way we can diagnose a hemorrhage in your brain."

For the first time, he met my eye. "Spinal tap? No way."

"Then you'll have to sign out against medical advice."

"No spinal tap!" he screamed.

As he exited, briefcase in hand, head still whipping around, I wondered: *Did a million-dollar lawsuit just walk out the door?*

■■■

In the mid-1990s, American medicine rebooted its approach to pain. Driven by wrenching stories of undertreated terminal cancer patients, then boosted by patient support groups mostly financed by pharmaceutical companies, pain control morphed from symptom to cause célèbre. Government regulators and hospital boards jumped on the bandwagon. Now, with doctors' pay tied to patient satisfaction scores, the pressure to prescribe first, ask questions later is relentless.

The predictable result? Roughly 16,500 deaths in 2010 from



prescription narcotic overdoses. That's four times the rate of 15 years ago. Prescriptions for narcotics have tripled in 10 years. Vicodin, a potent narcotic painkiller, is the No. 1-selling prescription drug in the country. The U.S. — nearly 5 percent of the world's population — ingests 80 percent of its narcotics.

■■■

My three patients all had the same diagnosis: drug-seeking. To an addict, the emergency department is a candy store. No, it's even better: Cook up a dramatic story, drop a fake name and you get the goods on the house.

■■■

The Long Island kid? He could pop his shoulder in and out at will. When he woke up, we showed him the damning call log — he'd phoned the hospital paging operator pretending he was the Las Vegas doctor — and he went hollering and kicking all the way out the door. For an encore, he later called 911 to report a patient (himself) being abused in the ER.

The businessman? A few weeks later, an uptown emergency department called. A worried doctor asked me about a scuba diving patient. This time, the caring doctor had mobilized an MRI team on a weekend and admitted the patient to intensive care before hitting on the spinal tap challenge. Now the overtrusting doctor was being investigated by the hospital for wasting resources.

And my fellow San Juan-er? When he realized no Dr. Garcia equaled no morphine, he stormed into the hallway. "F--- you!" he shrieked at the nurses. "I want an administrator! I want your names!"

Facing him just beyond fisticuffs range, I managed to hold him off until security arrived.

The death toll from runaway narcotic prescribing is finally goading states from Maine to California to take action with mandatory checking of prescription histories and educational campaigns. But this plague is far from over.

Treating symptoms always has been — and always will be — easier than diagnosing disease. Opiate overprescribing proves how readily the finely balanced gyroscope of clinical reasoning can be thrown off-kilter by outside agendas. At the inception of scientific medicine, pain was respected as a vital clue to diagnosis, not a driver of patient satisfaction scores.

The cure for the opiate epidemic is unbiased thinking. It is an old remedy, this clinical judgment, and the best one ever invented. ◘

Tony Dajer *is director of the emergency department at New York-Presbyterian/Lower Manhattan Hospital. The cases described in Vital Signs are real, but names and certain details have been changed.*

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The Doctor and the Salamander

Inspired by the regenerative abilities of an amphibian, Anthony Atala is driven to save lives by rebuilding organs.

BY **STEVE VOLK** PHOTOS BY **PATRICK MURPHY-RACEY**

Once upon a time, there was a little boy named Luke, who was as beautiful as a little boy could be — with thick, brown hair and a ceaseless, churning energy. Like every little boy, he grew up too fast. But unlike most little boys, he was born with a problem that grew even faster than he did.

By the time Luke celebrated his 10th birthday, his energy was gone. He felt tired pretty much all the time. He couldn't play with his friends. Sometimes, he couldn't muster the strength to leave his bed. He lost weight, till his bones showed through his skin, till he was just a fraction of himself.

Fortunately, in this time, there lived a doctor named Tony, who met Luke and his parents.

Dr. Tony spoke very quietly. He was gentle and patient. He had treated many boys and girls like Luke before, with spina bifida. He knew that part of Luke's spinal cord had grown outside his spinal column. Kids like Luke often grow up with bladders that do not grow with them, or that allow urine to leak and back up into the kidney. This is one of the worst things that can happen to a spina bifida patient. Now it was happening to Luke.

Luke had already undergone 15 operations in his life, but Dr. Tony wanted to perform one more surgery — an operation to solve Luke's problem. Because Luke had a broken bladder, Dr. Tony wanted to give him a new one. He described the procedure to Luke and his parents: He would take some healthy cells from Luke, urothelial cells that line the urinary tract and bladder. He



Anthony Atala, who heads the Wake Forest Institute for Regenerative Medicine, examines an ear scaffold created by a 3-D printer.

would place these cells in a petri dish, feed them and wait for them to grow. These cells from Luke would grow and multiply, creating an extension of Luke. And as they grew, Dr. Tony would begin to build a new bladder.

He would use collagen, the same tissue that creates the cartilage of the nose, and shape it in such a way that any child would mistake it for a white balloon. Then he would take the cells he'd grown and paint them on the balloon, until its color changed. When he was finished, the white balloon would become a pink and healthy bladder. Dr. Tony would use this new bladder to replace the bladder that was — everyone knew, but never said — slowly killing Luke.


Luke Massella

The procedure sounded crazy.

Who grows whole new organs for little boys?

But Luke and his parents believed in Dr. Tony and needed him to be right.

So in 2001, Luke Massella became one of seven boys and girls in the nation whom Dr. Tony supplied with a brand-new bladder, made from their own cells.

Seven years later, Luke captained his high school wrestling team.

Five years after that, he graduated from college.

The world changed, in some measurable way, for the better.

But the time had not yet arrived for happy ever-afters.

There is some magic in the story of Anthony Atala, the scent of fairy tale and dream. Born one of many siblings, in Peru, Atala is one of the most celebrated research surgeons in the world, yet we know almost nothing about his background. Atala is so private that in 2006, when a reporter from *The New York Times* asked about his childhood, the only response he offered was a chuckle.

Asked the same question again many years later in his office in Winston-Salem, N.C., Atala smiles warmly. His face radiates real joy. Then the chuckle comes, low and light, as if he is reacting to an old joke that never fails to please him. The effect is magical — creating a public portrait of Atala as a man who appeared out of nowhere, on a quest to save many, many millions of lives. His work, however, is the most magical thing about him.

A short rundown of the achievements of Atala and his research team at the Wake Forest Institute for Regenerative Medicine strains credulity. They discovered a new class of stem cells in amniotic fluid, perfect for creating organs out of patients' own cells without the risk of immunological rejection. They built blood vessels, skin, trachea, livers, kidneys, heart valves and bladders. Atala has successfully implanted lab-grown vaginas into four women. He hopes to conduct his first human trials of engineered penises for transplant within five years. The military is a major funder for his research.

And he has become a public figure, a famous face for science at its best and boldest, appearing on television shows and media outlets in segments tipping the end of chronic disease — a near-at-hand future in which any malfunctioning piece of us can be replaced with a whole new copy grown from our own living cells.

Atala has delivered two TED talks, subsequently seen by millions online. In both talks, he showed off the facet of his work that usually gets the most attention: his novel use of a desktop printer.

For the purposes of printing a kidney, Atala uses a printer cartridge loaded with human cells rather than ink, and a 3-D kidney-shaped substrate of collagen instead of paper. The printer, guided by computer imaging, drips cells, layer by layer, over the 3-D scaffold, and the inert mold comes to life. Over time, millions of cells begin to communicate and function as one organ. At one TED talk, Atala held out a pink, newly printed kidney in his gloved hands. The sense of wonder, awe, even mystification, was evident in the crowd's feverish applause.

In these talks, Atala only hinted at the status of his creations — at how close or far we are from transplanting these solid organs into humans — once.

In person, he rejects a timetable entirely. Ten years? Fifteen? Twenty?

Atala won't say. He *can't* say. Because he doesn't know. Consider: His bladder technology worked in seven children, including Luke Massella. Today, Massella coaches high school wrestling and has started a career in education. But 12 years after he saved Luke, the surgery still hasn't been approved for general use.

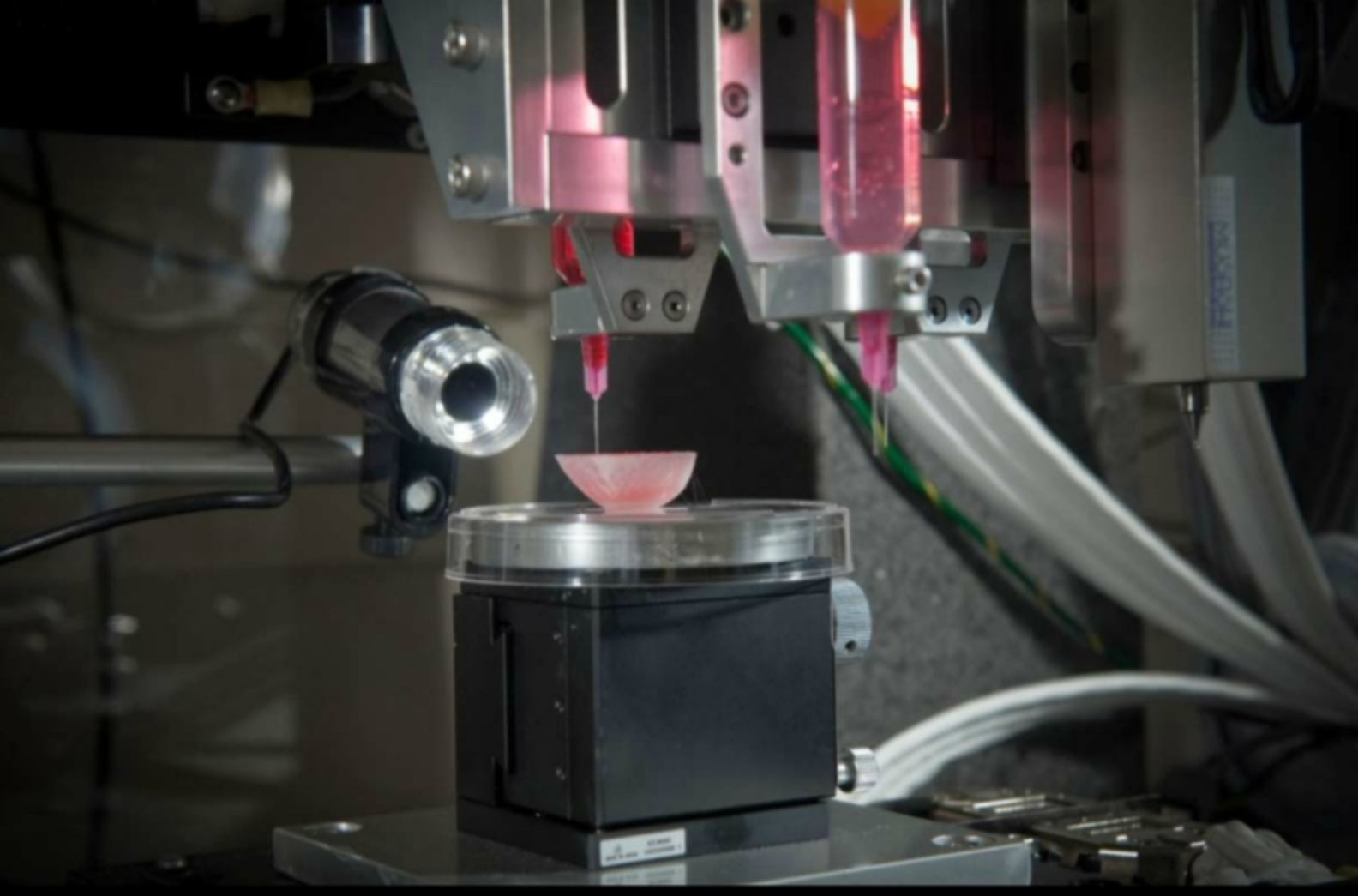
The governmental approval process for new therapies is notoriously slow. But Atala also faces an even more vexing foe: What nature does so endlessly, technology might prove forever unable to mimic.

Regenerative medicine is a multibillion-dollar industry, with funding from venture capitalists, government entities and militaries. We stare agog at what's been accomplished, like Atala's printer demonstration, and burst into applause. But premature celebration is not unknown in science.

Remember the Vacanti mouse?

In 1997, Charles Vacanti of the University of Massachusetts Medical School published the results of an experiment: He and his colleagues used cow cartilage cells and an ear-shaped mold to grow an ear on the back of a mouse. The Vacanti ear appeared in media the world over, hailed as a massive breakthrough in regenerative medicine. But 18 years later, no one is walking around with a Vacanti

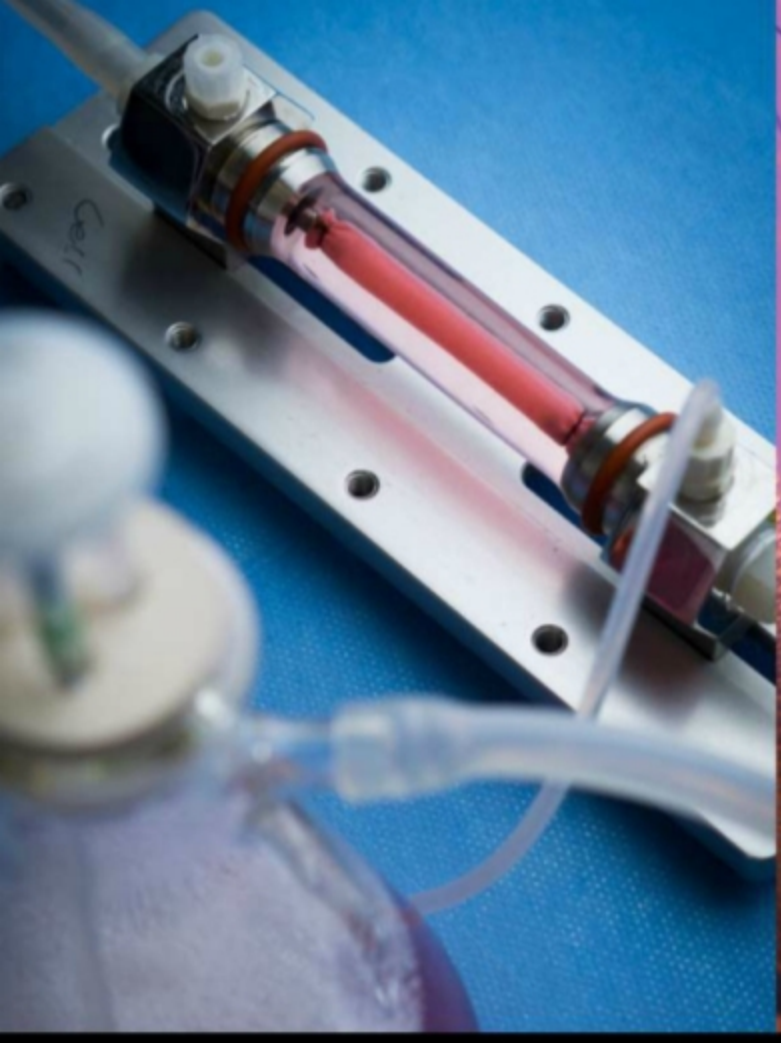
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Clockwise, from top: A 3-D printer lays down scaffolding and cells to create the beginnings of a kidney. A kidney stripped of cells awaits an injection of human kidney cells, part of the process of engineering a new organ. An ear scaffold provides the structure to grow human cells.









Clockwise from top left: Pink nutrient fluid is pumped through a synthetic human blood vessel, an effort to exercise it in preparation for implantation. Likewise, a pig's heart valve, which is stitched to a bioreactor, gets a workout. More than 300 people work at the Wake Forest institute.



ear on their head. A pair of research teams, using very different techniques, are still building toward a trial phase — meaning we are still a few years away from seeing the promise of the Vacanti ear become reality.

Joachim Kohn, a biomaterials scientist leading a staff of 30 at his Rutgers lab, says experience has rendered him skeptical about what regenerative medicine can achieve — and how the mainstream media tends to portray whatever advances come along. "When some story is published about our work," he says, "we start getting phone calls from desperate people who need help, and it makes me very sad to have to tell them that what they read about is actually not available."

At any given time, more than 1 million Americans await some form of tissue transplant. About 130,000 in the U.S. wait on organ transplant lists, hoping someone else's death will give them life. Each year, the number of people added to the wait list exceeds those who actually receive transplants. About 20 people die every day awaiting an organ that never comes. In fairy tales, needed items appear through magic. In real life, the number of organ donors simply doesn't meet the need.

Atala and Kohn are working to solve this problem through tissue engineering, by constructing whole new organs. But Kohn suggests the story of the Vacanti ear symbolizes regenerative medicine as a whole. "The ears kept breaking down," says Kohn. "They could not hold their shape."

The lesson, says Kohn, is that we are too eager to believe that nature can be mastered. Sometimes we even see what isn't there. "Go back and look at those pictures of the Vacanti ear that appeared in the media," he says. "Ask yourself: 'Would you really want to wear that on your head?'"

I did look. And Kohn is right. The Vacanti ear was … kind of gross. "Everyone said it looked like a human ear," says Kohn. "But it didn't. Not to the extent that anyone would actually want to use it."

And so the question is put to Atala: Is this real? Will we ever be putting entirely new livers and kidneys into ailing patients? "We may never get there," he says. "I believe we will. We have prototypes for everything we're working on. We've gotten that far."

But Atala explains that doing it once isn't enough. "This is science," he says, "and it needs to be reliable and reproducible. Doing it once is important because it proves it's possible. But we need to be able to get this process down so it's a success virtually every time."

The printer enables Atala to scale up the technology, eliminating the time it takes to create new organs by hand and the possibility of human error. Yet the printer is nowhere near as important as the schematic it follows — the bank of knowledge built by research teams. Right now that bank still needs shoring up. "It could be," he says, "that creating entire organs in a way that is reproducible may prove too difficult."

For Atala, a scientist, this statement is less an admission, with its connotation of confession, and more a matter of fact. His happy ending, a world where we can swap out bad parts for working ones, remains only a goal. Atala feels the need for these therapies sharply, a constant presence, like a rock in his shoe. Like Kohn, Atala receives calls from people around the world, asking if one of these incredible new therapies they've seen in the papers or on TV is available. The answer is no. The result is that Atala remains an optimist, buoyed by his vision of the future, yet wholly dissatisfied with now. He is, in this sense, the perfect protagonist for the scientific version of a fairy tale: a story in which a man approaches nature with just the right measure of humility and ambition, a story in which sudden bursts of insight enable him to best the obstacles that face him, so he won't need magic at all.

Today, at 56, Atala oversees 300 researchers and support personnel, including chemists, biologists and engineers divided into different teams working on cell therapy, a technology for what he calls partial transplants and the creation of new organs. To overcome the rugged individualism he says often dominates research science, he houses all the teams in open lab spaces, so the problems and solutions found by one group can be quickly shared.

In person, Atala has a gentle demeanor. His office is large and immaculate, reflecting the orderly, administrative side of his job. The small table at which he sits with guests is placed so far from his desk, his bookshelf and personal pictures of his family that all these more intimate items seem to be in another room entirely. The effect is that asking to inspect these items seems invasive.

I mention to him that the driver who brought me in from the airport spoke enthusiastically about what the institute means to Winston-Salem, and that he was proud to be from the same state, West Virginia, as Atala's wife. Atala blanches and changes the subject. Later, his press aide will tell me that Atala worries these sorts of biographical details are a distraction from his work. But at the moment, in his office, he regains his placid demeanor when the next question focuses strictly on his science.


Vacanti mouse

For Atala, the story of his professional quest starts in 1990, as he finished a residency at a University of Louisville hospital and planned for life as a clinician. He looked into a one-year post at Harvard. But a supervisor suggested he would be a good candidate for a particular two-year program there. This other program would require him to serve one year in clinical practice and another conducting research.

THIS PAGE: C. VACANTI, ET AL./PLASTICS AND RECONSTRUCTIVE SURGERY VOL. 100 ISSUE 2 1997/WOLTERS KLUWER HEALTH

"I don't want to be a researcher," Atala said.

At home, Atala told his wife about this other option. His own choice was clear. But his wife replied that, well, if she was going through all the trouble of moving to Boston, one year seemed like an awfully short time to stay. Two years, she said, would be *nice*. And that is how close Anthony Atala — one of the most accomplished researchers in modern medicine — came to disappearing into the bowels of a children's hospital.

Once he got to Boston, his work as a clinician created a new interest in research. As a pediatric urologist, Atala learned that the "state-of-the-art" operation available to kids like Luke involved fashioning a new bladder from a section of existing intestine. The drawbacks were obvious: The bladder holds liquid prior to evacuation; the intestine absorbs fluid. Complications from the procedure included continued illness and a risk of tumors.

"The operation was the best thing available," says Atala. In the meantime, the Harvard program required him to study the history of medical research. He found himself captivated by an animal that has inspired the fantasies of many doctors before him: the salamander. He came upon a peer-reviewed article that asked why a comparatively primitive lizard can regrow an entire limb, yet we can't.

Most doctors bypass the salamander, but Atala chased the dream. He was entranced by the idea that we *already* are like the salamander. We replace our entire bodies as our cells die off and regenerate through the decades. Every time we cut ourselves, our body forms clots, carries off dead tissue and bacteria, and — like a salamander — regrows skin at the wound site.

The problem is that these processes are incredibly slow. Bone takes 10 years to regenerate. Illness and disease work much faster. Still, Atala wondered if he could harness the body's own internal healing mechanism. He wondered if he might help the body produce better, faster results than it can achieve on its own. And ever since, he has tried to gin up human performance, to chase the salamander.

His work has focused on regenerating four major categories of human tissue.

First, at the simplest level, there are flat structures like muscle and skin. For these, Atala can work on a flat plane that he populates with cells.

Next up the scale are tubular structures, like blood vessels or the urethra, both of which have been successfully engineered and transplanted.

Third are the hollow, nontubular organs, like the crescent-shaped stomach or the balloonlike bladder. Such structures interact with the rest of the body in a more complicated way. The bladder connects to the kidney with a kind of valve, and to the urethra, requiring a muscle to contract and vacate urine. But in engineering terms, the bladder is just a flat sheet folded upon itself, like a balloon.

