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Up Close With

George Hightower

FUTURE VIROLOGIST

"Science isn't something you can look up in a book and find what's wrong or right."

FAVORITE FOOD

Pizza, any kind

MUSIC

"Anything and everything"

FIRST JOB

Dishwasher

FAVORITE TRAVEL DESTINATION

East Africa, for the natural beauty and diversity of its people and animals. "If you keep your eyes and ears open, any place is interesting."

PERSONAL HERO

"My mom. … She taught me the importance of caring and giving."

NICK ABADILLA

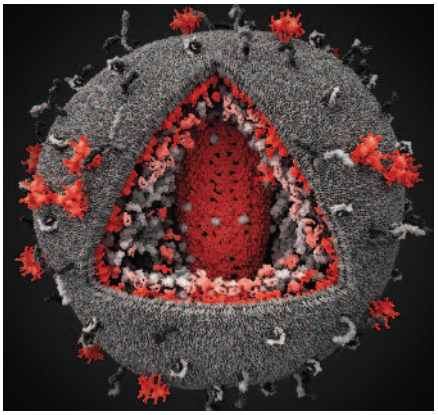
HIV on the Brain

BY AMBER DANCE

George Hightower likes to get lost.

Sometimes, that means rolling through southern Mexico on a local bus, not knowing exactly where the driver is going.

More often, it means mentally meandering through the DNA sequence of the human immunodeficiency virus (HIV), which causes AIDS. In so doing, he hopes to discover how HIV can attack the human brain, ravaging concentration, memory and judgment.



VISUAL SCIENCE COMPANY, WWW.VSCI.US

See structure-based images of HIV and rotate an illustration of an HIV particle 360 degrees at http://visualscience.ru/en/illustrations/modelling/hiv.

Hightower, a student at the University of California, San Diego (UCSD), is midway through a 9-year program to earn a combined M.D. and Ph.D. He aims to become an infectious disease expert who treats and studies viruses and bacteria.

Already, his work has revealed that some of HIV's many varieties are harder on the brain than others. The research might one day help doctors manage the effects of HIV brain infection and customize drug treatments based on the type of infection each person has.

But it's a lust for learning, as much as potential medical advances, that inspires Hightower to pore through the nearly 10,000 As, Ts, Gs and Cs in HIV's genome.

"It's the blueprint for life," he says, referring to the genomic letters. "I think that will always be exciting to me."

Writing the Textbook

Ever curious, Hightower fell in love with research during college at UCSD when he joined the laboratory of medical virologist and infectious disease physician Douglas Richman.

At the time, Hightower was enrolled in an immunology class. Although he loved learning about the body's numerous defenses against bacterial and viral invasion, he admits that memorizing a long list of immune cell types was less than thrilling.

Listening in on the seasoned scientists one day in the lab, he noticed that they weren't talking about that textbook list. They were debating whether certain cell types existed at all and what they might do if they were real.

NICK ABADILLA

[My] curiosity is really unlimited.

JONATHAN WINN

Hightower runs a weekend science academy at the San Diego school where these students just finished the Advanced Placement exam for calculus.

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These scientists were planning experiments that would fill future textbooks.

Hightower felt that exhilarating rush of being lost amid the unknown—and the challenge of finding his way. He was hooked.

Unlimited Curiosity

It's not just science that captures Hightower's interest, but many other subjects, including anthropology (his original college major), politics and philosophy. You might call him "Curious George."

"[My] curiosity is really unlimited," he says. "It pushes [me] to be a better learner."

He also seeks opportunities to share his experience and knowledge, especially with students who challenge tough odds because of their socioeconomic status.

Hightower attended Lincoln High School in Stockton, California, where his classmates had a variety of cultural and social backgrounds. This experience, combined with a desire to "give back" to the community, influenced him to work with the diverse student body at the Crawford Educational Complex in mid-city San Diego.

Inspiring Others

The Crawford complex is made up of four specialized high schools. Nearly half of the students are immigrants still learning English and 95 percent are living in poverty.

In 2009, Hightower read an article about Jonathan Winn, who teaches calculus at Crawford. Hightower was impressed with Winn's confidence in his students and his innovative approach to bringing college-level math to high school students.

Hightower e-mailed Winn to find out how he could help. That launched what Winn calls Hightower's "brainchild": a weekend science academy.

On Saturday mornings, about a dozen Crawford students join Hightower at the school. They create robots, build rubber band-powered cars, launch Mentos from soda bottles and explore other activities that demonstrate principles of science (mainly physics).

The high schoolers then take on the mentor role themselves, traveling to local elementary and middle schools to demonstrate and explain the experiments to younger kids.

In 2010, Hightower spoke at the induction of Crawford students into a math honor society. His theme was "Be Inspired."

"That, to me, is George Hightower in a nutshell," Winn says. "He spends a lot of time inspiring others."

As for Hightower's own inspiration, he mostly credits his mother, a physician who raised three children and taught school in East Africa. She now works for the World Health Organization in Ethiopia, helping hospitals in several countries improve patient care.

Origins of a Plague

At his own work, Hightower sits in a tiny cubicle—lab members call them "confessionals." Atop his desk marches a collection of rubber figurines: a baboon, a lemur, a gorilla and other primates.

Hightower's rubber figurines remind him that HIV started in apes and monkeys.

NICK ABADILLA

They serve as a constant reminder that HIV didn't start in humans: It came from apes and monkeys.

More than 20 species of primates carry their own version of HIV, called simian immunodeficiency virus or SIV. When this virus is in its original host species, it doesn't make the animal sick.

It pushes [me] to be a better learner.

The problems occur when the virus jumps from one species to another.

