Up Close With

Amy Palmer

BIOCHEMIST

CASEY A. CASS/UNIVERSITY OF COLORADO AT BOULDER

"I never would have guessed I would become a scientist."

FAVORITE HOBBIES

Rock climbing and snowboarding

FAVORITE WEEKEND ACTIVITY

Cooking a giant breakfast for the family

FAVORITE BOOK

The Power of One

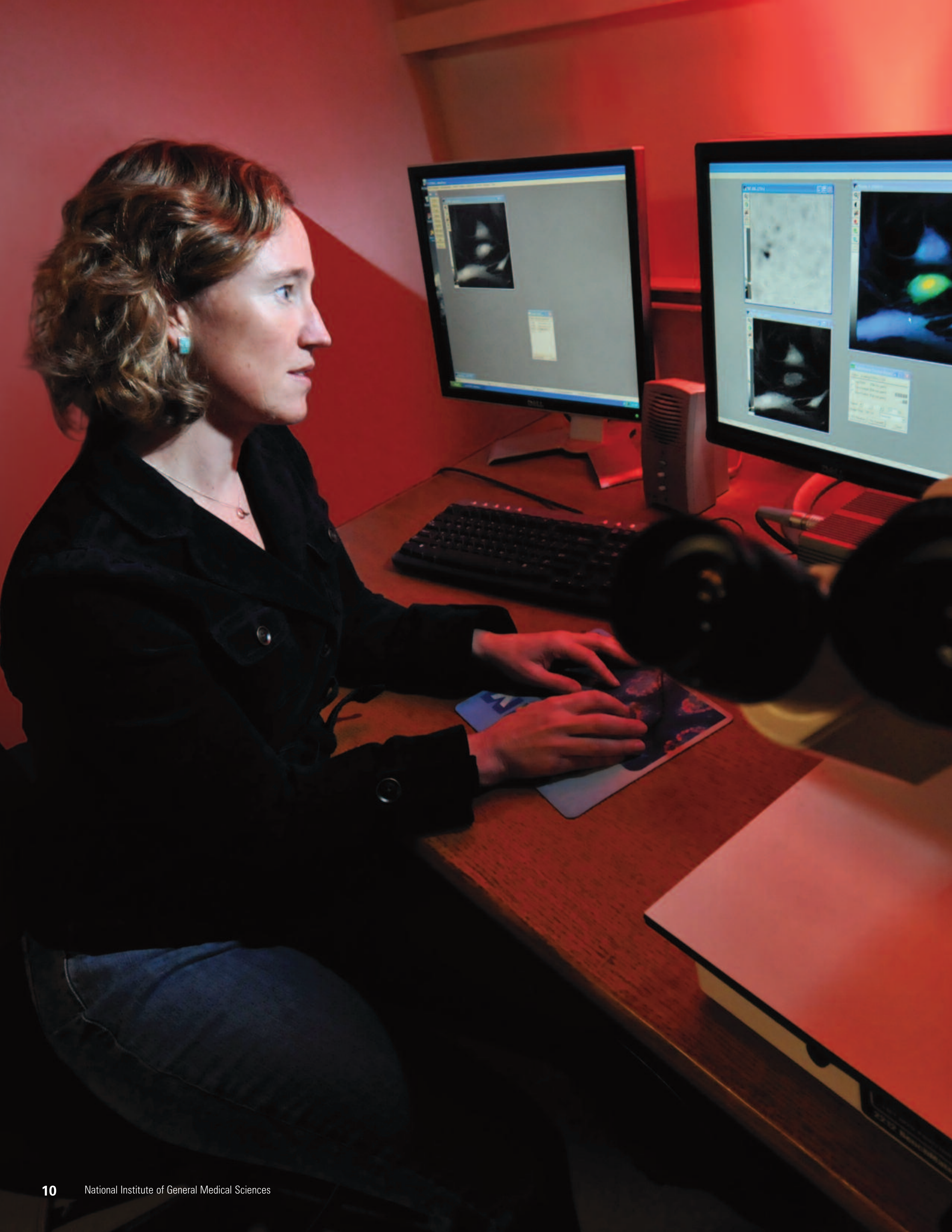
by Bryce Courtenay

FAVORITE FOOD

Cilantro—just about everything tastes better with cilantro on it

HIDDEN TALENT

Knitting



CASEY A. CASS / UNIVERSITY OF COLORADO AT BOULDER

Mesmerized by Metals

BY JANELLE WEAVER

Some kids have chemistry sets when they're 5. Amy Palmer was not one of them. In her teens, she considered becoming a gymnastics coach or writer, and almost majored in Russian instead of chemistry.

