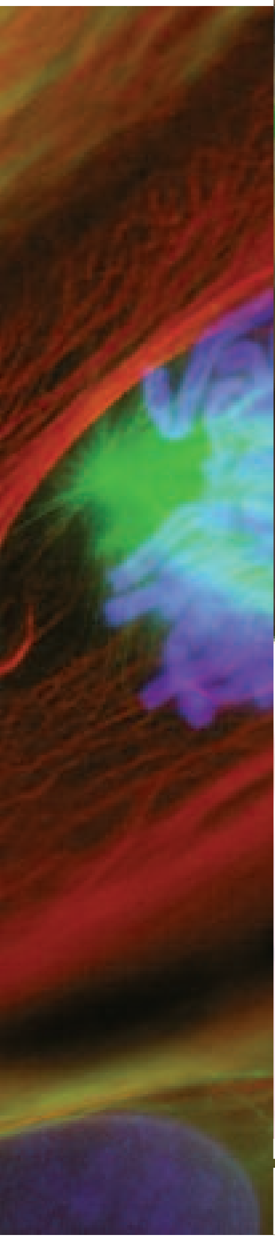
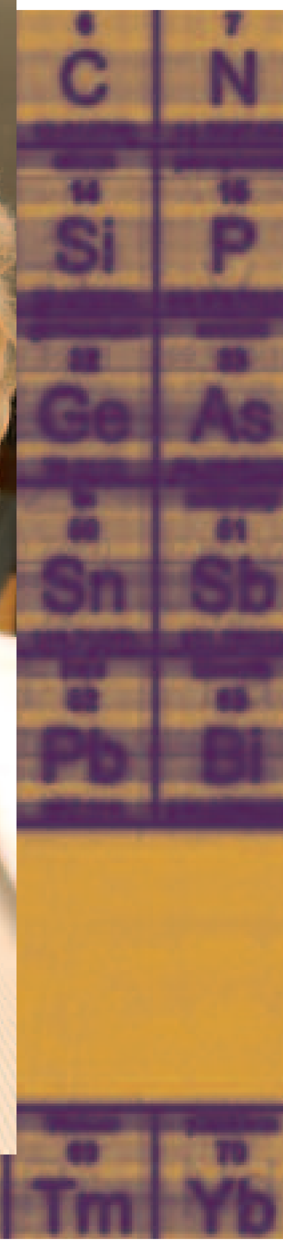
FINDINGS

March 2005





inside

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On the Cover

Photo of Andrés García: *Nicole Cappello*

Photo of Hilary Godwin: *Matthew Gilson*

Editor's Note

Should scientists genetically engineer grains to have extra vitamins?

Is it okay for a couple to choose the sex of their baby?

Should a 17-year-old girl whose aunt had breast cancer get a genetic test?

No one can claim to have the "right" answer to these or countless other questions that meet at the intersection of science and society. Yet all of us should be comfortable asking them and knowing where to find more information to develop an opinion based on the available facts.

Does that mean we should spend most of our free time in the library, reading scientific texts and journals? Should we become scientists or doctors?

These actions are not absolutely necessary for developing a critical mind. Of course, there are a great many things to be said for reading about science and going to graduate school. But have you ever thought about spending some time doing research in a lab? It's a fun, hands-on way to learn. If you'd like to give it a try, contact your local college or university and ask about research programs for high school students. If you're already in college, check out the undergraduate research opportunities offered there.

Even if you don't plan to do science for a living, chances are you'll have a better appreciation for those who do. And you'll also have a better idea of how to tackle really tough questions in a thoughtful, educated way.

