

Year 2015 | Volume 13 | Health | Natural Science | Technology | Social Science | Humanities | Business

# Research *at* Penn





# Moving Knowledge Forward



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In this brochure, you will read about some of the eminent research across the University's 12 schools from the past year.

A team of researchers is unraveling the mysteries of anesthesia, while another has uncovered a previously unknown pharaoh in Egypt. Scientists are finding new ways to ferry drugs across the blood-brain barrier, and others are making strides toward creating highly efficient solar panels. Designers are examining how to protect the Chesapeake Bay region from rising sea levels, and a legal scholar is examining whether U.S. companies are truly American-owned.

At Penn, research is aimed at expanding the frontiers of human achievement and understanding with the ultimate goal of improving the world.

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# Research *at* Penn

*Advances in Knowledge  
from the University  
of Pennsylvania*

Year 2015 | Volume 13 | [upenn.edu/researchdir](http://upenn.edu/researchdir)

Health | Natural Science | Technology | Social Science | Humanities | Business

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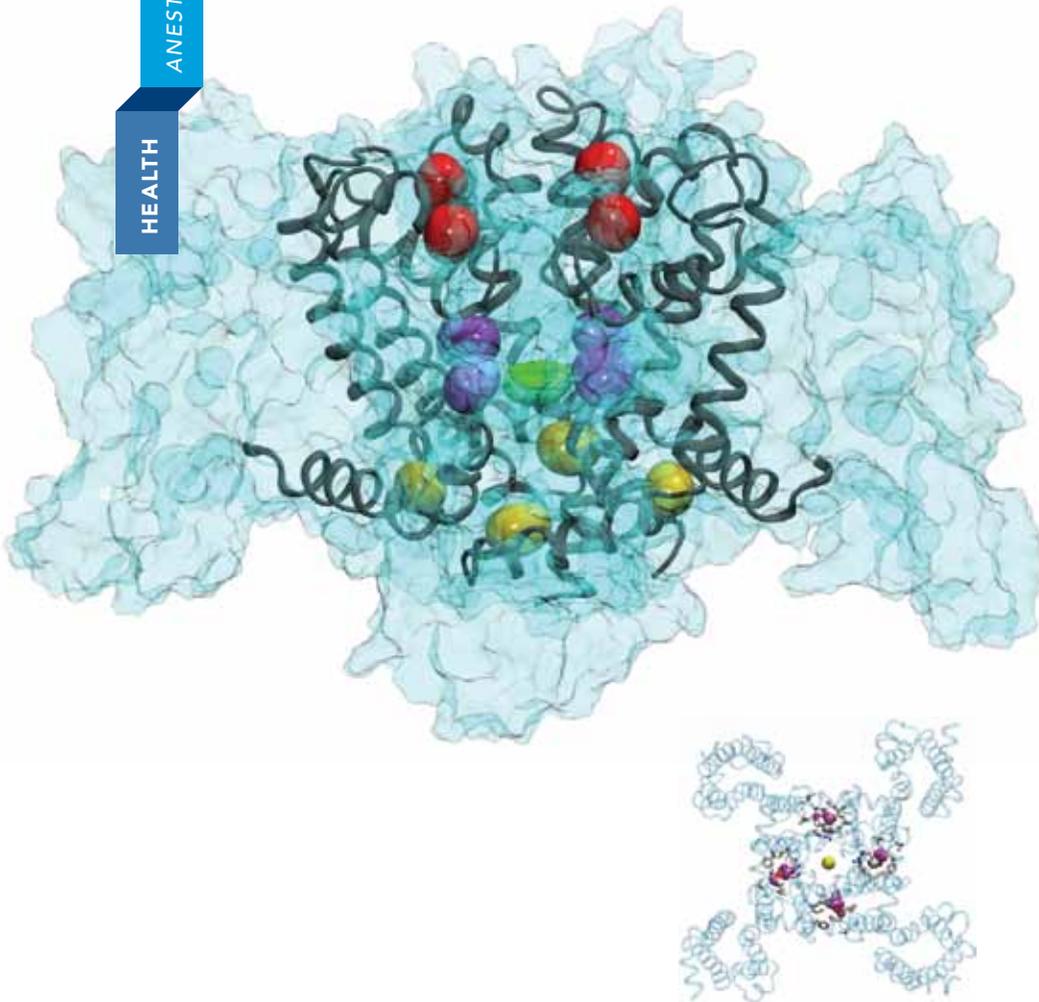
# Untangling the Mysteries of Anesthesia

**Anyone who has undergone surgery—from a simple filling at the dentist to a major cardiac procedure—has experienced anesthesia of some kind.** But despite its widespread use, how anesthesia works in the body remains a mystery.

New research by a team at Penn's Perelman School of Medicine has shed light on how one common anesthetic, sevoflurane, performs in a sodium ion channel. The study, published in the *Proceedings of the National Academy of Sciences*, is part of an ongoing research project led by Roderic Eickenhoff, vice chair for research and a professor of anesthesiology at the School of Medicine, that seeks to unravel the mysteries of anesthesia.

The multi-institutional team included researchers from Temple, Thomas Jefferson, and Drexel universities and the University of Pittsburgh, plus Associate Professors William Dailey and Ivan Dmochowski and Professor J. Kent Blasie, all from the Department of Chemistry in Penn's School of Arts & Sciences. This group found that sevoflurane binds to the sodium channel in three places, each having a different effect. One location is the channel pore and produces a simple pore-blocking mechanism, the second is in a gate that controls the opening and closing of the sodium channel, and the third is in another gate that controls sodium flow by changing the shape of the channel's pore.

“Even within these multiple sites, they’re not all working in the same direction to modulate the channel. They’re actually working against each other,” says Annika Barber, a postdoctoral researcher in the Department of Neuroscience in the School of Medicine and lead author of the paper. “For a single ion channel, a single protein, it’s just one player in a host of proteins that modulates the effect of anesthesia, but even within a single player, there’s more than one interaction that matters in terms of regulating the way that channel behaves.”



TOP: The three binding sites identified by clustering analysis, including the extracellular site (red), linker site (yellow), and cavity site (purple/green).

BOTTOM: A top view of the isoflurane molecule.

In order to examine how sevoflurane changes and manipulates the functions of the channel, Barber worked with the Institute for Computational Molecular Science at Temple to use molecular dynamic simulation—a 3-D computational modeling method—to force the anesthetic to stay in some areas of the channel protein and exit others. The team then worked with Manuel Covarrubias at Thomas Jefferson to integrate the 3-D behavior with electrical activity of the channel.

If researchers are able to see how different channels are affected by anesthetics, to attribute a functional effect to a specific site, they could theoretically begin to optimize the design of the drug for that particular site. This could lead to drugs with fewer side effects.

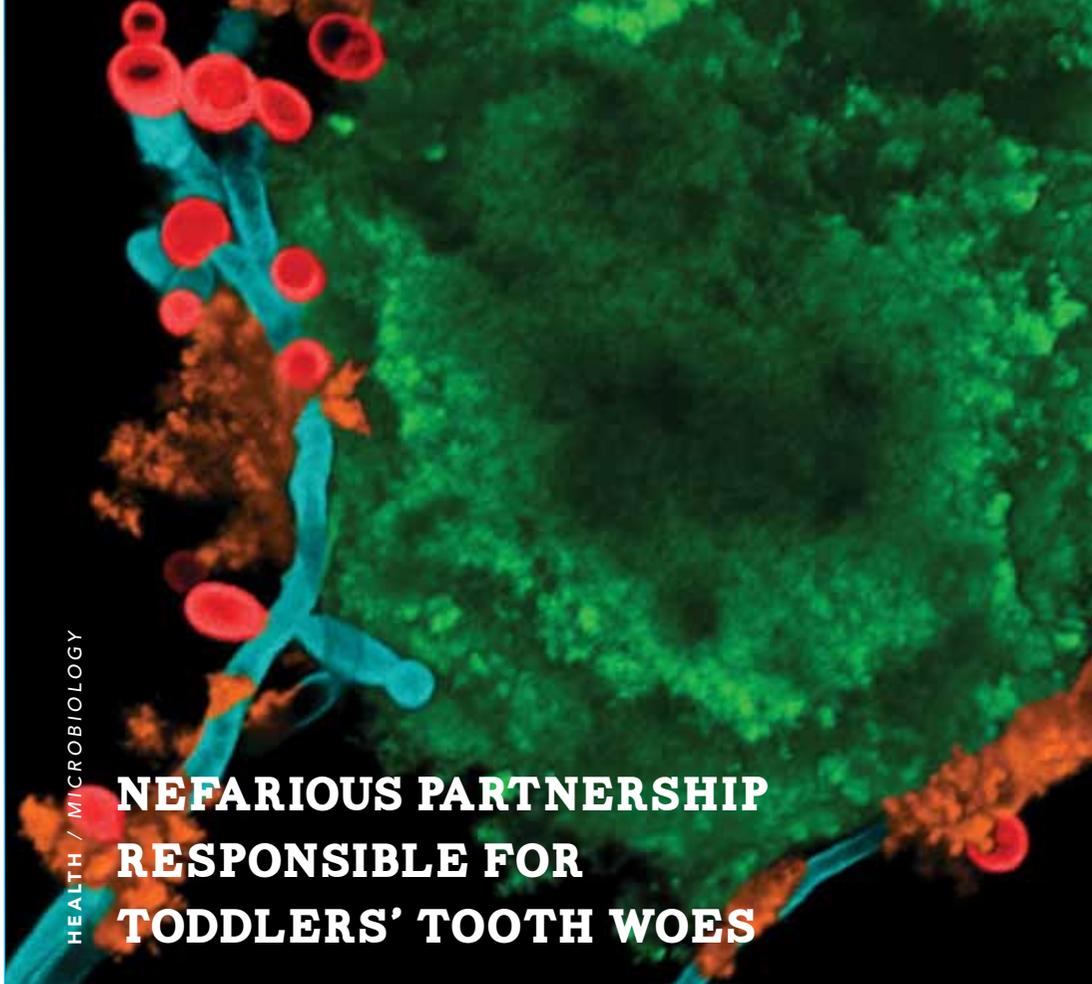
“If we understand the desirable properties of the existing drugs, even though that might be a difficult project, I would say there’s every reason to believe we could make something better,” says Max Kelz, associate professor of anesthesiology and critical care at Penn Medicine, who studies the relationship between anesthesia and unconsciousness. “It’s still fascinating that [anesthetics] exist in the first place, that they work as well as they do as often as they do. They can be thought

of as tools to probe some really fundamental questions in biology.”