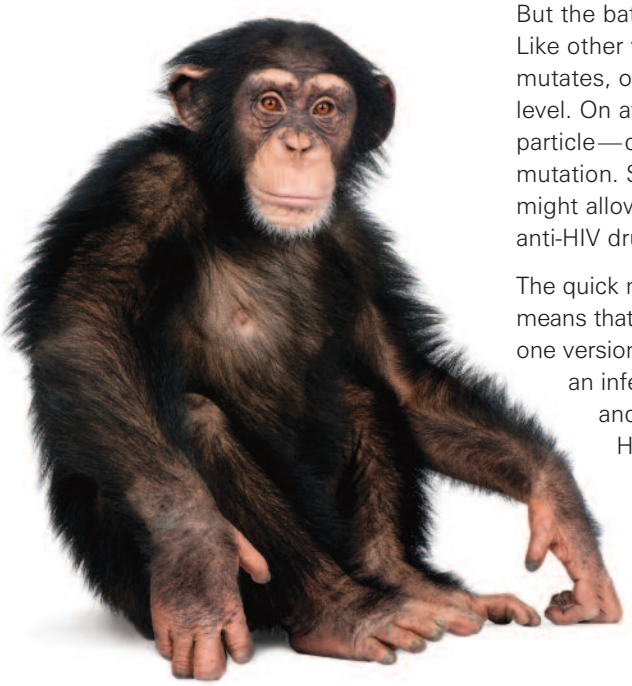
Scientists believe HIV originated as SIV in West African chimpanzees and monkeys. People hunting the animals for meat encountered the infected blood—and the virus gained a new host.

Viral Variety

HIV has made multiple jumps into humans, so there's more than one kind of the virus around. Each genetically distinct HIV version may cause a slightly different pattern of disease—it might make people sick quicker, be able to evade certain medicines better or be more likely to spread to the brain.

Worldwide, most infected people carry HIV-1, which is closely related to chimpanzee SIV and comes in a dozen different subtypes.

In some African countries, people have HIV-2, which appears to have originated in sooty mangabeys and comes in seven subtypes.



Scientists believe that HIV-1, the most common type worldwide, originated in chimpanzees.

Viruses are always evolving. Every winter, there's a new flu virus (and a new vaccine to combat it). And new viruses—like the one that causes SARS, or severe acute respiratory syndrome—keep emerging.

For infectious disease specialists like Hightower, that means the job will never get boring. "I can have a career 10, 15 years from now—working on a really important problem that we haven't even heard about today," he says.

Dodging Drugs

HIV is especially sneaky because it infiltrates the body's own defenses. It commandeers immune cells and turns them into factories that make new copies of itself.

The most common anti-HIV medications are protease inhibitors and reverse transcriptase inhibitors. They prevent the virus from reproducing inside human cells. These drugs have turned HIV from a death sentence into a long-term and manageable—but still serious—condition.

But the battle does not end there. Like other viruses, HIV frequently mutates, or changes at the genetic level. On average, every new virus particle—called a virion—has one mutation. Some of these mutations might allow the virion to evade anti-HIV drugs.

The quick mutation rate of HIV also means that a person doesn't just have one version of the virus. Davey Smith, an infectious disease physician and virologist who works with Hightower, says a single

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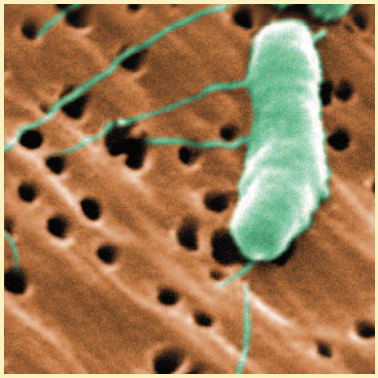

CDC/JANICE CARR

The bacterium that causes cholera (green) infects millions of people worldwide.

A Sweet Solution for Detecting Cholera

Poor sanitation and disasters like earthquakes and tsunamis can promote the spread of cholera, a water-borne, diarrheal disease that annually kills tens of thousands of people. Scientists devised a quick, inexpensive way to detect cholera toxin that might help limit the spread of the disease.

The new technique uses a special sugar and microscopic beads called nanoparticles. About 100 million nanoparticles lined up would measure just a millimeter.

A team led by chemist J. Manuel Perez at the University of Central Florida in Orlando created nanoparticles coated with the sugar dextran, which resembles the receptor the cholera toxin uses to invade intestinal cells. If cholera toxin is present in a water sample, it will bind to the sugar-coated nanoparticle and is then easily detected by a handheld machine.

The test would allow relief workers to identify contaminated water on the spot, instead of having to send samples to a lab. Workers could then restrict access to such water more quickly, possibly preventing a cholera epidemic.

The technique might also be adapted as an inexpensive cholera treatment that would be particularly valuable in the developing world. —*Erin Fults*

As long as I follow proper precautions, I'm safe.

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person can host a "swarm of variants" numbering in the thousands. Each of these variants might differ by just a single DNA letter.