Atala's biggest challenge is to create a solid organ, like the kidney.

Kidneys, bean-shaped organs about the size of a fist, act as a sophisticated filtration device, processing roughly 200 quarts of blood to remove 2 quarts of waste products and excess water. The waste removal function is carried out in each kidney by roughly 1 million nephrons, tiny vessels made up of even tinier urine-collecting structures called tubules. The kidneys also measure chemicals, including sodium and potassium, that are released back into the bloodstream in healthy amounts.

Even more daunting, solid organs are typified by a high level of blood flow — a network of blood vessels known as the vascular tree. These structures dwindle down to the size of the capillary, roughly 8 microns in diameter.



From left: A researcher injects cells into a cadaver kidney that's devoid of cells. A decellularization process removes cells from discarded kidneys, such as those that aren't suitable for transplants. A kidney scaffold awaits the addition of kidney cells.

SECOND FROM LEFT: WAKE FOREST BAPTIST MEDICAL CENTER

Estimates are tricky, but the human body likely holds about 60,000 miles of blood vessels, with many miles of them inside solid organs like the kidney.

The kidney looms as a major goal for Atala. About 82 percent of the people on the U.S. organ transplant list are waiting for kidneys and are usually suffering on dialysis. "People do it because they have to," he says, "but you don't want to live for years on dialysis. The quality of life can be very poor."

His entire career can be interpreted as an attempt to scale this ladder of regeneration all at once, rather than rung by rung. "It's all interconnected," he says. "Because when you solve one problem, like regrowing a cell, that brings you one step closer on every project."

At this stage, he has won enough victories to be celebrated in the media, but he remains circumspect. "I'm happy when something works," he says, "but I don't really celebrate in the way you might think because there's always more work to do until we're actually done. We solve one challenge, and we move on to the next."



From left: Student Sierra Marable works with induced pluripotent stem cells, or cells that have been coaxed back into a state in which they can transform into any of the hundreds of cells in the body. Decellularization of a ferret liver leaves behind only white tissue.

In the early 1990s, Atala was a young specialist in pediatric urology who had by this time made some progress in his thinking. He wanted to create three-dimensional scaffolds of various human organs out of safe, biodegradable material. He reasoned that the appropriate cells, grown outside the human body, could be reseeded onto the scaffold.

He was particularly interested in creating the simplest of solid organs, a phallus, which has just two different kinds of cells to manage. Injured adults, with genitals severely damaged or entirely destroyed in accidents or war, could only turn to cumbersome appliances for largely unsatisfactory solutions. Even worse, when babies born genetically male came into the world with penises too small to be functional, their parents were offered what Atala considered an insufficient, if not barbaric, "solution" — gender reassignment surgery.

Atala wasn't sure how to create a 3-D, working model of the phallus, or any other solid organ. But he figured solving that problem would heal a lot of misery. And so it came to pass that he attended a medical conference in Washington, D.C., on some subject entirely unrelated to regenerative medicine, when the answer arrived, suddenly, forcefully, as if an unseen figure had hollered it in his ear.

He didn't need to create a 3-D model at all.

Of anything.

3-D models already existed.

The penis itself.

The kidney.

The liver.

Atala had been experimenting with rabbits. But he couldn't just take the phallus from one rabbit and attach it to another, like Frankenstein. Just as in a human, the rabbit's immune suppression system would see this new organ as an invader and attack. But what came to Atala at the conference is that he might be able to decellularize the penis, to turn a cadaver phallus into the 3-D scaffold he needed. If he could wipe all the cells from the phallus, or any other organ, he could then reseed it with cells taken directly from the intended recipient, virtually eliminating the possibility of an immune rejection.

Back in his lab, Atala experimented. He plopped a phallus, livers and kidneys into still water with a mild detergent. He left them there for days, then viewed some tissue from each organ to see how many cells were removed. Unfortunately, he found, the organs were still virtually covered in cells.

Next, Atala placed the organs and detergent into the sort of shaker used to mix paint. The friction of the shaker

He was watching a kidney, in effect, regrow itself, the human body enacting its own salamander nature.

afforded him better results, but there were still too many cadaver cells to risk transplant.

Finally, he tried a centrifuge, which whirled at speeds that forced detergents deep into the organ tissue.

Again, he trimmed away some tissue, popped it under a microscope and looked.

Nothing.

The cadaver tissues, mostly composed of collagen, were essentially blank — empty canvases on which he could paint new cells.

He felt pleased, but like a hero on a quest, he knew the goblin at the door was merely a prelude to the dragon at the mountain's heart. The next challenge he faced required him to gain even greater mastery over the most fundamental level of biology, the cell.

The human body has an estimated 37 trillion cells or more working at any given time, each with a specialty that together produces one living entity: us. Learning to grow cells outside the body, while retaining their functionality, was thought to be an insurmountable problem. The belief was borne from scientific history. In the past, researchers studied specific cells by isolating them, injecting them with ferrous iron and literally *pulling* cells away from each other with a magnet. Such cells persisted for a short time or quickly died. But Atala tried his hand first at these old experiments, as a place to start.

He isolated the cells he thought he needed, at least to replicate these old experiments, and fed them the same nutrients they got in the body. He placed them on the scaffold, where they grew and sometimes even formed the 3-D structures they build in nature. Then, usually in less than a month, they fell apart. His first attempts at reseeding a phallus ended in penises that quickly lost their shape and scarred.

Atala started thinking through the possible differences between the phallus he was creating and the phallus as it exists in nature. The penis, he reasoned, is highly vascularized, "like a great big sponge" of blood vessels. So he added endothelial cells, which line blood vessels, and observed them through a microscope as they began to build the same structures they form in the body. At first, this raised



Atala holds a kidney cast, whose vessels have been injected with a colored material that solidifies. The kidney's complex vascular tree is especially challenging to engineer.

his hopes only a little. He had seen cells do this before, briefly, before collapsing. But "this time," he says, a rare sense of satisfaction creeping into his voice, "they kept going."

That step, of learning to grow the cells necessary to create a functional penis, took three years. "And it was a crucial step," he says, "not just on this project, but in the way it helped on all our other projects."

Atala would return, again and again, to what he learned: The idea, he says, "is to approximate, as closely as possible, the conditions found in the body in some controlled environment *outside* the body."

By 2009, Atala announced that his lab had transplanted phalluses onto adult rabbits, which successfully used the manufactured organs to breed. He seems to see the victory in a different context than the rest of us — less as an end itself than "just another step" toward eradicating as much illness, disease and misery as nature will allow.

On a summer weekend in the late '90s, on the south shore of Boston, Atala stalked across the sand, enjoying some rare free time from his work at Harvard. He walked, head down, watching the sand pass under his feet. The waves on Humarock Beach

roared steady as an engine, and the sand rolled beneath him like a conveyer belt, carrying spit curls of sea foam, seaweed and broken shells.

Then, in a story he often tells, he saw the stone.

Atala was drawn in, initially, by its shape — its slight curl, like that of a perfect kidney. He reached down, his fingertips scraping the sand, and plucked the rock free. The day was brisk, and he held the rock aloft, fixated on its one blemish: Along the entire length of the stone ran a single ridge, almost like a biology teacher's notation indicating what is known as the Brodel's line of the kidney.

The Brodel's line, in biology, denotes an avascular plane where the rich vascular tree of blood vessels and capillaries peters out. As Atala stood there, staring at the rock, what happened at the Washington, D.C., medical conference happened again: An idea, fully formed, arose in his mind with enough force to shift the entire world of medicine.

The media has focused on his most grandiose project — his attempt to grow whole organs. But what he realized there on the beach, all those years ago, is that he doesn't actually need to grow an entire organ at all.

"I just need 10 percent," he says.

Standing and staring at the line running along the stone, he knew he could part the delicate, dark-red tissue of the kidney along the avascular plane, across the organ's whole length, causing little blood loss or damage, and pop a kind of cartridge into this incision — a wafer of healthy kidney tissue. The kidney, in its own salamander-like way, would grow and incorporate the new tissue, just as it extends itself into new skin that forms after we're cut.

The logic that settled over him on the beach, however, went beyond the salamander to include a well-known truism in medicine: the human body's remarkable 10-times reserve. "Usually, a patient doesn't present with any serious symptoms till whatever organ is involved has lost 90 percent of its function," he says.

The patient doesn't collapse climbing the stairs, short of breath, until his lungs are functioning at 10 percent capacity. The heart patient doesn't succumb to chest pain until her artery is 90 percent blocked. "It's the same with the kidney or liver," says Atala. "If I can insert healthy tissue, equal to 10 or 20 percent of the size of the organ, I can keep that patient functioning and alive at a high quality of life."

Atala thinks of these serendipitous moments — when an answer to one problem arises suddenly, from some unlikely source — as a key aspect of his science. And in this instance, serendipity allowed him to envision a brand-new patient-treatment model, in which full organ transplants are rare and organ donor lists are eliminated. "Ideally, with this technology, you screen people and you augment the existing organ when they've only lost 40 or 50 percent of their function," he says. The patient never even reaches an emergency stage.

The very next week, Atala isolated the kidney cells he needed, then seeded them onto a decellularized scaffold. The different types of cells made the structures as they do in nature — for example, distal cells made distal tubules, a segment of the nephron that filters urine — but they didn't communicate. The frameworks they built were never connected. Atala, peering through a microscope, was like a pilot looking at an unfinished suburban development from an airplane. Structures dotted the landscape, but no roads ran between them.

Remembering what he learned from his work on the phallus, Atala tried another experiment. Seeking to approximate the conditions the cells experience in the body, he stopped isolating them in the first place. Like a chef making pesto with a mortar and pestle, Atala ground a section of healthy kidney tissue, extracting the various types of cells in a single pile.

"These cells already had a relationship, so to speak," says Atala. "So with this technique, that relationship was never really severed. They were talking to each other, and this way they continued to talk."

Looking through a microscope, Atala watched the ghostly, isolated structures he saw before connect — each to the other — healthy and alive.

"That one felt great," he says. "It was just what we hoped to see."

The words seem too small to encompass what he was really viewing — watching a kidney, in effect, regrow itself, the human body enacting its own salamander nature.

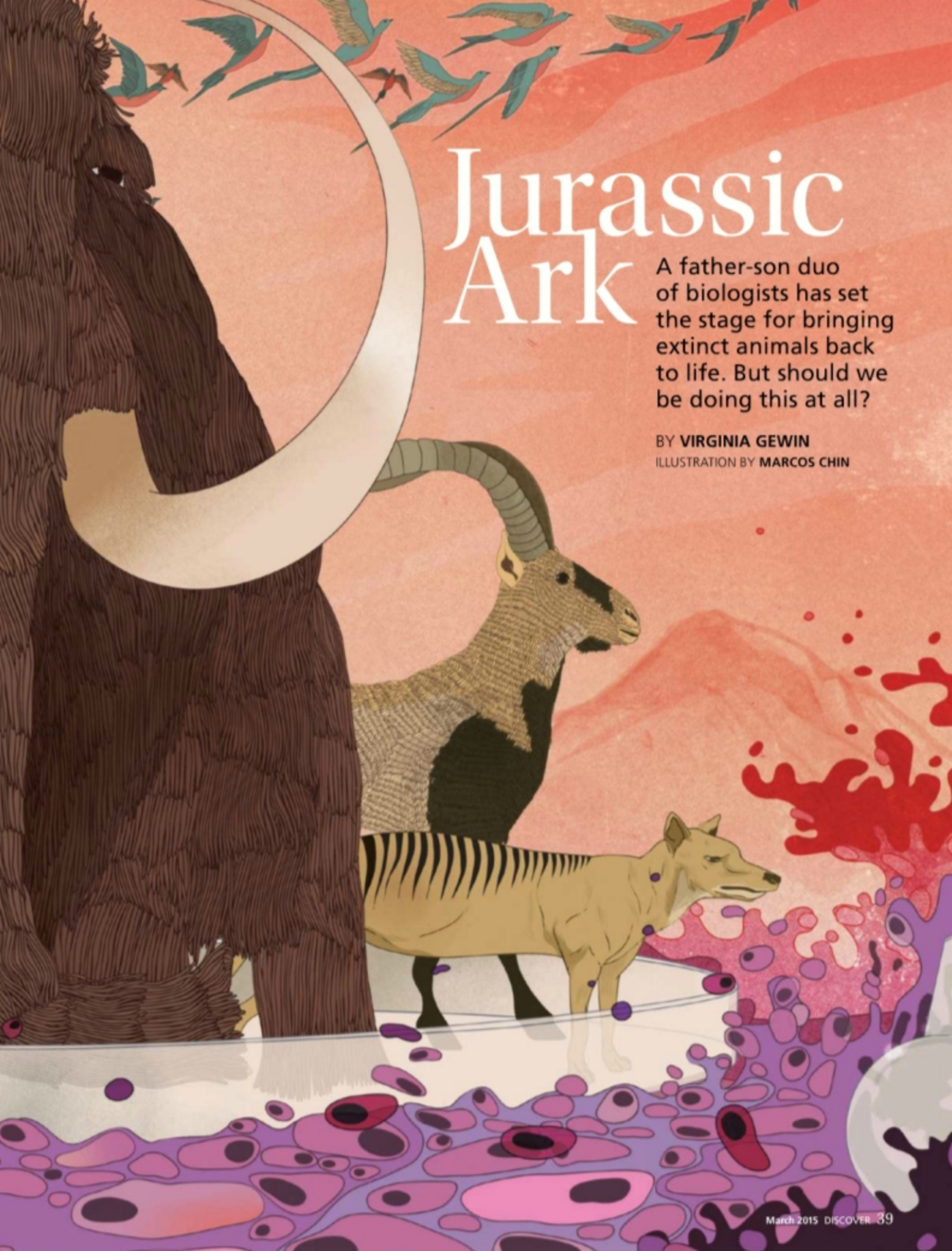
Atala continues to work on creating whole new organs. But he also has a team working on the model that occurred to him on the beach: Harvest and grow some healthy cells from a patient's damaged kidneys. Concurrently, decellularize a pig kidney, leaving only the casing. Then repopulate the organ with the patient's cells. Insert a section of that new kidney tissue, equal in weight to maybe 20 percent of the existing organ. With no cells from the pig, the recipient's body should accept this new section of kidney.

Atala is also pursuing this "wafer" model of creating partial transplants for other organs.

Though Atala always remains circumspect about the status of his projects, he says this partial transplant model is different: That team is far along in the process, successfully placing kidney cartridges into animals for trials lasting several months. The major problems, he says, all appear to be solved. Relatively speaking, partial transplants are closer. The most practical solution may not be as dramatic, or garner as much publicity as creating a whole new organ. Yet millions of happy ever-afters beckon. Because he saw the answer when it washed in with the tide — the ocean rolling back in from the future, sounding like an echo of a mystified crowd's applause. D

Steve Volk *is a freelance writer in Philadelphia.*





Jurassic Ark

A father-son duo of biologists has set the stage for bringing extinct animals back to life. But should we be doing this at all?

BY **VIRGINIA GEWIN**
ILLUSTRATION BY **MARCOS CHIN**

HENDRIK POINAR had no idea the bizarre turn his day was about to take.

Perched on a leather sofa in a downtown Toronto office, his host, a wealthy businessman, uncorked a $7,000 bottle of wine and outlined the multimillion-dollar offer: leave behind his research position at McMaster University's Ancient DNA Centre in Ontario and work full time to bring the extinct woolly mammoth back to life.

The businessman went on to describe a grand vision — a "Pleistocene Park" housed on 150 acres north of Toronto, where visitors would pay to see the herbivorous beasts. Throughout the three-hour lunch, he peppered Poinar with questions about the risks and feasibility of such an endeavor, trying to feel out how much skin Poinar was willing to put in the game.

Poinar was stunned. On this spring day in 2006, he was flying high on the heels of his recent study published in the journal *Science*. He and his colleagues had reconstructed the partial genome of a woolly mammoth found frozen in Siberia, and he was convinced that researchers like himself would soon be able to take bits of degraded tissue samples, extract ancient DNA and use them to piece together whole genomes of extinct animals. Poinar was thrilled that he was finally on the verge of uncovering genomic clues to past extinctions. But an ice age wildlife park wasn't quite what he had in mind.

Hendrik Poinar and his father, George Poinar Jr., an insect pathologist with a penchant for amber, have spent their careers exploring portals to the prehistoric past — tracing species' appearances, movements, adaptations and extinctions.

George, 78, is one of a vanishing breed of natural historians who have built whole careers out of careful observation. By focusing on creatures trapped in amber, he revealed the workings of bygone ecosystems. He has discovered the world's oldest-known bee and mushroom, the earliest evidence of flowering plant sex and, most recently, a fossilized ancestor of the bacterium that causes Lyme disease. But it was a cell nucleus in an amber-embedded fly that helped launch the study of ancient DNA, which quickly sparked notions of reviving extinct species and inspired Michael Crichton's novel-turned-movie, *Jurassic Park*.

Throughout his career, George, now a professor emeritus at Oregon State University, has kept his focus on creatures in amber. Hendrik, for his part, spent years plying through caves sampling preserved poop, probing permafrost and helping exhume mass graves, all to uncover well-preserved pockets of DNA that could shed light on how ancient creatures lived, died and evolved. In addition to sequencing the woolly mammoth genome, Hendrik has reconstructed the diets of extinct giant sloths, debunked a hypothesis about the origin of human immunodeficiency virus (HIV) and sequenced the genome of the bacterium that caused Black Death.



The passenger pigeon could be resurrected by splicing its genes into the genome of its cousin, the band-tailed pigeon.

Together the Poinars have helped set the stage for what promises to be a dramatic advance: resurrecting extinct species. George led early clandestine explorations of the notion before essential technology was invented. Later, Hendrik created blueprints of extinct life. With these blueprints in hand, scientists have begun exploring how to re-create an extinct species by manipulating the genome of its closest living relative. For example, a team could soon create something strongly resembling a passenger pigeon by altering a band-tailed pigeon's genes to craft the extinct bird's long tail, red eyes and peach-colored breast.

Today, Hendrik, 45, has almost completed the woolly mammoth genome. Harvard geneticist George Church is altering elephant genes to make them more mammoth-like, which could one day help produce elephant-mammoth hybrids. Australian researchers have begun sequencing the Tasmanian tiger's genome and hope to resurrect the extinct marsupial.

The prospects of de-extinction have inspired conservationists who want to use it to restore ecosystems and absolve the sins of past human-caused extinctions. The idea has proven so inspiring that affluent environmentalist and futurist Stewart Brand, the former publisher of the *Whole Earth Catalog*, launched a nonprofit group called Revive & Restore solely to advance the science of de-extinction and rally support for it.

Although it won't happen immediately, the technology and momentum suggest that some version of extinct animals will most likely roam the planet again. "Who wouldn't want to see a woolly mammoth?" Hendrik says. George hopes he's



ABOVE: LEAH NASH. BOTTOM FROM LEFT: ROBERT L. KOTHENBEUTEL/SHUTTERSTOCK; TIM ROUGH



George (left) and Hendrik Poinar, whose work helped make de-extinction possible, sit in George's home laboratory in Corvallis, Ore., where George studies specimens from his collection of amber-encased insects.

alive to see one revived — but he and Hendrik worry about what will happen when we do.

Back in Toronto, Hendrik met with his would-be benefactor a few more times before declining the offer. "I think he was surprised that I wasn't willing to take exorbitant sums of money to do this really cool stuff," Hendrik says.

It is, undeniably, cool. But as the technological pieces fall into place, it's startling to realize how close we may be to bringing back new versions of extinct species — and how ill-prepared we are.

OLD AMBER, NEW FINDS

The quest to resurrect ancient species began, as many scientific quests do, with a happenstance finding. In 1980, George Poinar and his future wife, Roberta Hess, an electron microscopist, cracked open a piece of 40-million-year-old Baltic amber containing a remarkably well-preserved female fly. Roberta spent days, using tiny pliers and a glass knife, slicing ultrathin layers of the fly's internal organs and preparing them to view through an electron microscope.

George, then 44, was trying to determine whether bacterial spores could survive in amber for millions of years, part of his larger efforts to trace the ancient origins of modern disease. When George was a boy, his mother gave him a book graced by a picture of a weevil trapped in amber, and that single image sparked a lifelong fascination with insects and other ancient creatures trapped in the fossilized tree resin.

As a professor of entomology at the University of California, Berkeley, George studied insects and their parasites, traveling to amber hot spots like the Dominican Republic, Canada, Mexico and northern Europe to collect and describe just about anything trapped in resin, from feathers to frogs. But the samples he saw never contained intact organelles — specialized cell structures with dedicated jobs. When Roberta peered through the microscope at samples from the fly, she was amazed to find mitochondria, ribosomes, muscle bands — and the nucleus, which houses the cell's genome. George returned from the university library one day to find a note Roberta left on his door: "SUCCESS!"

The findings, which garnered headlines when they were published in *Science* in 1982, raised a provocative question. Since the nucleus houses the cell's genetic material, could scientists resurrect ancient DNA? If so, that DNA would serve as a biological time machine that effectively allows scientists to revisit Earth's past and watch as proteins and species evolve.

On the surface, the notion seemed plausible, since intact tissues from woolly mammoths, which roamed northern grasslands and tundra until about 11,000 years ago, had been discovered recently in Siberian permafrost. But to most scientists, the idea seemed far-fetched.

Molecular tools were already reshaping biology, emphasizing the role of genetics, but the methods available were primitive. To characterize an ancient DNA fragment, scientists first had to clone it. That meant extracting it from tissue, treating it with enzymes to sew the ancient DNA into a small loop of bacterial DNA, then propagating that DNA in bacteria. Then they had to determine its sequence of nucleotide "letters," which was equally laborious. Even if DNA could be extracted from amber-preserved tissues, it, too, would likely be in fragments, which made isolating an ancient gene a daunting prospect.

George and Roberta's finding sparked the interest of a rag-tag group of scientists who banded together with George to form the Extinct DNA Study Group. They aimed to extract ancient DNA from organisms trapped in amber to sequence extinct genes, recover dormant life forms and study protein evolution.