Eckenhoff says doctors have become remarkably skilled at administering anesthetics—despite the mysteries that remain.

“Patients shouldn’t fear anesthesia,” he says. “But by the same token, they shouldn’t take it for granted. ... We need

a lot more work to understand how they work and what else they might be doing, and how to avoid those other things.” ■



HEALTH / MICROBIOLOGY

## NEFARIOUS PARTNERSHIP RESPONSIBLE FOR TODDLERS’ TOOTH WOES

Parents are admonished not to put their children to bed with a bottle, lest they rot their tiny teeth. Indeed, “bottle rot” is the familiar term for an aggressive and painful form of tooth decay that affects young children. In some cases, surgery is the only viable treatment.

Though researchers have known that sugar was to blame for this decay, called early childhood caries, a team led by Penn’s Hyun (Michel) Koo, a professor in the School of Dental Medicine’s Department of Orthodontics, wanted to better understand the mechanism.

Koo has spent 15 years studying how microbes construct the biofilms known, in the mouth, as dental plaque. Recently, he and other scientists had observed that in early childhood caries, these biofilms contained not only *Streptococcus mutans*—the bacterium implicated in most cases of tooth decay—but also a fungus, *Candida albicans*.

“We were puzzled,” says Koo. “*Candida* usually does not associate with *S. mutans*, nor does it colonize teeth very effectively.”

In research published in the journal *Infection and Immunity*, Koo and colleagues found that *S. mutans* uses an enzyme to produce extracellular polysaccharides and that this enzyme also attaches to *Candida*, allowing the fungus to produce these glue-like polymers in the presence of sugar. The fungus uses this “glue” to bind to teeth and *S. mutans*, two abilities it otherwise lacks. Under these circumstances, the fungus boosts plaque formation.

The enhanced biofilms also contained pockets of acidity next to the surface of teeth, which can dissolve enamel and cause cavities. The study, which was supported by the National Science Foundation and the National Institute of Dental and Craniofacial Research, found that the presence of *S. mutans* and *C. albicans* together doubled the number of cavities and boosted their severity severalfold in rats.

“Our data will certainly open the way to test agents to prevent this disease and, even more intriguing,” Koo says, “The possibility of preventing children from acquiring this painful and costly infection.” ■

# There's No Such Thing as 'Catching Up on Sleep'

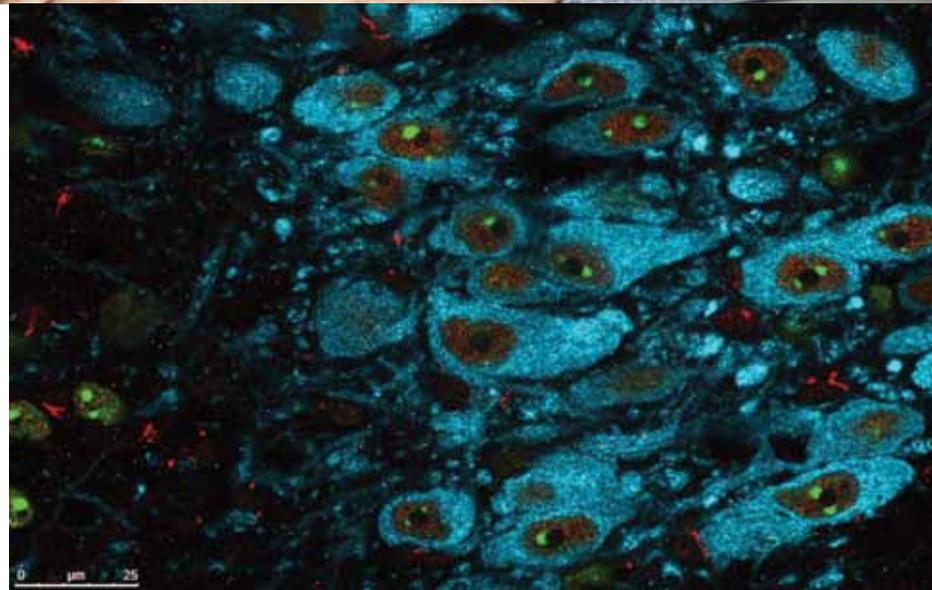
Unfortunately for night owls, the phrase “catching up on sleep” may be a misnomer. New research from the Perelman School of Medicine published in the *Journal of Neuroscience* suggests that chronic sleep loss may lead to irreversible physical damage to and loss of brain cells.

“We’ve known that when humans are sleep-deprived, their performance deteriorates,” says Sigrid Veasey, professor of medicine and member of the Center for Sleep and Circadian Neurobiology at Penn Medicine. “If you’ve memorized a love poem or something for a test, that didactic information is fine. But the ability to stay focused on tasks or integrate matters—those are things that are more vulnerable to sleep loss.”

Despite the assumption that full cognitive recovery could be achieved following periods of short- and long-term sleep loss, Veasey and her colleagues have, for the first time, determined that extended wakefulness is irreversibly harmful to the locus coeruleus (LC) neurons, which are essential for alertness and optimal cognition. The research was funded by the National Institutes of Health National Heart, Lung, and Blood Institute.

The research team examined groups of mice experiencing periods of normal rest, short wakefulness, or extended wakefulness, modeling a shift worker’s typical sleep pattern consisting of three consecutive days of eight hours of sleep loss during the normal sleep time.

Veasey and her colleagues found that in the mice that experienced several days of shift worker sleep patterns, LC neurons began to display reduced sirtuin type 3 (SirT3) proteins—an important component of mitochondrial energy production, redox responses, and metabolic homeostasis maintenance. Those mice also showed increased cell death, losing 25 percent of LC neurons.



Researchers found that extended wakefulness is irreversibly harmful to LC neurons in mice (pictured), which are essential for alertness and optimal cognition.

The findings demonstrate sleep’s vital role in restoring metabolic homeostasis in mitochondria in LC neurons to ensure their optimal functioning during waking hours.

“There are 40 million people in the U.S. who perform shift work—night and early morning—and are only getting about six hours of sleep a night,” Veasey says. “Those individuals could be losing neurons, and that’s highly relevant. We’re now excited to figure out how much of an issue this is in humans and how we can protect the brain.” ■

## Increasing Condom Use in South African Men

**W**ith 6.2 million cases, South Africa has the highest number of HIV-positive individuals in the world. As with other sub-Saharan countries, a majority of cases in South Africa are transmitted through heterosexual exposure, most often passing from a male to his female partner during unprotected sex.

Because gender-based power relations generally prevent South African women from talking to their partners about condom use, the need to educate men on the role they play in the epidemic is urgent and clear. However, according to authors of a Penn-led study published in the *American Journal of Public Health*, few interventions to change the men's behavior have been developed and evaluated.

"This study was the first randomized control trial conducted in South Africa to show that you could increase condom use in men," says John B. Jemmott III, professor in Penn's Annenberg School for Communication and the Department of Psychiatry in Penn's Perelman School of Medicine.

Led by Jemmott and Loretta Sweet Jemmott, professor in Penn's School of Nursing, and funded by a grant from the National Institutes of Health, the intervention was a multi-institutional collaboration among researchers from the

Centers for Disease Control and Prevention, Haverford College, Temple University, and the University of Fort Hare in East London, South Africa. Penn participants also included two of John Jemmott's Penn Medicine colleagues, Anita Heeren and Craig Carty.

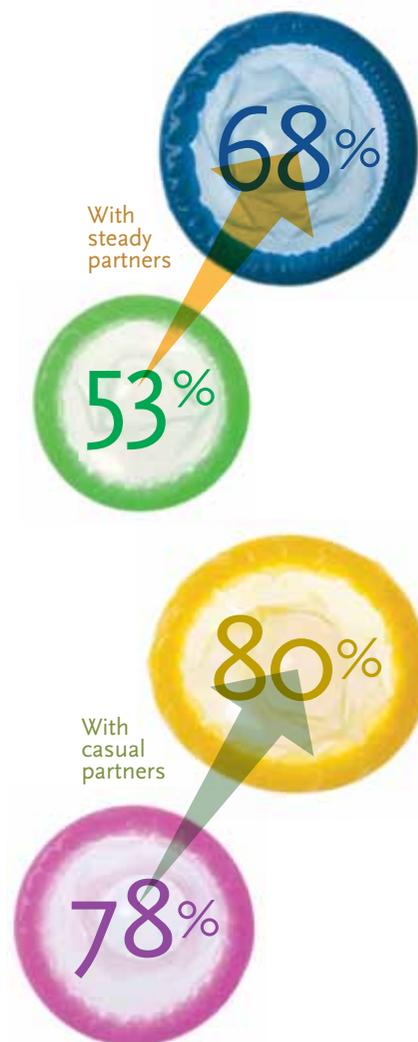
Starting in 2008, 1,181 men were recruited from townships outside the city of East London to participate in either an HIV/sexually transmitted infection risk-reduction intervention or a control intervention promoting healthy diets and regular exercise.