Alison Davis

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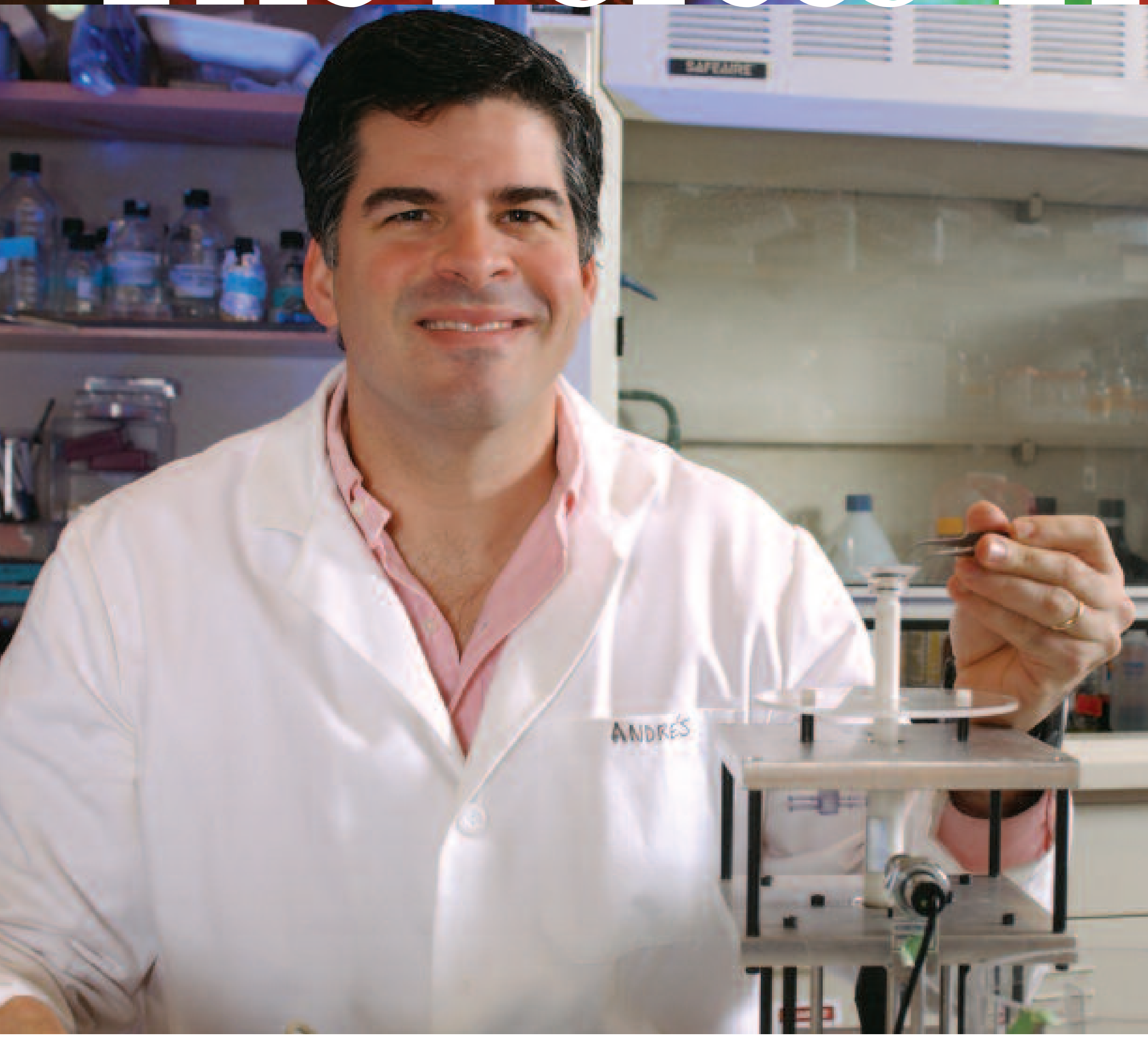
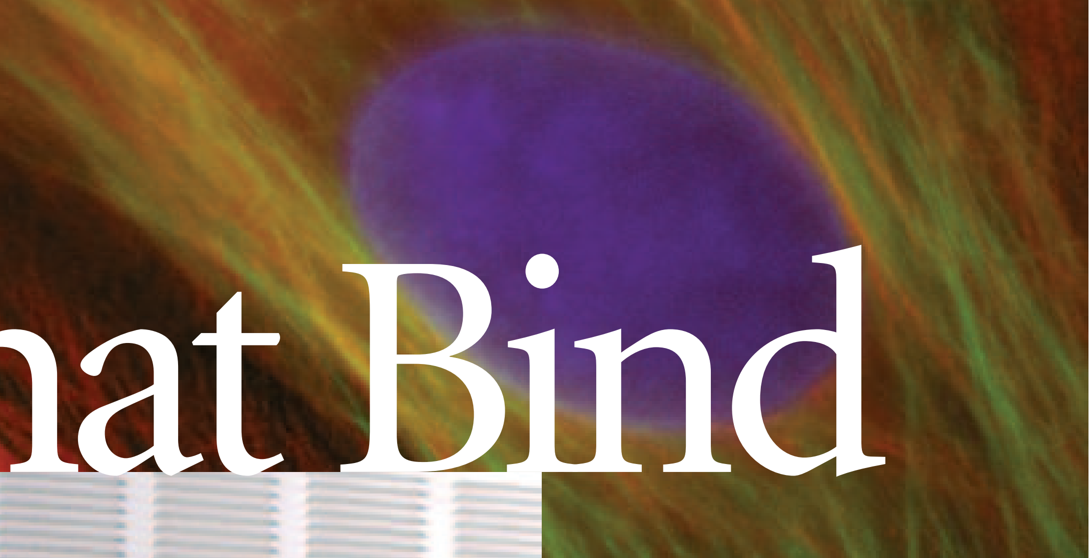
The Forces Th





hat Bind

CONLY L. RIEDER

NICOLE CAPPELLO

By Emily Carlson

In one way, Andrés García is different than a lot of other dads. Like many fathers, he plays sports with his two boys, sometimes watches cartoons with them, and leads his older son's Cub Scout den.

But García offers his kids something else, opening their eyes to a world beyond imagination. While visiting their father at work, the boys, 6 and 9, watch objects that are normally invisible to the human eye spring to life under the lens of a microscope. They see a magical machine spit out particles of gold to make new biomaterials that could one day replace broken bones.

García, 35, is an engineer who solves biological problems. He hopes that his work will yield a synthetic bone that could one day help heal fractures and improve the performance of artificial joints. García collaborates in this effort with his wife, Michelle LaPlaca, who is also a biomedical engineer.

An associate professor of mechanical engineering and bioengineering at the Georgia Institute of Technology (Georgia Tech) in Atlanta, García thrives on the challenge of being a successful scientist and a great dad. He and his wife already had kids when they started working at Georgia Tech in 1998. Before long, their careers took off. The young engineers won awards for their work and got research grants to start exciting new projects.

Despite the pressure to push ahead even faster, the couple always made time for their kids, Andrés and Rafael.

"Early on, Michelle and I said that family would be one of our top priorities."

"Here was this biomaterial that improved my life."

Andrés García is an engineer at Georgia Tech. By studying cell stickiness, García aims to create new biomaterials that can heal bones and other body tissues.

Sticking to It

To balance work and family, García makes the most of his time on campus. "You have to be very efficient," he says, explaining that he starts doing research the minute he steps into the lab.

With the goal of designing new types of biomaterials—synthetic products that interact with living systems—García and his graduate students study the mechanics of cellular adhesion, the process by which cells attach to a surface.

Just like tape sticks to paper, a cell sticks to a three-dimensional scaffolding that keeps it in place. This scaffolding, called the extracellular matrix, surrounds the cell and contains nutrients, proteins, and other molecules necessary for living. The matrix holds together the millions of cells that make up our blood vessels, organs, skin, and other tissues.

Paradoxically, the same mechanism that makes cells stick to a surface also helps them change shape and move around the body. Without adhesion, cells in the bloodstream couldn't grab onto vessel walls, crawl to the site of a cut, and repair a wound. Cellular adhesion also plays a major role in the development of embryos into babies.

On the other hand, cellular adhesion can cause problems, too. Gone wrong, this process helps cancer cells spread to other organs and allows arteries to harden, which can lead to heart disease.

Cells can stick to a variety of surfaces because they have specialized proteins that poke through their outer surfaces. These proteins link the extracellular matrix with the signaling circuitry inside the cell. Where the two connect, molecules gather and form tiny "feet" that take a cell where it needs to go. In scientific language, the feet are called focal adhesions.

In the case of cellular adhesion, stickier isn't necessarily better. Too much adhesion makes cell movement difficult, resulting in a sort of molecular flypaper that keeps cells stuck on a surface. And too little sticking power provides no traction whatsoever, preventing a cell from moving forward.