"I always found the humanities more interesting," she says. "I never would have guessed I would become a scientist."

Palmer discovered her love for science in college. A professor offered her a rare opportunity to work in a well-regarded research lab investigating the health effects of toxic metal exposure. But to accept the position, she'd have to give up her spot in the Russian foreign study program in St. Petersburg.

She had faced a similar decision before, when a Dartmouth swim coach insisted that she, a competitive swimmer since kindergarten, decide between the swim team and the lab.

At both crossroads, she opted for research—an activity that attracted her because of her natural curiosity and drive for making discoveries.

"I didn't know why someone would let me work in their lab. I was not the perfect student," Palmer says. "But I gave it a shot, and [it was the] opportunity that defined the direction I took in my life."

Now a biochemist at the University of Colorado at Boulder, she uses creative chemistry to track the movement of metals and other molecules in living cells, especially when those molecules play a role in human diseases.

Beyond the hardware store: Metals like copper, zinc and iron are essential nutrients, needed in tiny amounts throughout our bodies.

Metal Overload

Throughout her research career, Palmer has focused on the role of metals in biology. Some metals, like iron, copper, calcium, zinc and magnesium, are essential for health (see "Metal Match," page 13).

Calcium ensures strong teeth and bones and is necessary for muscles to move, brains to send signals and hearts to beat.

Iron helps carry oxygen to tissues and is important for cells to produce energy, make DNA and grow. It's why our blood, when exposed to oxygen, is red.

But an excess of metals in our bodies can cause organ failure, nerve damage, cancer or even death. So, Palmer explains, there must be careful controls on how metals get where they need to go. That's where her research comes in.

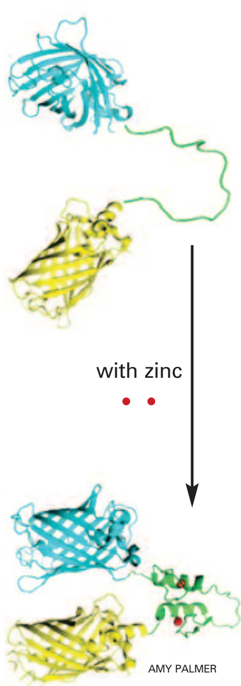
Her work has the potential to make an impact on people's health.

Zinc Zealot

Much of Palmer's work focuses on zinc, a metal used throughout our bodies to ensure proper immune responses and a healthy nervous system. Zinc also regulates the function of some genes, enables many proteins to carry out their vital roles and helps speed chemical reactions in our bodies. A zinc imbalance is linked to Alzheimer's disease, diabetes and prostate cancer.

When Palmer was doing research in college, it was impossible to track the movement of metals inside cells. Once she had a lab of her own in Colorado, she developed four fluorescent sensors to detect zinc in living cells.

These sensors allow Palmer—and other scientists—to see how cells use and store zinc. They can detect different levels of zinc in various parts of the cell and follow its flow during processes like nerve signaling, bacterial invasion and disease progression.



When zinc (red) binds to the floppy part (green) of Palmer's sensor molecule, it yanks together the two fluorescent proteins (blue and yellow).

"When she tackles a problem, she tackles it hard," says Tom Trainor, a chemistry professor at the University of Alaska Fairbanks whom Palmer met when they were both graduate students at Stanford University. "She's focused on getting whatever she sets her mind to."

Palmer made her zinc sensors using two fluorescent proteins, one that glows blue and the other that glows yellow. She linked these proteins together with a zinc-sensing segment, which swings around loosely like a slack rope.

When this slack area binds to zinc, it constricts and yanks the two proteins together, causing the blue protein to transfer light energy to the yellow protein, which then glitters like ink from a yellow highlighter.

Palmer visualizes the yellow gleam by peering through a microscope specially designed to detect fluorescent molecules. She can track the levels and location of zinc for as long as she'd like.

Metals and Memory

In her latest experiments, Palmer has her microscope trained on cells from a part of the brain called the hippocampus, which helps mammals store memories.

The hippocampus is also the first area of the brain to be damaged by Alzheimer's disease, which robs patients of the ability to form new memories.

Tracking zinc in the brain region called the hippocampus (blue) might shed light on Alzheimer's disease.

By tracking the movement of zinc inside hippocampus cells, Palmer hopes to gain insights into what role the metal might play in forming memories and the progression of Alzheimer's disease.

She'd also like to determine which proteins, nerve signals and other factors influence the movement of zinc inside brain cells.