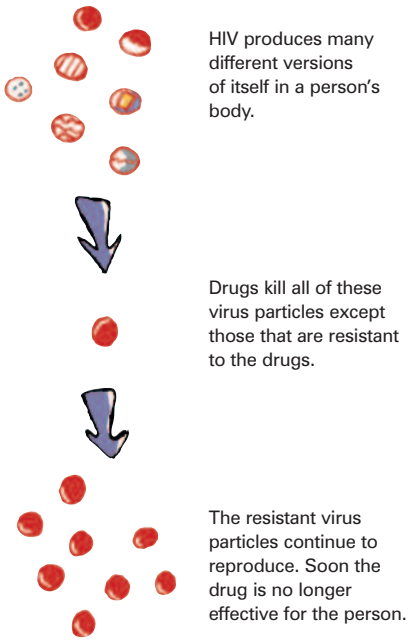
Evolution in Action

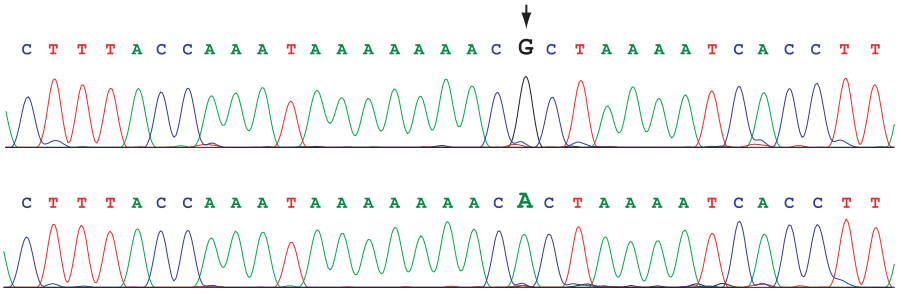
HIV's genome is diabolically simple. It contains only nine genes. Worldwide, more than a hundred laboratories are studying those genes in an effort to understand and combat AIDS.

By studying how HIV's genes change within their human host, scientists can better understand how more complex animals and plants evolve to match their environment.

"What I love about this research is it brings up some very basic concepts in evolutionary biology," Hightower says. "A lot of systems are so complex, you can't [easily investigate] these basic questions."

How HIV Resistance Arises





This readout from a DNA sequencer shows two sequences that vary by just one letter. Two high school students used DNA sequencing to bust several seafood joints in New York (see "DNA Sequences Expose Fishy Sushi," page 7).

Beeline to the Brain

Hightower is looking for the genetic mutations that affect HIV's ability to infect the brain. Identifying these will help scientists understand why some people have cognitive effects and others don't.

He is collaborating with Sanjay Mehta, an infectious disease specialist at UCSD. Mehta estimates that about a third of people with HIV have cognitive problems. Of those, only a third have severe symptoms.

Hightower and Mehta are working with scientists at UCSD's HIV Neurobehavioral Research Center who provide them with raw materials for the research—blood samples from HIV-positive people and test results that evaluate the people's ability to think and remember.

Does Hightower worry about working with HIV-infected blood?

"As long as I follow proper precautions, I'm safe," he says.

But just in case, there's a stash of HIV medicines in the lab fridge. If taken immediately after an accidental exposure to HIV and then for at least a month, these would prevent infection.

Color-Coded DNA

Hightower carries the vials of blood to a biosafety hood, a special cabinet that ensures the airflow moves away from him, so no HIV particles blow his way.

Using common laboratory procedures, he separates out the virus's genetic material and zeroes in on the

NICK ABADILLA

Before handling HIV-infected blood, Hightower dons gloves, safety glasses and a lab coat.

gene he's most interested in—reverse transcriptase, an enzyme found in HIV but not in humans.

Then, Hightower makes several copies of the gene and feeds them into the DNA sequencer. A boxy tabletop machine, the sequencer looks like a featureless, over-wide computer tower.

After a few hours, it displays a graph with overlapping, multicolored peaks and valleys. Each colored line—red, green, blue or black—corresponds to a different letter in the DNA sequence.

By comparing the DNA sequences of HIV variants, Hightower has discovered that, ironically, people infected with drug-resistant variants of HIV have fewer cognitive problems.

It sounds a bit backwards—a tough, drug-avoiding virus is soft on the brain. But in fact, it makes sense. A mutation that makes a virion resist drugs is likely to make it weaker, not stronger, Hightower says.

How come? Imagine an army tank that needs to pass through a low tunnel. The soldiers can remove the gun turret. The tank then fits through the tunnel—but it has lost its most powerful weapon.

Similarly, a mutation that enables HIV to resist drugs might make it slower to reproduce or less able to sneak into the brain.

Nature's Balance

When not at the lab or working with students, Hightower looks to nature to recharge his spirit.

He regularly runs along the beach near campus. It's a habit that started when he was in college.

"No matter how broke I was, I could go to the beach," he says.

Pounding the sand three times a week, Hightower dropped from 235 to 170 pounds. He lost so much weight

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DNA Sequences Expose Fishy Sushi

A pair of high school sleuths sequenced the DNA from their dinners to determine that New York City sushi wasn't always what it claimed to be.

The students, Kate Stoeckle and Louisa Strauss, collected 60 seafood samples from around New York in 2008. They discovered that one-quarter of the samples were mislabeled.

What was advertised as white tuna, an expensive fish, was really cheap tilapia. Flying fish caviar was actually plain old smelt. Red snapper turned out to be Atlantic cod.

Stoeckle and Strauss relied on a technique called DNA bar coding, which scientists use to identify species.

Instead of sequencing all of an organism's DNA, bar coders read just one gene, in this case, the one that encodes cytochrome c oxidase.

Cytochrome c oxidase is part of the electron transport chain, which all life forms use to make energy in the form of ATP.

Because each species has a slightly different code for cytochrome c oxidase, bar coders can pinpoint a species by just reading the one gene.

The students started their experiment with a sushi-buying binge. They preserved bits of the fish in alcohol.

Then they enlisted the help of Eugene Wong, a graduate student at the University of Guelph in Ontario, Canada. He compared the bar codes from the sushi with a database of bar codes from more than 5,000 fish species.

The experiment was possible because DNA sequencing is getting faster and cheaper. Reading a bar code costs as little as $5—less than a plate full of sushi.—*A.D.*

TRAUMA.ORG IMAGE DATABASE

Flooded with fluid, a lung with ARDS (left) shows up white on an X-ray, while a normal lung (right) is black.