"It's like walking on ice," explains García. "You move your legs, but you don't go anywhere."

Measure of Strength

But cellular adhesion is much more complicated than creating friction between two surfaces. It requires force (see sidebar on page 7).

Cells, like people, need to exert force to move around. This force lets us run, talk, and even breathe. Cells apply their force through focal adhesions, explains García.

The molecules that create this cellular muscle power are fairly well known. What gives them their strength, however, is less understood because adequate tools haven't been developed to measure adhesion strength reliably and reproducibly, says García.

One way to fashion the right tools is to bring together biology and engineering. But, according to García, that's difficult.

"The biggest challenge is to integrate emerging concepts from engineering and cell biology, two very diverse disciplines," he says. "Very few people are trained in both."

Biologists, García explains, are generally more interested in studying the complexities of living systems. Engineers, on the other hand, like to use a different approach. They tend to take the systems apart so they can measure them, he says.

By merging these two problem-solving approaches, García built a tool to determine just how tightly cells stick to a surface and then find out what can change that adhesion force.

Accurate measurements of cellular adhesion strength, says García, will help researchers understand how cells control their stickiness and why they attach to certain surfaces but not others. Scientists could also use this information to design new medicines or even medical devices that aid or hinder a cell's ability to migrate.

Cells walk along body surfaces via tiny "feet," called focal adhesions, that connect with the extracellular matrix.

NICOLE CAPPELLO

A cell-spinning device designed and built by García and his coworkers measures how much force is required to pull cells off a surface.

Putting Ideas in Motion

The idea that synthetic materials can do all this has kept García excited about his research for more than 20 years. When he was 11 years old, the engineer experienced first-hand the awesome ability of implanted devices to substitute for the real thing.

"I developed a condition in my thigh bones that required the use of surgical pins to prevent further degeneration," he says. "After recovering, I was able to run and play basketball again. I was really excited—here was this biomaterial that improved my life."

Although he initially thought he wanted to be an orthopedic surgeon, García's interest gradually shifted more toward basic research. He saw research as the wellspring of exciting new discoveries and technologies.

After college, García earned a Ph.D. in bioengineering from the University of Pennsylvania in Philadelphia. He stayed on as a postdoctoral fellow in the School of Medicine to learn more about cell biology and started to focus his attention on cellular adhesion.

The first step in building a tool for studying adhesion was to create a special surface that would let García control where and how strongly cells stick. Without this material, he says, he wouldn't have been able to accurately measure adhesion strength.

One Size Fits All

If cells have enough room to move around freely, they change shape and shift the position of their focal adhesions. For example, when a spherical cell attaches to a surface, it flattens out and the focal adhesions shift from the center to the edges.

To keep the size and place of the cellular feet constant, García decided on a one-size-fits-all approach. He created a surface in which he could confine each cell to its own space.

Borrowing photolithography methods commonly used to etch patterns onto small electronic circuit boards, García and other scientists generated plates with tiny indentations big enough to hold just one cell each. The researchers treated the surface of the plates with gold and a blend of chemicals that enabled cells to grab on in certain spots. With this lab-made material, García could manipulate the focal adhesion complexes and examine their strength under various conditions.

Now able to precisely control cellular adhesion, García needed a way to measure how much force kept the cells stuck down. Relying on his engineering background, he built a spinning device that he likens to a low-speed blender.

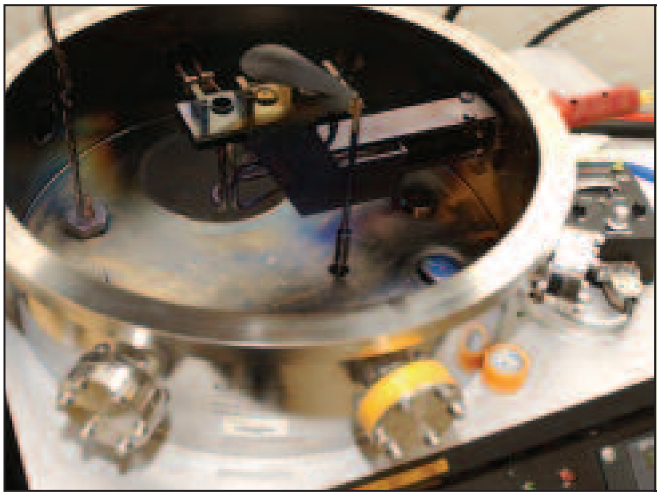
Here's how it works.

García puts the plate containing cells on a disk holder that spins inside a chamber filled with liquid (see photo, left). Like the blades of a blender, the disk holder and plate circle around, bathed in fluid, at a particular speed. As the disk spins, it generates a three-dimensional flow pattern that applies precise detachment forces to adherent cells. It's kind of like the wind blowing in your face when you drive around with the car windows down, García says.

He knows exactly how much force he needs to apply to detach the cells, so by counting the number of cells still sticking to the plate at the end of the experiment, he can calculate adhesion strength.

To the surprise of some of his colleagues, García's experiment did what it was supposed to do, and it worked over and over again.

"A lot of people thought we wouldn't be able to get reproducible results or that the device wouldn't work as we expected," says García. "It's exciting to test something, and sometimes you get surprising results."



NICOLE CAPPELLO

García uses a "gold-making machine," or electron beam evaporator, to build surfaces for his cell adhesion experiments. Inside the chamber, an electron gun heats a piece of gold until it evaporates, depositing a thin layer of gold onto a glass slide where cells can grow in a special pattern.