The group corresponded for more than a year and finally met in March 1983 in Bozeman, Mont., where they contemplated what one member called a "far-out" idea. Somewhere, they mused, a mosquito that fed on a dinosaur might be trapped in amber, and white blood cells from the dinosaur might be preserved in the mosquito's stomach. If so, they might be able to transplant a white blood cell nucleus into an egg from a frog or other animal that has been enucleated, or stripped of its own nucleus. Then, by using standard tissue culture methods,

THE QUEST TO RESURRECT ANCIENT SPECIES

Some key points along the path to de-extinction.

1980

» George Poinar and Roberta Hess discover intact nuclei in 40-million-year-old fly in amber.



1981

1982

1983

» Polymerase chain reaction (PCR) technique is developed to copy DNA fragments.

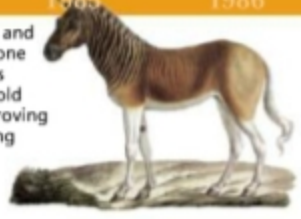
» Extinct DNA Study Group holds its first (and only) meeting.

1984

» Allan Wilson and Russ Higuchi clone gene fragments from 140-year-old quagga pelt, proving DNA in nonliving tissue can be reproduced.

1985

1986



TIMELINE FROM LEFT: GEORGE POINAR; PHOTO RESEARCHERS/SCIENCE SOURCE



George Poinar examines slides of insects and arachnids in his home lab. He works to understand ancient creatures and the diseases they carried.

they might be able to grow dinosaur tissue in the lab.

The notion of replicating extinct life forms was crazy enough that the group agreed to keep their work secret and not talk to the media. "We thought they would make fun of it or wouldn't take it seriously or would shut us down," George recalls. They also contemplated ethical dilemmas that still trouble scientists today. Was it OK to bring back an extinct species, or something like it, simply out of scientific curiosity? What if it is not adapted to the current environment, or if it suffers? What if it unleashes a dormant pathogen and spreads disease?

At the time, George had begun collaborating with molecular biologist Allan Wilson, a colleague at Berkeley who had just cloned gene fragments from the 140-year-old pelt of a quagga, an extinct brown-and-white-striped zebra relative. The work proved for the first time that DNA from nonliving tissue could be reproduced, and Berkeley quickly became a hotbed of ancient DNA research. The scientists detected some evidence of fossil insect DNA in amber samples, but they couldn't rule out contamination by microbial or human DNA. Grants to fund additional work were denied, Wilson was diagnosed with cancer (he died in 1991), and the project was shelved.

With such dim prospects in the near term, George lost hope — that is, until six years later, when Hendrik entered the field.

GOLD RUSH FOR ANCIENT GENES

As a boy, Hendrik sometimes followed his dad into the field to collect insects, but he was far more content in George's lab. There he played with desiccated, ghostlike roundworms, which he could disintegrate with a touch or bring back to life with a few drops of water. He became fascinated with their state of suspended animation, poised between life and death.

Like his dad, Hendrik loved to ponder events that shaped the natural world. But he admits to being frustrated by the limited explanations George could offer based on observations alone. "I needed something more concrete," he says. "I wanted to understand the molecular mechanisms that allow organisms to sit in an animated state."

To do that, Hendrik had to examine the genes of long-dormant or dead organisms. Few scientists thought that ancient DNA could last thousands of years, in part because DNA breaks down into smaller fragments when exposed to microbial activity, sunlight, heat and humidity. But as an undergraduate molecular biology researcher at California Polytechnic State University (Cal Poly) in San Luis Obispo in the late 1980s, Hendrik was determined to test the notion anyway. Since amber preserved ancient animal and plant tissue so well, it seemed as good a place as any to look for preserved DNA that could tell the tale of vanished creatures.

Hendrik began working in the lab of Cal Poly microbiologist Raúl Cano, and Hendrik teamed up with his father, who eagerly gave him samples of 40-million-year-old amber from the Dominican Republic containing stingless bees. To extract DNA cleanly from such samples without contaminating it, Hendrik developed a new method. He quick-froze the amber in liquid nitrogen, which is cheap, harmless to cells and extremely cold. Warming the amber then fractured it, exposing the internal tissue for DNA extraction. Hendrik recovered several short gene fragments, which represented just one-ten-thousandth of 1 percent of the bee's total genetic information. With George as a co-author, it was Hendrik's first scientific paper, published in *Medical Science Research* in 1992.

The next year, the Poinars and Cano built on that work,

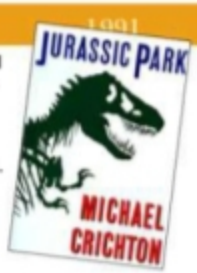
ABOVE AND OPPOSITE: LEAH NASH

1987
» First commercial PCR machine lets biologists fish out genes from minuscule tissue samples.



Baby Blue, a PCR prototype

1990
» Michael Crichton's novel *Jurassic Park* is published.



1992
» Hendrik and George Poinar report new freeze-fracture method to extract ancient DNA from amber.

1993
» The Poinars and Raúl Cano use PCR to obtain DNA from 120-million-year-old amber-trapped weevil.
» *Jurassic Park*, the film, is released.

1994
» Svante Pääbo and Hendrik Poinar start developing rigorous new methods to counter dubious claims of DNA from plants and dinosaurs millions of years old, including the Poinars' weevil claim.

1995

reporting what they described as DNA sequences from a 120-million-year-old amber-encased weevil. They published the work in the journal *Nature*, timed to coincide with the premiere of the blockbuster movie *Jurassic Park*.

Just a couple of years earlier, George learned that he and Roberta were thanked in the acknowledgments of Crichton's 1982 novel, and he realized then that a tall, lanky fellow who visited his lab years earlier was Crichton. George's Baltic fly nucleus convinced Crichton that dinosaur DNA could plausibly be extracted from an amber-entombed mosquito. When the Poinars' *Nature* paper was published, several reporters asked Hendrik and George the same question: Could extinct animals ever be brought back to life? Interviewed by Katie Couric on the *Today* show on the night of the movie's premiere, Hendrik assured her that dinosaurs would never roam Earth again.

Is it OK to bring back an extinct species, or something like it, simply out of scientific curiosity? What if it is not adapted to the current environment, or if it suffers? What if it unleashes a dormant pathogen and spreads disease?

The next dozen years saw researchers rush into the field to hunt for ancient DNA. Many were enticed by the tantalizing prospect of finding prehistoric genetic material that could shed light on extinct species and evolution itself. These scientists used polymerase chain reaction (PCR), a powerful, new method at the time, that makes millions of copies of degraded ancient DNA fragments. They scrambled to outdo one another by publishing DNA sequences that were ever more ancient, with one fantastically claiming to have sequenced 80-million-year-old DNA from dinosaur bones. But it soon became clear that PCR was yielding plenty of fool's gold — DNA from humans or modern-day microbes that had contaminated samples. In fact, the so-called dinosaur DNA turned out to from a human Y chromosome.

By the late 1990s, Hendrik had completed a doctorate in molecular biology with Svante Pääbo, a Swedish paleobiologist who trained with Wilson at Berkeley. Pääbo and Hendrik recognized that some of their early samples could have been contaminated. To prevent such errors, over time the two established several protocols to combat contamination, using bleach, ultraviolet lights and positive-pressure clean rooms. They also emphasized the need to replicate findings in a second laboratory, and they policed research in the field. "My dad taught me how to think outside the box, but Svante shaped me to be meticulous," Hendrik says.

In 2000, Hendrik co-authored a powerful letter in *Science* that outlined the rigor required, titled, "Ancient DNA: Do it right or not at all." The ancient DNA gold rush waned in the early 2000s, and Hendrik became convinced that if some technological breakthrough didn't happen soon, the field would soon die.

CHEATING EXTINCTION

As researchers struggled to reconstruct ancient genomes, the world's first de-extinction had already, surreptitiously, taken place. In 2003, Spanish scientists had used the same cloning method that helped create Dolly the sheep to resurrect the Pyrenean ibex, a wild goat endemic to the French mountain range. They injected intact nuclei from the last living ibex into more than 400 enucleated eggs of the domestic goat. They then implanted those eggs into surrogate mothers — either Spanish ibexes or ibex-goat hybrids. Six of the seven animals that became pregnant miscarried, and the other gave birth via Caesarean section to a kid that died after just 10 minutes. More recently, an Australian team used the same strategy to resurrect the gastric-brooding frog, a fantastical creature that swallowed its eggs and coughed up babies. They managed to transfer the extinct frog's nuclei into the egg cells of a barred frog, but so far, the embryos have yet to fully develop.

Such methods may help resurrect recently departed species, but it will be all but impossible to find tissues with intact nuclei for long-gone species. To resurrect these species, scientists plan to use the extinct organism's genetic code as a blueprint. That became feasible in 2005 when the first commercial next-generation (next-gen) DNA sequencing machines became available. (See "Making a Woolly Mammoth," page 45.) "This is what we had been waiting for," says Hendrik. Today, next-gen sequencing allows scientists to sequence an entire human genome in hours for less than $1,000, far faster and cheaper than ever before. And the same technology enables researchers



Hendrik Poinar holds a giant tooth from a massive mammoth.

TIMELINE FROM LEFT: SCIENCE MUSEUM LONDON/FLICKR/CREATIVE COMMONS; NAJAH FANNY/CORBIS/SABA; LONELY_THINK/STOCK; R. DYDEKIEWIND OXEN SHEEP & GOATS OF ALL LANDS, LIVING AND EXTINCT (1896)/BIODIVERSITY HERITAGE LIBRARY

1996 1997 1998 1999 2000 2001 2003 2004

» Dolly the sheep provides proof that animals can be cloned by somatic cell nuclear transfer.





» Hendrik Poinar co-authors "gold criteria" to ensure reliable sequencing of degraded ancient DNA.



» First de-extinction: Pyrenean ibex. Results not reported until 2009.

NEXT-GEN SEQUENCING AND ANCIENT DNA

To characterize the genes and genomes of long-gone organisms, scientists first extract whatever DNA remains from scarce bits of preserved tissue. They then chemically label the DNA — typically tiny, degraded fragments contaminated with microbial DNA from the environment and human DNA from being handled — to form a library consisting of thousands of DNA fragments. They use one of several proprietary methods to determine the sequence of nucleotide "letters" (A, C, G and T) that encode genetic information. A computer program uses telltale genetic signatures to distinguish fragments of ancient DNA from contaminating DNA. It then connects simulated DNA fragments with overlapping sequences to reconstruct longer stretches of ancient DNA and, eventually, sections of the genome.

Today, Hendrik Poinar and other ancient DNA researchers can sequence more DNA in one week than a well-equipped research team relying on 1990s-era technologies could have done in 20 years. And since the cost of genome sequencing has plummeted to one-thousandth of its initial cost, it's clear that the Neanderthal, a 700,000-year-old horse and the woolly mammoth will simply be the first of many ancient genomes to be sequenced. – VG

to uncover the genetic blueprint of an extinct animal.

To turn that blueprint into a living organism, scientists will also need a surrogate mother. A modern relative is the best bet. Beth Shapiro, an ancient DNA researcher at the University of California, Santa Cruz, is using the band-tailed pigeon genome as a guide to piece together a draft passenger pigeon genome. Ben Novak, a biologist funded by Revive & Restore, the nonprofit group Brand established, will use that blueprint to try to revive the extinct bird. So far, Shapiro and Novak have amassed 88 passenger pigeon samples from museum collections, but it will be a long, hard slog to determine which genes distinguish a passenger pigeon from a rock pigeon, and what the genes do, Shapiro says.

It's the woolly mammoth that's probably the furthest along toward de-extinction. Hendrik plans to publish the most complete woolly mammoth genome yet, and George Church's team at Harvard is already introducing specific DNA variants — genes for hair, tusks, subcutaneous fat and cold resistance in blood — into cultured cells from Asian elephants, with the goal of preparing the rebuilt mammoths for life on the tundra. But even making an elephant whose genes are 9 percent mammoth might take 20 years, and we may never re-create an exact duplicate of the extinct species, Church says.

Because it's so hard to replace all the genes that make a woolly mammoth — or a passenger pigeon or dodo or Steller's sea cow — a unique species, the re-created animals won't be *exactly* what went extinct. Some will be clones, like the baby Pyrenean ibex. Some could be genetically engineered hybrids. Others will likely be wholly synthesized — new beasts altogether.

TAKING SECRETS TO THE STAGE

In March 2013, 30 years after the only Extinct DNA Study Group meeting, Hendrik strolled onstage before a standing-room-only crowd at the TEDx conference on de-extinction in Washington, D.C. With an image of an amber-ensconced insect from *Jurassic Park* on a giant screen behind him, Hendrik described how he and his father used to imagine long-gone insects waking up and crawling out of the resin. He described how the woolly mammoth disappeared, like 99 percent of all animals ever to walk the Earth, then he walked the audience through the steps needed to resurrect one. But he ended on a cautionary note: "I have to admit that part of the child in me would love to see these creatures walk across the permafrost, but part of the adult in me wonders whether we should."

In the past, scientists played their cards close to the vest as they developed, then commercialized, powerful new technologies. Often, they were sure that what was best for the science was best for society. And time after time, their secrecy and paternalism fed fears that sparked a public backlash — over technologies as diverse as test-tube babies, cloned animals like Dolly the sheep and genetically modified organisms. "The reason we're in this situation with [the backlash against] genetically modified organisms is because we didn't talk about it clearly enough, early enough," Church says.

The TEDx conference, which was organized by Stewart Brand and his wife, genomics entrepreneur Ryan Phelan, represented a historic break from that tradition — a high-profile bid to convince the public that de-extinction was feasible and worth doing. Proponents like Church contended that the herbivorous woolly mammoths could help preserve essential carbon-storing grasslands in the Arctic north, while Brand made the case that resurrecting species would atone for human-caused extinctions.

Hendrik and Ross MacPhee, curator at the American Museum of Natural History, pushed successfully to include philosophers, historians and ethicists at the conference to weigh the promise and the perils of de-extinction. The fact that humans will effectively be creating organisms that could never have existed before is a terrifying prospect, says MacPhee. "It's *Brave New World*-ish."

It's been nearly two years since that conference, and no extinct animals have yet been resurrected. This buys us all time to discuss, publicly and openly, the impacts of such life-altering endeavors, Hendrik says. There's time to consider whether bringing back ancient animals might cause them to suffer, release dormant diseases or harm today's already struggling

TIMELINE FROM LEFT: 454 LIFE SCIENCES, A ROCHE COMPANY; BOENSCH, B./CORBIS; MICHAEL J TYLER/SCIENCE SOURCE; TEDX DEEXTINCTION/FLICKR/CREATIVE COMMONS; TED HOROWITZ/CORBIS

2005
» First commercial next-generation (next-gen) sequencing system is released.

2006
» Hendrik Poinar uses next-gen sequencing to partially sequence woolly mammoth genome.



Roche 454 next-gen sequencer

2008

2009



2010
» Svante Pääbo publishes draft sequence of Neanderthal genome.

2011
» Australian team creates embryo of extinct gastric-brooding frog.



2012
» The nonprofit Revive & Restore is founded to enhance biodiversity by reviving endangered and extinct species.



MAKING A WOOLLY MAMMOTH

Reviving a woolly mammoth will be no easy feat, but below are two plausible methods. The first requires remarkable luck to find a mammoth cell with a viable nucleus. The second requires painstaking efforts — which are underway — to modify the Asian elephant's genome to resemble the mammoth's. Eventually, scientists might use mammoth genome sequences to synthesize chromosomes, which could be placed in a nucleus that then is placed in a cell and grown into an embryo, which could be implanted in a surrogate mother.



The Asian elephant is the woolly mammoth's closest living relative.

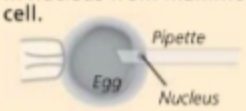


Cloning With Somatic Cell Nuclear Transfer

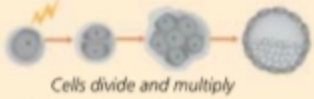
Starting with a viable nucleus

Cell with intact nucleus

1 Extract egg from Asian elephant donor, then swap in nucleus from mammoth cell.



2 Electrically shock the egg to stimulate cell division, creating an embryo.



3 Implant embryo into the uterus of a surrogate mother elephant.



4 After gestation, Asian elephant mother gives birth to a cloned baby mammoth.



Building a Hybrid With Genome Engineering

Starting with mammoth genome

Ancient DNA fragments

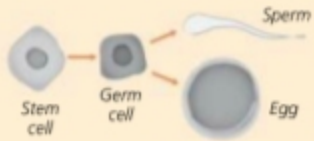
1 Cultivate Asian elephant stem cells.



2 Modify their genomes to substitute mammoth genes that confer cold resistance using genome-engineering tools.



3 Convert modified stem cells into germ cells, which form modified elephant sperm and egg.



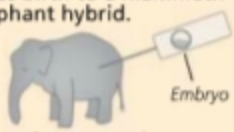


The elephant genome is modified with mammoth genes for cold resistance, such as long hair, extra subcutaneous fat and an altered blood protein.

4 Fertilize the modified elephant egg with modified elephant sperm, creating embryo of mammoth-elephant hybrid.



5 Implant hybrid embryo into the uterus of surrogate mother elephant; mother gives birth to a mammoth-elephant hybrid.



6 See if the baby has mammoth cold-resistance traits. Make additional changes, if needed, creating a herd of mammoth-elephant hybrids that can flourish on the tundra.



ALISON MACKEY/DISCOVER. ASIAN ELEPHANT: JAN HAVLICEK/SHUTTERSTOCK. MAMMOTHS: OZJA/SHUTTERSTOCK

species and ecosystems.

On a summer afternoon, an unfinished Yahtzee game is evidence of the family vacation underway at George's home on the Oregon coast. George and Hendrik take part in a favorite pastime — friendly debate. Should we resurrect extinct organisms? "Sure, if we can," George says. Hendrik bristles, suggesting it's just this attitude that is the problem. "It's this idea that science marches ahead and does things just because we can," he says.

The generation gap between father and son lays bare a subtle, but momentous, shift taking place in modern science. George and his contemporaries feared that taking their concerns public could have jeopardized their ability to move the science forward.

Hendrik and his cohorts, on the other hand, worry that a lack of transparency could foster a destructive mistrust of science that jeopardizes us all.

As Hendrik and George have shown, the discovery of ancient DNA created a de facto time machine, and new genetic technology is speeding its development. And, at least in fiction, the only thing certain about a time machine is that it will tamper with the present.



2013

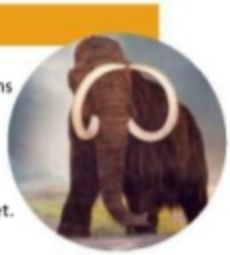
» Ethics discussion is part of pioneering TEDx de-extinction conference.

2014

» George Church uses genome-editing techniques to begin altering Asian elephant genome to resemble woolly mammoth's.

2015

» Hendrik Poinar plans to publish the most complete woolly mammoth genome yet.



Virginia Gewin *is a freelance science journalist covering environmental issues from her perch in Portland, Ore.*

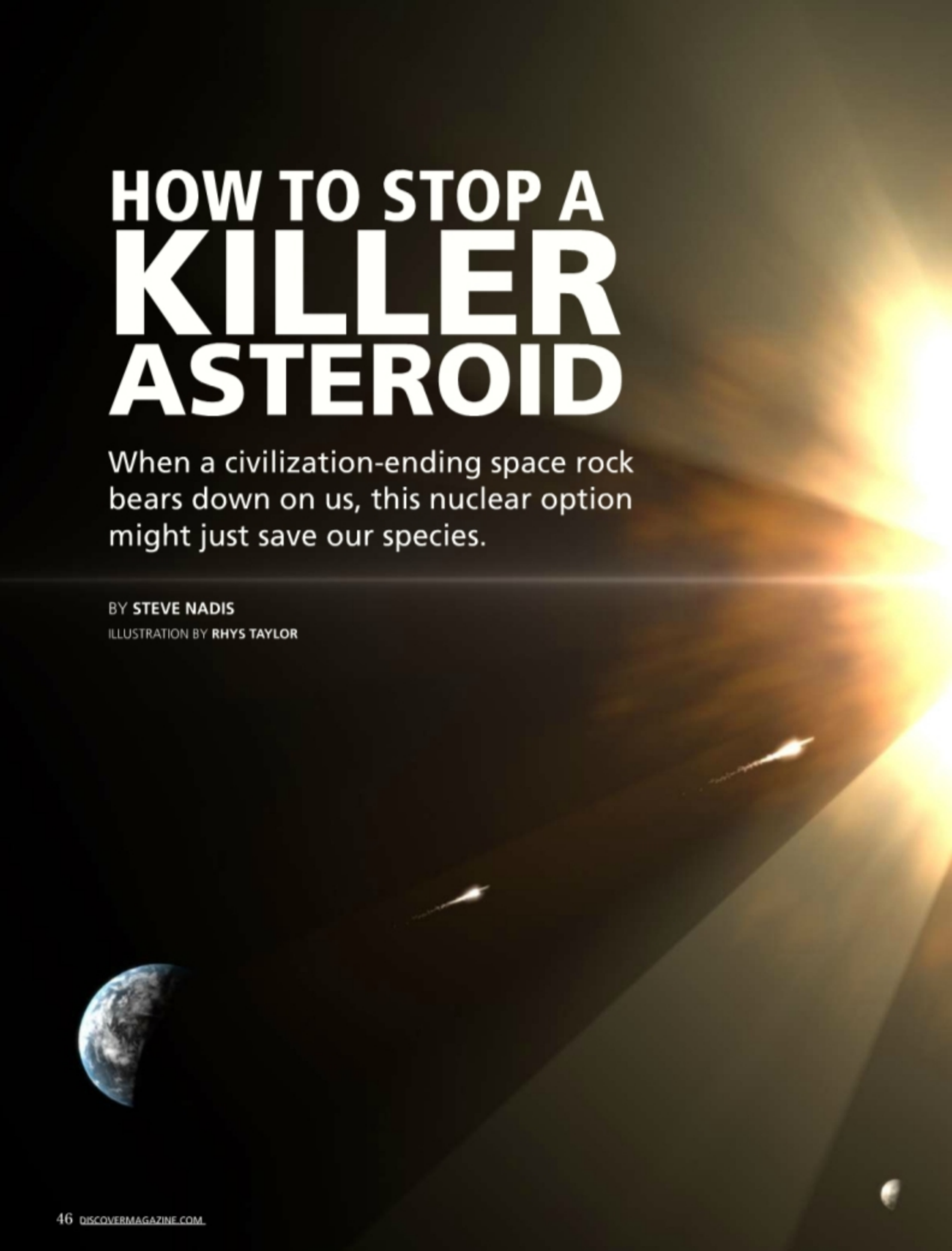
Do you think extinct animals should be brought back to life? Weigh in at **DiscoverMagazine.com/Extinct**

HOW TO STOP A KILLER ASTEROID

When a civilization-ending space rock bears down on us, this nuclear option might just save our species.