Ultimately, she hopes her work will have medical applications. She envisions a zinc-tracking technique that would enable early diagnosis of diseases like Alzheimer's and drugs that could control the level or location of zinc to prevent or treat such diseases.

Finally, she plans to expand beyond zinc and develop fluorescent sensors for other biologically important metals such as copper, which in high levels can cause liver damage, kidney failure, coma and death.

"Her work has the potential to make an impact on people's health, and that's a big deal to her," Trainor says.

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FIND MORE @

To see the hippocampus inside a brain, check out the animation at http://en.wikipedia.org/wiki/File:Hippocampus.gif

Metal Match

Several metals are vital to life. By eating a balanced diet, you probably get enough of these essential nutrients. But if you lack one or more, you could experience symptoms ranging from tiredness and hair loss to severe brain damage.

Too much of certain metals can be equally disastrous (see main story).

See if you can match the metals with what they do in our bodies.

A: Iron
B: Manganese
C: Calcium
D: Magnesium
E: Zinc
F: Copper

☐ **1.** The most abundant metal in our bodies (about 1 kg in the average person), stored in bones and teeth. Also critical for proper muscle and nerve function, hormone release and more. Found in dairy products, broccoli, figs and sardines.

☐ **2.** Found in pennies, electrical wires and the Statue of Liberty's skin, this metal is also needed for firm skin, cartilage and ligaments, and to remove dangerous "free radical" molecules in the body. Rich sources include beef liver, lobster, shiitake mushrooms, chocolate and nuts.

☐ **3.** The most widely used metal for making machinery, skyscrapers, cars and ships. It is also found in red blood cells, where it is responsible for carrying oxygen to our tissues. Abundant in red meat, beans and spinach.

☐ **4.** Used in batteries and to prevent rust on cars, fences and bridges, this metal is used throughout our bodies in many ways, including immune function, brain activity, and growth and development. To get lots of it, eat oysters, fortified cereal, baked beans or beef.

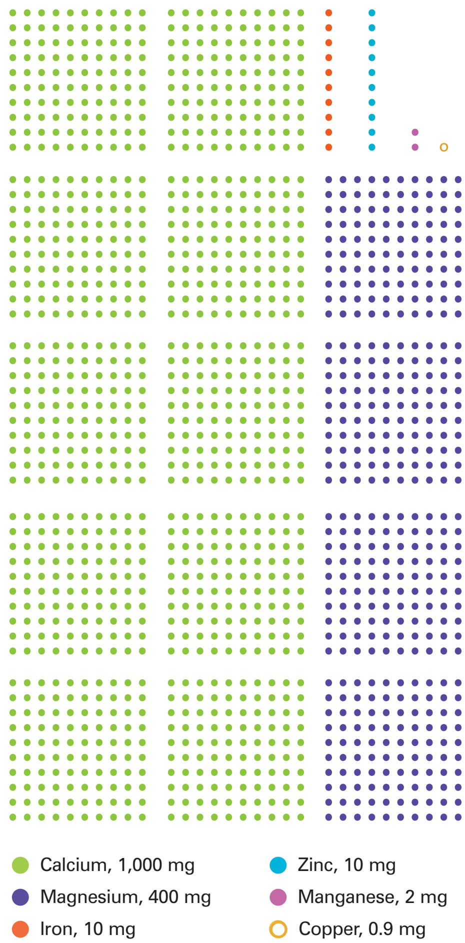
☐ **5.** Used in flares and fireworks. Needed for healthy muscles, nerves, bones, a strong immune system and a steady heart rhythm. Abundant in whole grains, spinach and pumpkin seeds.

☐ **6.** An essential additive in steel and used to make pink-colored glass, this metal is stored mainly in the liver and kidneys. It helps our bodies make DNA and RNA, break down food into energy and heal wounds. Good sources are oat bran and other whole grains, pineapple and chickpeas.

—Alisa Zapp Machalek

Recommended Daily Amounts (approx.)

Each dot represents 1 milligram (mg)



Adapted from the U.S. Department of Agriculture's Dietary Reference Intake Tables, developed by the Institute of Medicine's Food and Nutrition Board.

Answers: 1.C 2.F 3.A 4.E 5.D 6.B

"I want to bring excitement and


Sepsis is usually treated in a hospital intensive care unit, where IV antibiotics and fluids help fight infection and keep blood pressure from dropping too low.

Seeking the Causes of Sepsis

If you read about Kevin Tracey in the September 2010 issue of *Findings*, you know that sepsis, or body-wide inflammation, is a top killer that remains difficult to understand and treat.