Breathing Easy: Inflammation Under Control

You may never have heard of ARDS (acute respiratory distress syndrome), but it is a leading cause of death in intensive care units. Doctors don't know exactly what triggers it, and there are no specific drugs to treat it.

ARDS often follows a serious injury or infection. It begins when an overzealous inflammatory response floods the lungs with fluid, preventing oxygen uptake and causing major organ failure.

Immunologist Laurie Kilpatrick at Temple University School of Medicine in Philadelphia may have discovered how to rein it in. By studying ARDS in rats, she was able to prevent many of its symptoms by blocking the action of a specific enzyme.

This enzyme, known as delta-protein kinase C, activates white blood cells called neutrophils. Part of our first-line defenses, neutrophils spew out toxins to kill bacteria and other invaders. These chemicals also inflame nearby tissues. Blocking delta-protein kinase C shuts down neutrophils and seems to halt the cascade of inflammation.

The finding points to a possible drug target for ARDS and could also help explain what causes this out-of-control inflammatory reaction. —*Hadley Leggett*

A big part of science is sharing ideas.

NICK ABADILLA

Running on the beach helps Hightower keep physically and mentally fit.

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from his 5' 8" frame that high school friends didn't recognize him at a recent reunion.

To bring nature into his own living space, Hightower built a greenery-covered enclave on his patio.

He began by scavenging plants abandoned by departing graduate students. His favorites are cacti and other succulents that grow in strange, Dr. Seussian shapes.

The garden is now a welcome sanctuary for reading and bird watching.

Globe Trotter

Hightower also continues his interest in other cultures. Fortunately, science offers opportunities to travel.

In 2010, he worked with scientists in Ethiopia. He also attended a meeting of Nobel laureates in Lindau, Germany.

His favorite part of the Lindau meeting was the informal chats with other attendees and with laureates—including some of his personal heroes.

A big part of science, Hightower says, is just sharing ideas, trying to get unlost together.

His most recent trip was a honeymoon in Mexico. Not surprisingly, they got lost, he chuckles.

Hightower embraces those puzzling times during travel, and in the laboratory, too.

"Even when I'm most frustrated … there's no place I'd rather be." ● ● ●

FIND MORE @

Learn about HIV/AIDS biology and research at http://www.niaid.nih.gov/topics/hivaids/understanding/pages/default.aspx

See a timeline of HIV milestones at http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm117935.htm

Get basic facts on HIV and AIDS from the Centers for Disease Control and Prevention (http://www.cdc.gov/hiv/topics/basic) and from AIDS.gov (http://www.aids.gov/hiv-aids-basics)

KEITH WELLER

Up Close With

Cara Altimus

NEUROSCIENTIST

"Everyone is really interested in science. They just don't know it."

BEST THING TO DO ON A RAINY DAY

Walk over all the bridges in downtown Baltimore

PETS

Two dogs, Tuxedo and Zinnia, and a cat, B.B. Queen

FAVORITE COLOR

Red

ALTERNATE CAREER

Geologist

MOST UNUSUAL BIRTHDAY GIFT

Jigsaw (the power tool, not the puzzle), from my parents

A Light on Life's Rhythms

BY STEPHANIE DUTCHEN

A dozen bleary-eyed students lay draped across the furniture in a university lounge at dawn. By the flickering light of the movie *Ratatouille*, each one gently played with one or two lab mice.

It was part of graduate student Cara Altimus' study on the effects of sleep loss on the mice. Altimus couldn't exactly hold 20 mice herself to keep them awake, so she convinced her labmates to help "Pet a Mouse for Science."

Research on the brains of mice sheds light on the inner workings of our own.

Because mice and humans use similar neurological processes to control many behaviors, studies like this promise to help us better understand the effects of insufficient or disrupted sleep on night shift workers, people with sleep disorders and even students who pull all-nighters to cram for exams.

Now a 26-year-old neuroscientist at the Johns Hopkins University School of Medicine in Baltimore, Maryland, Altimus is burrowing deeper into the brain. She uses genetic and behavioral experiments to uncover how networks of cells, proteins and genes control learning, memory, mood and the daily rhythms of our bodies.

"What gets me excited is circuits—not electrical circuits, but how cells and components interact," says Altimus. "When you think about it, our memories are just cells talking to each other."

Sand Science

Altimus says the first inklings that she might become a scientist came when, as a kid, she "watched sand move around."

She grew up on St. Simons Island, a major shipping port off the coast of Georgia. Every storm that hit the island swept in mounds of sand that clogged the shipping channels. Altimus watched as engineers scrambled to clear the sand without "messing with" its natural movement up the coast.

"We watched experiments in action," she recalls. "As a family, we would try to predict what would happen" to the sand over time if the engineers hauled it out to sea or dumped it on land.

In high school, she did a science fair project on whether the color of sand related to its proximity to sediment-rich rivers or the ocean.

"We took the family boat to every nearby beach," she says. "It took a whole summer. I took it super-seriously."

KEITH WELLER


graph
composition book
100 sheets

Her first discovery … changed the field.

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By the time she went to college at the University of Georgia, she thought she would become a geologist. On a 10-week van trip across the country, she helped a group of geologists map rivers and canyons, filling notebook after notebook with field observations.

But Altimus ultimately found geology "too static." She turned to ecology, then genetics, and that led her into neuroscience. Now she perturbs genes and sleep patterns instead of sand.

In a twist of fate, in 2010 Altimus married a geologist. She and her husband, John, have spirited debates about just how "static" geology is, and compete to identify rocks or find fossils faster.

With a grin, she says, "He's not always the best."