BY **STEVE NADIS**

ILLUSTRATION BY **RHYS TAYLOR**



Detonating a nuclear device near an incoming asteroid's surface would vaporize just a portion of its top layer, providing a big enough push to knock it off course.

Nothing fills movie theaters like the end of the world, which may be why Hollywood keeps turning out apocalypses. Yet most big-screen disaster scenarios pale in comparison to the genuine cataclysm that befell Earth some 66 million years ago, when a 6-mile-wide asteroid slammed into our planet. It left behind a roughly 120-mile-wide crater in the Yucatan and wreaked global environmental havoc. Many scientists believe this was the event that wiped out the dinosaurs and about 80 percent of all animal species. Events of this magnitude are rare, but astronomers assure us something similar will happen again.

Nature provided a little reminder on Feb. 15, 2013. First, a 56-foot-diameter rock exploded without notice above the Siberian city of Chelyabinsk, releasing the energy of more than 30 Hiroshima-size atomic bombs. Later that day, a totally unrelated 150-foot-wide asteroid named 2012 DA14 made a close approach, coming within about 17,000 miles of hitting us — some 5,000 miles closer than many TV and weather satellites.

Astronomers believe millions more large, undiscovered and potentially deadly asteroids lurk out there and could catch us unawares. Testifying before Congress a month after Chelyabinsk and 2012 DA14's flyby, NASA chief Charles Bolden said that if we had just a few weeks' notice before an impending asteroid impact, he could offer only one word of advice: "Pray."

Testifying before Congress, NASA chief Charles Bolden said that if we had just a few weeks' notice before an impending asteroid impact, he could offer only one word of advice: "Pray."

John Remo, a 73-year-old physicist living in New Mexico, finds that remark troubling. For Remo, a scientist at the Harvard-Smithsonian Center for Astrophysics, Bolden's statement serves as a painful reminder that we, as a country and a world community, have done little to prepare humankind to fend off asteroids bound for Earth, even though it's within our means to do so. We have the rockets and technical know-how, but have not yet put the pieces together — or mustered the will to do so.

For the past two decades, Remo has devoted himself to rectifying that oversight. In particular, he's focused on the option of "last resort," which may, in extreme circumstances, be our first and only resort: using nuclear blasts in outer space to push a menacing asteroid out of harm's way and onto a benign trajectory. His most recent research has helped quantify the amount of push a nuclear device could deliver in a dire emergency, when no other technology could save us.

In other words, the same devices that laid waste to Hiroshima and Nagasaki and brought the world to the brink of destruction might offer our only means of salvation in the face of an asteroid-induced Armageddon. It comes down to a question of awareness and resolve, Remo says. "Can we humans do what the dinosaurs could not — amass our expertise and technological resources in the defense of our planet?"

TAKING AIM AT ERRANT ROCKS

Remo got his Ph.D. in quantum optics in 1979 after developing the mathematics that would make lasers more powerful, stable and efficient. His journey through graduate school took longer than usual because he taught at several universities, traveled quite a bit and undertook extensive research in astrophysics, looking in particular at how the composition of asteroids and meteoritic fragments affects their size. He became absorbed in this line of study, even though it set him back on his dissertation. At the time, Remo wasn't thinking about near-Earth objects, bodies in the solar system whose orbits may one day intersect with Earth's. He was more interested in the solar system's origins, viewing each extraterrestrial rock he came across as "a poor man's space probe."

Upon graduating from the Polytechnic Institute of New York, he decided he could best maintain his independence, and carry out the most innovative work, by forming his own company. His firm, Quantametrics, developed technology for high-powered space lasers, working for clients like the "Star Wars" missile defense program and NASA, which relies on lasers for certain types of astronomical observations. The holder of about 20 patents, Remo continued his research on meteorites on the side, and both strands of work brought him into contact with scientists at various national labs.



JOHN BURCHAM

Meteor Crater, 4,100 feet wide and 550 feet deep, formed about 50,000 years ago when a nickel-iron asteroid slammed into a spot near present-day Winslow, Ariz. The crash released the energy equivalent of millions of tons of TNT. Impacts of this size happen every few thousand years.



Physicist John Remo holds a slice of the Leoville chondrite, a meteorite billions of years old. He has tested many varieties of space rocks in his research.

Owing to his combined expertise, he spoke at a 1992 Los Alamos National Lab conference on asteroid defense. This was the first major meeting to explore options for intercepting near-Earth objects that threatened Earth, and it brought about a rare commingling of astronomers and weapons lab researchers.

The civilian scientists who attended, notes astronomer Clark Chapman of the Southwest Research Institute, "went expecting it to be unusual, and we weren't disappointed." There was talk of "fringe stuff like antimatter weapons," he says, "and other outlandish proposals." Edward Teller, the father of the hydrogen bomb, spoke of developing a nuclear device 10,000 times more powerful than anything yet devised.

However, most of the ideas discussed at Los Alamos focused on deflection, giving an asteroid a push to dislodge it from a dangerous course. The most straightforward way to do this is the "kinetic energy" approach — simply ramming a spacecraft into an asteroid. But during the conference, Remo was struck by a realization already familiar to attendees more experienced in the subject: When you're talking about deflection, nothing can match the energy density of nuclear weapons.

Pound for pound, nuclear explosives — which derive their power from runaway chain reactions in their radioactive fuel — carry about a million times the energy density of chemical explosives. If you need to move a big rock (more than 3,300 feet), or if you're in a hurry to move a smaller rock (about 330 feet), nukes may be your best shot. The devices could be armed once they're out of Earth's atmosphere, and the intervention can occur far enough from our planet to keep any fallout or explosion risk well beyond the biosphere — the goal being to save the world without harming it.

Of course, the energy density of a nuclear device is not the whole story. Remo also realized during the conference that we can't predict how an asteroid will respond to a nuclear blast without a clear understanding of the object's material properties. Contrary to what intuition might suggest, a crumbly, carbonaceous asteroid can actually be nudged far more readily than a solid, iron-filled body. The biggest unknown at the time was how much momentum the nuclear radiation would impart to the asteroids — how big a push the blast would provide. "That question can only be addressed experimentally, not theoretically," Remo says.

He resolved to figure out just that, and for many years Remo used the



Pieces of asteroids, called meteorites when they land on Earth, come in three main types (from left): stone, iron and stony-iron.

TOP: MARK HOLM. BOTTOM FROM LEFT: ERWIE MASTROIANNI/DISCOVER (2); ROBERT HAAG

proceeds from his laser work to privately support his asteroid studies. (He eventually received funding from the National Nuclear Security Administration and other federal agencies.) "John's experiments were the first to use real extraterrestrial objects — a collection of meteoritic material of various kinds," says Barry Shafer, a physicist formerly based at Los Alamos. And Remo was just getting started.

CREATING A NUCLEAR KICK

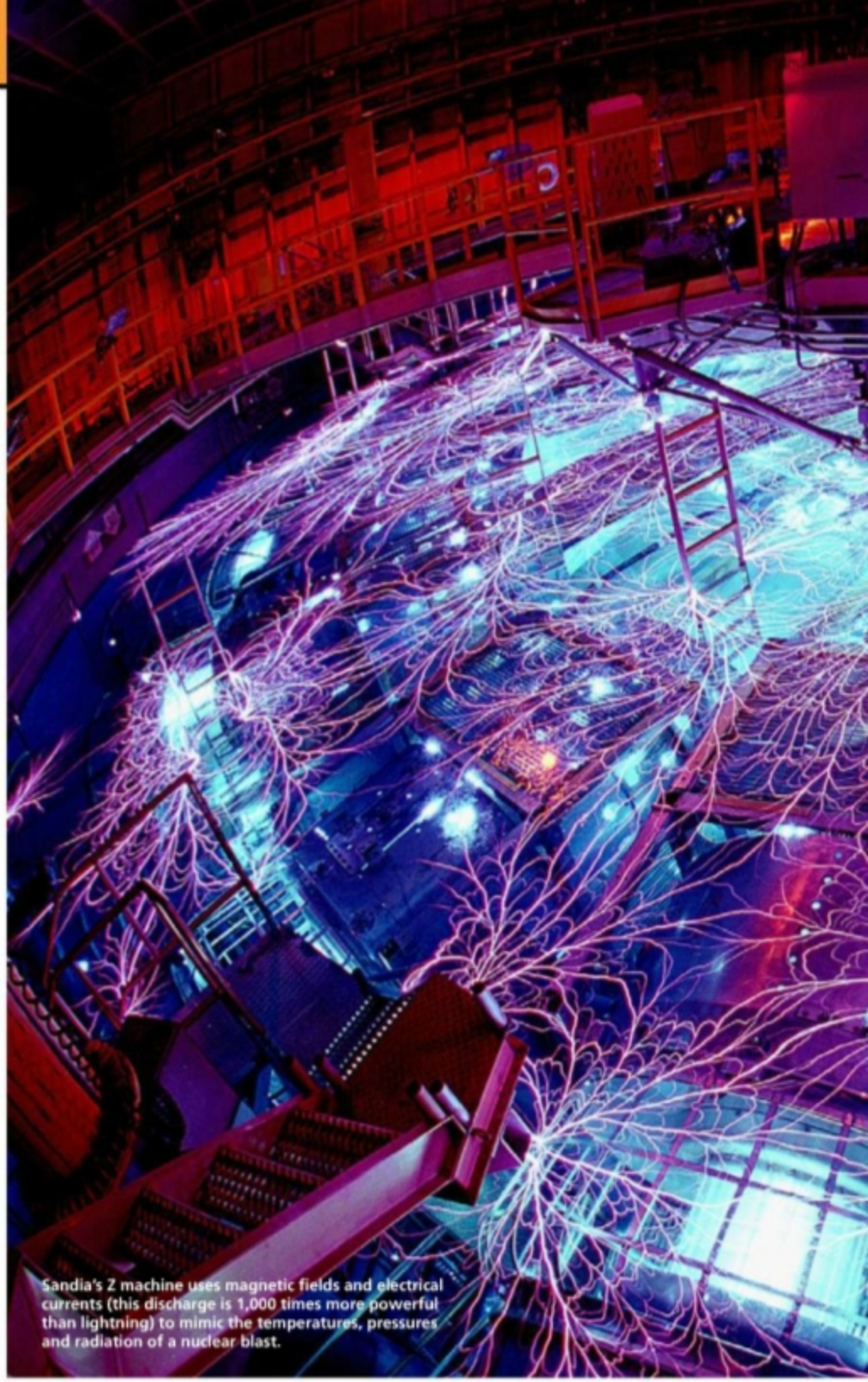
Here's the basic scenario that Remo had in mind for a hypothetical asteroid encounter: With a collision imminent, we'd launch a rocket into space. When close enough to its target, the rocket would set off a nuclear bomb (or possibly several) close to — though not in or on — the asteroid. The blast would vaporize a thin portion of the body's surface. The hot gases produced would immediately expand and rise from the surface, providing a concerted kick, or thrust, that would propel the asteroid away from Earth.

After spending about 10 years gathering meteorite samples, in 2000 Remo finally gained access to the perfect device for exploring the nuclear option: Sandia National Laboratories' Z machine, which happens to be the world's most powerful nuclear blast simulator, apart from nuclear weapons themselves.

A former particle accelerator reconfigured to its present guise in 1996, the Z machine is a platform for studying the physics and effects of nuclear explosions. It reproduces, for a fraction of a second, the high temperatures and intense radiation (predominantly in the form of X-rays) that accompany each detonation. The machine offered Remo his best hopes for figuring out how the X-rays from a nuclear blast would interact with, and possibly deter, incoming asteroids of varying compositions.

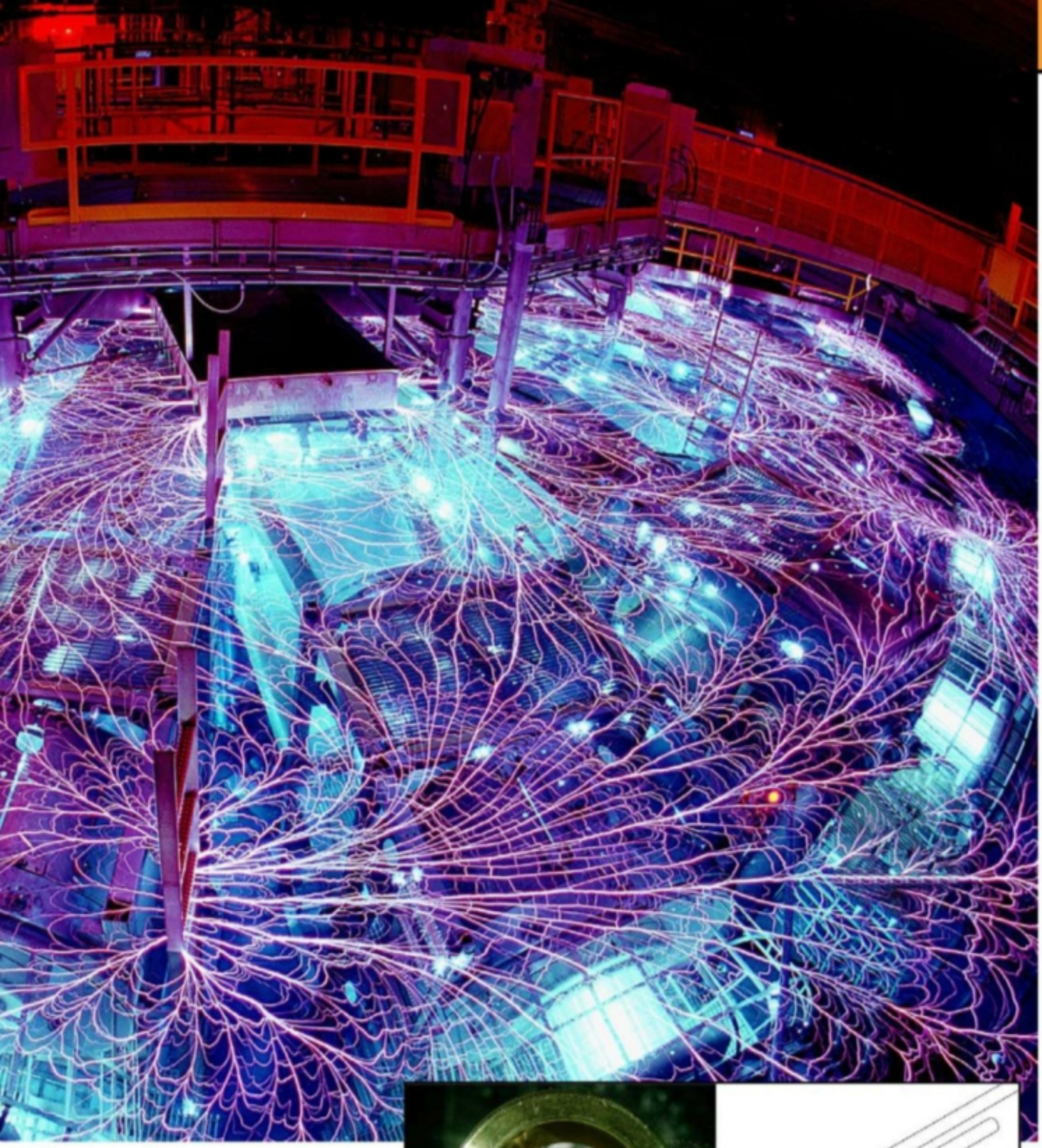
People have been investigating the effects of nuclear weapons for decades, but Remo offered a novel twist, says R. Jeffery Lawrence, a physicist who recently retired from Sandia: "He initiated studies of how X-rays interact with the stuff that asteroids are made of."

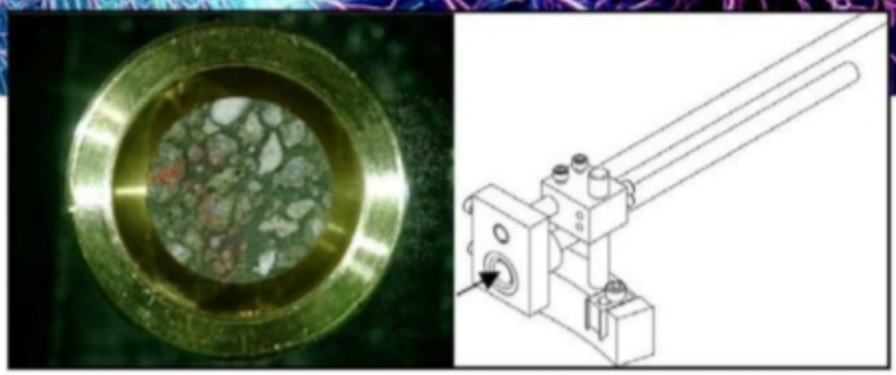
To simulate a nuclear "kick" in the lab, Remo and his longtime collaborator, Sandia physicist Michael Furnish, mounted small, disk-shaped samples of meteoritic material about 10 centimeters from the Z machine's X-ray source. When the X-rays briefly bombarded the disks, a little of their surfaces boiled off, providing an impulse that pushed the disks away. Remo and Furnish used a system invented at Sandia to calculate the velocity of each disk in the face of the X-ray barrage and became the first to effectively move asteroids (albeit minute ones) with radiation.



Sandia's Z machine uses magnetic fields and electrical currents (this discharge is 1,000 times more powerful than lightning) to mimic the temperatures, pressures and radiation of a nuclear blast.

ABOVE: SANDIA NATIONAL LABORATORIES





Remo and his colleagues would place small samples of meteorites (such as the roughly half-inch-wide chondrite at left) just inches away from the extreme energy pulses of the Z machine (right).

Remo and Furnish continued their tests, off and on, whenever the Z machine was available. In 2005, Remo, a lifelong New Yorker, moved from Long Island to the high desert of Placitas, N.M., so he could pursue this research more readily. "You can't do experiments by telephone," he says. All told, they tested about a

INTERNATIONAL JOURNAL OF IMPACT ENGINEERING
VOLUME 35, ISSUE 12/JOHN REMO/ELSEVIER (2)

dozen samples of different meteorite materials — some stony, some iron, some solid and some powdery — and studied the materials' response to varying levels of radiation by moving the targets closer to or farther from the X-ray source.

By 2010, Remo felt they had compiled "a complete body of work" on how radiation affects meteoritic substances. They enlisted Lawrence to help tally the results and do some computer modeling. Their joint findings were published in a 2013 paper in the *Journal of Plasma Physics*.

"The experiments show, first and foremost, that we can generate X-rays at a level sufficient to deliver the equivalent of a hammer blow to an object," says Lawrence. More specifically, they found that the motion induced by a blast was consistent for a given class of materials, such as stony versus metallic meteorites. "If we know from reconnaissance that it's a stony asteroid or a nickel-iron asteroid," explains Remo, "we can have a pretty good idea in advance how it will respond to an X-ray blast."

Remo fully believes that "when push comes to shove, and our survival is at stake, people will take advantage of any means available to protect the planet."

Prior to the Z machine studies, that response "had been a major uncertainty for a long while," says Harvard planetary scientist Stein Jacobsen. "John [Remo] deserves credit for coming up with a way to get a handle on this problem in the laboratory. He took the initiative and convinced Sandia to let him do these experiments."

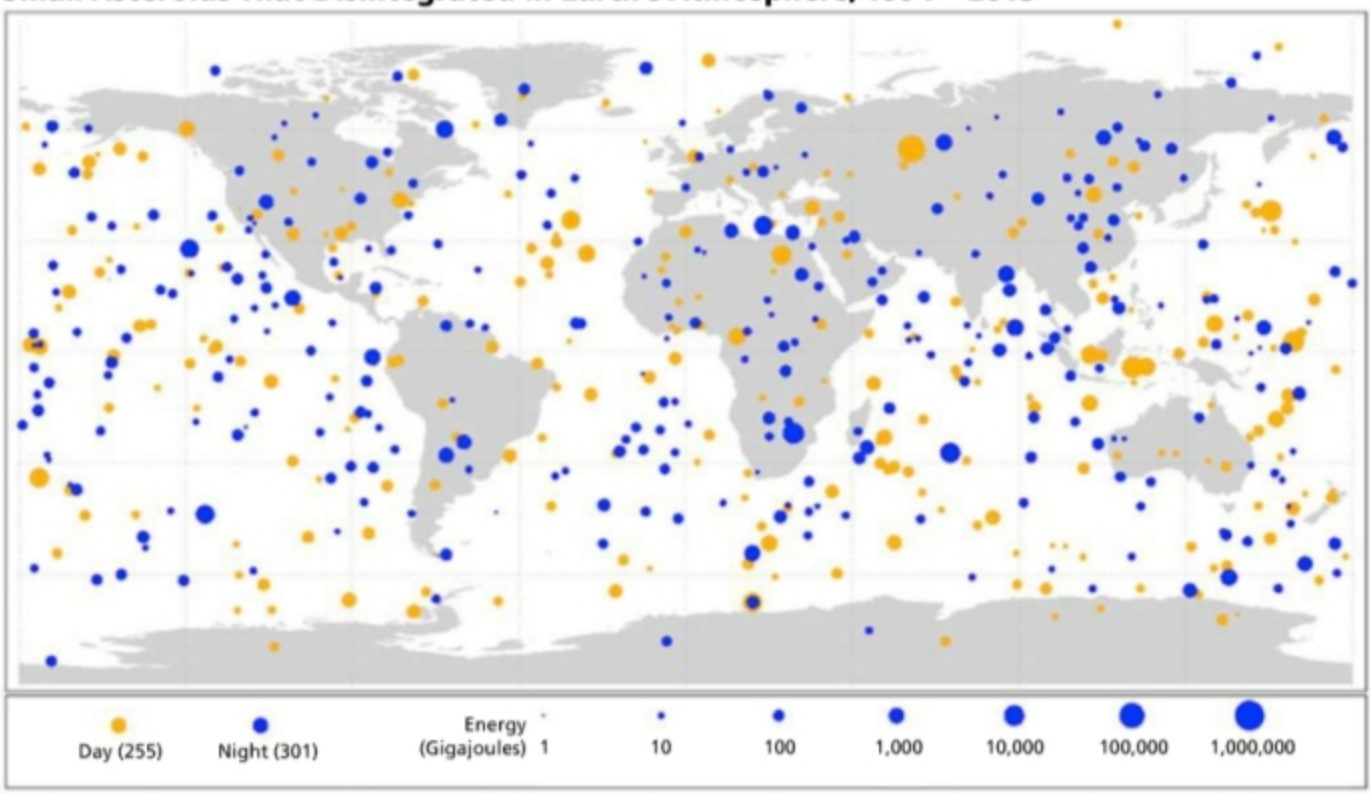
BEYOND THE LAB

Going from a meteoritic sample less than a centimeter in diameter to an asteroid up to a kilometer or more in diameter involves a pretty big leap. Yet Remo feels scientifically justified in making that leap because the radiation interacts with a material's atomic properties, and those properties are the same for small and large bodies. Their minute experimental samples are still thick enough to absorb all the radiation.