Gaining Momentum

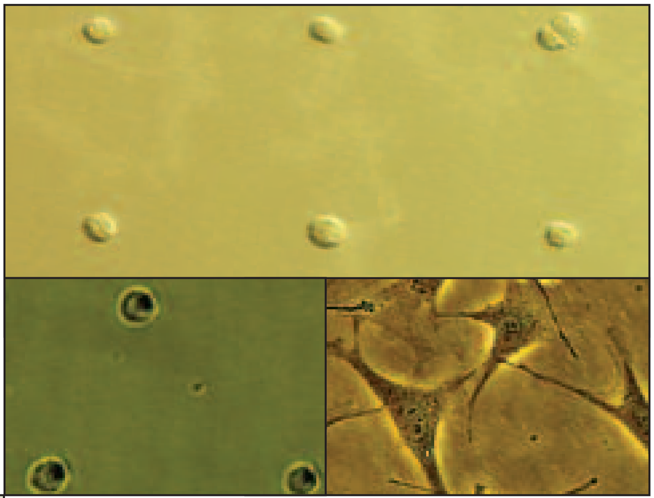
García uses his spinning gadget to find out what factors beef up adhesion strength. Through his experiments, he has learned that cellular stickiness depends on the size of the focal adhesion complexes. The more feet a cell has in one spot, the stronger the grip. García has also discovered that adhesion strength depends on the molecular makeup of the cells themselves. Without certain kinds of proteins, a cell loses its ability to develop forces enabling it to strongly stick to a surface.

Taken together, this information leads not only to a better understanding of focal adhesion mechanics, but also to a new framework that García and other researchers can use to study the role of cell stickiness in human health and disease.

Knowledge gained in García's lab could have broader implications for the field of biomaterials, too. For example, understanding how cells stick to synthetic materials could lead to new medical devices that doctors implant in the body.

As García explains, the body often "labels" implanted devices as foreign and launches an immune attack, like it would do with a virus. The result can be chronic inflammation, which is a bad thing. A better understanding of cellular adhesion could yield new biomaterials less likely to trigger such reactions.

In fact, García has already developed a material that directs cells to produce substances such as bone mineral. Similar materials might be used to make bone grafts and coatings for artificial hip and knee joints as well as other tissues.



ANDRÉS GARCÍA

García's gold-making machine creates a specialized surface (top) on which cells grow in a pattern (bottom, left). Without a patterned surface to adhere to, cells stretch out any which way when growing on a glass slide (bottom, right).

Managing the Load

Out of the lab by 5:00 p.m. most days, García spends the next few hours with his family, coaching his sons' baseball and basketball teams or helping them with homework. Once the kids are tucked in, García and LaPlaca often work more by reading scientific papers, writing manuscripts about their research, or planning experiments. The long nights aren't necessarily fun, says García, but he and his wife understand and appreciate the load each one carries.

"It's a good thing we're both in similar situations," he says. "We really help and support each other, both professionally and emotionally."

An example is attending out-of-town scientific meetings. Going to these conferences is an important part of being a researcher. There, scientists talk to each other, discuss their findings, and get new ideas.

García and his wife take turns going to these meetings so one parent will always be home with the kids. When they want to go to the same conference, they juggle their schedules.

"I'll go for the one day, come back, and then Michelle will go for one day," says García. "It's a matter of setting priorities and sharing the load."

If necessary, they'll turn the trip into a family excursion. "We'll take the kids, and they'll sit in the back of a session. They ask really good questions!" jokes the engineer.

The Perfect Balance

In between work and family, García finds time for another passion: sports. For most of his life, he has found himself on the basketball court several times a week. Now he plays an occasional round of hoops with his graduate students or a game against another engineering department. Three days a week, he starts off his day with a 3-mile jog.

"I run at 5:45 a.m.," García says, "and I make the most of it."

García always makes the most of his free time, including plane rides to and from meetings, some of which take him overseas. Like most scientists, García uses this time to catch up on reading scientific journals. But he freely admits he can only read so many in one sitting. For variety, he'll read thrillers, murder mysteries, and other books. Recently, he finished a biography of Benjamin Franklin.

Back at the lab, García does more experiments that help connect engineering and biology, with the hope of blazing new frontiers in medicine. He can't help but share his excitement with young Andrés, Rafael, and their friends who visit the lab.

García hopes these experiences match the marvel he felt that day in the doctor's office when he first saw the healing power of science. ■

Forces Are With You

CONLY L. RIEDER

When you turn the page of a magazine or kick a soccer ball across the field, you exert force that sets something in motion. Similarly, your body uses force to move itself. Force is a measure of the energy exerted over a given distance. It is the push or pull on an object necessary to make it move or change direction. For this to happen, the object (or person) must interact with another object, either close-up or at a distance. Here are a few examples of forces at work.

Applied force is the force one object exerts on another. This happens when you push a book across a desk or use your bicep muscle to lift your arm. When your heart pumps, it creates pressure that forces blood throughout your body.

Gravitational force is the pull that massive celestial bodies, like Earth and its moon, exert on objects. Your skeleton supports your body and stops gravity from tugging your organs and tissues to the ground.

Frictional force happens when one object slides across the surface of something else. For example, brake pads rub against metal rotors to stop tires from turning. Since friction resists movement, your body fights it in certain ways. For example, it reduces friction in joints like your shoulder or knee by coating them with slippery fluids that allow them to move freely.—*E.C.*

Getting the Le

ead Out

"The ultimate high is making a new discovery."

MATTHEW GILSON

Hilary Godwin is a chemist at Northwestern University near Chicago. Godwin studies the chemistry of lead poisoning.

By Karin Jegalian

Ask Hilary Godwin about her childhood summers at camp, and you might be surprised by what you hear.

For Godwin, summer camp meant hiking the mountains of northern California and helping her dad collect snakes. Her father, along with her stepfather and stepmother, is a herpetologist—a biologist who studies reptiles or amphibians.

Scrambling around outside, watching animals in action, Godwin saw, up close, how scientists work. Her efforts even earned a mention in the small print at the end of some of her father's research papers.

As a child, it didn't occur to Godwin, now 37, that she would be anything other than a scientist when she grew up. She knows that's not the case for everyone, yet she thinks most people can appreciate science even if they do not pursue it as a career.

Although many people see science as a bunch of facts, Godwin says, that's not really accurate.

"[The facts] are not what excite most scientists. It's the sense of discovery and the challenge of the unknown."

To Godwin, excitement is the essence of science, and that's the main lesson she tries to teach to her students.

"The ultimate high is making a new discovery or thinking you might have made one," she says.

Field Work at Home

Today, Godwin tries to re-create in her own lab some of the excitement that filled her summers years ago. In addition, each year the chemist at Northwestern University, located just outside Chicago, runs an intensive summer science workshop for incoming freshmen.