More than Meets the Eye

When she started graduate school at Hopkins, Altimus joined the biology department and "rotated in every kind of lab I could."

That included studying gonad formation in flies, neural development in zebrafish and light's effect on body temperature in mice.

She decided on the lab of neuroscientist Samer Hattar, where she studied the "master clock" in the brain. This clock, driven by hundreds of genes and proteins, keeps our bodies running on a roughly 24-hour cycle (see "How the Body Keeps Track of Time—Or Doesn't," page 13).

Our brains also use ambient light as an external cue to align our daily, or circadian, rhythms with our environment.

Altimus wanted to know more about how light and darkness help set our inner clock and what happens when our clock is out of synch with the world around us.

When she started her research, scientists already knew that light enters the eye, strikes the retina and triggers nerve impulses that travel along the optic nerve to the brain.

Altimus' first discovery in Hattar's lab was that light information actually has two possible paths to follow: "image-forming," which creates a picture of what we see, or "non-image-forming," which relays information about how light or dark it is out there.

It turns out that the non-image-forming path has a big impact on us without our conscious control. It helps align our master clock, constricts our pupils when it's bright outside and even affects our mood and alertness.

"This was her first discovery, and it was a major paper and changed the field," says Hattar. "I still get shivers."

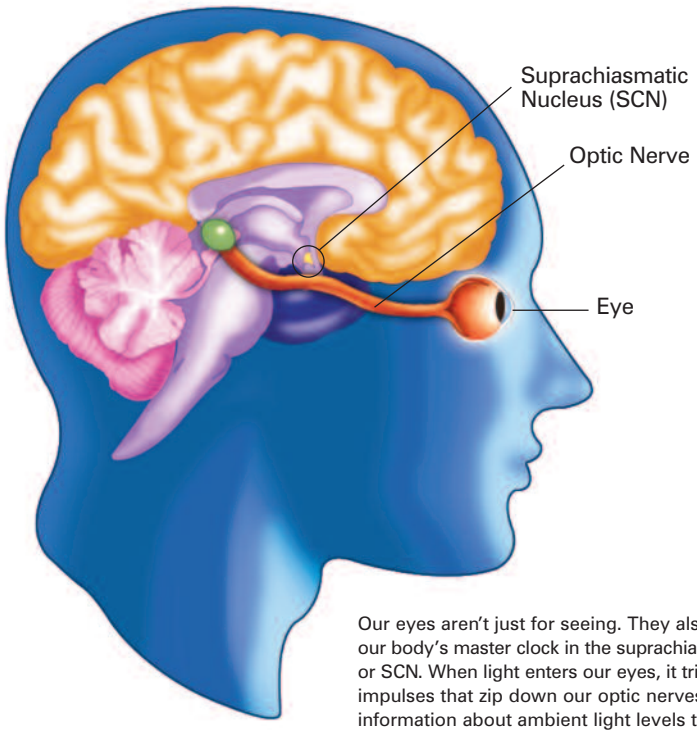
But how do cells in the retina work together to sense the amount of light around us and adjust accordingly? Learning about this process, known as photoentrainment, became Altimus' next major project.

Responding to the Light

There are three kinds of light-sensitive cells in the eye: rods, which help us see in the dark; cones, which allow us to see in color; and a tiny smattering of another cell type containing a light-sensitive protein called melanopsin.

The team believed that rods and cones were transmitting image-forming information, while the melanopsin cells were responsible for photoentrainment.

story continues on page 14



Our eyes aren't just for seeing. They also help regulate our body's master clock in the suprachiasmatic nucleus, or SCN. When light enters our eyes, it triggers nerve impulses that zip down our optic nerves and relay information about ambient light levels to the SCN.

How the Body Keeps Track of Time—Or Doesn't

The daily, or circadian, rhythms of our bodies rise and fall to the tick-tock of biological clocks. These clocks are found in a vast array of organisms, telling trees when to bud or shed their leaves, reminding bears and toads to hibernate, synchronizing biological activities in fruit flies, even keeping an internal beat in microbes.