The skill-building, risk-reduction intervention program, Men Together Making a Difference, included role-playing, "circle of men" talking groups, and videos that members of the team created specifically for the program.

The intervention's success, evidenced by participants' increased use of and discussion about condoms with their partners one year after the intervention, was largely due to the researchers' ability to tailor the activities to the language and customs of the culture. They used an authentic ceremonial drum in the circle of men, for example, and created a video that included scenes in shebeens, or drinking clubs where much of the high-risk sexual behavior was initiated, which provided strategies for being safe sexually while drinking.

"Being able to see what occurs in these settings was critical to designing a program that really matched their culture," Loretta Sweet Jemmott says. "This was a solid, community-based, culture-driven intervention. You can't just take what we did in these neighborhoods in South Africa and do the exact same thing in another country—but you can adapt it to use with men in other countries." ■

INCREASE IN CONDOM USE  
FOR MEN ONE YEAR  
AFTER THE INTERVENTION



TALKING TO THEIR  
PARTNERS ABOUT  
CONDOM USE

10%  
for men with  
steady partners

10%  
for men with  
casual partners

**If you've had chicken pox once, you're likely protected for life, due to the immune system's built-up defenses.**

Penn researchers have found that people can also develop immunity to specific strains of Lyme disease, with the protection lasting six to nine years.

Because there are about 16 strains of Lyme that can affect people in the United States, this protection means one person could experience more than one bull's-eye rash in his or her life. But this new understanding of the immune system's response to the Lyme bacteria may help shape vaccine development efforts

down the road, eventually giving rise to a way of preventing infection from multiple strains at once.

Previous work in mice had suggested that strain-specific immunity might exist, but this is the first time it's been examined in humans with naturally occurring Lyme disease infections.

In the new study, Dustin Brisson, an associate professor in the School of Arts & Sciences' Department of Biology, and colleagues used data from an earlier report that had identified the strain of each infection in 17 patients who had Lyme more than once. That research confirmed that the

## PROTECTION AGAINST SPECIFIC STRAINS OF LYME DISEASE CAN LAST YEARS



patients' subsequent infections were almost all caused by different strains of the bacteria, indicating that additional tick bites were to blame, rather than relapses of the original infection.

"We wanted to see if so few patients were infected by the same strain multiple times because they were protected against subsequent infections with the same strain," Brisson says.

Using a statistical approach, the team found it would be nearly impossible to arrive at the data presented by the 17 patients if no strain-specific immunity was present. Incorporating data into their model from 200 additional Lyme disease patients, they also determined that the immunity lasts around six to nine years. The study, which was supported by funding from the National Institutes of Health and the Burroughs Wellcome Fund, was published in *Infection and Immunity*.

"If you could make a vaccine that covers several of these strains," Brisson says, "you could substantially reduce the probability of infection in vaccinated people. The vaccine could last several years, perhaps requiring a booster once every several years." ■



## LYME DISEASE HAS EVOLVED TO EVOLVE

**Dustin Brisson studies *Borrelia burgdorferi* not only to try to prevent Lyme disease, but also to understand evolution.** In a recent study published in *PLOS Pathogens*, he has found evidence that the bacteria's ability to change is a trait that evolution has favored over time.

Brisson says it makes sense that this species could evolve to maximize its ability to adapt to future conditions. "Pathogens face a very strong selection pressure from the host's immune system," he says. "If they don't adapt, they will die."

In the study, Brisson examined *B. burgdorferi*'s "cassettes" of DNA, which are normally not expressed but can be inserted in a gene critical for long-term infection. Variations in these cassettes serve as a kind of ace in the hole, increasing the variety of challenges the Lyme bacteria can pose to their mammalian host. Brisson's team found strong evidence that, over time, natural selection has favored more diverse cassettes—diversity to keep the immune system guessing and the bacteria thriving. ■

## Prolonged Exposure Therapy Aids Adolescent Girls with PTSD

**Research has shown that there is a high prevalence of post-traumatic stress disorder (PTSD) among adolescents—especially among girls.** Despite the large numbers, an evidence-based treatment for PTSD has yet to be established for adolescents.

Findings from the Perelman School of Medicine's Edna Foa, a professor of clinical psychology in the Department of Psychiatry, could potentially change that. Her recent study shows that a modified version of prolonged exposure therapy—in which participants repeatedly recount their traumatic

experiences—shows greater success than supportive counseling for treating female adolescents with PTSD who are survivors of sexual assault.

“There are numerous studies on PTSD treatment of adults, and a number of studies have been done on PTSD treatment for children, but we saw a gap of research on treatment of adolescents,” Foa says. “We couldn't assume that treatment of PTSD in adolescents was the same as treatment for children—adolescence has its own developmental issues and difficulties that need

special considerations. We decided to focus on [PTSD from] rape and sexual abuse, which is more prevalent among girls than boys, and this is why we focused on girls in our research.”

In the six-year study of 61 adolescent girls, ages 13 to 18, with sexual abuse-related PTSD, Foa and her colleagues examined the benefit of a prolonged exposure program modified to meet the developmental stage of adolescents and compared it with supportive counseling. Each patient received as many as 14 60- to 90-minute sessions of either type of therapy by counselors who provided treatment at Women Organized Against Rape, a rape crisis center in Philadelphia. The research, published in the *Journal of the American Medical Association*, was funded by the National Institutes of Health.

“We gave [the patients] the opportunity to revisit the memory, process it, and gain current perspective on it,” Foa says. “Whether they felt guilt, ashamed, or fearful, repeatedly retelling and revisiting what happened to them helped [the patients] separate the trauma from the present and realize that it happened in the past.”

Foa says the patients who received the modified prolonged exposure therapy showed a significantly greater reduction of PTSD and depression symptoms, and an improvement in overall functioning, compared with patients who received supportive counseling. These differences were maintained throughout a 12-month follow-up period.

“We also found that this treatment could be successfully delivered by counselors or social workers who were trained to conduct counseling and were not familiar with prolonged exposure before the study was conducted,” Foa says. “The next step will be to widely implement prolonged exposure in community clinics that treat adolescents who suffer from PTSD.” ■



“Whether they felt guilt, ashamed, or fearful, repeatedly retelling and revisiting what happened to them helped [the patients] separate the trauma from the present and realize that it happened in the past.”



## Quality Trumps Quantity When It Comes to Learning First Words

*“We see that the more an environment maximizes the ‘here and nowness’ of speech, such as when a parent is gesturing or looking at the object in question, the more likely it is that an interaction will be highly informative.”*

**How much parents say to their children when they are very young has been shown to predict their vocabulary when they begin school**, which in turn predicts success throughout their educational careers.

A study now shows that early vocabulary improvement is likely to have more to do with the quality than quantity of these interactions.

The study, supported through the National Institute of Child Health and Human Development, was led by professors John Trueswell and Lila Gleitman, both of the Department of Psychology in Penn's School of Arts & Sciences, and published in the *Proceedings of the National Academy of Sciences*. They collaborated with researchers from Drexel University and the University of Chicago.

Trueswell and Gleitman's previous research suggested that children learn their first words in "eureka" moments—that is, only after "highly informative" examples of speech that clearly connect the word to the thing to which it refers. To test how important these examples were compared with the overall quantity of speech, they designed a three-year study of 50 families. Their first step, however, was to determine what constituted highly informative speech.

To do this, the researchers showed adult volunteers short video clips of parents interacting with their children at home, each centered on one instance of the parent saying a common noun. To simulate the experience of a child who has yet to learn any words, the video was muted until the parent reached the target, which was replaced by a beep. The volunteers were then asked to guess the target word.

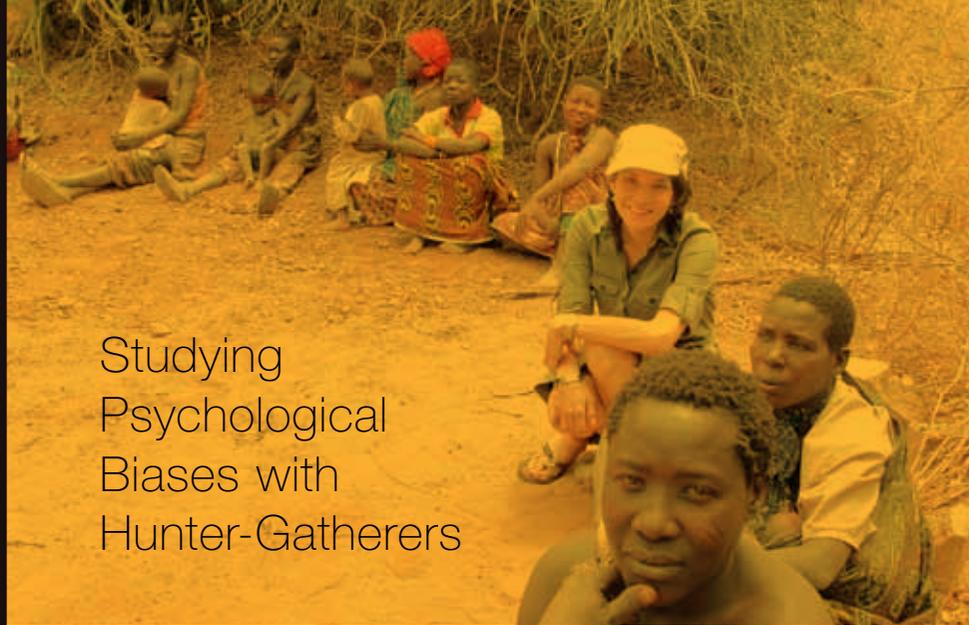
"Identifying a particular word's referent, especially when you don't know any words to begin with, is not a simple task," Trueswell says.