The experience is designed to get the students doing research. They collect soil and water samples and test them for the presence of heavy metals like lead. Godwin has discovered that looking at real-life problems that affect people in the community really inspires her students.

MATTHEW GILSON

Undergraduate students working in Godwin's lab get a real taste for research.

"One of my favorite parts of this program is taking the students out into the local community to gather samples. This is the closest I come to doing 'field work' as an adult."

From the very beginning, Godwin saw that science could be thrilling and fun. To her, research is more than solving puzzles, it's finding new puzzles to solve.

Her personal puzzle is the mystery of what makes lead act as a poison when it gets inside a person's body, especially if that person is a young child. Godwin has been studying why lead is poisonous for more than 8 years, ever since establishing her own lab.

Good-for-Nothing Lead

By tracking atoms of lead inside cells, Godwin hunts down which molecules—particularly proteins—pick up the lead that finds its way into the body. In doing so, she hopes to explain how lead exposure can contribute to health problems such as learning delays in children.

Believe it or not, some metals are perfectly safe to ingest, albeit in very small amounts (see sidebar on page 13). In fact, several metals are required for good health. Glance at the label of a multivitamin bottle and you'll see some of these listed.

Metals such as calcium and iron are important dietary staples. We also need zinc, copper, and potassium, in addition to tiny amounts of other metals such as selenium, manganese, and cobalt.

Often, metals work along with the body's enzymes to help these molecules do their job of speeding up chemical reactions. Our bodies couldn't function without enzymes, and many enzymes are helpless without metals.

All bets are off for lead, however.

"There's nothing good about lead," says Godwin, explaining that no one has dug up any evidence that lead does anything useful in the body.

While some pediatricians say there are no safe levels of lead, especially in young children, most of us do have trace levels of it because lead is all around us. For thousands of years, lead was part of many products, from eating utensils to ink. Before 1978, it was also a component of house paint. This poses a health hazard for children living in older homes, since they can suffer lead poisoning by eating or touching chipped or peeling paint. Lead dust can contaminate toys and other household objects.

In addition, until the mid-1980s, lead was added to gasoline to aid combustion. While gas stations no longer sell leaded gas, residue from fuel used years ago is present in soil in some areas, especially next to roads and highways.

Lead, which is sometimes present in chipped or peeling paint in houses built before 1978, is a health hazard.

Lead dust in soil can settle on clothes and shoes or become airborne. Lead used in plumbing, often to seal pipe joints, contaminates some water supplies, especially in neighborhoods with older homes.

Once lead gets inside the body, it can hurt virtually every organ but seems to do the most damage to the developing brain and nervous system.

Doctors worry most about the effects of lead on fetuses, babies, and young children because their bodies are growing so quickly. Often, the first symptom of lead poisoning in children is high blood levels of the metal found during routine testing. Ironically, such routine testing showed that Godwin's own son, who is now 3 years old, had high levels of lead in his blood at one point.

"It brought home to me how helpless you can feel as a parent," she says, adding that her 1920s-era home, while charming, nevertheless harbored the hidden health risk of exposure to leaded paint.

In addition to taking the necessary steps to reduce lead exposure in her home, Godwin decided to get certified as a lead risk assessor, a person who is licensed to find lead hazards in buildings.

A Chemist is Born

Growing up amid so many biologists—in addition to the herpetology crowd, Godwin's mother researched ants and now teaches biology—you would think Godwin was destined for a career in biology.

In fact, at one point she dreamed of studying chimpanzees and being the next Jane Goodall. A famous primatologist, Goodall pioneered the study of chimpanzee behavior in the wild, beginning in the 1960s.

But Godwin ended up a chemist, lured by the fascination of making her first molecule from scratch. After taking a few social science courses in college at the University of Chicago, then joining a research lab in the school's chemistry department, Godwin found that she felt more at home with chemistry, a quantitative, measurement-based field of study.

She earned a Ph.D. in chemistry at Stanford University in Palo Alto, California, and by the time she graduated, she already had a job offer to run her own lab at Northwestern. But first, she decided to spend a few years as a postdoctoral fellow at Johns Hopkins University School of Medicine in Baltimore, Maryland.

While there, Godwin learned of work done by other scientists showing that lead can slice through RNA, a major type of genetic material in our bodies. Could this explain why lead is poisonous, she wondered? Godwin read up on the topic and realized that, in fact, no one really knew what makes lead toxic.

An Uncommon Bond

According to the Centers for Disease Control and Prevention, 2.2 percent of children in the United States between the ages of 1 and 5 years have blood levels of lead greater than or equal to 10 micrograms per deciliter. This amount has been linked with harmful health effects, in particular learning disabilities and behavior problems.

Godwin (bottom and top, right) started field work as a child, spending summers at "snake camp" with her father and twin sister, Laura (top, left).

HILARY GODWIN

Until the last decade, very little was known about why this particular metal is so harmful. Godwin and other researchers have begun to sleuth the molecular mystery. Her research has shown that lead interferes with the function of proteins that turn genes on or off. She has discovered that lead usually does its dirty work by displacing atoms of zinc and calcium in these proteins.

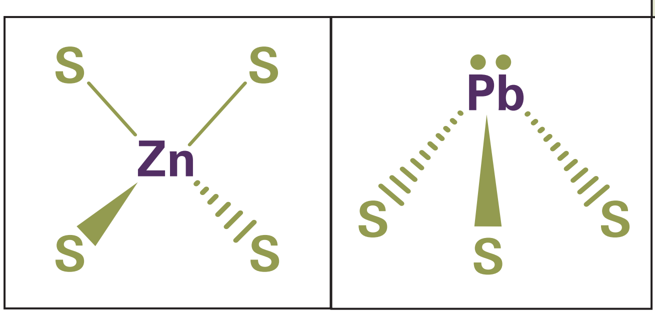
Zinc displacement occurs even with relatively low levels of lead in the body, Godwin says. With lead in zinc's place, the proteins can't do their jobs properly.

A protein's precise shape is crucial to what it does, and even a subtle disruption can affect its function. When lead takes the place of zinc, the protein's shape changes. This is because lead forms different chemical bonds than zinc does. Zinc forms four, equally separated chemical bonds, while lead forms three, and these are at different angles (see drawing).