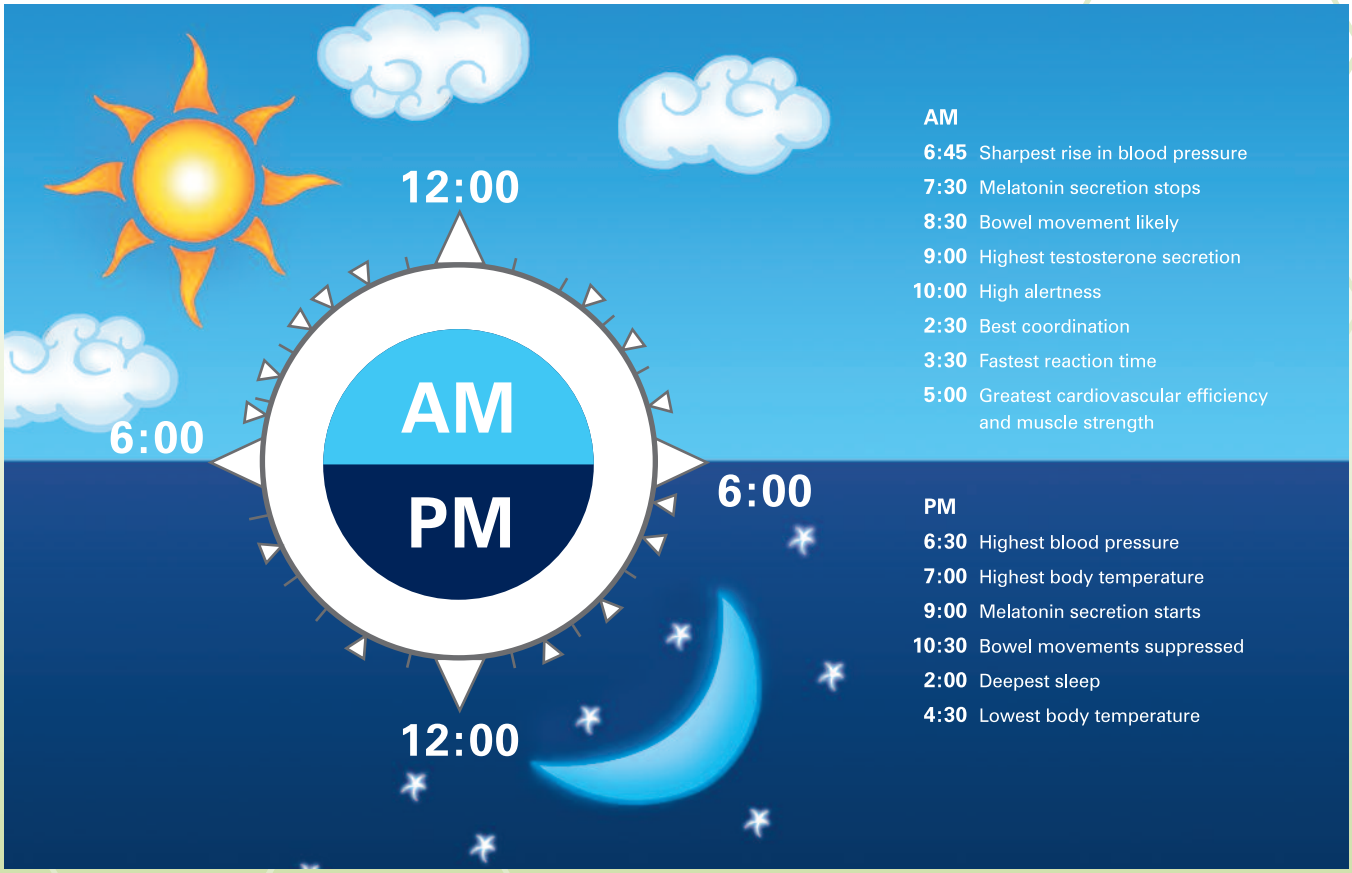
Our own master clocks are located in a tiny area of the brain called the suprachiasmatic nucleus or SCN. (We also have an array of little clocks throughout our bodies, from the lungs and liver to individual cells.)

Smaller than a pea, your SCN is located near the center of your brain, a few inches behind your eyeballs. It sits just above your optic nerves, which relay information from your eyes to your brain, so it's ideally positioned to receive information about the amount of incoming light. It adjusts your sleep/wake cycles accordingly. When there's less light, such as after sunset, the SCN directs your brain to produce more of a sleep-inducing hormone called melatonin.

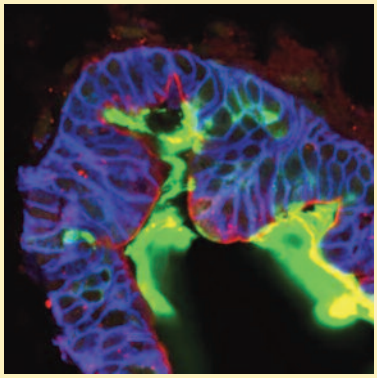
If this process goes awry, or if your daily routines go against your body's natural clock, you could end up with a sleep disorder or other health problems.

Some people have "delayed" or "advanced" sleep phase disorders, where they get sleepy too late or too early. Others with seasonal affective disorder get the blues as daylight wanes in the fall and winter.

You've experienced temporary circadian rhythm disruptions if you've had jet lag, felt groggy after waking up too early one day or had trouble falling asleep at night after staring at a bright computer or TV screen for hours. —*S.D.*



Our body's master clock, located deep in our brains, regulates the cycles of many bodily functions.



JAMES WELLS

This lab-grown tissue exhibits all of the major intestinal cell types and functions to secrete mucin (green).

Got Guts?

For the first time, researchers have coaxed human cells to form 3-D tissues that look and work like organs.

The "organoids" function like intestines. They contain all the major intestinal cell types and display characteristic intestinal structures, including fingerlike projections. They are able to absorb nutrients and secrete proteins, just like our own intestines.

Developmental biologist James Wells and his team at Cincinnati Children's Hospital Medical Center created one batch of organoids from human embryonic stem cells and one from induced pluripotent stem (iPS) cells. Like embryonic stem cells, iPS cells, which came from human skin biopsies, can turn into virtually any cell type in the body.

The two cell types were put in separate laboratory containers and exposed to growth-promoting proteins. Within a month, the cells in each container morphed into four different cell types and formed a tissue that resembled a fetal intestine.

The study will shed light on how human intestines develop and function. The work might also be useful in treating certain bowel diseases or designing drugs that are more easily absorbed through the intestines. —*Erin Fults*

In science, there's a lot of stuff to

continued from page 12

But if people (or mice) don't have working melanopsin cells, their brains still sense light and align their circadian rhythms. Clearly, melanopsin cells aren't the only ones contributing to photoentrainment.

That left two options: rods and cones. Because cones are the main players in image formation during daylight hours, most scientists suspected they would also be the ones involved in photoentrainment.

Altimus proved otherwise.

Through genetic engineering of mice, she showed that rods, rather than cones, help with the heavy lifting of photoentrainment.

"This is where she soared," says Hattar.

She went on to discover that light and dark both affect sleep patterns, and that melanopsin plays a role in the process.

Night Shift

Driven by concern about the health impact of night shift work, Altimus investigated the effects of exposure to light at the wrong time of day.

