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

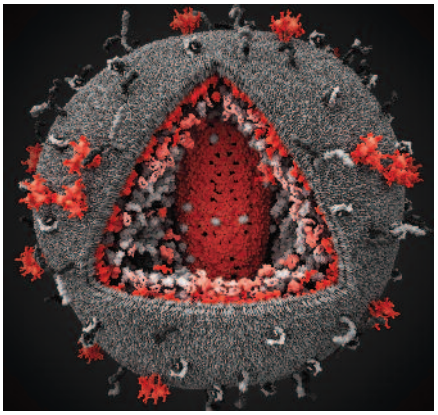
HIV on the Brain

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.

continued from page 3

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.

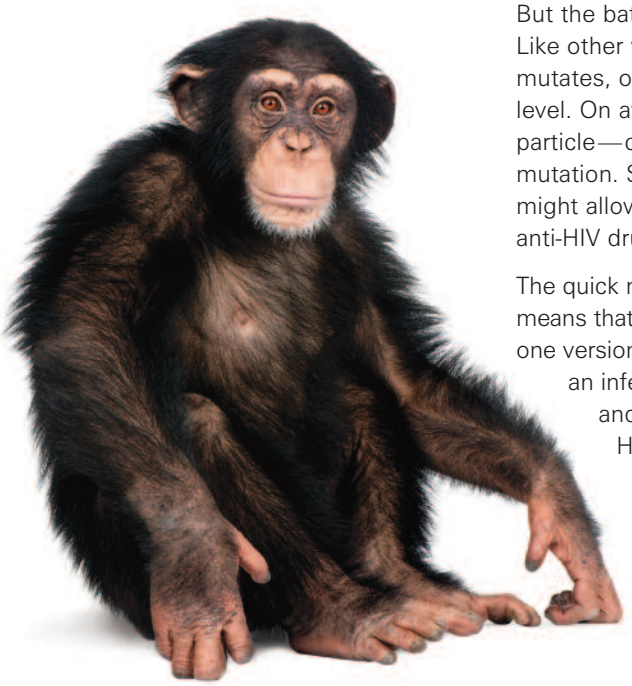
Scientists believe HIV originated as SIV in West African chimpanzees and monkeys. People hunting the animals for meat encountered the infected blood—and the virus gained a new host.

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

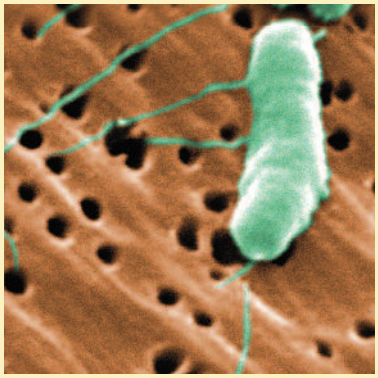
HIV is especially sneaky because it infiltrates the body's own defenses. It commandeers immune cells and turns them into factories that make new copies of itself.

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

story continues on page 6



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.

continued from page 5

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

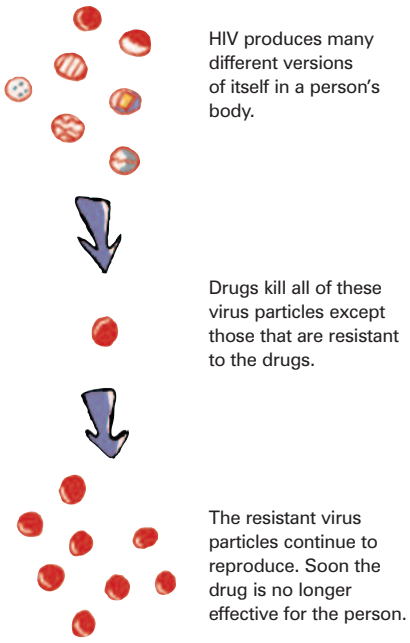
Evolution in Action

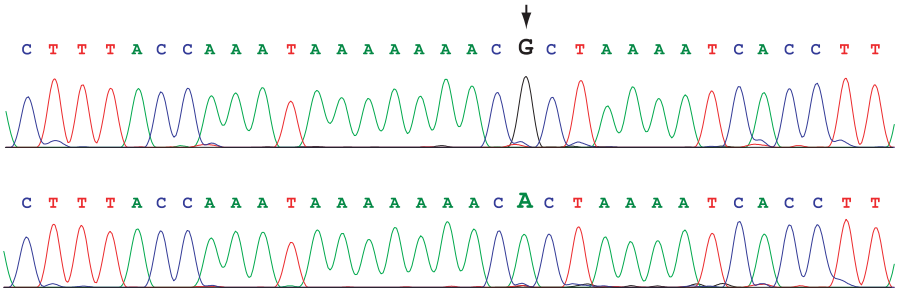
HIV's genome is diabolically simple. It contains only nine genes. Worldwide, more than a hundred laboratories are studying those genes in an effort to understand and combat AIDS.

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

story continues on page 8

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.

continued from page 7

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)