Researchers in Godwin's lab measure how tightly proteins bind to lead and other metals. One of the experiments they do is to test a certain protein's vulnerability to the effects of lead. In such an experiment, Godwin mixes a protein sample with lead and another metal to which the protein normally binds. If the lead sticks more tightly than the other metal, it's a hint that the test protein will be affected by lead, she explains.

For example, some zinc-binding proteins in the body are known to be crucial for normal development in children and for maintaining proper blood pressure in adults. Lead in place of zinc in these proteins can cause developmental delays in kids and high blood pressure in adults. Lead also knocks out zinc from a protein that helps form molecules of heme, which, among other things, carries oxygen in the blood. This snag may explain why lead can cause anemia, or low levels of red blood cells.

Lead also takes the place of zinc in a protein involved in making sperm, perhaps accounting for increased infertility rates in men exposed to high levels of lead at work. And when atoms of calcium in the body are bumped out by lead—which happens when lead levels are quite high—nerve impulses get messed up. Because of the way cells amplify electrical signals, just one lead-corrupted protein can have a significant effect.



Zinc (Zn) and lead (Pb) each form a different pattern of chemical bonds. In place of zinc, lead can twist a protein's shape and interfere with how the protein does its job in the body.

Pioneering Spirit

Godwin loves science and working in the lab, and she thinks the experience is important for nearly everyone. It's not that she wants to turn everyone into a scientist, but Godwin says that doing research is the best way to understand how science works. She wants students to experience science as scientists do.

Although students routinely learn about "the scientific method," they rarely do so while actually exploring something for themselves, Godwin points out. She wants to create teaching experiences that mimic true discovery instead of just telling students that science is *about* discovery. Students who get a real taste of research may not decide to make a career of it, but she thinks they will certainly be better informed in public discussions about science.

Throughout her life, Godwin has been exposed to unusual experiences and pioneering ways. As the first woman chemistry professor at Northwestern, she is mapping a course for other women in science.

Recently, Godwin achieved another first when she was appointed chairperson of the entire chemistry department. She is the first woman to hold the post.

In this capacity, Godwin is eager to help young faculty with their careers—to make sure that these researchers are able to balance work and family life, and to help them learn to be managers and mentors as well as scientists.

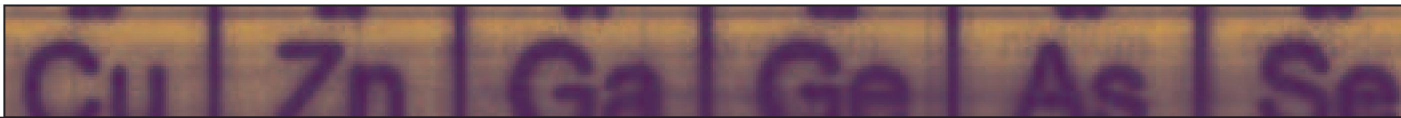
Godwin calls chemistry, like other fields that depend on hands-on work, an "apprenticeship science." Students and postdoctoral researchers do much of the work, and professors act as trusted advisors.

Second only to the thrill of discovery, what Godwin likes best about being a scientist is mentoring young people. She says that being a scientist is not just a career, it's a way of thinking. Godwin believes that growing up with scientists affected how she thinks and how she views the world, and it similarly affects how she is raising her son.

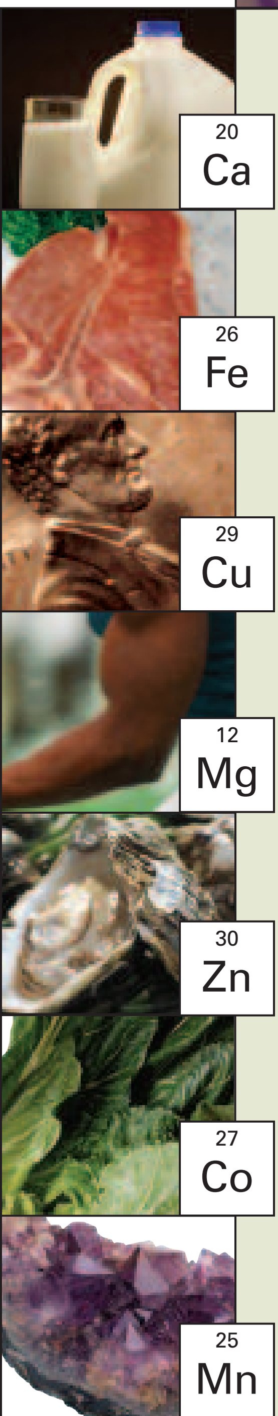
In her home, questions abound and everything is a potential experiment. The kitchen counter doubles as a lab bench where the materials and variables can be munched when the experiment is done.

Family vacations are an opportunity to get out "in the field," for example, by scuba diving or watching animals in their natural environments.

Or hunting for snakes in the mountains . . . now a Godwin family tradition. ■



Healthy Metals



Lead is bad for you, but many metals are vital to life. Some of these "good metals" are listed below. Cells usually need them in just miniscule amounts.

[Ca] Calcium. Did you know that this essential component of bones and teeth is a metal? In our bodies, calcium is abundant in bones and is critical for proper muscle and nerve function. Good dietary sources include dairy products, broccoli, figs, and sardines.

[Fe] Iron. Iron is not only found in skyscraper steel and frying pans, it is also in the bloodstream. Iron from foods like meat, beans, and spinach helps carry oxygen throughout our bodies.

[Cu] Copper. The metal copper is found in old pennies, high-quality plumbing, and electrical wires. It's also in lobster, crabs, beans, and nuts. In our bodies, copper helps mop up dangerous "free radicals," highly reactive chemicals that have been linked to an increased risk of cancer and heart disease.

[Mg] Magnesium. Magnesium is a metal used in flares and fireworks. Our bodies need magnesium for strong bones and teeth, as well as for muscle contraction and relaxation. Food sources include vegetables, especially dark green, leafy ones.

[Zn] Zinc. This metal is present in a range of household products, from batteries to cosmetics. In our bodies, many proteins need one or two zinc atoms to fold into the right shape. Zinc is important for controlling gene activity and regulating hormones. Good dietary sources include oysters, chick-peas, whole grains, and nuts.