She found that when she shifted the sleep patterns of mice by turning on a light when it was supposed to be dark (a regular experience for night workers), the animals had temporary learning problems.

To detect learning, she gave the animals new objects—typically Christmas ornaments—and let them sniff, nudge and climb all over them. Sometime later, she would show the mice the ornaments again to see whether they recognized them.

She discovered that, even when the mice got a normal amount of sleep, if their sleep cycles were misaligned with their environment, they didn't seem to remember the objects. This suggests that shift work might cause trouble with learning and remembering, even for those workers who get 8 hours of sleep during the day.

The retina spreads out in this image like flower petals with the optic nerve at the center. Nerve cells containing the light-sensitive protein melanopsin are shown in blue.

DAVID MCNEILL, HATTAR LAB

Construction Zone

When Altimus began her research, Hattar's lab didn't have all the equipment she needed.

She lacked the budget and the patience to wait, so she built what she needed herself.

Armed with amateur experience in woodworking and a stubborn determination, she made a water maze—a setup that can cost $10,000—from a $350 cattle tank. Then she built a camera mount on the ceiling to record the mice's movements.

She made boxes to hold the cages where the mice ran on their wheels. She built a crate to house a tool that measured the mice's ability to track a moving pattern. And she put together a contraption shaped like a plus sign to see how much time the mice spent in closed versus open spaces, a measure of their anxiety levels.

It wasn't all perfect—sometimes she had to build things twice—but today, the lab staff still uses much of what she built.

process. You need to think about things for a lot of time.

Knack for Numbers

Altimus also has another uncommon and useful skill.

"I am slightly obsessed with numbers," she says. "I remember the first phone number I ever dialed and my parents' credit card number from when I was 16."

She loves quantifying things, from tracking gas prices to calculating the perfect speed to drive to work so she makes the most green lights.

This talent helps her out in the lab, where she can look at data and quickly recognize changes in a mouse's wheel-running behavior or sense if a piece of equipment isn't calibrated properly.

Work and Play

Altimus also prizes her ability to stay fully engaged in her work for hours, something she got better at when she took music classes.

"In science, there's a lot of stuff to process. You need to think about things for a lot of time," she says.

As a result, she sometimes finds it hard to stop working at the end of the day. After meeting her husband for dinner, Altimus often finds herself going back to the lab to solve a nagging problem while John reads scientific papers and keeps her company. Or they'll go to his office and she'll catch up on her own paperwork.

In college, Altimus taught classical guitar to underprivileged children.

KEITH WELLER

"We are both really interested and excited by our work," she says. "We get bogged down if something doesn't make sense, and we try to solve it right then."

Spending evenings together in the lab is one way Altimus and her husband make time to see each other while juggling busy schedules. They also carve out 20 minutes each morning to sit and have breakfast.

"We don't really rest. We get antsy if we're not doing something," she says.

Instead of watching TV, they read and debate the news. When they're not at work, they hike, bike and take advantage of Baltimore's cultural events, from museum exhibits to symphony concerts.

Altimus also plays classical guitar and tutors high school students in biology.

In the midst of everything, she still finds time to bake. The latest in a "long line" of bakers, she whips up cookies, cakes and pastries for her labmates and other staff.

Learning About Learning

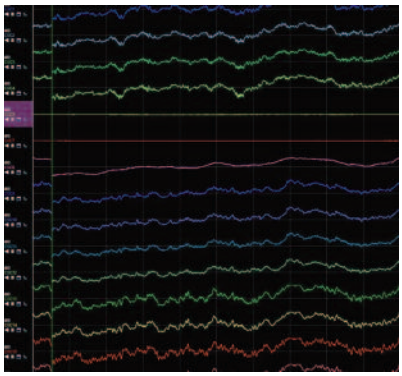
After 5 years in Hattar's lab, Altimus completed her Ph.D. degree in 2010. Since her subsequent departure, Hattar and others have missed more than her cookies.

"I wanted Cara to stay [in my lab] forever," Hattar says. "She is innovative, doesn't get scared, reads the literature, works hard and gets things done. And she can build stuff."

Altimus is now a postdoctoral researcher in the lab of Hopkins neuroscientist David Foster.

Even though she has been in his lab for just a few months, Foster says Altimus "is not only persistent and works really hard, she is creative. That is a very potent and rare thing, to see both in the same individual."

Altimus is setting up experiments that will give her a front-row seat to a live performance—watching and recording the brain activity of rats and mice as they navigate their way through mazes in search of food.



CARA ALTIMUS

Altimus studies the brain activity of rats and mice to understand how human brains work.

She's following up on an intriguing finding Foster made: As rats run through a maze, their neurons fire in a certain order, seemingly taking note of landmarks. Then, when the rats reach the food and stop to eat and groom themselves, the same sequence of neurons fires again—but in reverse.

It's as if their brains are reviewing the path backwards to remember how they got to their tasty snack.

Foster calls it "reverse replay." He suspects human brains do it, too.

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Chemical tags on certain DNA letters can change the activity of genes without altering the DNA sequence.

Starved Parents, Obese Children?

Whether you are well nourished—even before you become a parent—might affect the health of your descendants.

Researchers observed decades ago that if food was scarce during a man's lifetime, his grandchildren had higher-than-average rates of diabetes, obesity and cardiovascular disease.

Clearly, the descendants were inheriting *something* that increased their risk of these diseases, but what was it? Normally, gene sequences are passed unchanged from parent to child.

A new study by biochemist Oliver Rando of the University of Massachusetts Medical School suggests that changes in the activity of genes—seemingly without changes in their DNA sequence—might be responsible.

Rando found that when male mice were fed a low-protein diet, the activity of hundreds of genes in the animals' offspring changed. In particular, genes that manufacture fats were more active. Making too many fats can lead to obesity and related diseases. These same genes also displayed an altered pattern of chemical tags that regulate gene activity through a process called epigenetics.