"We see that the more an environment maximizes the 'here and nowness' of speech, such as when a parent is gesturing or looking at the object in question, the more likely it is that an interaction will be highly informative," Gleitman says.

If more than half the adults could guess an example's target word correctly, it was considered highly informative. Using this rubric on the study participants, the researchers found that the parents who most frequently used highly informative examples did so roughly 10 times as often as those who did so the least.

The effect of this discrepancy was clear: The more frequently a child heard highly informative examples of speech, the better he or she did on a vocabulary test at the end of the study.

Increasing the quantity of speech was beneficial, but only because it increased the number of chances parents had to provide highly informative examples. The results are also promising in that the rates of these quality examples were not correlated with socioeconomic status. ■



## Studying Psychological Biases with Hunter-Gatherers

NATURAL SCIENCE / BEHAVIORAL ECONOMICS

**One of the most widely studied psychological biases is known as the endowment effect.** It causes us to overvalue things we currently possess, simply because we possess them. Given one of two items of equal value at random and then proposed a trade, people overwhelmingly stick with whatever they were first handed.

Most people who have participated in such experiments, however, are WEIRD, an acronym meaning they are from cultures that are Western, educated, industrialized, rich, and democratic.

To better understand the degree to which this bias in experiments is innate or the product of environmental factors, researchers visited one of the few remaining places where such studies can be conducted: Hadzaland, a remote area of Tanzania where some of the last hunter-gatherer societies live.

The study, published in the *American Economic Review*, was led by Coren Apicella, an assistant professor in Penn's School of Arts & Sciences' Department of Psychology, and Eduardo Azevedo, an assistant professor in Wharton's Department of Business Economics and Public Policy. They collaborated with colleagues from Yale University and the University of California, San Diego.

Owing to geography, different Hadza camps have varying amounts of contact with outsiders. Isolated camps share all possessions communally, while others sell traditional wares to visiting tourists and buy items from a nearby village.

Apicella conducted different versions of the endowment effect experiment with participants from several camps.

"The more isolated Hadza traded about 50 percent of the time, which is what rational people should do," Azevedo says. "People near the village traded about 25 percent of the time, which is much closer to the 10 percent we see with the Western students that usually participate in these experiments."

One explanation for this discrepancy is that the bias is a learned behavior that comes with exposure to capitalism. Alternatively, both groups might experience the bias, but it is suppressed in the more communal groups by social pressures.

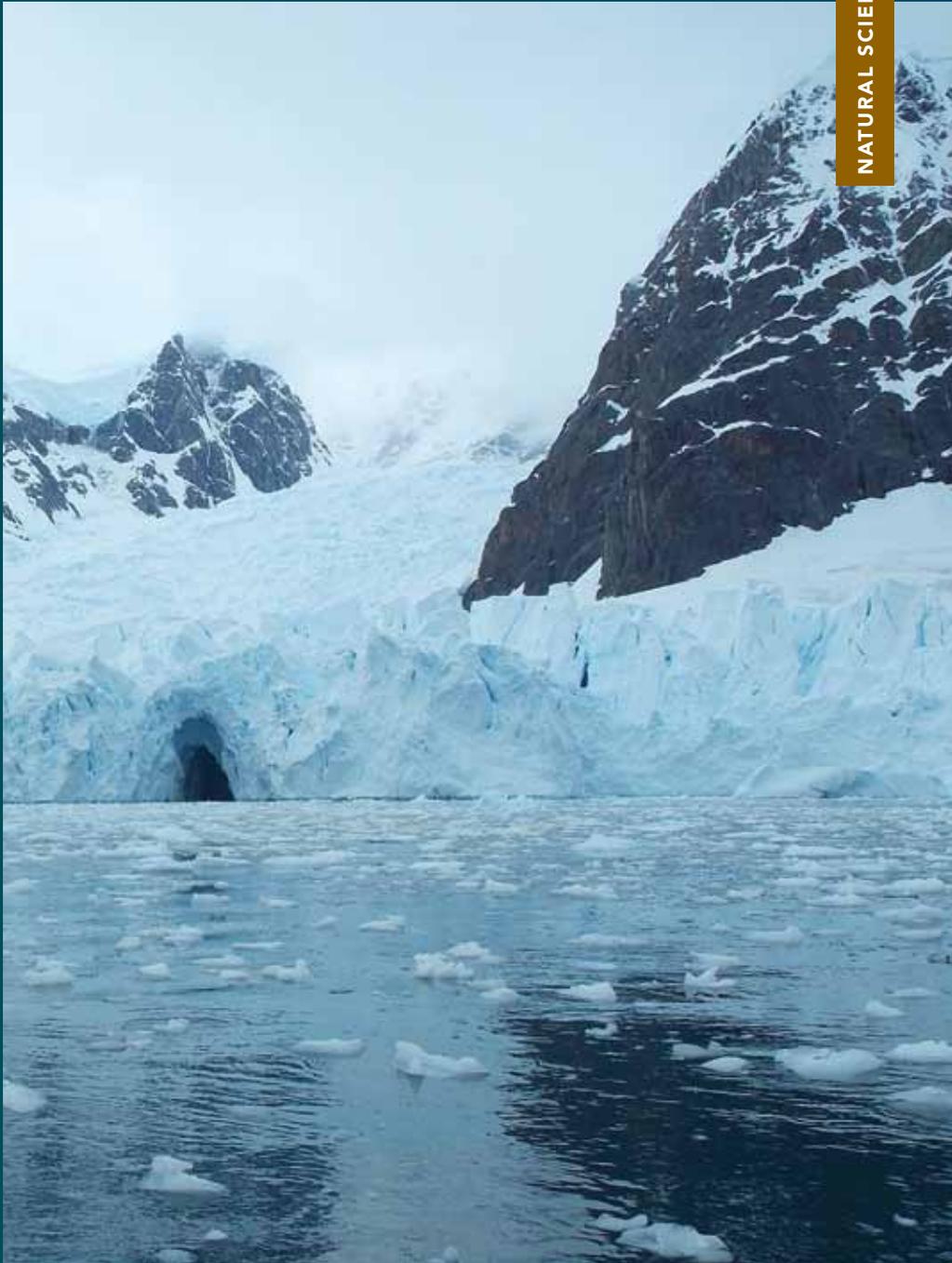
"We need to study this further to see which explanation holds," Apicella says. "Either way, the results suggest that these isolated hunter-gatherers are more rational than the average Western consumer when it comes to economic decisions."

The research was supported by funding from the Science of Generosity Initiative of the University of Notre Dame, the John Templeton Foundation, and the National Institute on Aging. ■

# How Changing Oceans Affect Earth's Global Climate

EARTH & ENVIRONMENTAL SCIENCE

NATURAL SCIENCE



## WEB EXTRA



[goo.gl/rzLyyX](https://goo.gl/rzLyyX)  
Watch a video  
of Irina Marinov  
discussing her work.



*These studies predict global decreases in natural carbon uptake and oceanic photosynthesis due to warming over the 21st century, with different parts of the ocean responding in critically different ways.*

**F**ar below the ocean surface, deep currents channel heat and carbon around the globe, regulating our planet's climate like a thermostat.

But anthropogenic climate change may be altering this thermostat, according to Irina Marinov, assistant professor in the Department of Earth & Environmental Science in Penn's School of Arts & Sciences. Marinov's research group uses advanced computer models and hardware to study ocean and atmosphere dynamics. The group's recent research shows how climate change profoundly alters major ocean currents and the ocean's natural capacity to store carbon.

In a recent *Nature Climate Change* publication, Marinov, Penn Postdoc Raffaele Bernardello, and McGill University collaborators argue that the Antarctic Bottom Water—a current of cold, dense, deep water that carries carbon and heat from the Antarctic coast to the equator and northern latitudes—is weaker than it was in pre-industrial times. Greater precipitation around Antarctica is increasing the freshness of surface ocean waters, diminishing the convective turnover needed to replenish the massive current.

"This is worrisome because it might slow down the uptake of anthropogenic carbon and heat by the ocean, creating a positive feedback loop for climate change," Marinov says.

Related studies published in the *Journal of Climate* and *Global Biogeochemical Cycles* investigate the ocean's natural ability to absorb carbon dioxide through phytoplankton, microscopic photosynthetic organisms. These studies predict global decreases in natural carbon uptake and oceanic photosynthesis due to warming over the 21st century, with different parts of the ocean responding in critically different ways.

"In the Northern Hemisphere, surface waters are warming relatively quickly," Marinov says. "This decreases ocean mixing and nutrient replenishment of the surface ocean, causing phytoplankton, and hence the uptake of atmospheric carbon dioxide via ocean photosynthesis, to decline. But in the Southern Ocean, alterations to the jet stream are increasing surface nutrients, and we see the opposite pattern."

Future directions for Marinov's group include exploring Southern Ocean-atmosphere feedbacks and "teleconnections," climate signals propagating quickly at large distances.

"Oceans change slowly, over centuries and longer," says Marinov. "But when local ocean temperature changes get propagated through the atmosphere, we start seeing global climate effects very quickly. Teleconnections involving the atmosphere and ocean may be crucial to our planet's future climate." ■

***“These cells acquired the ability to propagate and migrate, beginning the process of metastasis and moving to distal sites in the body.”***

## Identifying a Trigger for the Spread of Breast Cancer

Certain forms of breast cancer are slow to spread, while others are fast and invasive. Knowing the difference can help doctors and patients make treatment decisions, but sometimes it's hard to predict the course a particular cancer will take.

A study led by the School of Veterinary Medicine's Manti Guha, a senior research investigator, and Narayan Avadhani, professor of Biochemistry in the Department of Animal Biology, lends insight into why some breast cancers are particularly quick to spread and points to a potential biomarker for identifying aggressive forms of the disease. Writing in *Oncogene*, they found that cancers with low levels of mitochondrial DNA (mtDNA) experience a kind of metamorphosis, coming to resemble stem cells with the ability to move around the body and spread disease.