Tracey discovered that the nervous system is involved in this immune response and that stimulating a particular nerve could protect animals—and possibly humans—against sepsis.

Other scientists are looking elsewhere.

Trauma surgeon Carl Hauser at Beth Israel Deaconess Medical Center in Boston focuses on mitochondria. These cellular power plants can spill into the bloodstream after an injury. Because they're biologically similar to bacteria, mitochondria can ignite a sepsis-like immune response.

At the Oklahoma Medical Research Foundation in Oklahoma City, cardiovascular biologist Charles Esmon points to histones, the spool-like structures that wind DNA into tidy shapes. Esmon found that histones can enter the bloodstream during an infection and cause sepsis. He also discovered that Xigris®, a drug used to treat sepsis, works by chopping up histones.

Because histones are also linked to multiple sclerosis, lupus and other diseases, finding ways to inactivate them could have benefits beyond fighting sepsis. —*Emily Carlson*

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Salmonella Surge

Nudged by one of her students, Palmer is now using chemistry and imaging techniques to address another biological question: How does *Salmonella* attack cells?

Salmonella is a rod-shaped bacterium that causes severe diarrhea, fever and abdominal cramps. Every year, there are approximately 40,000 *Salmonella* infections reported in the United States. There have been outbreaks related to contamination of alfalfa sprouts, peanuts, salami and black pepper. Last year, there was a massive recall of eggs due to *Salmonella* poisonings across the country.

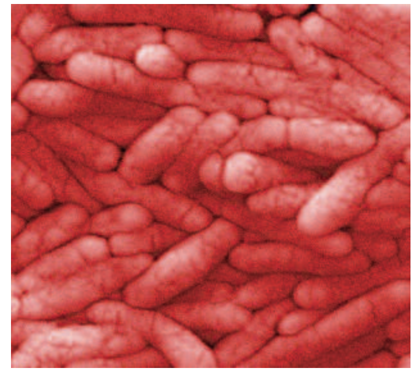
During an infection, *Salmonella* uses what looks like a miniature syringe to inject more than 60 proteins into cells in the infected person's intestinal lining. The cell's natural response is to engulf the bacterium. But rather than destroying *Salmonella*, this action just welcomes it in.

As *Salmonella* enters human or animal cells, a piece of the host cell's membrane engulfs the bacterium, forming a compartment called a vacuole. From this protected spot, the bacterium ejects another round of proteins that help it evade the host cell's defenses, prolonging the infection.

Seeing the Light

By using fluorescent sensors to track different *Salmonella* proteins, Palmer is figuring out how they enable the bacterium to infect and survive inside a host cell. She discovered that labeling proteins and tracking bacterial infection required a different technique than the one she used to track zinc.

She couldn't just attach her fluorescent proteins onto the *Salmonella* proteins, because the resulting complex was too big to get through *Salmonella's* narrow, syringe-like projection. So she split the problem in half—literally.


JANICE HANEY CARR/CDC

Rod-shaped *Salmonella* bacteria like those magnified here can invade the intestines, causing food poisoning.

She and her research team divided the barrel-like fluorescent proteins down the middle. They put the left half into the host cell and attached the right half to proteins in *Salmonella*.

Then they waited for the yellow glow. The fluorescent proteins only light up once the two halves unite within an infected cell. When the scientists see the light, they know that *Salmonella* has successfully infected the host cell. Then they track where the fluorescent proteins go and what they do.

Palmer tracked *Salmonella* proteins between 4 and 24 hours after infection. Her team found that some proteins home in on the vacuoles and create tubules that shoot out from them, like legs dangling from a spider. The tubules carry the vacuole around inside the cell and might help *Salmonella* spread from cell to cell.

Other *Salmonella* proteins wander over to the cell's "post offices"—compartments called Golgi bodies that package proteins, carbohydrates and fatty lipids for delivery to other parts of the cell. Palmer's team and other scientists suspect that *Salmonella* proteins may intercept these nutrient parcels and deliver them instead back to the bacteria.

Palmer is now working on ways to track multiple proteins simultaneously to see how they coordinate an attack. She is also collaborating with the U.S. Department of Agriculture to study how *Salmonella* invades pigs, cows and chickens. Eventually, her work may reveal how *Salmonella* maintains its niche in the cell, allowing infections to persist.

What Matters Most

When Palmer's not on campus, she's most likely spending time with her family—Alexis Templeton, a geology professor at CU-Boulder, and their two children, Ethan (5) and Ellie (3).

Palmer works hard to maintain a balance between her work and family life, says colleague and friend Deborah Wuttke, a biochemist at CU-Boulder. "She has an incredible ability to multitask and a strong commitment to both family and her professional life."