Scientists are still trying to understand how epigenetic changes occur and how such changes might affect the metabolism and disease risks of future generations. —*Kirstie Saltsman*

There's always more to be done . . .

continued from page 15

Altimus will conduct similar maze experiments in mice, which are easier to genetically modify than rats. She'll study a range of brain processes, like how certain neurons get "recruited" at different times during memory formation, how reverse replay happens in normal brains and how it may go wrong in diseased brains.

It's complicated work because the brain is intimidatingly complex—countless genes and proteins are working simultaneously. She can't just study one at a time, then piece them together to get the whole picture.

Foster explains, "It's like trying to make a blueprint of a car by saying where all the atoms should go."

Altimus hopes to improve scientists' basic understanding of what happens in our brains as we go about our daily lives.

That knowledge, in turn, might lead to better treatments for brain disorders like Alzheimer's disease.

"The whole field is feeling its way, but the motivation is very clear: preventing cognitive diseases," says Foster.

Mice are nocturnal. Those in a laboratory spend most of the day asleep and most of the night running on their exercise wheels.

In the meantime, Altimus says that, for her, the greatest reward of science is "the day-to-day."

"It's that stereotype of you in a room, seeing something that suddenly makes sense," she continues. "Or thinking about it until it makes sense. Or maybe it doesn't make sense, and then you try something else."

Does she ever worry about running out of ideas or new things to try?

No. "There's always more to be done," she says. "It's science." ● ● ●

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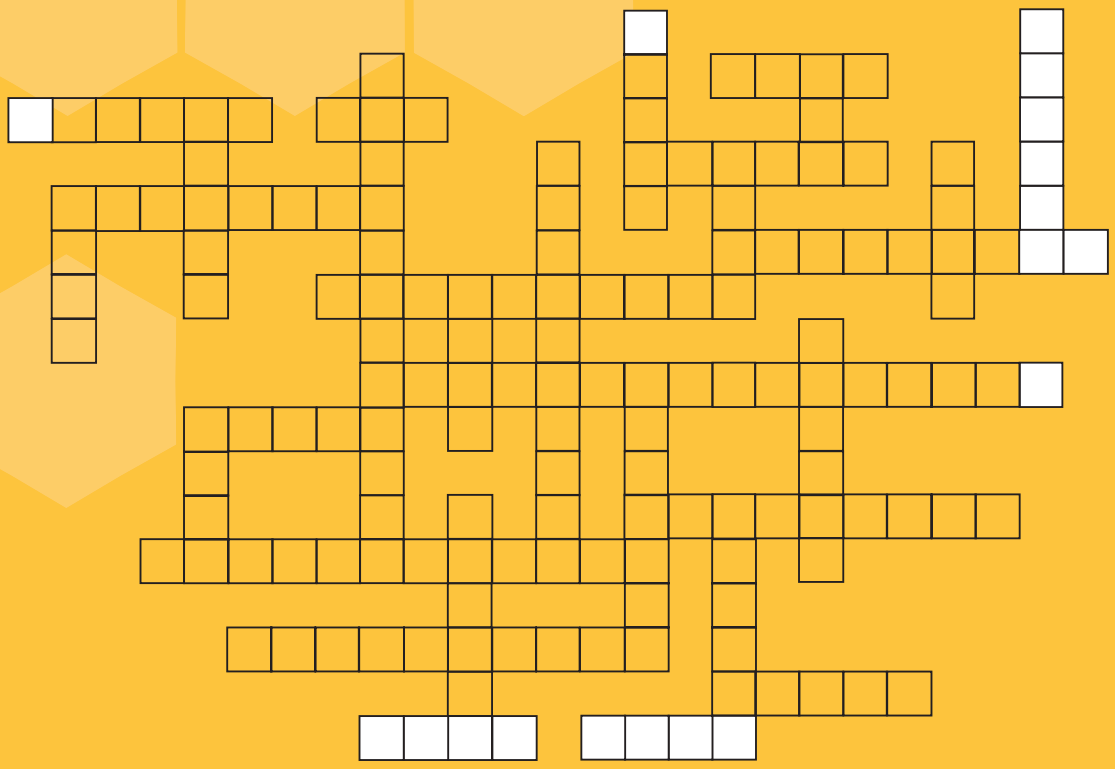

ACROSS

4. School Hightower attends
6. When traveling across many time zones, people can experience _____
8. A type of light-sensing cell in the eye
10. HIV attacks the _____ system
13. DNA change
14. The daily rhythms that control sleep and many other biological functions
15. HIV jumped to humans from this species
18. The brain senses light and aligns its cycles accordingly through this process
20. The body uses external signals like light and dark to set its biological _____
22. Cheap way to ID species
24. The scientific field that focuses on the nervous system, including the brain
25. Studying learning and memory in mice could reveal more about this brain disease
26. Raw fish dish
27. # genes in HIV
28. Creature infected with a virus

DOWN

1. HIV sometimes affects the _____
2. HIV emerged in West _____
3. University where Altimus conducts research
5. Abbreviation for the part of the brain that houses the human "master clock"
7. Through natural selection, organisms _____ to their environment
9. A light-sensitive protein found in some nerve cells in the eye
11. Altimus works with these animals in the lab
12. HIV causes this disease
13. Altimus measures brain activity in mice while they navigate through a _____
16. Abnormal sleep patterns can affect learning, memory and _____
17. Individual virus particle
19. Altimus has an uncanny ability to remember these
20. The type of eye cell that lets us see in color
21. "S" in SIV stands for
23. Mutations can make HIV _____ drugs

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