[Co] Cobalt. Mixed with other metals, cobalt is used in jet engines. It also gives a brilliant blue color to pottery, glass, and tiles. Cobalt forms the core of vitamin B12 and is important in the body for making red blood cells. This metal is found in meat, dairy products, and leafy green vegetables.

[Mn] Manganese. This metal helps to give Sacajawea dollar coins their shiny, golden luster and amethysts their purple hue. In our cells, it helps break down fats, carbohydrates, and proteins to convert food into energy. Manganese is present in whole grains and cereal products.—*K.J.*

Needle-Free Injections

For the millions of Americans afraid of needles, help may be on the way. A new medical device now available in some hospitals and clinics can inject medicines without the jab of a needle. The device, called SonoPrep®, is initially being used to numb skin for painful procedures such as the insertion of catheters or intravenous tubing.

SONTRA MEDICAL CORPORATION

Traditionally, doctors numb skin before doing these procedures by injecting a local anesthetic medicine through a needle. This method can take up to an hour and it hurts, whereas SonoPrep does the job painlessly in just 5 minutes.

SonoPrep works through ultrasound technology. Developed with NIGMS funding by **Robert Langer** of the Massachusetts Institute of Technology in Cambridge, the device uses battery power to apply low-frequency sound waves to skin for 15 seconds. This ultrasonic energy subtly rearranges the distribution of fat molecules, creating tiny canals in the skin.

Small quantities of liquid can flow into and out of these channels, enabling the painless delivery of anesthetics or other medicines. The skin isn't harmed by the process, and within a day it returns to normal.

Langer, a chemical engineer and the inventor of many novel methods to deliver medicines, has much more in mind for SonoPrep. He licensed the technology to a company, Sontra Medical Corporation in Franklin, Massachusetts, that plans to test the needle-free injection system for various other medical uses, including vaccination.

Plans are also under way to test SonoPrep's ability to measure blood sugar in people with diabetes and give just the right amount of insulin when needed. —*Alison Davis*

Finding a Single Microbe

Outbreaks of the potentially deadly bacterium *E. coli* O157:H7 pose a serious health risk. As few as 10 to 100 of these microbes in contaminated food or water can kill people who are especially vulnerable to infection, such as young children and the elderly.

Unfortunately, finding such miniscule amounts of bacteria in food or body fluids is very difficult and time-consuming. Standard techniques require a lot of sample material and can give false results. Better methods for the quick and accurate detection of bacteria are urgently needed for protecting public health.

To make progress on this front, NIGMS grantee **Weihong Tan** of the University of Florida in Gainesville used nanotechnology. A key goal of this new area of science is to learn how to build structures and devices at the nanometer scale. (There are 25 million nanometers in 1 inch.)

The chemist designed a tiny, nanometer-sized biosensor to detect *E. coli* O157:H7 by attaching an antibody, a protein that can grab tightly onto the microbe, to a "nanoball." When it detects as little as a single bacterium, the nanoball-antibody combination glows brightly. This is because the microscopic nanoball biosensor is packed with thousands of dye molecules that give off a fluorescent signal on contact with the microbe.

To test the practicality of this approach, Tan spiked samples of ground beef with very small amounts of *E. coli* O157:H7, then mixed the spiked and unspiked samples with nanoball biosensors. The technique worked: only the contaminated samples lit up.

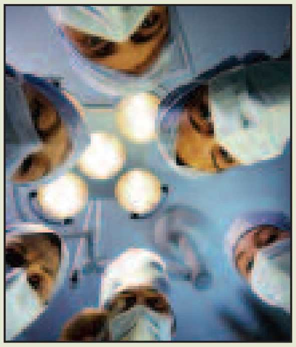
While the approach will require scaling up for more widespread use, Tan believes it will speed the development of rapid and highly sensitive new tools for disease surveillance and diagnosis. —*A.D.*

Seeing Red

Hair color, like many other aspects of our appearance, is inherited. But genetic factors also influence less visible characteristics, such as how we respond to medicines.

Anesthesiologists have long observed that people with naturally red hair may need more anesthesia and have wondered if heredity plays a role. NIGMS grantee **Daniel Sessler** of the University of Louisville School of Medicine in Kentucky decided it was time to put the issue to the test.

Sessler, an anesthesiologist, recruited 10 women with naturally bright red hair and an equal number with black or dark brown hair. He gave the women a commonly used inhaled anesthetic, then applied a small electric shock to each woman's thigh and watched for a reflex movement, an indication that the anesthetic dose was too low. The women did not feel or remember the shock.



Sessler adjusted each woman's dose until she had a reflex movement only half the time, a standard method for determining the appropriate individual dose of an anesthetic medicine. He found that nearly all of the red-haired women needed 20 percent more anesthetic than did those with dark hair.

Just about all people with red hair share a common genetic variation that affects hair and skin color. After analyzing DNA from the women in the study, Sessler identified this genetic variation in 90 percent of the red-haired women who needed more anesthesia. In a separate study, he discovered that redheads also get less pain relief from local anesthesia, the kind you often get at the dentist.

While the study findings do not directly link hair color genes to anesthesia response, they do suggest that health care providers should monitor anesthesia doses carefully in redheads. More broadly, the research opens the door for further study of the role of heredity in anesthesia response. —*A.D.*

Bone Marrow Powers Wound Healing

The body automatically springs into action to heal a wound. It does this by grouping together certain cells in the bloodstream so they can form a clot and short-circuit a potential infection.

Researchers have long known that the infection-fighting cells come from bone marrow, the spongy material inside bones. But recently, scientists discovered that the bone marrow-derived cells also play a role in healing wounds and keeping skin healthy.

NIGMS grantee **Frank Isik** of the University of Washington Medical Center in Seattle made the discovery using experimental mice whose bone marrow cells were engineered to glow green under a fluorescent light. He took the glowing bone marrow cells from these mice and put them into another set of mice that were genetically the same but hadn't gotten the cells that could glow.