Mammalian cells contain between 100 and 1,000 copies of mitochondrial DNA, but previous research had found that as many as 80 percent of people with breast cancer have low mtDNA content in the affected tissue.

To understand the link between reduced mtDNA and cancer spread, Guha and Avadhani experimentally reduced mtDNA levels in normal, non-cancer-forming human breast cells and in cancerous breast cells.

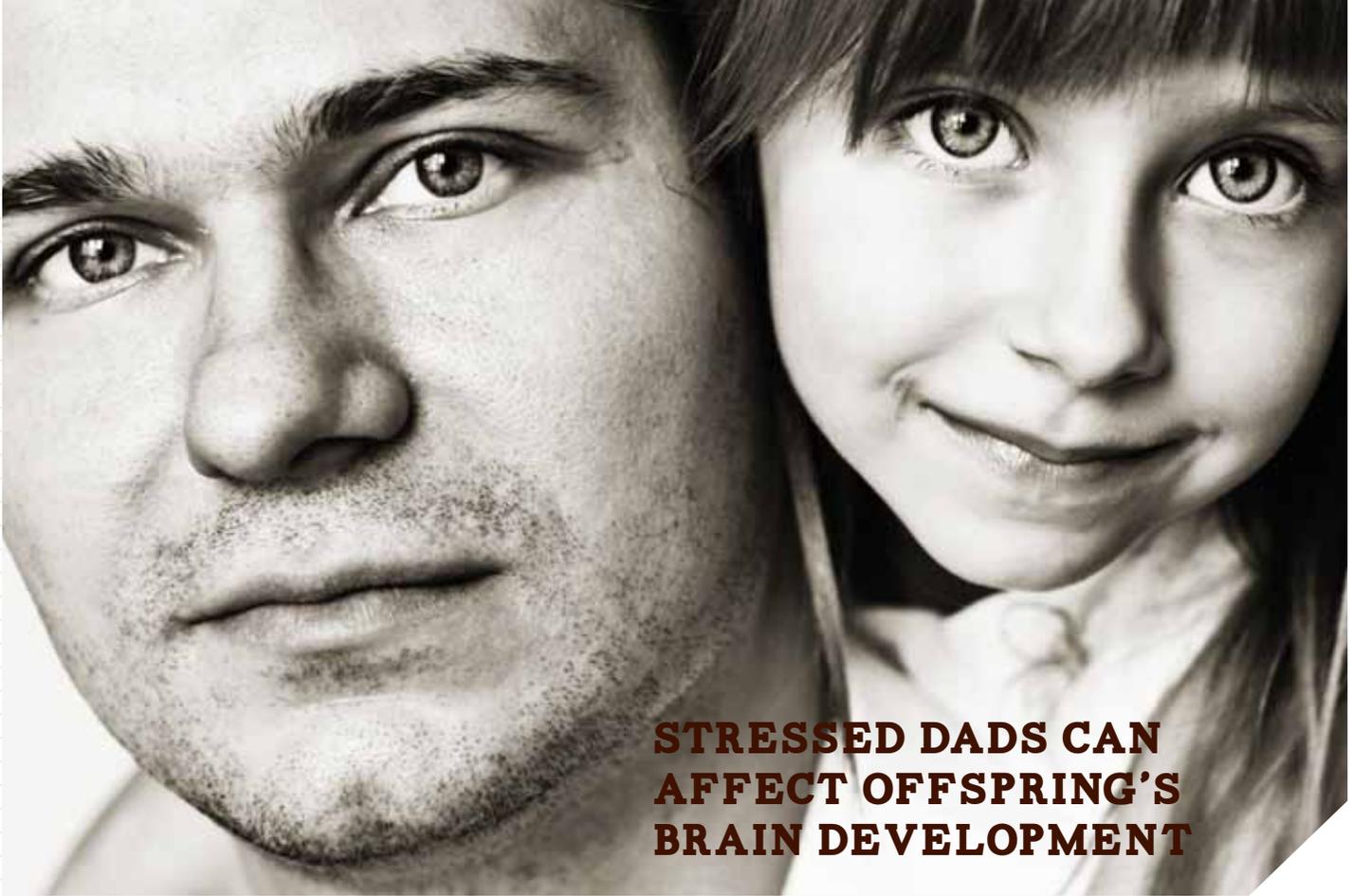
The effect was striking. Cancerous cells with reduced mtDNA had altered metabolism and a disorganized structure, similar to cancer cells that have begun to spread, while the normal breast cells became invasive and began to resemble cancer cells. The cells with reduced mtDNA also became self-renewing and expressed cell surface markers typically found on breast cancer stem cells.

“These cells acquired the ability to propagate and migrate, beginning the process of metastasis and moving to distal sites in the body,” says Avadhani.

As the Penn team continues to study the pathway that leads from low mtDNA to metastatic cancer, they hope to identify biomarkers of aggressive disease that could help customize treatments and eventually develop strategies to intervene and prevent cancer spread.

Their work was supported by the National Institutes of Health and the Harriet Ellison Woodward Trust. ■





## STRESSED DADS CAN AFFECT OFFSPRING'S BRAIN DEVELOPMENT

**Researchers investigating neurodevelopment disorders in children usually begin with the mother.** Logically, they retrace the mother's actions, examining what she ate, her stress level, any infections she may have had, or any other mitigating factor she was exposed to during pregnancy.

Tracy Bale, a professor of neuroscience in the School of Veterinary Medicine and the Perelman School of Medicine, has shown that fathers can affect neurodevelopment, too. Stress on preadolescent or adult male mice can produce long-term changes to their sperm that reprogram the region of their offspring's brain that governs responses to stress.

Bale says the findings suggest one way in which paternal-stress lifetime exposures may be linked to stress-related neurodevelopmental disorders like autism, schizophrenia, and ADHD. The study was published in the *Journal of Neuroscience* and co-authored by Penn Vet's Ali Rodgers, Christopher Morgan, Stefanie Bronson, and Sonia Revello. Funding was provided by the National Institute of Mental Health.

Bale says male mice are ideal study subjects because, unlike females, they do not partake in the rearing of their offspring, which eliminates confounding factors outside of germ-cell formation such as maternal behaviors, allowing a more clear interpretation of the contributing mechanisms.

The researchers conducted the study by exposing adult male mice to six weeks of chronic stress before breeding them. The mice were stressed by altering their environ-

ment in unpredictable and novel ways, such as putting marbles in their cage, changing their home cage multiple times, or exposing them to a predator's odor—all things that are unfamiliar and stressful to a mouse.

The researchers then examined these males' offspring for stress responsiveness as adults. Surprisingly, the researchers found that both male and female offspring from these stressed dads showed a significant change in

*The findings have potential impact among humans in that it may one day be possible to screen sperm for epigenetic marks to predict disease risk.*

how they responded to stress, even though they had never interacted with their fathers. These studies also found epigenetic changes in the stressed dads' sperm, demonstrating that the environment was able to change the germ cell to produce differences in these offspring.

Bale says she was "shocked" when she discovered that stressed fathers could impact neurodevelopment in such a robust way. She says the findings have potential impact among humans in that it may one day be possible to screen sperm for epigenetic marks to predict disease risk.

"If you determine marks that are predictive of an increased risk, I think the average parent would want to know," she says, "and then you could keep a closer eye on those children, looking for earlier signs and allowing for earlier interventions." ■



**RIGHT:** Labeled cells in a dog's retina show a small area dense with cone cells (labeled red), much like a human fovea.

# Discovering an Anatomical Feature Shared by Dogs and Humans

**B**e they Fido, Fang, Spike, or Spot, dogs have been an important part of people's lives for tens of thousands of years. That is why it's all the more surprising that a team of Penn researchers have only just discovered a feature of the eye that canines and humans have in common.

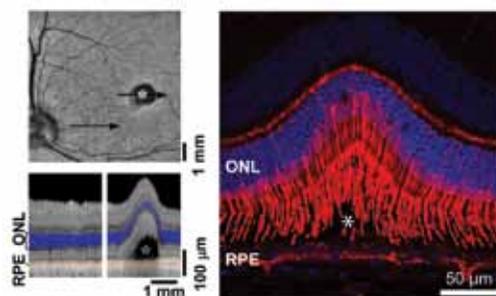
The find is a photoreceptor cell-packed region of the retina that is crucial for viewing details in the center of our field of vision, and it appears to be involved in genetic blinding diseases in both humans and dogs.

"It is absolutely unexpected and very hopeful in terms of having an ability to understand this very unusual part of the human retina," says William Beltran, an associate professor of ophthalmology at the School of Veterinary Medicine, who co-led the study with Artur Cideciyan, research professor of ophthalmology at the Scheie Eye Institute at Penn's Perelman School of Medicine.

In humans, this region of the retina is called the fovea. Tiny but mighty, the fovea is packed with photoreceptor cells called cones, at densities that surpass 100,000 cones per square millimeter. We rely on the fovea to see fine details while reading, driving, or looking at objects of interest.

In the new study, the Penn team, which also included vision scientists Gustavo Aguirre and Karina Guzewicz of Penn Vet and Samuel Jacobson of Penn Medicine, used advanced imaging techniques to take a closer look at canine retinas.

#### BEST1-mutant



The fovea-like area in dogs with a form of macular degeneration was affected much like foveas in humans with the disease.

While the highest previously reported cone density in canine retinas was 29,000 cones per square millimeter, Beltran and Cideciyan's work revealed an area where cone densities reached more than 120,000 cells per square millimeter, comparable to the density present in the human fovea. They also found that the back end of this region corresponded with an area dense with cells that transmit signals to the brain.