"The X-rays won't penetrate any deeper into the asteroid than into the laboratory target" — just beneath the surface, he says.

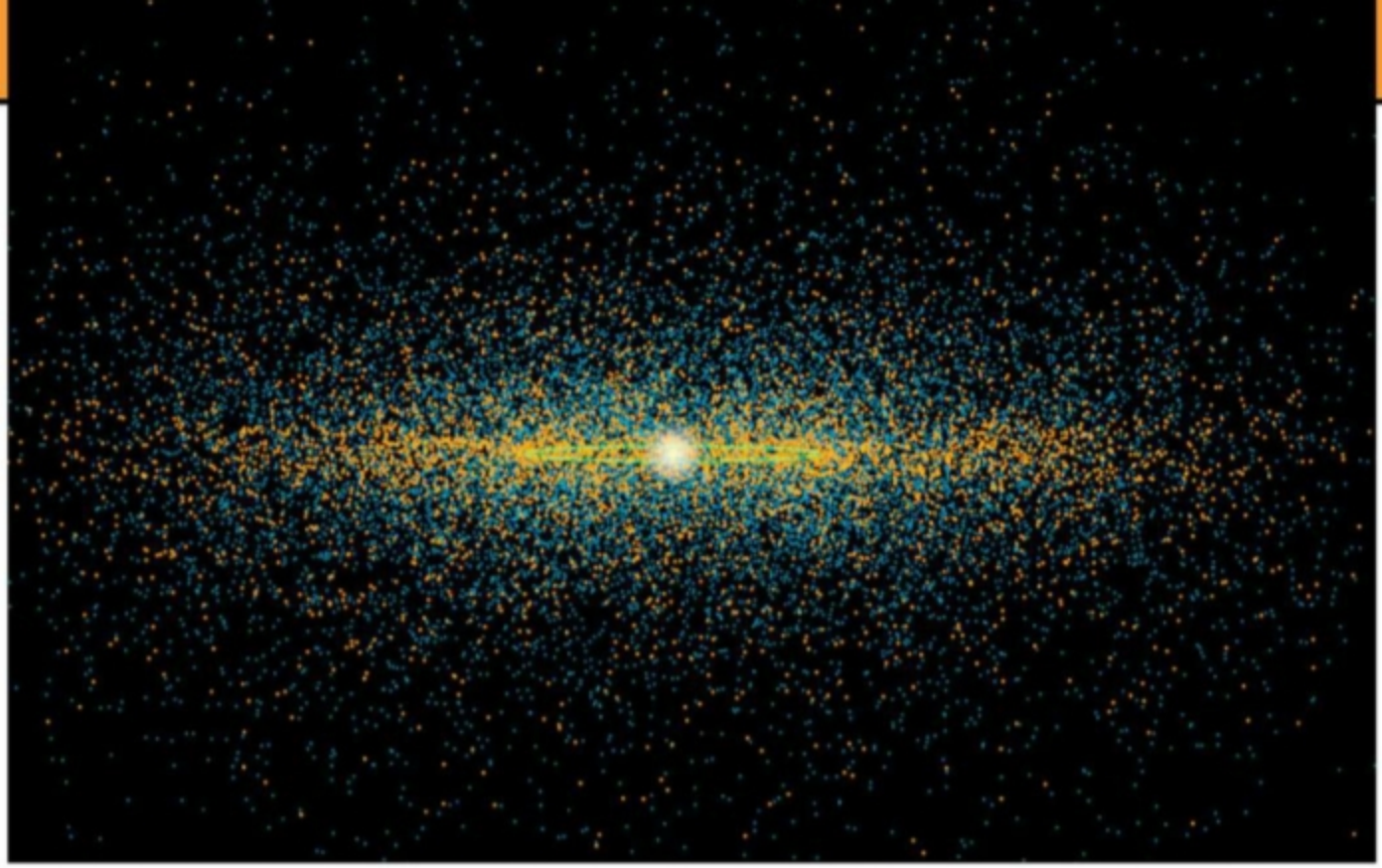
Eventually Remo would like to see some of these ideas, and technologies, put to a test. But before trying it out in space, researchers first need to work everything out on paper in systematic fashion, like determining how far from a given asteroid the bomb should go off. His rough calculations indicate that, ideally, one would want to detonate the device from a distance of

Small Asteroids That Disintegrated in Earth's Atmosphere, 1994 – 2013



Small asteroids hit our planet's atmosphere with surprising frequency. Impact energy is measured in gigajoules; for reference, 1 gigajoule (1 billion joules) is about two-thirds the energy of a lightning bolt. Luckily these asteroids, which range from 3 feet to almost 60 feet, are small enough to disintegrate in our atmosphere in bright flashes known as bolides, or "fireballs." However, experts agree it's only a matter of time before something larger slips through and makes it to the ground.

NASA/PLANETARY SCIENCE



This edge-on view of our solar system (with Earth's orbit shown in green) includes a snapshot of the most potentially troublesome asteroids. Near-Earth asteroids are blue, and the subset of them known as potentially hazardous asteroids — those with orbits coming within 5 million miles and big enough to survive the descent through Earth's atmosphere — are highlighted in bright orange.

roughly two asteroid diameters away.

In addition, Remo would like to see a comprehensive review of all the components needed for this option: the launch vehicles, guidance systems, sensors and cradle holding the nuclear explosives. A 2007 paper he helped write recommended six nuclear missiles, released individually at intervals of about an hour. The bombs would go off in six separate blasts, each with a yield of up to 1.2 megatons (equivalent to about 100 Hiroshima-scale bombs).

With a series of separate pulses, Remo says, you could monitor the effects, making adjustments as you go along. Having several smaller explosions instead of one really big blast also reduces the chances of fragmenting the asteroid, which would make it more difficult to handle, Remo adds. "We want to give it just the right amount of energy — enough to give it a good kick but not so much that you break it into bits."

CAN WE DO IT?

An operation of this sort might take months to pull off, from launch to interception, depending on the size and orbit of the object in question, and how prepared we are. With enough warning, it's definitely possible.

Remo doesn't even consider the technical challenges of conducting an actual space test all that daunting. Seventy-plus years into the era of nuclear energy, Remo says, "that technology is advanced and well-tested. We know how these devices work. And we don't need any major advances in rocketry, either." Ideally, he'd like to test this defensive capability in space, using unarmed warheads to demonstrate that, when the situation arrives, we really could set off the blasts as needed.

Tests involving actual nuclear warheads, however, would be problematic for political reasons, given that several international agreements prohibit bringing nuclear weapons into space, let alone firing them. But these statutes are not cast in stone, and they could be overridden in a life-or-death situation, with the fate of Earth hanging in the balance.

"If a near-Earth object is approaching Earth and we are in great peril, then the U.N. Security Council can make its own decisions about what to do," says Hans Haubold, a senior officer with the United Nations Office of Outer Space Affairs in Vienna, who has co-authored several papers with Remo. "The world powers could meet and determine what technology makes sense for dealing with a particular threat."

Remo fully believes that "when push comes to shove, and our survival is at stake, people will take advantage of any means available to protect the planet — if it comes to that. But they still have to go through the decision-making process, and I'm trying to help them make an informed decision."

If we ever face the prospect of an imminent assault on Earth from a large wayward rock, Remo hopes we can offer a bit more than divine intervention, which was all that Charles Bolden had for Congress in 2013. "I'm not anti-religious," Remo says. "I'm not against praying. But if you're going to pray, maybe you should pray that the rocket works." ◼

***Steve Nadis**, a Discover contributing editor, is co-author of* A History in Sum: 150 Years of Mathematics at Harvard. *He lives in Cambridge, Mass.*

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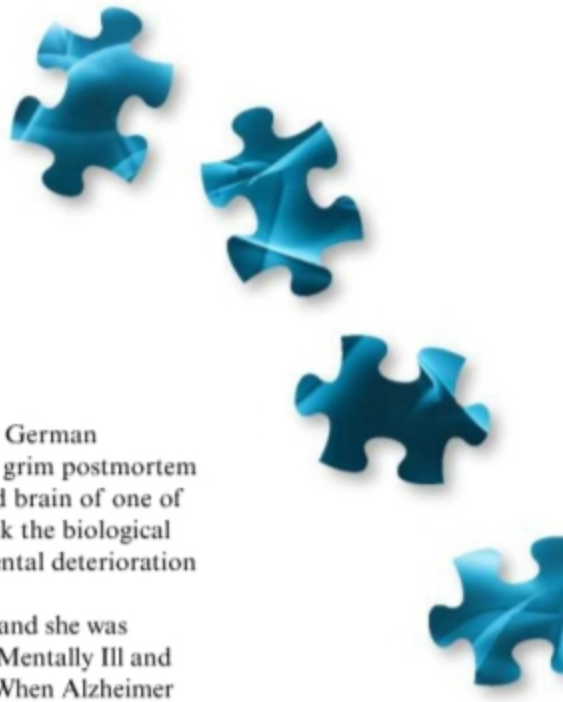


ILLUSTRATION: DAN BISHOP/DISCOVER. HEAD: DIGITAL STORM/SHUTTERSTOCK. PUZZLE: MILAGLIP/SHUTTERSTOCK

Cracking the Alzheimer's Code

Are we close to conquering one of the most ***puzzling diseases*** of our time?

BY **LINDA MARSA**



More than a hundred years ago, German physician Alois Alzheimer did a grim postmortem analysis of the dementia-ravaged brain of one of his patients. He hoped to unmask the biological roots of her severe and rapid mental deterioration and bizarre mood swings.

Her name was Auguste Deter, and she was admitted to the Hospital for the Mentally Ill and Epileptics in Frankfurt in 1901. When Alzheimer first interviewed the 51-year-old woman, she was enveloped in a fog of confusion, and she exhibited delusional behavior: She was intensely jealous of her husband; she sometimes would start screaming, thinking people wanted to kill her; and she became wild and uncontrollable. She died five years later.

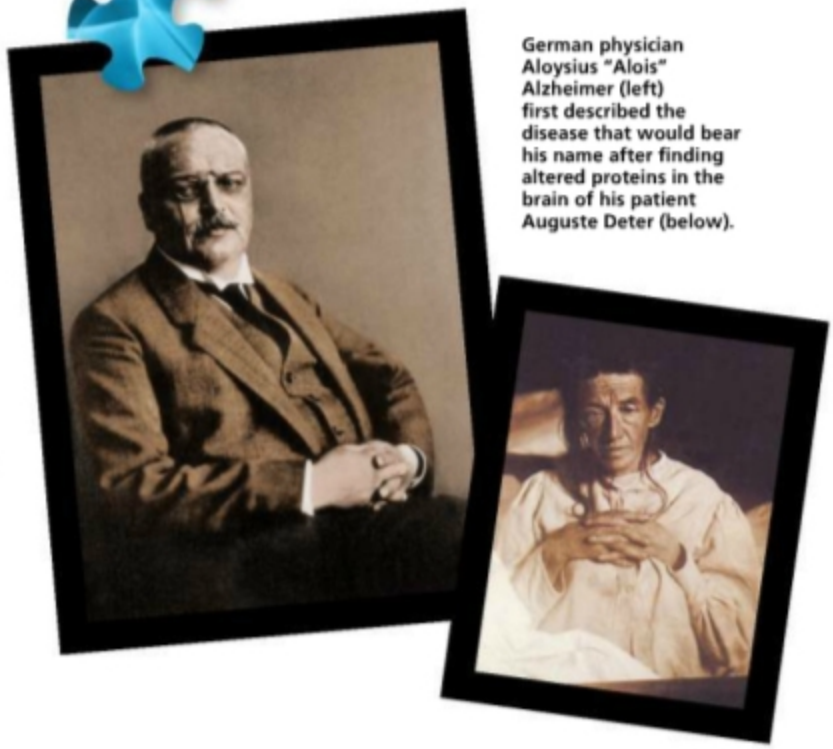
When Alzheimer examined thin slices of her brain under a microscope, he noticed that nestled right next to the labyrinth circuitry of healthy nerve cells were small clumps of hard, barnacle-like



bundles of proteins called amyloid plaques and that many of the fibers extending from the ends of the nerve cells — different proteins called tau — were thickened and tangled. This aberrant brain circuitry — the amyloid plaques and tau tangles — became the twin hallmarks of the disease that bears his name.

For years, scientists have struggled to understand how these proteins work. Why do they go haywire? What comes first — plaques or tangles? And which one is the miscreant that drives nerve degeneration? Are amyloids the toxic bad boys, or the tau tangles? Each camp has long had its devotees. But recent technological advances and a series of remarkable discoveries in the past two years have provided key clues about how Alzheimer's disease ravages the brain.

Although researchers are reluctant to utter the word *cure*, they're tantalizingly close to answering many of the questions that have stymied Alzheimer's research, and they're finding ways to prevent this devastating brain-wasting disease — or at least reduce the damage it causes. "Within our lifetimes, we will conquer Alzheimer's," says Anne Young, a Harvard neurologist and director of the MassGeneral Institute for Neurodegenerative Diseases in Boston. "It's an incredibly exciting time, and everything we dreamed of is coming to reality."



German physician Aloysius "Alois" Alzheimer (left) first described the disease that would bear his name after finding altered proteins in the brain of his patient Auguste Deter (below).

THE LOOMING AVALANCHE

More than 5 million Americans have Alzheimer's, and it's the underlying cause of 500,000 deaths each year. Barring a medical breakthrough, the incidence of the disease is expected to reach epidemic proportions as the nation's 76 million baby boomers move into old age. The number of Alzheimer's patients is expected to hit 100 million worldwide by 2050, including as many as 16 million in the U.S. Such huge demand for care would put unbearable strains on society and could bankrupt health care systems.

This looming avalanche of Alzheimer's has lent greater urgency to the search for treatments. In 2012, the Obama administration earmarked $156 million over two years to fund research, bringing the total to $530 million a year; the goal is to defeat Alzheimer's by 2025. That may seem ambitious, but there is now reason to believe this target may be within reach.

Until now, the quest for effective Alzheimer's treatments has been marked by costly and high-profile failures, mainly because we haven't focused on the right targets — and we're stepping in too late. Scientists believe that by the time the disease rears its ugly head, patients likely have sustained irreversible damage, which may explain why the drugs tested in clinical trials don't do much good.

But there is hope on the horizon: Scientists recently mapped out many of the neural pathways through which Alzheimer's develops. Powerful, new high-resolution visualization tools can peer deep inside a living brain, allowing scientists to track the cascade of events that leads to Alzheimer's. Genetic discoveries have shed light on the underlying biological mechanisms of the disease. Unpacking how these bits of renegade DNA work may provide more clues on how to stop the disease.

This deepened understanding of what drives neurological deterioration should lead to smarter therapies, while new diagnostic tools could allow intervention before too many neurons are destroyed. In the not-too-distant future, "we'll be able to identify those most at risk based on their genetics, do imaging tests to determine the onset and then institute therapies that nip it in the bud," says Rudolph Tanzi, a neurologist at Harvard Medical School. "That's the mantra: early prediction, early detection and early intervention."

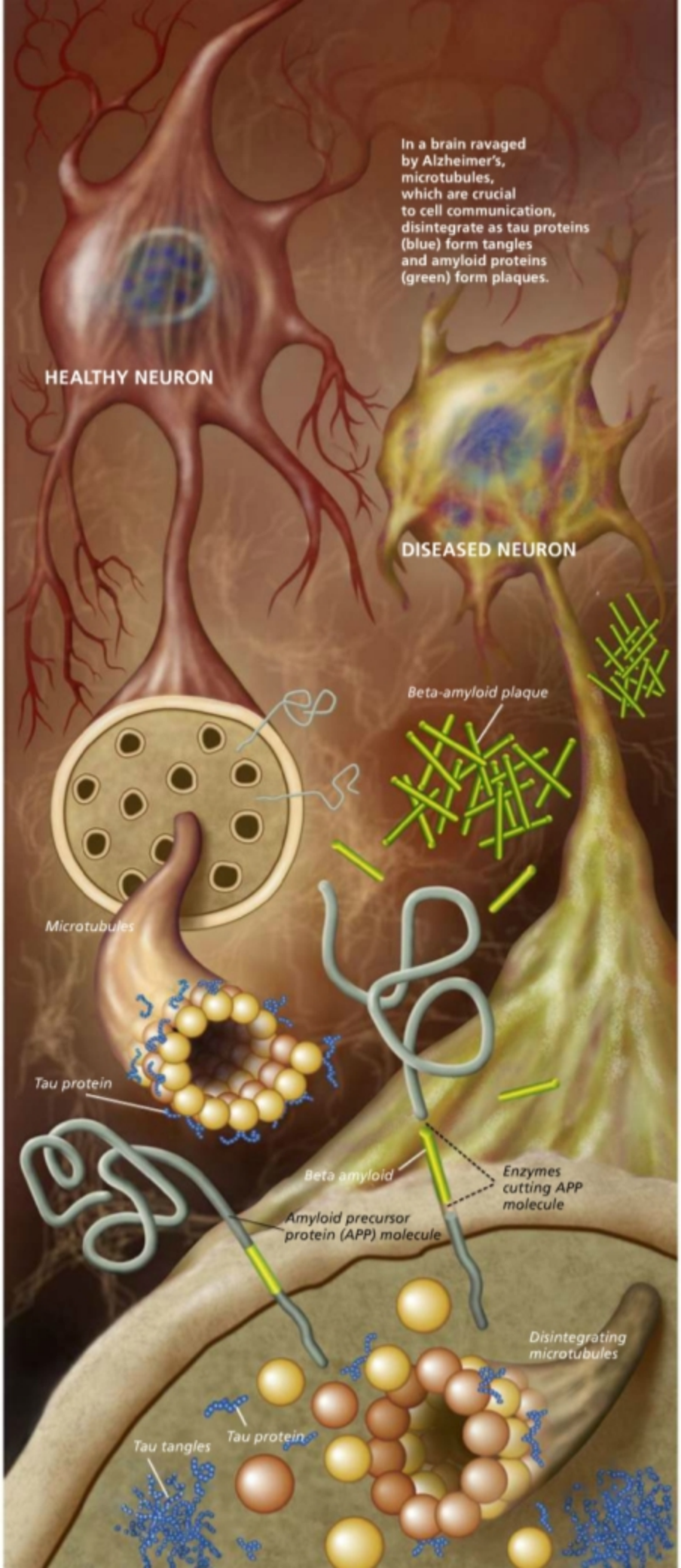
But Alzheimer's is not divulging its secrets easily.

A DEADLY CASCADE

We now know that plaques are clusters of protein fragments called beta-amyloid peptides. They collect outside the nerve cells in the brain and disrupt the signaling system between neurons, blocking them from relaying messages. This communication breakdown explains why Alzheimer's patients suffer progressive memory loss, confusion and increasing difficulty doing daily tasks.

In contrast, the tau protein wreaks havoc *inside* nerve cells, causing

THIS PAGE, FROM LEFT: JESSICA WILSON/SCIENCE SOURCE; PHOTOTAKE, INC./PHOTOTAKE. OPPOSITE: AMY SMITH



the accumulation of spaghetti-like strands that choke the neurons. This disrupts the flow of electrical signals that travel through the nerve cells, ultimately causing them to wither and die. The buildup of twisted tau deposits also destroys surrounding nerve cells and eventually wastes away vast swaths of brain tissue. Other vital structures, the axons and dendrites — known collectively as neurites — that project from the nerve cells and send and receive messages are dependent on this neural transport network. When this network is disrupted by tau tangles, it can trigger a chain reaction of damage in the memory and cognitive circuitry of the brain, accelerating mental deterioration.

Amyloid and tau are both naturally occurring proteins. The body produces amyloid plaques and then eliminates them in a normal biological process of decay and renewal. In some instances, amyloids may even serve a protective function; recent studies indicate they can act as molecular guardians that mute the body's autoimmune reactions. They also mop up the errant cells involved in inflammation after an injury. But for reasons that are yet unknown, when Alzheimer's develops, this protein divides improperly and creates a form called beta amyloid, which is toxic to neurons in the brain. When this happens, the brain generates plaques, which accumulate around the neurons and eventually disrupt the signaling system between brain cells.