Though full of energy, Palmer recognizes that you can't excel at everything all at once. Her career and family are her top priorities.

So, at least for now, Palmer has less time for her hobbies, such as rock climbing. During graduate school, Palmer, Templeton and Trainor would spend weekends climbing in the mountains of California.

"It was one of my biggest passions," Palmer says.

"She was set on being a good climber and taking the lead," Trainor says. "She had a healthier perspective than most scientists in terms of balancing life inside and outside the lab."

The formula is simple for Palmer: "It's a matter of figuring out what matters the most and making compromises," she says. "If I have to choose between finishing a paper now and going to my son's preschool graduation, of course I'm going to the graduation."

Palmer is also grateful for the support of Templeton, who understands the lifestyle and stresses of academic life. She remembers how Templeton helped her address one particular challenge—knowing when to shut her door.

"I would leave it open all the time and never get any work done," she says.

Finally, Templeton gave her a crucial tip. "Now, if I close it most of the way, the students know not to bother me unless it's really important," Palmer says.

Opening the Door

Palmer's friendly and helpful nature makes it difficult for her to deliberately shut the door, even partway, on her students.

"I never had a professor like her," says Jose Miranda, one of Palmer's graduate students. "She always took the time to make sure everyone understood, and her door was always open. When I'm a professor, I'm also going to have an open-door policy."

Teaching is what initially attracted Palmer to an academic career. "I want to bring excitement and innovation into the classroom," she says.

To learn how, she obtained a master's degree in science education while working on her Ph.D. in biophysical chemistry at Stanford.

"I realized that not everyone learns the same way that I do, and I should adopt a lot of different strategies to reach the most students."

The dedication to teaching is a major factor that attracted her to CU-Boulder, which had initiated the Science Education Project under the direction of Nobel laureate Carl Wieman. The project works to improve science teaching by using research-validated classroom techniques and technology.

"It gave me the courage to try out different things in the classroom," Palmer says. She relates chemistry to daily life, intersperses lectures with discussions and encourages students to interact and ask questions.

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AMY PALMER

Palmer and her partner, Alexis Templeton, take a break from academic life during their annual family vacation to Maine.

Research on an enzyme that repairs sun damage in plants and animals could reveal new ways to prevent and treat skin cancer in humans.

Sun Damage—More Than Skin Deep

Too much sun makes your skin wrinkled, burned and leathery. It also damages your DNA, increasing your risk for cancer. Plants and many animals have an enzyme called photolyase that can repair sun damage. Humans lack it.

Recent studies revealing the workings of photolyase provide a ray of hope for preventing or treating sun damage in people. The research was led by Dongping Zhong, a physicist and chemist at Ohio State University in Columbus.

The scientists first exposed a strand of DNA to ultraviolet (UV) light, causing the same kind of damage as the sun. Then they added photolyase. Using an ultra-fast laser as a sort of high-tech flashbulb, they were able to see photolyase in action as it repaired the UV-damaged DNA.

Zhong's group discovered that photolyase sends an electron and a proton to repair the damaged genetic material. After this process, the electron and proton return to the enzyme—possibly to start over and heal other areas.

More research on photolyase might lead to new treatments for skin cancer and better sunscreen products.—*Jilliene Mitchell*

As a scientist, you create knowledge…

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Palmer's students soon realize that understanding natural phenomena can be pretty cool.

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One course she teaches is physical chemistry, or, as she calls it, "Chemistry for the Unwilling."

"Most students think they'll hate it," Palmer says. "My goal is to get them to realize that it's cool to understand something about the physical phenomena you see in the world."

According to Wuttke, Palmer is one of the most popular teachers in the rigorous course's history.

"She completely turned [the course] around by bringing in modern teaching tools. She holds her audience with rapt attention," Wuttke explains.

Palmer hopes that her teaching will have a tangible impact, moving some of the students, as she once was, from "unwilling" to "potentially interested" in a research career. For these students, the next step is to gain laboratory experience.

"Listening to lectures is not the same thing as being a scientist," Palmer says. "As a scientist, you create knowledge; you don't just learn what's been done before."

And Palmer hopes that students who experience research will become hooked, like she did.

"There's no one path or right answer, and every question leads to more questions," she says about a research career. "It's an incredible endeavor to be a part of."

MATTHEW GILSON

Hilary Godwin

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Read about a scientist who studies a metal that is toxic at virtually any level—lead—because it displaces healthy metals like zinc. Go to http://publications.nigms.nih.gov/findings/mar05/lead.html