When the team examined dogs with genetic mutations that cause macular degeneration in humans, they found the canines' fovea-like region was affected in a similar way to how human foveas degenerate in the disease.

"Our findings are very promising from the human point of view," says Cideciyan. "They could allow for translational research by allowing us to test treatments for foveal diseases in humans and macular degenerative diseases in dogs."

The study was published in *PLOS ONE* and supported by the National Institutes of Health, the Foundation Fighting Blindness, and the Macula Vision Research Foundation. ■

## ONE MOLECULAR PATHWAY, THREE FORMS OF BLINDNESS

The term "blindness" may seem straightforward, but it can actually refer to a plethora of diseases. A recent study by School of Veterinary Medicine researchers Sem Genini, William Beltran, and Gustavo Aguirre, however, has identified a molecular pathway that leads to vision loss in three types of blindness—a route that could be targeted by a single therapy.

The researchers studied canine models of three inherited vision diseases, each caused by its own genetic mutation: rod cone dysplasia 1, X-linked progressive retinal atrophy 2, and early retinal degeneration. In *PLOS ONE*, they report that all of the diseases involved activation of a particular pathway that causes photoreceptor cell death.

"What this shows is that there is an early trigger that is quite similar among all three diseases," Aguirre says.

That could mean that the same drug could be employed to treat all three of these diseases—and perhaps others that use the same cell-death pathway. ■

## Ferrying Alzheimer's Drugs Across the Blood-Brain Barrier

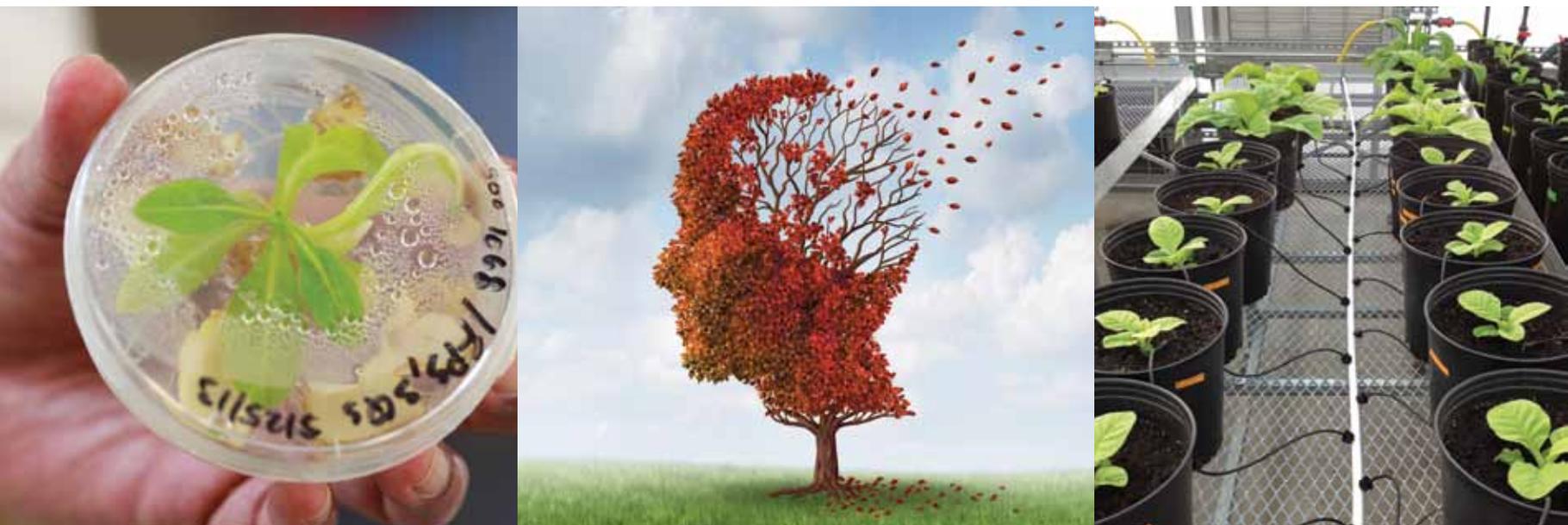
**Tightly packed walls of cells known as the blood-brain and blood-retina barriers not only protect vital tissues but also make it difficult for drugs to reach the brain or eyes.**

"Drug companies have been able to come up with compounds that can clear Alzheimer's plaques from the brain, but they've often failed to get the compound across the blood-brain barrier," says Henry Daniell, a professor in the School of Dental Medicine's Departments

barrier crossing was a success: The researchers found the compound in both the brain and retina, reporting their finding in the journal *Molecular Therapy*.

"We were quite thrilled," Daniell says. "If the protein could cross the barrier in healthy mice, we thought it was likely that it could cross in Alzheimer's patients' brains, because their barrier is somewhat impaired."

Indeed, when they took tissue from the brains of either mice or humans who had Alzheimer's and exposed it to the



of Biochemistry and Pathology and director of translational research.

Now a team led by Daniell has found a way to navigate through the barriers to break up the sticky beta amyloid plaques that accumulate in the brains of Alzheimer's patients. The discovery offers hope for treating Alzheimer's as well as other brain and eye diseases.

To traverse the barrier, Daniell's team paired a small molecule, cholera toxin B subunit (CTB), which is known to be able to cross the blood-brain barrier, with another molecule, myelin basic protein (MBP), which can degrade the beta amyloid chains that build up into tangles in the brain.

The researchers inserted the fused genes into plant chloroplasts, bred the plants that incorporated the new gene, and then fed the freeze-dried plant material to mice. The

CTB-MBP compound, evidence of brain plaques decreased up to 60 percent in mice and 47 percent in humans.

As a final test, the researchers fed the CTB-MBP-containing plant material to 15-month-old mice with Alzheimer's—the equivalent of 80-year-old humans. Remarkably, the brain plaques in these mice decreased between 40 and 70 percent, a sign that perhaps this approach could be used to treat people who already have early signs of the disease.

The study was supported by the National Institutes of Health and other organizations. ■

### WEB EXTRA



[goo.gl/xkzCxR](http://goo.gl/xkzCxR)

In a video, Henry Daniell discusses his work directing drugs across the blood-brain barrier.

**Imagine a game where you and an opponent each begin with a million dollars.** You are given a choice: You can keep the money or give it to your opponent. If you're both selfish, you get to keep your money. If you're both generous, you're rewarded with an extra million to split. But if you're generous and your opponent isn't, you lose everything to him or her.

The "prisoner's dilemma" is a staple of game theory. When applied to the game of life, this survival of the fittest raises questions about the evolutionary origins of cooperation.

A paper published in the *Proceedings of the National Academy of Sciences* by Postdoctoral Researcher Alexander Stewart and Professor Joshua Plotkin, both of Penn's Department of Biology in the School of Arts & Sciences, offers an explanation. While others have suggested that cooperative strategies can be successful in such a scenario, the researchers offer mathematical proof that only generous strategies succeed in the long term.

"Since Darwin, biologists have been puzzled about why there is so much apparent cooperation, and even flat-out generosity and altruism, in nature," Plotkin says. "Our paper helps provide an

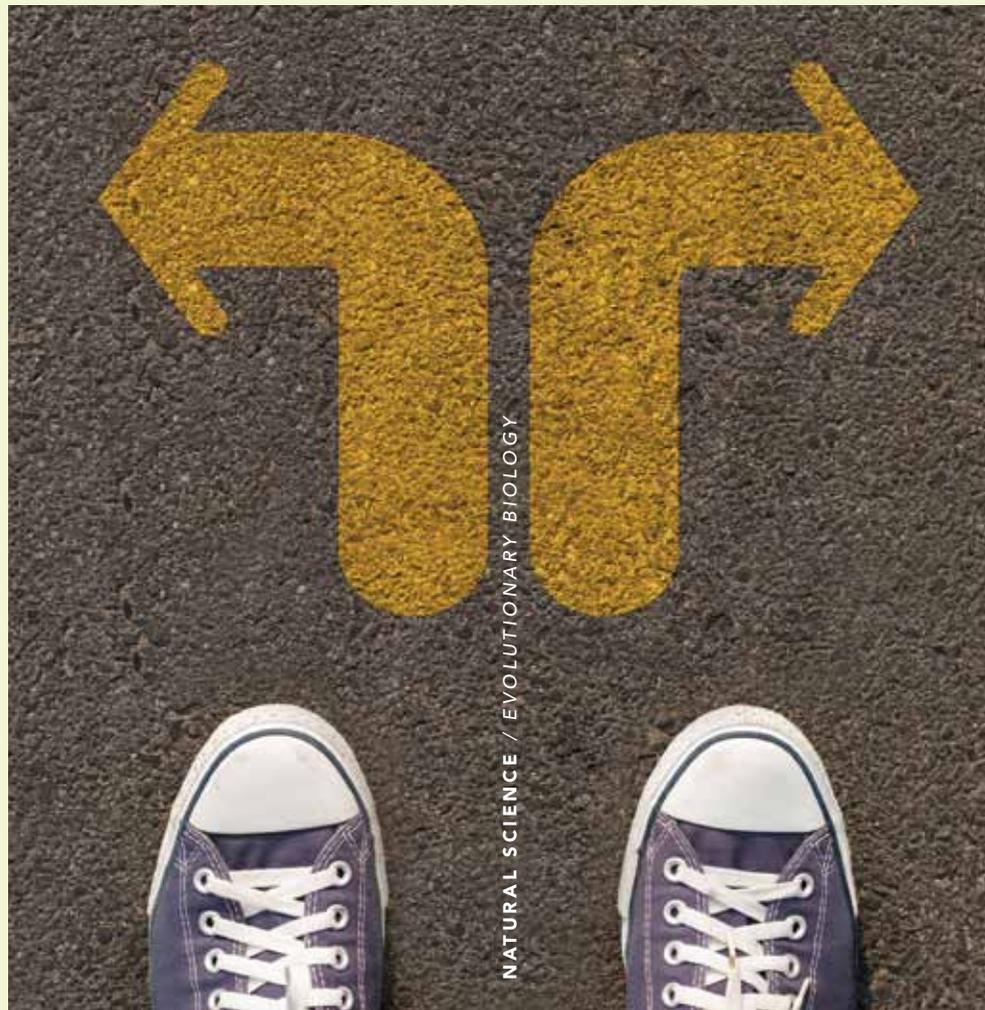
## SHARE OR STEAL: *The Evolution of Cooperation*

explanation for why we see so much generosity in front of us."