Tau proteins, for their part, are vital to the structural integrity of neurons, acting like girders that stabilize synapses — the bridges that allow electrical impulses to cross between neurons. But at some point, tau goes astray, too, and the nerves lose their structural support, causing the cells to collapse and die. In fact, tau tangles may be the real culprits behind memory loss, since they're directly linked to cognitive deficits. People can have amyloid plaques and still function normally, but once they have tau tangles, dementia is evident.

"Tangles drive the dementia and drive the nerve degeneration," says Tanzi, who also is director of the Genetics and Aging Research Unit at Massachusetts General Hospital. "If you don't get tangles, you don't get the disease. Once tangles form, they spread like wildfire and keep spreading. But the biggest gaping hole in our understanding is, how does amyloid drive tangle formation?"

Scientists are beginning to find some clues, through genetic fingerprints and with technologies that allow researchers to watch plaques form.

PEERING INSIDE THE BRAIN

Until recently, the only way to look at human plaques was by analyzing the brains of people who died from the disease — a challenge one scientist compared to looking at a car wreck and trying to puzzle out the accident's cause. We can't just simply peel away a living person's skull to watch what happens in real time or slice off samples to scrutinize under a microscope.

Although the postmortem studies of Alzheimer's patients revealed a mess of plaques and tangles, scientists knew they would need to figure out ways to study living brain tissue to unlock the disease's secrets. Traditional imaging techniques like MRI and positron emission tomography (PET) wouldn't work. They're good at providing snapshots as small as a millimeter and can tell us about brain activity, but they can't capture the formation of human plaques or tangles, which are about 100 microns, or a tenth of a millimeter — about twice the thickness of a cat's whisker.

So until recently, much of what scientists learned was gleaned by inference or from studying mouse models of the disease. But the lab animals are not good surrogates. In the past few years, however, powerful new visualization tools, coupled with novel tracer chemicals that can illuminate even the tiniest bits of brain tissue, have given scientists a glimpse into the inner workings of the human brain.

In 2012, the FDA approved Amyvid, a radioactive dye that attaches itself to amyloid proteins so they can be highlighted on a PET scan. Similar radioactive tracers also have come online. Using chemicals like these in combination with new imaging tools, such as the multi-photon confocal microscope, has enabled researchers to explore the minuscule world of the neuron and observe brain cells in action with far more precision. This microscope is powerful enough to detect objects as small as a single micron — one-thousandth of a millimeter — and plaques are about 10 microns across.

"You can see individual connections between neurons, and watch in real time images of plaque formation," says Bradley Hyman, a neurologist at Harvard Medical School.

TRACKING RENEGADE DNA

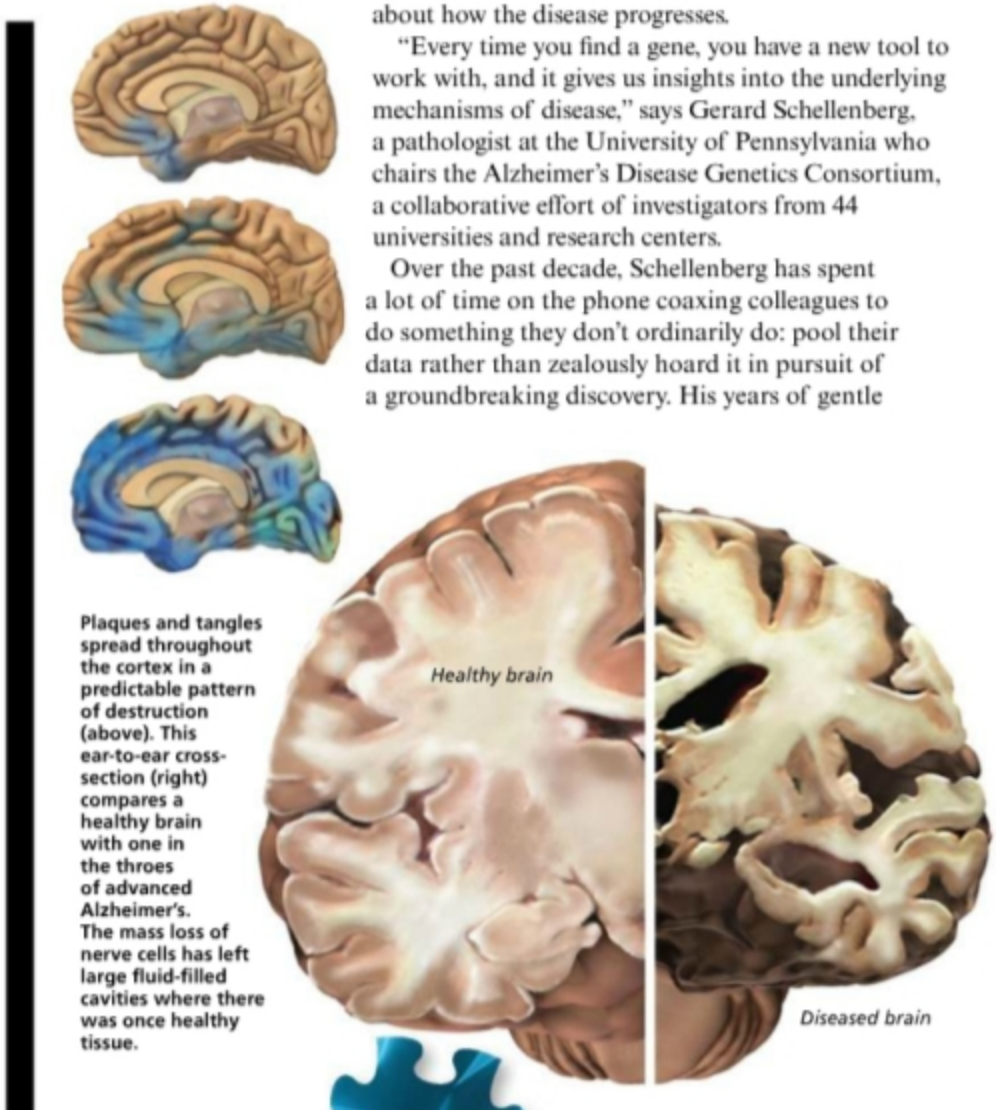
Using these new imaging tools, scientists can now track how errant genes associated with Alzheimer's behave. Although neural degeneration in Alzheimer's disease is a complicated process that happens over many years, the instigating event could be caused by just a few genes going awry. These snippets of renegade DNA are the research target.

Alzheimer's disease can tear through generations of families. In the early-onset form, it claims victims in the prime of their lives, in their 40s and early 50s. It envelops them in a fog of confusion and ultimately erodes relationships and memories. Scientists have spent much of the past three decades hunting down genes linked to this inherited form of the disease. In the past three years, they've uncovered more than a dozen of them.

Spotting the bits of mutant DNA that underlie Alzheimer's may soon lead to genetic tests that can tell whether someone is at higher risk so he or she can take preventive steps. They can also tell us about how the disease progresses.

"Every time you find a gene, you have a new tool to work with, and it gives us insights into the underlying mechanisms of disease," says Gerard Schellenberg, a pathologist at the University of Pennsylvania who chairs the Alzheimer's Disease Genetics Consortium, a collaborative effort of investigators from 44 universities and research centers.

Over the past decade, Schellenberg has spent a lot of time on the phone coaxing colleagues to do something they don't ordinarily do: pool their data rather than zealously hoard it in pursuit of a groundbreaking discovery. His years of gentle



Plaques and tangles spread throughout the cortex in a predictable pattern of destruction (above). This ear-to-ear cross-section (right) compares a healthy brain with one in the throes of advanced Alzheimer's. The mass loss of nerve cells has left large fluid-filled cavities where there was once healthy tissue.

LEFT: NATIONAL INSTITUTE ON AGING/NATIONAL INSTITUTES OF HEALTH. RIGHT: STACY JANNINGS/ALZHEIMER'S ASSOCIATION



Spotting the bits of mutant DNA that underlie Alzheimer's may soon lead to genetic tests that can tell whether someone is at higher risk.

arm-twisting paid off in the creation of the consortium, which collected genetic data from more than 11,000 people with Alzheimer's and a nearly equal number of older people who showed no signs of dementia.

Using genotyping to determine genetic differences, the researchers began to see patterns emerge. They identified four new genes that were more common in those who had the disorder. When three other research groups from the United States and Europe added their patient profiles, swelling the overall numbers to 54,000, their findings were confirmed. The newly unmasked genes play a role in three distinctively different bodily functions, including systems that control inflammation and cholesterol and the regulation of how brain cells clean up toxic proteins. These discoveries build upon previous findings about genes linked to Alzheimer's, such as the *APOE-4* gene, which is a powerful marker for late-onset Alzheimer's disease; about 40 percent of those diagnosed have this DNA variant.

In fall 2013, this international consortium identified 11 more genes that increase the risk of developing Alzheimer's disease, bringing the total number of genes associated with the more common late-onset form of the disease to 21. This expanded collection helps paint a clearer picture of the factors that ratchet up risks. It also offers unprecedented glimpses of the biological pathways that drive the disorder.

Some of the newly spotted genes regulate how nerve cells talk to each other in the brain's memory centers, such as the hippocampus; others are related to immune response and inflammation. This discovery lends more weight to the growing evidence that inflammation — and our immune system's hyperactive reaction in mopping up the cellular debris left by the wayward plaques and tangles — plays a key role in the spread of the disease. "We're starting to connect the dots between the genes and the clinical symptoms," says Tanzi, who is involved in the work. "Plaques and tangles get the process going and nerve cells start to die. But it's not until inflammation kicks in that the process takes off like wildfire — and this is what drives the dementia."

Recent research also has illuminated how the deadly cascade that leads to brain atrophy is set in motion: The buildup of amyloid plaques sparks mutations in the genes that signal the formation of the renegade tau proteins. But which genes? To try to find out, Tanzi is studying the DNA of 3,000 families with multiple members affected by the late-onset form of the disease. The hope is to identify many, if not all, of the other genes and gene mutations that influence risk.

PLAN OF ATTACK

But the real heavy lifting comes with deciphering exactly what these genes do, and creating a mosaic with these bits and pieces that can provide a fuller picture of how the genetic variants work to cause destruction. A startling discovery in 2013 may contain a crucial puzzle piece that could lead to the development of therapies that can stop the disease in its tracks.

It began in 2008, when Harvard researchers fingered the *CD33* gene in a genome-wide dragnet of genes in families affected by Alzheimer's. At the time, they hadn't identified the gene's function. But in a postmortem analysis of brain tissue from patients with late-onset Alzheimer's, scientists noticed there was too much of the *CD33* gene in cells called microglia, which are dispatched by the immune system to repel foreign invaders. There seemed to be a direct relationship between the presence of *CD33* and the number of destructive amyloid plaques.

Normally, these microglia cells are beneficial. They clear out molecular debris, such as dead and dying nerve cells and deposits of the sticky amyloids that could impair brain function. But the microglia cells are hypervigilant and swing into action at the first sign of trouble. Somehow, when the microglia cells are armed with the renegade *CD33*, they go into overdrive, launching an indiscriminate search-and-destroy mission that strafes healthy neurons with friendly fire when too many amyloids start piling up.

"Instead of cleaning up when neurons die, the microglia assume they're under attack when they see too much cell death and kill nerve cells as collateral damage," says Tanzi, who led the research team. "It is now clear *CD33* is the main switch that triggers the microglia to change from a neuroprotective to a neurotoxic function." Finding a compound to block this rogue gene and turn it off, he believes, could stem the damage inflicted by the amyloids.

In fall 2013, Tanzi's group made what has been hailed as a "paradigm shifting" genetic discovery that helped settle the debate over whether it's amyloids or tau proteins that trigger late-onset Alzheimer's. After conducting experiments with a newly developed strain of mice that are good surrogates for Alzheimer's, they found that a gene called *ADAM10* makes an enzyme called alpha secretase, which prevents the formation of beta amyloid. But the mutant form of the *ADAM10*

gene did exactly the opposite: It blunted the action of the enzyme, resulting in the production of more of the toxic proteins. "People with this gene mutation usually get Alzheimer's at around age 70 because of the buildup of amyloids due to the reduced activity of the protective enzyme," says Tanzi. Researchers are now testing modulators of these enzymes in the lab to see if they can fix this defect and prevent plaque production.

But it's not just the bad actors that are being fingered. Researchers have also uncovered snippets of DNA that seem to *halt* the development of the brain disease, even in people whose genes put them at higher risk. Icelandic scientists studying the DNA of 1,795 of their citizens unearthed a rare errant gene — only 1 in 10,000 people of European descent carry the mutation — that slows production of plaques in the brain. They found that people who were 85 or older and didn't have Alzheimer's — or any decline in mental acuity, for that matter — had the mutant gene four to five times more often than those who had the disease. What the researchers found especially astonishing is that this was true even in octogenarians with two copies of the *APOE-4* gene, which is present in about 90 percent of 80-year-olds with Alzheimer's. About 25 of the people over age 85 had two copies of *APOE-4*, yet not one of them had the disease.

The next step is to figure out how the protective mutant gene works and then create a treatment that mimics its action. Accomplishing that feat would represent a giant leap toward a genuine cure. "The gene has been cloned, and we know it interferes with the production of toxic amyloid fragments," says Ralph Nixon, a professor of psychiatry and cell biology at New York University School of Medicine and a past chair of the Medical and Scientific Advisory Council of the Alzheimer's Association. "But we don't know precisely the mechanism by which it is operating — that's the work that needs to be done."



It's not just the bad actors that are being fingered. Researchers have also uncovered snippets of DNA that seem to halt the development of the brain disease.



HOPE ON THE TREATMENT FRONT

Advances in deciphering the genetics of Alzheimer's not only ferret out common DNA variants that more reliably predict risk, they also provide new clues to potential biological targets for drugs to prevent, stop or even reverse the disease. Until now, most promising treatments have fallen by the wayside. Drug companies have lost billions in Alzheimer's therapies that looked good in early research but failed in larger clinical trials, leading one report to characterize the field as "a graveyard of hope."

But those treatments were tested on people who already had symptoms of the disease. Recent studies in those with an inherited form of early Alzheimer's detected the presence of rogue amyloid proteins up to two decades before symptoms emerged, suggesting that we're intervening too late, when the damage is irreparable.

"That led to a search for individuals who are guaranteed by their genetics for developing Alzheimer's and identifying them at an age before they have symptoms," says Nixon. "Then we could treat the disease before it is like a locomotive that just can't be stopped."

In the past few years, two studies were launched to find out whether drugs that shrink plaques can halt the onset of the disease before symptoms appear in those genetically predisposed to develop Alzheimer's. One study, known as DIAN (Dominantly Inherited Alzheimer's Network), involves more than 260 people in the U.S., Britain, Germany and Australia. The other, the Alzheimer's Prevention Initiative, encompasses 300 members of an extended family of about 5,000 who live in Medellín, Colombia, and the surrounding mountain villages.

The DIAN study is composed of families with an inherited form of early Alzheimer's; many relatives have the disease or have died from it. People who harbor the mutant gene sometimes have symptoms in their 30s and 40s, usually around the same age that their parents started to show signs. On average, most develop symptoms before age 45 and are diagnosed with dementia by age 51. No one with this rogue DNA escapes this terrible fate.

DIAN participants were given one of two drugs, called gantenerumab and solanezumab. Both are antibodies that bind to amyloid proteins and help remove the toxic proteins from the brain before they have a chance to turn into plaques. In the study of the Colombian family members who develop early-onset Alzheimer's, scientists are testing another drug, crenezumab, which acts similarly to the other drugs. If these therapies can somehow halt or slow the development of memory loss, confusion or plaque formation, it might be possible to slow the progress of the disease.

Because the subjects in these closely watched studies are at such a high risk, researchers should know within the next few years if the experimental drugs will halt or delay the onset of the disease. "The

characterization of these families has been so thorough, based on all their siblings and parents, that we know when any one person will start to develop cognitive deficits," says Ronald DeMattos, an Alzheimer's researcher at Indianapolis-based Eli Lilly and Co., which makes solanezumab and is co-sponsoring the DIAN trial. "If they progress more slowly than usual within that time frame, that would suggest these treatments are having their desired effect."


Rudolph Tanzi

But what about people who don't have a strong familial history of the disease? In the past year, two other long-term clinical trials began to test therapies that might either prevent or delay Alzheimer's in healthy volunteers who are not genetically at risk of developing the early-onset form of Alzheimer's. One study, called A4 (the anti-amyloid treatment in asymptomatic Alzheimer's trial), will test solanezumab in 1,000 cognitively normal people age 65 to 85, who have abnormally high levels of amyloid proteins. Participants will be selected based on the results of a PET brain scan to detect the presence of the haywire proteins.

The other trial, called the TOMORROW study, will give an FDA-approved diabetes drug, pioglitazone, to healthy volunteers to see if it can delay the first symptoms of cognitive impairment. The clinical trial will eventually encompass 5,000 participants who harbor two specific genes linked to Alzheimer's: *APOE* and *TOMM40*. An observational study conducted by German scientists in 2014 suggests that long-term use of this drug may protect against dementia. Using prescribing information from a German database, they looked at 145,000 adults 60 or older who did not have dementia. During follow-up six years later, they found that 10 percent of the cohort — about 14,000 people — developed dementia, but the risk was lower in those who were taking the diabetes medication. "People with diabetes may have an increased risk of Alzheimer's," says Keith Fargo, director of scientific programs and outreach at the Alzheimer's Association. "The drug may reduce these odds by controlling glucose metabolism and because it has an anti-inflammatory effect. Many researchers now believe inflammation plays a big role in Alzheimer's."

And in another advance, a research team led by Tanzi has concocted what they call "Alzheimer's in a dish." The team used human embryonic stem cells — which can transform into any cell of the body — and cultured them in a mixture of chemicals to grow human brain cells. Then they implanted Alzheimer's genes into the neurons, which obligingly began churning out the telltale clumps and tangles that characterize the disorder.

"Within six weeks, the nerve cells produced amyloids, and within eight weeks, we got tangles," says Tanzi. "This is a much better model than what we have, and it's faster and cheaper. We can now screen drugs within two months in a dish."

This discovery will solve one of the key stumbling blocks in devising therapies: the lack of a human model that can shed light on how the disease progresses. Scientists characterize the advance as a game changer that could dramatically accelerate the testing of new drug candidates.

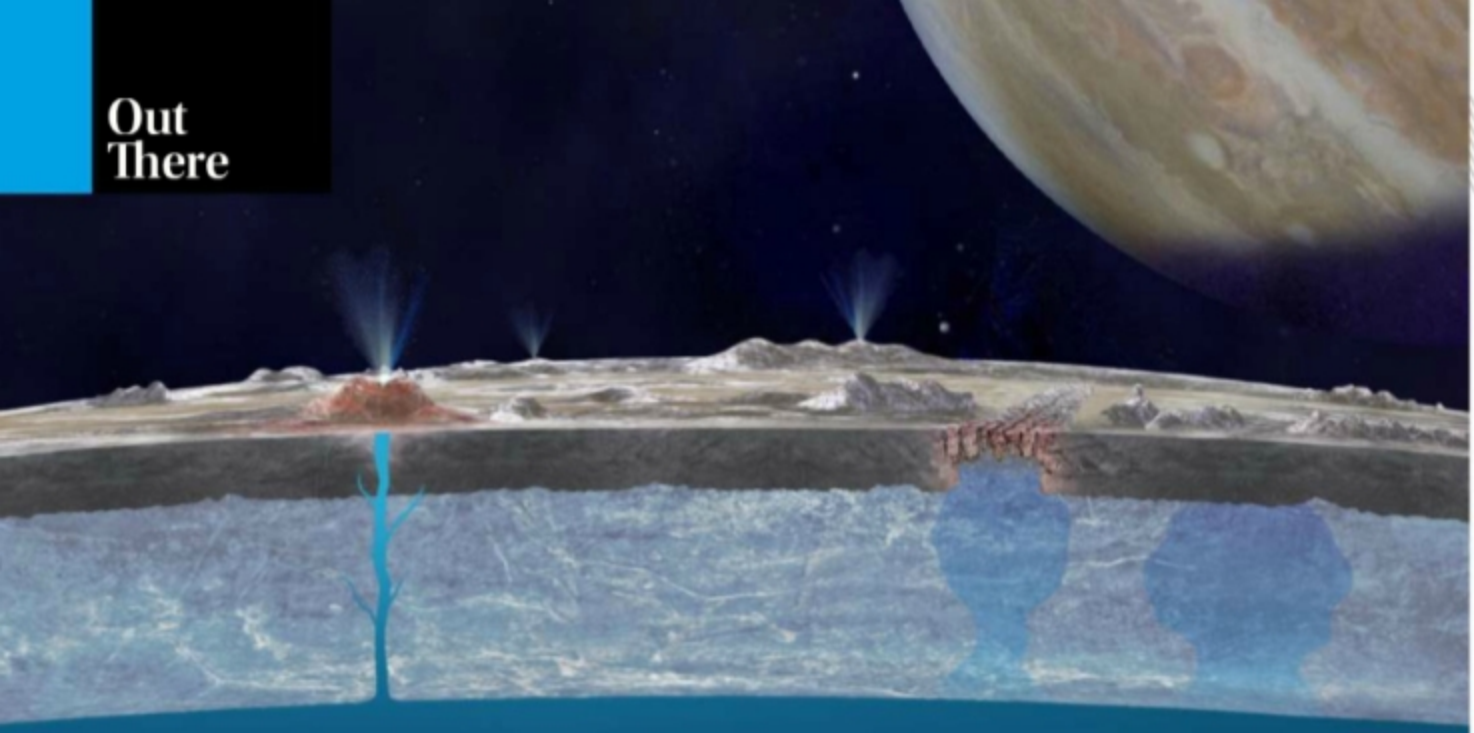
It's likely that a combination of strategies will be needed to halt the disease's progression, using a cocktail of medications aimed at different targets in much the same way AIDS and many cancers are now treated.