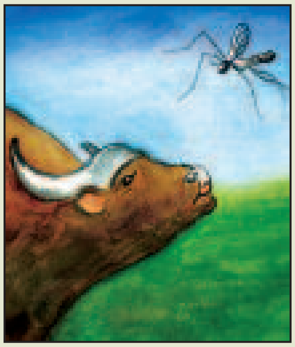
Isik, a plastic surgeon-researcher, then made a small incision in the back skin of the transplanted mice. To his surprise, as long as 6 weeks after the mice had been wounded, and well after they were no longer at risk for infection, the luminescent cells derived from the bone marrow remained in their healed skin.

Isik also discovered that only the bone marrow-derived cells were able to make a particular type of collagen found not just in healed wounds, but in skin all over the body. This led him to conclude that cells from bone marrow help form the tough, yet expandable, matrix of skin.

Isik now wonders whether diseases that interfere with wound healing, such as diabetes, do so because they affect bone marrow cells. In time, this line of research may reveal targets for drugs to speed wound healing. —*A.D.*

Wild Ox vs. Mosquito

Warm, summer evenings by the lake can be so peaceful and relaxing…except for the torrent of mosquitoes that seems to attack every uncovered inch of your skin. In some places in the world, the outcome is worse than simple itching.



Mosquitoes in the steamy rainforests and jungles of Southeast Asia and India transmit life-threatening diseases that include yellow fever. Although an effective vaccine for this infectious disease has been available for more than 60 years, the number of people infected has been rising. For this reason, yellow fever has re-emerged as a serious public health threat.

Fortunately, nature provides some protection for the wildlife living in these muggy climates. For example, large beasts such as oxen (also known as gaurs) that inhabit these tropical areas ooze a natural skin secretion called gaur acid. Scientists think that this chemical protects gaurs by discouraging the landing and feeding of *Aedes aegypti*, one type of mosquito that carries and transmits the yellow fever virus.

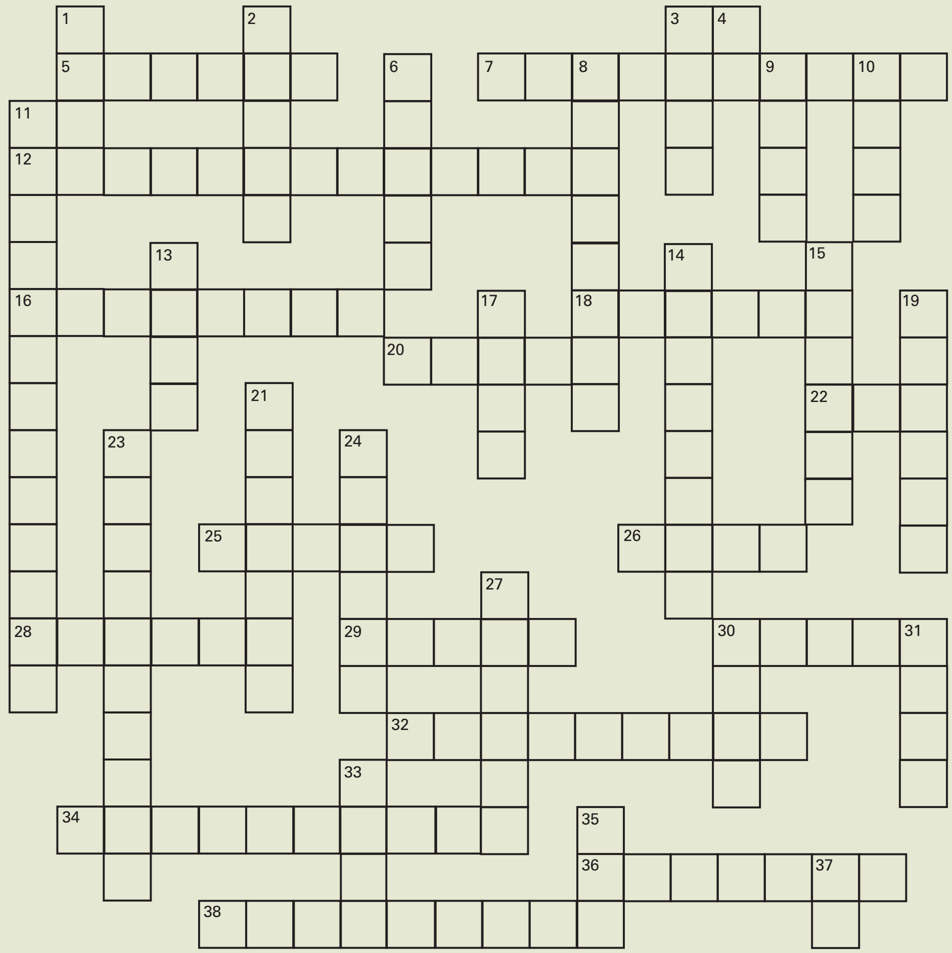
In the future, people may benefit from this treasure in nature's medicine chest. NIGMS grantee **P. Andrew Evans** of Indiana University in Bloomington recently learned how to make gaur acid in his lab.

It was no easy feat, considering that before the chemist began working on the problem nobody knew how gaur acid's molecular pieces snap together. Using a helper molecule called a rhodium catalyst, Evans produced gaur acid in just seven chemical steps.

He anticipates that the method could be industrialized fairly easily to make large quantities of this natural insect repellant. —*A.D.*

These stories describe NIGMS-funded medical research projects. Although only the lead researchers are named, science is a team sport and it is important to realize that many researchers work together to carry out these studies.

The Last Word



ACROSS

3. Spanish yes
5. lead is one
7. game of hoops
11. male pronoun
12. space outside a cell
16. scientist who builds things
18. chemist Hilary
20. liquid color
22. cow sound
25. wow
26. 1 of 206 in the body
28. slithery reptiles
29. calcium is one
30. better than good
32. just one microbe
34. medicine before surgery
36. science of living things
38. not natural

Puzzle answers can be found at
http://www.nigms.nih.gov/findings/

DOWN

1. peak
2. cause of motion
3. observed
4. info. tech.
6. units of living matter
8. power
9. chemical attachment
10. no-good metal
11. Hilary Godwin's father, for one
13. pickle flavor
14. stickiness
15. not enough red blood cells
17. lead displaces, sometimes
19. blossom
21. Hilary, for one
23. sound wave technique
24. reaction helper
27. engineer Andrés
30. wild ox
31. player's group
33. focal adhesions
35. alphabet's first 3
37. stop opposite

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