Earlier examinations of this paradox had two players repeatedly facing off, allowing them to employ different long-term strategies. One such strategy was essentially extortion—a selfish player forcing an opponent into being generous.

Stewart and Plotkin explored a format of the game that more resembled societies. Instead of a head-to-head competition, they envisioned a population of players matching up against one another. The most successful players got to "reproduce" more, passing on their strategies to their offspring.

They found that extortion strategies wouldn't do well within a large, evolving population because an extortion strategy doesn't succeed against itself. Generous strategies are the opposite; players suffer more than their opponents over the long term if they don't cooperate.



"Since Darwin, biologists have been puzzled about why there is so much apparent cooperation, and even flat-out generosity and altruism, in nature."

"You might think being generous would be a stupid thing to do, and it is if there are only two players in the game," Stewart says. "But if there are many players and they all play generously, they all benefit from each other's generosity."

The study received support from the Burroughs Wellcome Fund, David and Lucile Packard Foundation, James S. McDonnell Foundation, Alfred P. Sloan Foundation, Foundational Questions in Evolutionary Biology, U.S. Army Research Office, and U.S. Department of the Interior. ■

# A New Paradigm in Solar Power

### Current solar panels need two materials to work:

One or both absorb the light that excites electrons, but it is the interface between them that gets those electrons to flow in one direction, producing electrical current.

Single-phase materials that can do both of these tasks only work with ultraviolet light. This part of the spectrum is powerful but only a fraction of the light produced by the sun. Having a material that could perform this trick for visible light—the bulk of the sun’s output—could pave the way for super-efficient solar panels.

Researchers at Penn and Drexel University have now used computer modeling to devise such a material, known as a perovskite crystal.

The study, published in *Nature*, was led by Professor Andrew M. Rappe and Research Specialist Ilya Grinberg of the Department of Chemistry in Penn’s School of Arts & Sciences, along with Professor Peter K. Davies, chair of the Department of Materials Science and Engineering in the School of Engineering and Applied Science. It was supported by the Energy Commercialization Institute of Ben Franklin Technology Partners, the Department of Energy’s Office of Basic Energy Sciences, the Army Research

OPPOSITE: An illustration of the perovskite crystal fabricated in the experiment.



These solar panels would be inherently more efficient, as some of the sunlight’s energy is lost when electrons wait to make the jump from one material to the other.

Office, the American Society for Engineering Education, the Office of Naval Research, and the National Science Foundation.

The researchers began their search for the new material by theorizing composites of existing ones based on the two qualities they needed to combine.

“We know a family of materials that can give electrons a direction in which to flow, and we know a family of materials that can absorb visible light,” Rappe says. “The challenge was to find compatibility between those two properties.”

After several failed attempts to experimentally produce the specific materials they had theorized, the researchers had success with a combination of potassium niobate and barium nickel niobate, fine-tuning the ratio of these metal atoms in the final product.

Solar panels made out of this material would be easier to manufacture than their existing two-material counterparts. They would also be inherently more efficient, as some of the sunlight’s energy is lost when electrons wait to make the jump from one material to the other.

Future research will go toward improving the material’s efficiency and scaling it up to useful sizes. ■



# Probing RNA with a Precision Molecule

Though every one of the body's cells has the same protein-making instructions encoded in its DNA, the proteins they need to produce at a given time are constantly changing. A snapshot of this information can be gleaned from a cell's RNA molecules, which ferry the instructions to the cellular factories where proteins are assembled.

Accessing a cell's full complement of RNA, known as its transcriptome, is, therefore, a powerful research tool. However, existing techniques are unable to target individual cells without removing them from their natural tissue environments.

A multidisciplinary Penn team, featuring researchers from the Perelman School of Medicine and the Departments of Chemistry and Biology in the School of Arts & Sciences,

has now demonstrated a process to do just that, known as transcriptome in vivo analysis, or TIVA.

In a study published by *Nature* and supported by the National Institutes of Health, Pennsylvania Department of Health, the PhRMA Foundation, and the McKnight Foundation, the team physically isolated the RNA of a single cell within living tissue in mouse and human cells by "tagging," or capturing, it with a custom-built molecule.

This method provides a unique opportunity to assess how cells really work in the body—especially the changes that occur with disease.

"Our data showed that the tissue microenvironment shapes the RNA landscape of individual cells," says Jim Eberwine, professor of pharmacology at Penn Medicine.

The TIVA tag is a precise molecular machine, containing the multiple chemical tools necessary for its complex mission. These tools include a means of entering cells, a fluorescent marker for tracking its location, and, most important, a site that binds to RNA that can be activated at the appropriate time and place.

This final aspect was critical to the researchers' goal of targeting a single cell still embedded in live tissue. Unable to introduce the TIVA tag to the target cell without damaging its neighbors, the researchers designed a binding site with a removable chemical cage; the tag can't begin capturing RNA until a laser with a specific wavelength breaks the cage open. That way, the researchers could have the molecule enter

CONTINUED ON PAGE 33



## Heart Attack Gel Prevents Lasting Damage

**Heart attack and heart failure remain the leading causes of death worldwide;** if the former is not itself fatal, it often contributes to the latter. Now, a team of bioengineers and cardiac surgeons has developed an injectable gel that could break this link.

A study demonstrating the gel's efficacy was published in the journal *Nature Materials*. It was led by Jason Burdick, professor of bioengineering in Penn's School of Engineering and Applied Science, and Brendan Purcell, then a postdoc in his lab. Joseph Gorman and Robert Gorman of the Department of Surgery in Penn's Perelman School of Medicine, as well as researchers from the University of South Carolina, contributed to the study.

"For heart attack patients, the first priority is restoring blood flow to the heart," Burdick says. "What's neglected, however, are the secondary effects that occur after a heart attack."

These secondary effects include the release of enzymes intended to quell inflammation in the heart. If this response is sustained too long, the enzymes can damage muscle tissue, weakening the walls of the heart. Such conditions can lead to congestive heart failure.

The body produces inhibitors to these tissue-degrading enzymes, and lab-grown versions have been used in clinical trials. However, lacking a way to specifically target the heart, this kind of treatment can lead to side effects in tissues where enzymes and inhibitors are already in balance.

"That's where our approach came in," Purcell says. "And to really fine-tune the targeting, the innovation with this material is that it releases the inhibitor in response to the activity level of the enzyme."

The inhibitors are held inside molecular cages within the gel, the bars of which can be broken down by the enzyme. The more the enzyme is present, the more the gel breaks down and the inhibitor is released, leading to a dynamic balancing act.

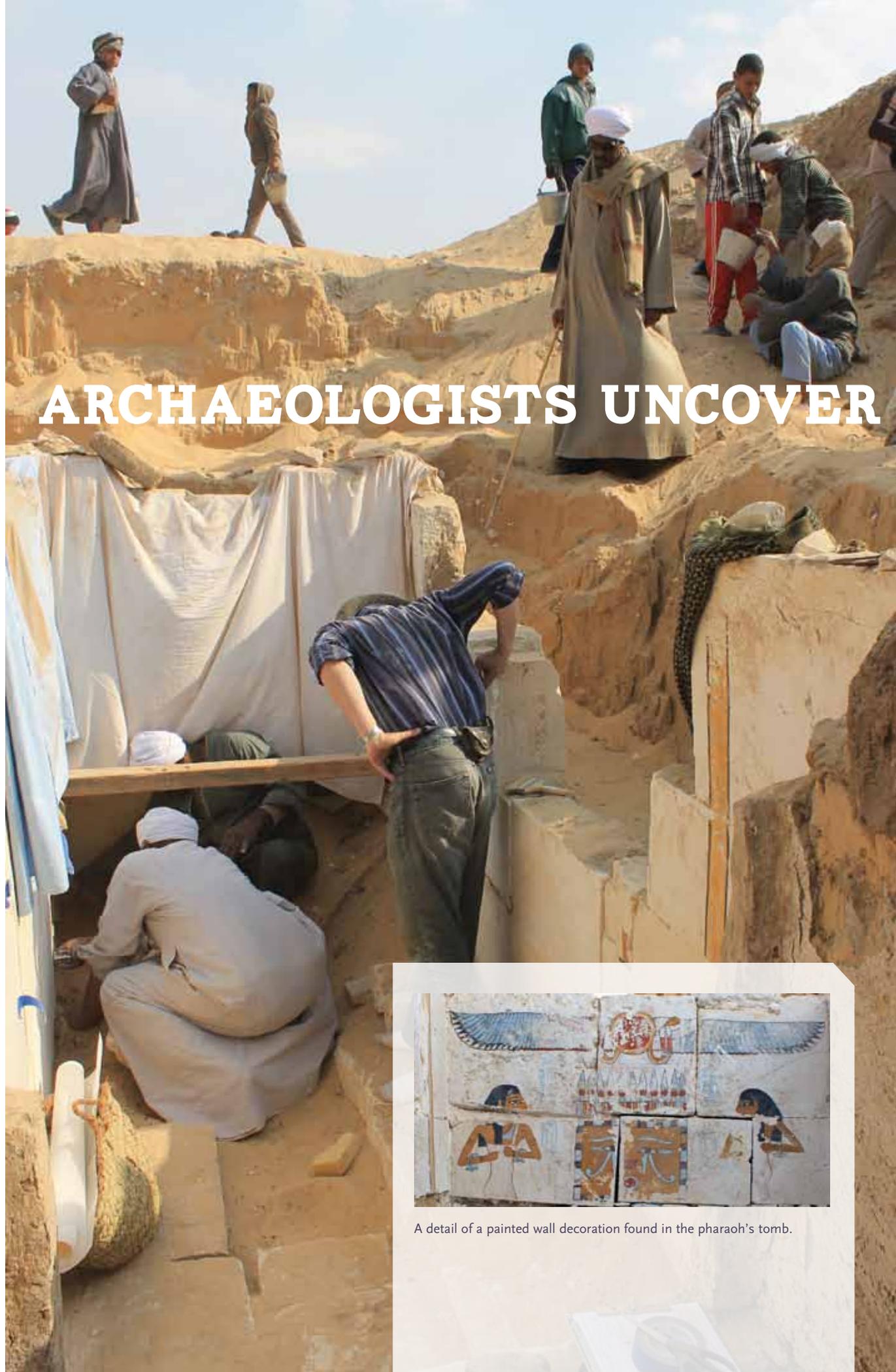
Testing the gel both in vitro and in vivo with pigs showed that the release of inhibitors closely matched the presence of the enzyme, and that the gel improved important post-heart-attack traits, such as the amount of blood pumped with each beat.