"We've been operating under the assumption that a single drug would do the trick in terms of reversing the deficits," says Frank LaFerla, director of the Institute for Memory Impairments and Neurological Disorders at the University of California, Irvine. "But it's like trying to put out a raging fire with a bucket of water. Once a fire reaches that point, you need to bring out the firetrucks and helicopters." D

Linda Marsa *is a contributing editor for* Discover *and author of* Fevered: How a Hotter Planet Will Hurt Our Health and How We Can Save Ourselves (Rodale).



JOSH REYNOLDS



Alive on the Inside?

Many small, frozen worlds seem to have warm underground oceans, making the search for alien life more exciting — and more confusing.

BY COREY S. POWELL

The watery depths of Jupiter's moon Europa might interact with its icy crust (as illustrated above), making the existence (and detection) of life there more likely.

"Follow the water." That's been a guiding principle in the modern search for extraterrestrial life, based on the overwhelming evidence that all living things on Earth — no matter how exotic or extreme — require water to survive. For the past two decades, this emphasis on water has focused attention on Mars, where NASA has intently sought evidence of ancient rivers or modern trickles. Each eroded pebble and layer of sediment there has been heralded as an important clue.

Lately, though, the celestial dowsing process has been pointing in a sharply different direction, away from the majestic deserts of the Red Planet and toward a motley assortment of small, frozen bodies. The shift began in the late 1990s, when the Galileo spacecraft gathered evidence that Jupiter's moon Europa has a thick layer of water beneath its icy crust. No need to mince words: "Thick layer of water" is another way of saying "a vast, global ocean," one that just happens to be sequestered underground (or rather, under ice). Europa may hide twice as much water as all Earth's oceans put together.

Any thought that Europa was an anomaly soon evaporated with the discovery of geysers on Enceladus, a 300-mile-wide satellite of Saturn. Then the, er, floodgates opened as scientists began reporting evidence of water sloshing around inside Jupiter's moon Ganymede, Saturn's Titan and Mimas, and perhaps Neptune's Triton. There may be water layers inside Pluto and the dwarf planet Ceres, too.

> **No need to mince words: "Thick layer of water" is another way of saying "a vast, global ocean."**

"Instead of being the exception, maybe it's normal to have an ocean in an icy body," says Louise Prockter, a Europa expert at Johns Hopkins University. "And there are so many icy bodies we haven't even looked at yet."

Taken together, the evidence suggests that little ice worlds contain much, perhaps most, of the warm, wet real estate in the solar system. That epiphany inevitably leads to a pair of captivating questions. Could organisms really eke out a living in the eternal darkness of a subterranean ocean? And if so, does that mean our Mars-obsessed space program has been diligently looking for life in all the wrong places?

EUROPA UNION

As soon as I mention life, Prockter pauses and offers a gentle but firm disclaimer that she is not looking for

NASA/JPL-CALTECH

"bugs" on Europa. "I've been horribly misquoted in the past," she sighs.

True enough, but her work is central to addressing those existential questions. If anything lives on Europa, it probably needs a way for fresh materials to circulate from the surface down into the ocean. And if we want to find that alien life, it will be a lot easier if some stuff from the oceans migrates back up to the surface. The underlying issue, then, is whether the icy crust of Europa is dynamic and vital, or if it is more of an immobile casket. That's where Prockter comes in.

About two years ago, she sat down with Simon Kattenhorn, a friend and colleague at the University of Idaho, and mapped out an enigmatic region where Europa's landscape resembles a jigsaw puzzle. When the two researchers fit the pieces together, re-creating the original landscape, they found "a big hole in the middle" — a place where the original crust went missing. It almost surely ended up below the surface, shoved by the pieces' motion, where it got recycled into the moon's interior.

If old crust is disappearing in some places, then new crust must be forming elsewhere. That fits with other evidence that the cracks on Europa's surface are slowly spreading, presumably pulling up stuff from below in the process. "There is material on the surface that's quite likely ocean material," Prockter says.

Bolstering that view, the Hubble Space Telescope recently detected large, intermittent clouds of water vapor hovering around Europa's southern hemisphere. The strong implication is that liquid water lurks just below the surface, perhaps in glacial lakes akin to Lake Vostok in Antarctica. During local high tide, fissures in the ice crack open and water squirts out, forming a plume. That discovery parallels the current interpretation of the jets on Enceladus, driving home Prockter's larger point: "We think of Europa as the poster child for icy satellites. If we can understand Europa, we'll make great leaps toward understanding these other bodies."



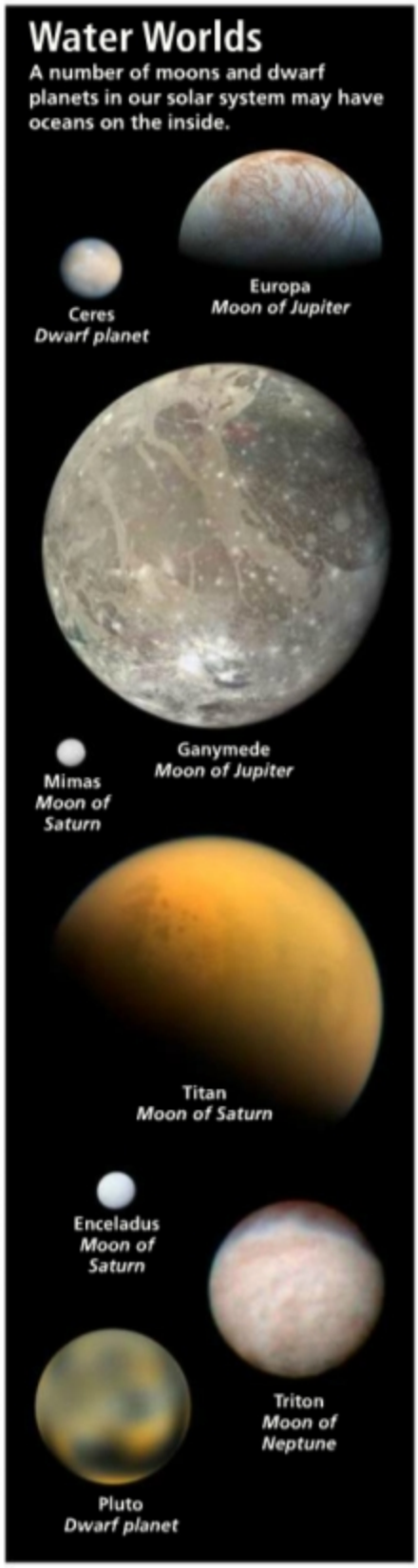
Sunlight glints off Kivu Lacus, a 48-mile-wide hydrocarbon lake on Saturn's moon Titan, seen in a near-infrared image from the Cassini probe.

Europa and Enceladus seem to represent one extreme of the water worlds, places where the ice is thin and the ocean is just barely out of reach. With geothermal heat welling up from below and energetic compounds raining down from above, it's not hard to imagine how life might gain a foothold on those moons. For Ganymede, Mimas and the rest, the liquid layer is probably locked away deeper, dimming prospects for life. Titan is a special case because it has hydrocarbon lakes on the surface in addition to a likely ocean underneath, making it a doubly liquid world that is literally awash in organic chemicals.

"There's still a lot to be discovered on Titan; I hope there will be repeat missions, not just one," muses Caltech's Ed Stone. As lead scientist on the historic Voyager project, he oversaw the original reconnaissance of Titan in the 1980s. But in 2012, NASA rejected a proposed spacecraft mission to Titan's lakes in favor of another trip to — you guessed it — Mars.

TAKE ME TO THE OCEAN

More broadly, the efforts to learn more about the hidden water worlds have proceeded at an agonizing half-pace. True, this year Ceres and Pluto will get robotic visitors, the



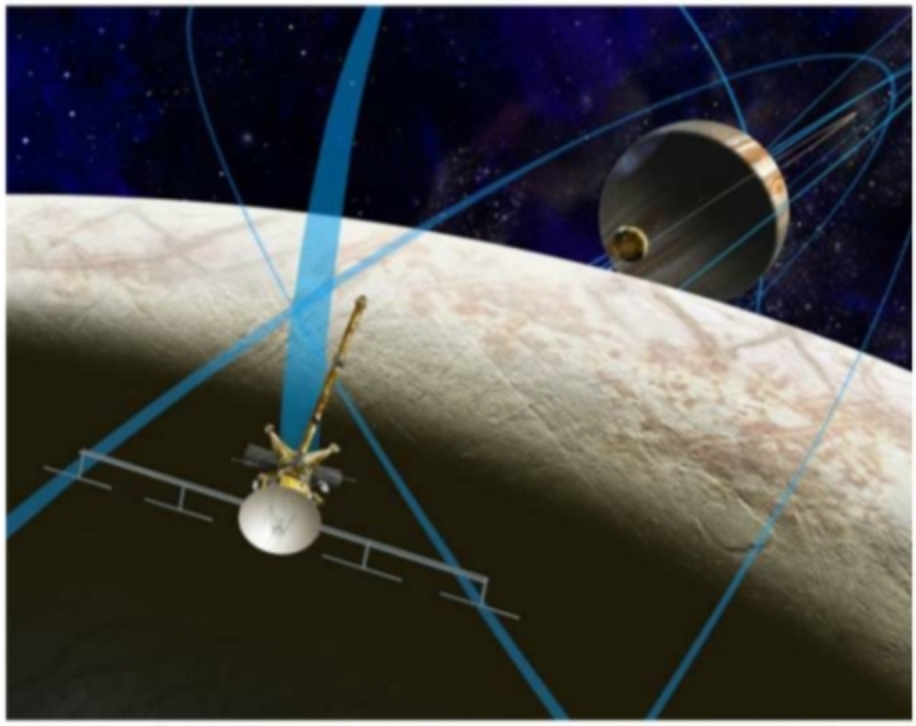
TITAN: NASA/JPL-CALTECH/UNIVERSITY OF ARIZONA/UNIVERSITY OF IDAHO. WATER WORLDS FROM TOP LEFT: NASA/ESA/SWRI/CORNELL UNIVERSITY/UNIVERSITY OF MARYLAND/STSCI; NASA/JPL-CALTECH/SETI INSTITUTE; NASA/JPL-CALTECH (5); NASA/ESA/M. BUIE (SOUTHWEST RESEARCH INSTITUTE)

Dawn and New Horizons probes, respectively. The results should clarify those dwarf planets' inner structures, but they're unlikely to reveal much about life. Meanwhile, Europa, the archetype of the breed, hasn't received a second look since Galileo's termination 12 years ago.

The obstacles are both practical and political. Europa has the best-understood and most-accessible of the buried oceans, but even a probe on the surface would have a hard time figuring out what is happening beneath its ice.

At the same time, NASA's obsession with Mars means little money is left over for a Europa mission — and the money needed would be substantial. Not only is Europa much farther from Earth, but it also orbits within Jupiter's fierce radiation belts, so any probe there would need protection against destructive particle blasts. A meaningful exploration of Europa would probably cost at least $2 billion.

But wait! Help is on the way — from Congress of all places. Support there is steadily growing for the Europa Clipper, a concept that NASA has been nurturing and refining for the past few years. Prockter, who helped define the spacecraft's scientific goals, is cautiously optimistic that this mission will really happen. NASA is currently evaluating proposals for specific instruments.



NASA's proposed Europa Clipper mission would give us an unprecedented look at Jupiter's fractured satellite (foreground in this illustration). The probe's long, looping orbit around planet and moon would find out if the watery Europa might be capable of hosting life — assuming NASA can fund it.

In its latest guise, the Europa Clipper would make repeated, rapid swoops past Europa before retreating to safer distances from Jupiter. Here at last is where the real answers could begin. Flying through the moon's liquid plumes, the Clipper could map their sources and get a direct sample of Europa's ocean, tasting for hints of biochemistry. Further ahead, some researchers envision submarines somehow breaching the Europan ice to take a direct look, or radiation-hardened rovers conducting life-science experiments at the edges of the geysers. But these are all distant possibilities, decades away at least.

"There might be a massive, well-developed ecosystem under the ice that we'll never get to see — at least not anytime in the near future," Prockter says wistfully.

It reminds me of President Kennedy's words in 1962: "We choose to do these things not because they are easy, but because they are hard." I'm also thinking about the Space Age lesson we've learned over and over since then: Each time we summon our resources and tackle the hard things, we achieve a new and deeper relationship with the universe.



The subsurface ocean of Europa contains more than twice as much water as Earth's oceans. That's a lot of real estate for possible Europan life, with energy provided by geothermal heat.

Corey S. Powell**, editor at large of* Discover, *also writes the magazine's Out There blog. Follow him on Twitter, **@coreyspowell

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William Cho (landscape); Mike Reynolds (eclipse)

Unraveling the Mystery of Ancient Egypt's Roots

The earliest mummies reveal how culture and climate created the world's first state.

BY **GEMMA TARLACH**

Pyramids and pharaohs: iconic images of ancient Egypt, but what came before the massive tombs and elaborate burials? New analysis of old evidence is shaking up conventional thinking about how early, how quickly and even why prehistoric nomadic societies coalesced into the world's first formal state.

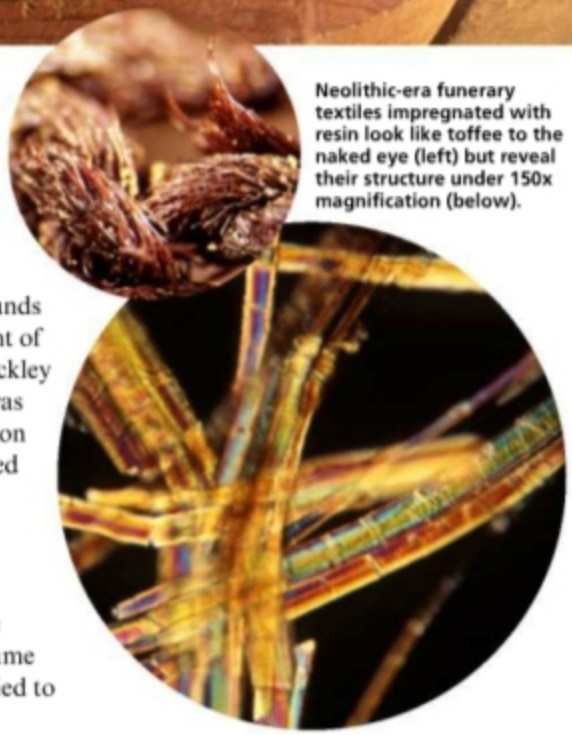
A key to understanding the surprising new chronology of ancient Egypt's foundation can be found in tiny, "toffee-like" shards of material, some of which are more than 6,000 years old.

In 2014, researchers rewrote the timeline for mummification — moving its start back in time by millennia — when University of York archaeological chemist Stephen Buckley analyzed several fragments of funerary textiles and reed matting dating from 4500 to 3350 B.C. The fragments spanned two key periods in prehistoric Egypt: the Late Neolithic, or Badarian period, and the Predynastic, or Naqada period. The material, excavated in Egypt in the early 20th century, was residing in the Bolton Museum in northwestern England. The fragments were significant because the location, and the archaeological context in which they were found, had been accurately recorded — a rare find for material this old.

Using gas chromatography-mass spectrometry (GC-MS), Buckley hoped to succeed where two previous attempts by chemists had failed: to extract and identify the components of a dark golden-brown substance that had been applied to the funerary fabrics in preparation for burial.



Mummification in ancient Egypt was at its height when Ramses II (above) reigned during the second millennium B.C., but the practice was established 3,000 years earlier.



Neolithic-era funerary textiles impregnated with resin look like toffee to the naked eye (left) but reveal their structure under 150x magnification (below).

"GC-MS is great for separating out a complex mixture into individual compounds and then giving you a fingerprint of each separated compound," Buckley says, acknowledging his work was still difficult due to contamination by 20th century materials applied during conservation work.

What Buckley's analysis revealed surprised even him. The components of the toffee-like material, and their relative proportions, were nearly the same as the recipe of a mixture applied to

FROM TOP: PATRICK LANDMANN/PHOTO RESEARCHERS/SCIENCE SOURCE; RON OLDFIELD AND JANA JONES/UNIVERSITY OF YORK; OLDFIELD



Researcher Stephen Buckley has found Egyptian mummification methods were consistent for millennia.

JOANN FLETCHER

textiles during mummification at the height of the practice in Egypt, around 1500 to 1000 B.C.

In addition, certain ingredients, such as resin from coniferous plants, showed evidence of being heated and processed before application, confirming that collecting, making and applying the concoction were intentional acts, not merely an accident of nature or guesswork.

"They had an understanding of empirical science. They were conducting experiments and making observations," says Buckley.

The study Buckley and colleagues published in the journal *PLOS One* showed that mummification was established much earlier in Egypt than we knew — as early as 4300 B.C., during the Badarian period, rather than about 2500 B.C., after the foundation of the Egyptian state, as previously thought.

The findings also complement a new and more precise chronology for ancient Egypt, published in 2013 by another group of researchers. That chronology revised the time of the shift between two prehistoric periods — a crucial transition between earlier nomadic herding societies of the Badarian and the later Naqada society, settled and practicing intensive agriculture in the Nile Valley, that would give rise to the Egyptian state.

During the Neolithic, Egyptians had an understanding of empirical science. They were conducting experiments and making observations.

ESTABLISHING A NEW TIMELINE

When estimating the course of events in prehistoric Egypt, archaeologists traditionally had worked with a *relative* chronology based on the evolution of pottery styles. That conventional approach had established that the nomadic societies of the Badarian period transitioned to the agriculture-based settlements of the Naqada period about 4000 B.C.

In 2013, however, a multidisciplinary team took a new look at — and applied a new method to — existing archaeological evidence. Researchers combined radiocarbon dating with statistical modeling to create an *absolute* chronology that was less subjective than previous timelines. They pinpointed the start of the Naqada period to approximately 3800 to 3700 B.C.

When looking back over millennia, a couple of centuries might seem like a modest change. But the absolute chronology's new start date of the Naqada period, 3800 to 3700 B.C., is important because it establishes that the period between nomadic herders transitioning to permanently settled farmers and then into a unified political state was much faster than we thought.

Archaeologists working with the traditional relative chronology had placed the foundation of ancient Egypt as late as 2900 B.C. The new absolute chronology puts the unification of the region into a state, under one ruler, at 3100 to 3050 B.C. Transitioning from nomadic herders to an organized political state built on permanent agricultural settlements in a mere six or seven centuries is lightning fast in the world of ancient state formation. By contrast, the period between the establishment of permanent settlements and intensive agriculture in Mesopotamia and the rise of the ancient Sumer civilization as a unified political entity was nearly two millennia.

Again, Buckley's chemical analysis of those toffee-like bits provides a clue as to how prehistoric Egyptian society coalesced so quickly.

The analysis proved that the practice of mummification was already established as early as the fifth millennium B.C. and that the core recipe already had been worked out and would remain nearly unchanged throughout the course of the civilization. That implies that the scattered, nomadic herders of the early Badarian period were not so disorganized, or so primitive, as archaeologists had commonly believed.

"They were incredibly complex," says Michael Dee of the University of Oxford, a co-author of the

first absolute chronology. He also co-authored a 2014 paper in *Antiquity* that found people of Neolithic Egypt and northern Sudan already shared well-established, consistent beliefs and practices about decorating the body in life and in death. That shared belief system made sudden cohesion into a formal state possible.

"It's not surprising that they could bind together so quickly," says Dee. "You could see in the culture they already shared the start of what would become a culture around the king, entombing him in grand pyramids."

Buckley agrees, noting that the ingredients he identified in the mummification materials — including some sourced from as far away as modern-day Turkey — indicated a sophisticated culture with established rituals and symbolic values attached to materials used in preparing the dead for burial.

THE ROLE OF CLIMATE IN A RISING CULTURE

But why did nomadic herders, ranging for millennia across much of what is now Egypt and northern Sudan, choose suddenly to settle and begin intensive agriculture in the relatively restricted area of the Nile Valley?

Some archaeologists believe that climate change was the catalyst.

In 2006, researchers pointed to data from 150 sites across the eastern Sahara that showed the region underwent significant desertification over several centuries, beginning about 5300 B.C. Conditions became so arid that even once-inhabited oases and highland refuges were abandoned by 3500 B.C. — just as previously nomadic populations were settling into Nile Valley farming communities, driven to the fertile floodplain by the encroaching desert.

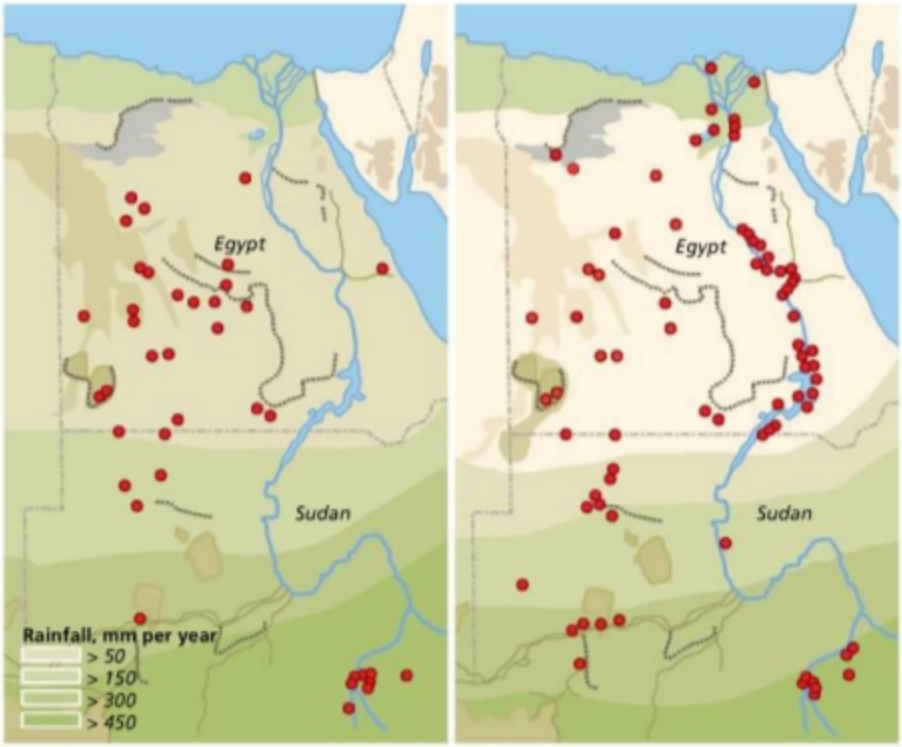


"There was a drying up of the Sahara, and people headed to the Nile Valley, that's true," says Dee. "But there's more nuance. The people settling the Nile Valley already shared long-term cultural identities that tied them more closely together than anything to do with climate change."

The overall pace of desertification quickened about 3800 to 3700 B.C., the date of the onset of the agricultural, Nile Valley-based Naqada period, according to the absolute chronology. In an intriguing way, Buckley's chemical analysis of funerary textiles also supports the idea that it was climate change that forced the nomadic herders into farming the Nile Valley instead.

In his analysis, Buckley identified unusual fatty acids that appeared to have come from marine sponges in the material from earlier Badarian-era specimens. The compounds were in only one of the Naqada samples, however, and even then were found in a much lower amount (2 percent compared with more than 20 percent in the Badarian samples).

Buckley believes the marine-based fats in the mummification of Badarian-era bodies represented the connection the nomadic herders had to the sea, scores of miles from the Nile Valley. As desertification funneled them into the valley itself, and into intensive agriculture, they lost that connection. Land animal fats, such as those from sheep, replaced the ingredient once derived from marine sponges — and would, millennia later, provide tangible evidence explaining ancient Egypt's mysterious origins.



In 2006, researchers used radiocarbon-dated material from 150 archaeological sites in the eastern Sahara to map a change in settlement patterns that coincided with increased desertification of the region. From 7000 to 5300 B.C. (left), human settlements, indicated above by red dots, were established throughout the area. From 5300 to 3500 B.C., as the desert encroached, settlements clustered in the fertile Nile Valley.

Gemma Tarlach *is senior associate editor at* Discover.

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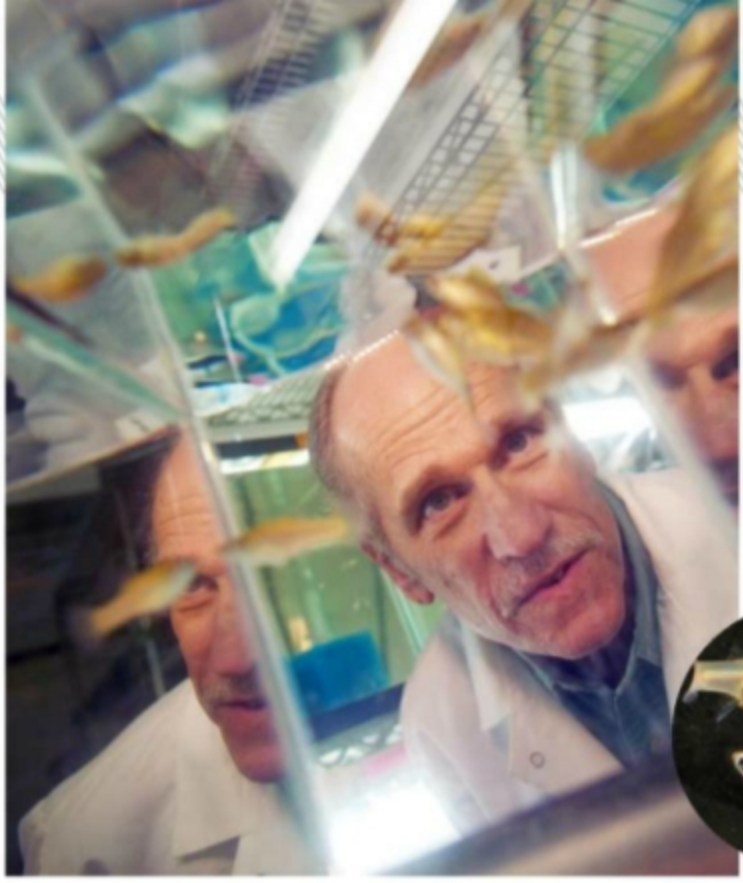
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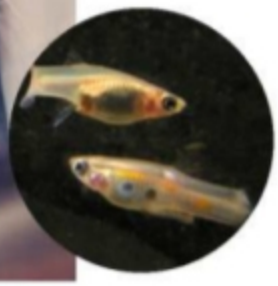
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Life in the Fast Lane

Some species are evolving far more quickly than Darwin ever imagined.

BY **JANE BRAXTON LITTLE**





Biologist David Reznick examines a few of his lab subjects. Reznick's study of Trinidad guppies (below) revealed that the fish can evolve rapidly.

As a graduate student in the late 1970s, David Reznick set out on a modest quest to test a key part of the theory of evolution. Reznick wanted to examine Charles Darwin's concept of the struggle for existence — specifically, how predator-prey interactions shape the evolution of new species. Enthusiastic and ambitious, he intended to do it in the wild. "I wanted to watch evolution happen," says Reznick, now an evolutionary biologist at the University of California, Riverside.

So in 1978, he flew to Trinidad in search of guppies. Armed with a topographic map traced onto a piece of notebook paper, he headed into the Caribbean island's rugged Northern Range. Working under a canopy of tropical trees amid squawking birds, multicolored butterflies and boas, he collected 1,600 guppies, a colorful fish species so prolific that the females can produce dozens of babies every three to four weeks. Reznick was curious to see if predators could affect genetic adaptation in guppies over a short time.

It was not considered a promising experiment. A century earlier, Darwin had assumed that evolution takes tens to hundreds of thousands of generations to produce new species — a plodding path so slow it is essentially invisible. That theory still held sway when Reznick began grad school in 1974. Scientists had studied evolution in controlled laboratory experiments, but watching it happen in a natural setting in a human lifetime was considered improbable at best, more likely impossible.

"I was hanging my career on the idea that you could change the environment and see things evolve significantly in time to get tenure," Reznick says. "People thought my thesis was cute, but doubted I would live long enough to see the results."

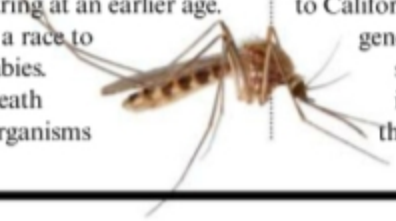
Undaunted, in 1981 Reznick returned to Trinidad's swift streams to test his theory. He transplanted guppies from a site where they had to fend off cichlids, an aggressive, wide-mouthed fish, to a new site with no predators and no other guppies. Reznick also introduced cichlids to guppy sites without predators.

He found that within four years — a mere six to eight generations — male guppies had significantly changed their reproductive patterns. Those transplanted from a high-predation site to a stream without predators were larger, matured later and reproduced more slowly. Where Reznick had introduced predators, the guppies adapted by maturing at an earlier age. Survival became a race to produce more babies.

"The risk of death alters the ways organisms allocate resources for survival," Reznick says.

The results of his federally funded study prompted what he calls one of his proudest moments in science: a *National Enquirer* story with the headline, "Uncle Sam wastes $97,000 to learn how old guppies are when they die." Actually, Reznick chuckles, "I learned a great deal more than that." His work with the guppies changed his thinking about how quickly species can evolve. And it helped launch a paradigm shift in scientists' thinking about evolution.

In the decades since Reznick's first trip to Trinidad, other studies have demonstrated a fast drive toward adaptation that scientists have come to call "rapid evolution." Researchers who once assumed evolution required millennia are documenting species adapting in mere decades, or even shorter time frames. Mosquitoes that colonized the London Underground in 1863 are now so different they can no longer mate with their above-ground relatives. Chinook salmon from Alaska to California needed just a human generation to become smaller and shorter-lived after an increase in commercial fishing in the 1920s. Adaptation is



FROM TOP: LONNIE DUKA/COURTESY OF UNIVERSITY OF CALIFORNIA RIVERSIDE; PAUL BENTZEN/DALHOUSIE UNIVERSITY; KIM TAYLOR/NATURE PICTURE LIBRARY

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Anole lizard

happening right under our noses, in our lifetimes.

Most recently, evolutionary biologist Yoel Stuart found that green anole lizards on islands in Florida's Indian River Lagoon needed just 20 generations to adapt to an invasion of brown anoles. Driven to higher perches by the invaders, the green anoles became better at clinging to branches by developing larger toepads with more scales — in just 15 years. It's more evidence of "evolutionary change on observable time scales," says Stuart, now at the University of Texas at Austin.

Many of the extraordinary adaptations happening around us may be because of us. As human activity disrupts climate patterns and modifies habitats, rapid evolution appears to be an increasingly common strategy for survival.

The effect of warming temperatures on tawny owls is one of the first documented examples of adaptation to climate change in a wild population. Finnish ornithologist Patrik Karell and others found in a 2011 study that the coloration of the owls morphed in response to warming winters in Finland.

Tawny owls come in two colors, pale gray and reddish brown. Until recently, natural selection favored the pale shade, which gave owls a better chance at survival in a snowy landscape. As winters became milder, Karell noticed a steady increase in the proportion of reddish-brown owls.

"Even subtle alterations shape how organisms evolve," Reznick says.

Species are evolving at speeds that Darwin could not have imagined. But not all species can adapt quickly enough to evade harm. When a non-native species arrives in an ecosystem, the native species often are ill-equipped to defend against the foreign invader. Ash trees in North America, for example, lacked "evolutionary accommodations" to protect against the emerald ash borer when it arrived from Asia, Reznick says. As a result, tens of millions of ash trees across the continent are threatened by the green beetle, which is thought to have hitchhiked to the U.S. in wood crating or pallets.

Today's evolutionary biologists have the analytic power to track species adaptation like never before. Advances in molecular biology allow them to identify the very genes that help individuals move away from their ancestors as they adapt to new conditions. For example, a team of scientists at Harvard Medical School and Princeton identified *BMP4* as the key gene that sculpts the beaks of the Galapagos finches that gave Darwin his first inklings of the theory of evolution.

"We are no longer forced to infer evolution from its historical footprints in the fossil record or from dusty collections of moths," Reznick says.

Reznick and his team continue to transplant guppies in the tropical streams of Trinidad. Along with other new tools of evolutionary biology, such as DNA analysis, they are using a technique Reznick developed to mark individual guppies so they can more easily recapture them later. This marking method allows his team to reconstruct the pedigree of individual guppies and measure their reproductive success. The research is answering questions about how predator-prey interactions shape evolving species, but it has also generated new questions: If environmental forces can change guppies, could the guppies themselves also change their ecosystems? Intrigued, Reznick has turned his attention to how ecological and evolutionary processes interact.

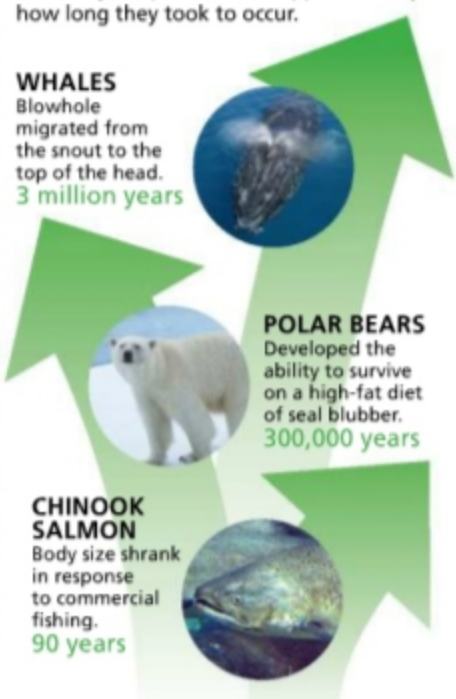
Now he's not only monitoring guppies; he's also watching their predators to see how the interaction changes the ecosystem. His team wants to know how guppies adapt to predators as well as how predators evolve in response to guppies — the ecological cause-and-effect relationships.

"What hardly anyone's thinking about is that the animals and plants left behind may have evolved and are different from what they were before predators were eliminated," Reznick says. This raises fundamental questions about ecological restoration, invasive species, natural selection and what else changes when the fittest actually survive.

Documenting the rapid evolution of species in natural settings turns Darwin's "mystery of mysteries" into a real-time scientific adventure. And while Reznick has succeeded in watching evolution happen, he's beginning to think his earlier calculations underestimated how quickly species actually adapt in nature. "What's exciting," says Reznick, "is that it is now feasible to incorporate evolution into our thinking about how the world is changing."

TIME FOR A CHANGE

Adaptation drives evolution, but timelines for those changes vary wildly. Below are three key adaptations and approximately how long they took to occur.



Jane Braxton Little *writes about science and natural resources from northeastern California.*

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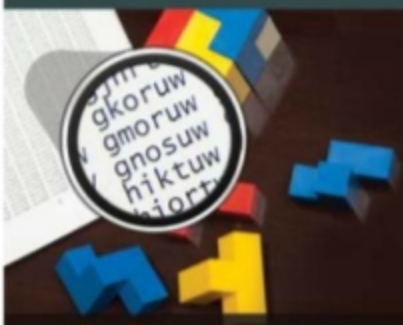
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Nuclear Accidents

BY KRISTEN POPE



A road sign warns of radioactivity near Chernobyl, the site of the world's worst nuclear accident.

ANATOLI KLIASHCHUK/DEMOTIX/CORBIS

1 The worst nuclear accident in history, the 1986 Chernobyl disaster in Ukraine — then part of the Soviet Union — will leave measurable radioactive contamination in a 15,000-square-mile area for 300 years. **2** Shortly after the accident, needles on pine trees in a 1.5-square-mile area around the crippled nuclear plant turned red. The trees now growing there resemble mangled, warped bushes and lack central stems. **3** Scientists studying barn swallows near Chernobyl from 1991 to 2006 discovered 11 types of abnormalities, including malformed beaks and deformed feathers. **4** The brains of 48 species of birds around Chernobyl have been found to be 5 percent smaller than average due to radiation-caused oxidative stress, possibly decreasing cognitive activity. **5** Researchers measured a higher and less variable mean level of radiation — compared with post-disaster measurements at Chernobyl — around Japan's Fukushima Daiichi Nuclear Power Plant after its 2011 meltdown. **6** Six months after the Fukushima meltdown, 28 percent of pale grass blue butterflies in the area had deformities such as altered wing patterns and malformed antennae and legs. **7** The first-ever study of radiation exposure on wild primates, conducted in 2012, found that monkeys near Fukushima had significantly lower red and white blood-cell counts compared with monkeys elsewhere in Japan. **8** But nuclear accidents aren't bad for all species. Melanized fungus contains melanin that actually helps it convert gamma radiation into energy. **9** Spiders in the Fukushima region also seemed to benefit after the disaster. Their numbers increased, possibly because radiation slowed their insect prey and made them easier to catch. **10** Scientists predicted that Pacific bluefin tuna subsistence fishermen in Japan and California would face only minor risks from Fukushima's excess radiation, with two additional cancer deaths per 10 million people during their lifetime. **11** After Chernobyl, the Swedish government made a special allowance for the level of radiated reindeer meat the Sami — a subsistence culture in northern Scandinavia — could consume, allowing them 1,500 becquerels of radiation per kilogram of food, five times the level allowed for the general population. **12** Even with the allowance, 29 percent of reindeer meat in Sweden's Sami lands was deemed unsafe and destroyed in 1987. **13** Ukrainians were also concerned about radioactive meat after Chernobyl, slaughtering 15,000 cows they feared were contaminated just a few days after the accident. **14** Cuba received 60 percent of its food from the former Soviet Union; some believe radiation from Chernobyl dramatically altered Cuban birth ratios. After a steady birthrate for decades, male births skyrocketed in the wake of the accident, peaking in 1996 with 118 boys born for every 100 girls. **15** Fears of contamination caused the United Kingdom to test sheep grazing in upland regions for Chernobyl radiation until 2012. **16** A product we developed for animals plays a role in protecting all of us from nuclear mishaps: Cat litter is often used to absorb and stabilize volatile radioactive chemicals stored in nuclear waste facilities. **17** In 2013, a New Mexico nuclear-waste storage facility switched the type of cat litter used in storage drums. An unexpected chemical reaction caused a drum to rupture and leak radiation. **18** Another unusual nuclear incident occurred in Mayapuri, India, in 2010. Workers sliced into radioactive cobalt-60 that was accidentally left in research equipment and sent to a scrap metal yard. Eight workers were hospitalized with radiation poisoning, including one who died from the exposure. **19** One of the workers reportedly carried a piece of the isotope around for days, unaware of the danger. **20** Survivors of nonlethal nuclear accidents can carry something else around: worry. Researchers found that people living near Pennsylvania's Three Mile Island exhibited higher levels of stress more than a year after the nuclear plant's 1979 incident compared with individuals outside the area. ■

Kristen Pope *is a freelance writer and editor who specializes in matters of science and conservation.*

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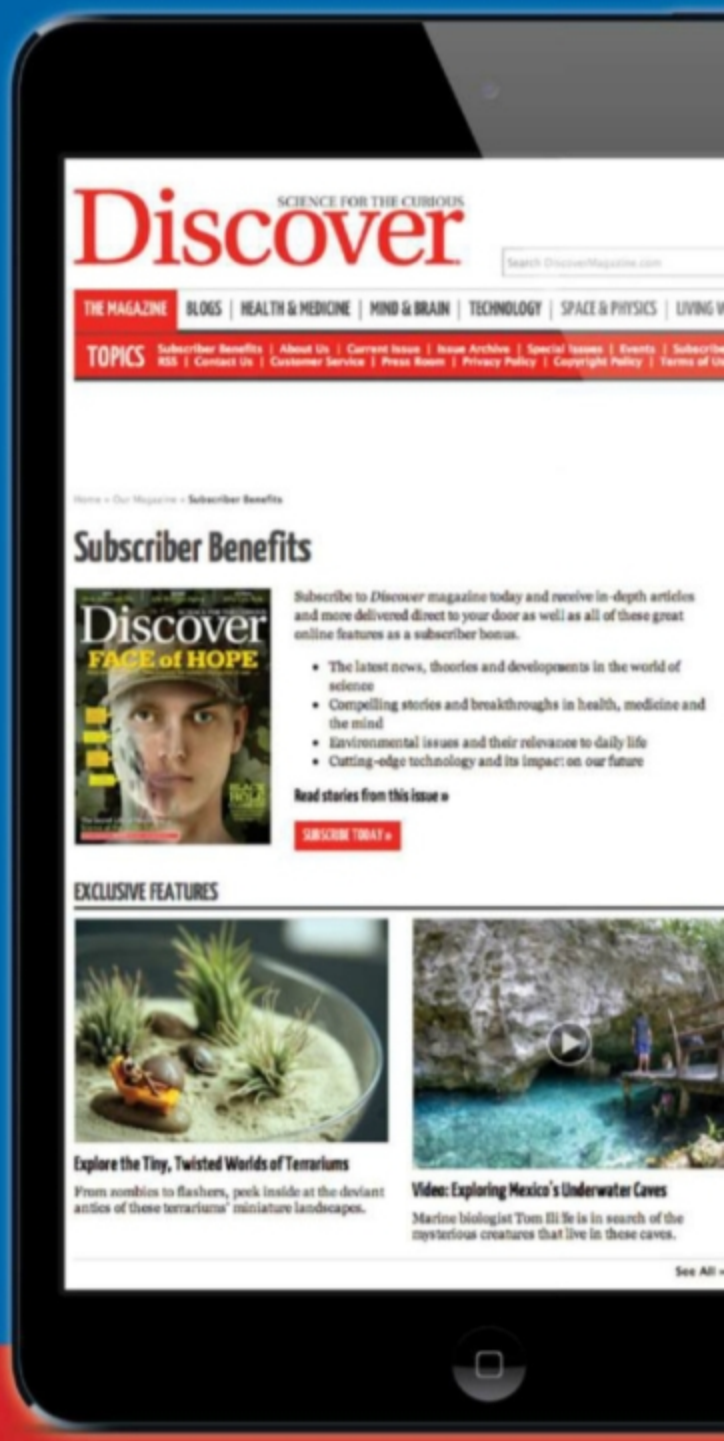
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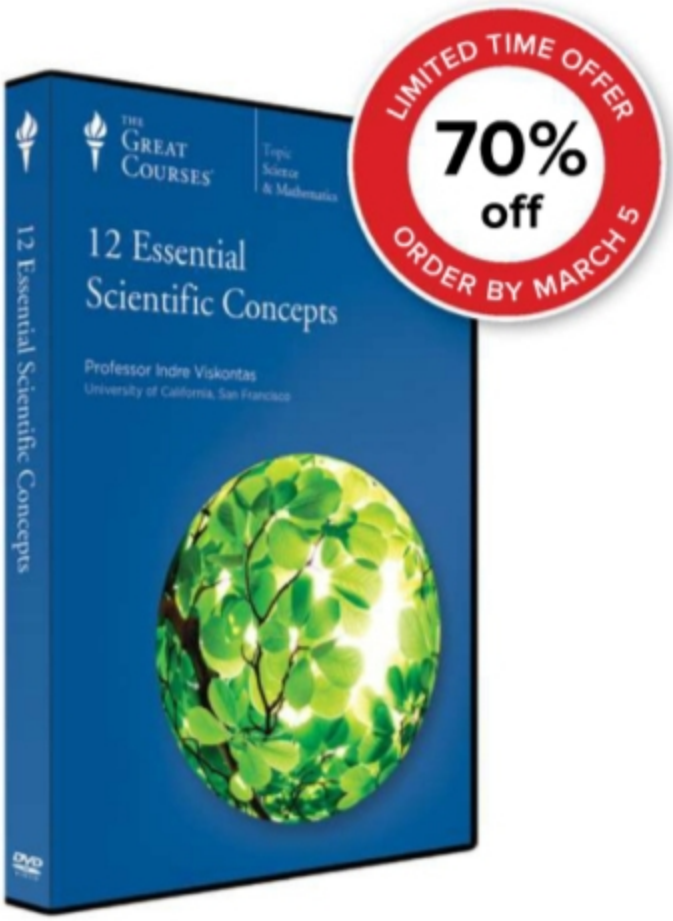
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