The team is hopeful that these results will pave the way toward clinical use in human patients.

The research was supported by the National Institutes of Health and the Veterans Affairs Health Administration Center. ■

Team members work to excavate the burial chamber of Pharaoh Woseribre Senebkay, with sheets covering a painted wall decoration.

# ARCHAEOLOGISTS UNCOVER



A detail of a painted wall decoration found in the pharaoh's tomb.



# TOMB OF AN UNKNOWN PHARAOH

**Just west of the Nile River in Upper Egypt, Penn archaeologists recently unearthed an unknown pharaoh—and with him, an entire forgotten Egyptian dynasty.**

The Penn team, led by Josef Wegner, an associate professor in the Department of Near Eastern Languages and Civilizations in the School of Arts & Sciences and associate curator in the Penn Museum of Archaeology and Anthropology's Egyptian Section, uncovered the tomb of Pharaoh Woseribre Senebkay, a king who ruled over an unknown Abydos dynasty around 1650 B.C.E.

Wegner's discovery suggests that Senebkay is potentially one of the first in a series of as many as 20 undiscovered pharaohs that ruled over the small kingdom. Penn graduate students Kevin Cahail,

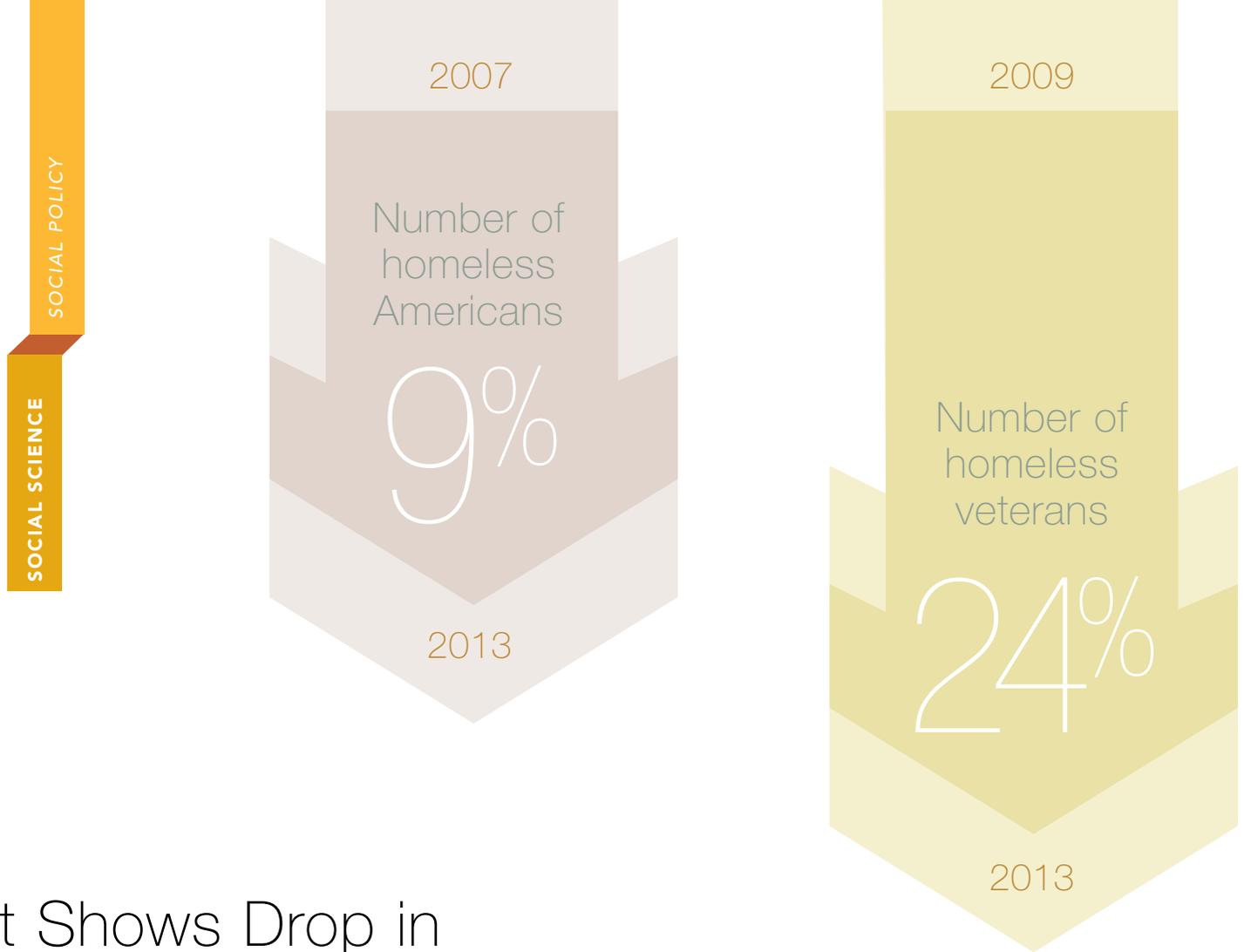
a Ph.D. candidate in Egyptology, and master's students Matt Olson and Paul Verhelst also played key roles on the excavating team.

"It's exciting to find not just the tomb of one previously unknown pharaoh, but the necropolis of an entire forgotten dynasty," Wegner says. "Continued work in the royal tombs of the Abydos dynasty promises to shed new light on the political history and society of an important but poorly understood era of ancient Egypt."

Wegner and his team first stumbled upon Senebkay's tomb after excavating a series of chambers constructed of mud-brick, which usually designated a common person's tomb. But upon further examination, they encountered a stone slab, and then a tomb consisting of four chambers, including a limestone burial chamber adorned

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## Report Shows Drop in U.S. Homelessness Rate

**In 2007, the U.S. Department of Housing and Urban Development submitted an Annual Homeless Assessment Report (AHAR) to Congress**, a first-of-its-kind study providing baseline data on homelessness in America.

Dennis Culhane, a professor in Penn's School of Social Policy & Practice, was a co-principal investigator of the initial AHAR and each report submitted since. Recent findings have shown that homelessness in America is on the decline.

Between 2012 and 2013, the number of homeless Americans dropped by nearly 4 percent, and since 2007, the number of homeless individuals has decreased by 9 percent.

Culhane credits the drop in numbers to an increased federal focus on placing people who are chronically homeless in subsidized housing units with support services. The initiative began with the George W. Bush administration in 2003 and has continued through the Barack Obama administration.

"All total, you have 110,000 new vouchers out there in the last 10 years targeted to chronic homeless people, most of whom are unsheltered," Culhane says. "That's a pretty big investment."

Homelessness among veterans has declined every year since 2010. Between 2012 and 2013, veteran homelessness declined

by 8 percent; between 2009 and 2013, it decreased by 24 percent.

The Obama administration has made fighting homelessness among veterans one of its top priorities. Culhane, who is also director of research for the National Center on Homelessness Among Veterans at the U.S. Department of Veterans Affairs, says funding to reduce veteran homelessness has increased from \$400 million when Obama took office to \$1.4 billion. He says there is no doubt that a significant portion of the reduction in the number of veterans who are homeless is due to an increased focus from the president and Congress.

Data for the AHAR is collected through an information system that tracks every entry and exit from a community's shelter system, and boots-on-the-ground observation. On the last Wednesday of every January, field workers in nearly 3,000 municipalities count the number of people in unsheltered locations, such as parks, bridges, cars, and abandoned buildings, or on the street.

On a single night in January 2013, there were 610,042 people experiencing homelessness in the United States. More than one-third of all homeless people were living in unsheltered locations, and nearly one-quarter were children. ■

**While working on a book on the question of efficacy in Western medicine,** Robert Aronowitz, chair of the Department of History and Sociology of Science in Penn's School of Arts & Sciences, came across what he calls "a treasure trove of evidence" about the history of prostate cancer.

A historian and medical doctor, Aronowitz noticed many references from the 1950s and early 1960s alluding to the "Bowery series." Further research revealed that a urologist, Perry Hudson, experimented on more than 1,200 homeless and alcoholic men from New York City's Bowery neighborhood in the 1950s and '60s, one of the first attempts to screen asymptomatic men for prostate cancer and cure the diagnosed men with radical surgery, castration, and sex hormones.

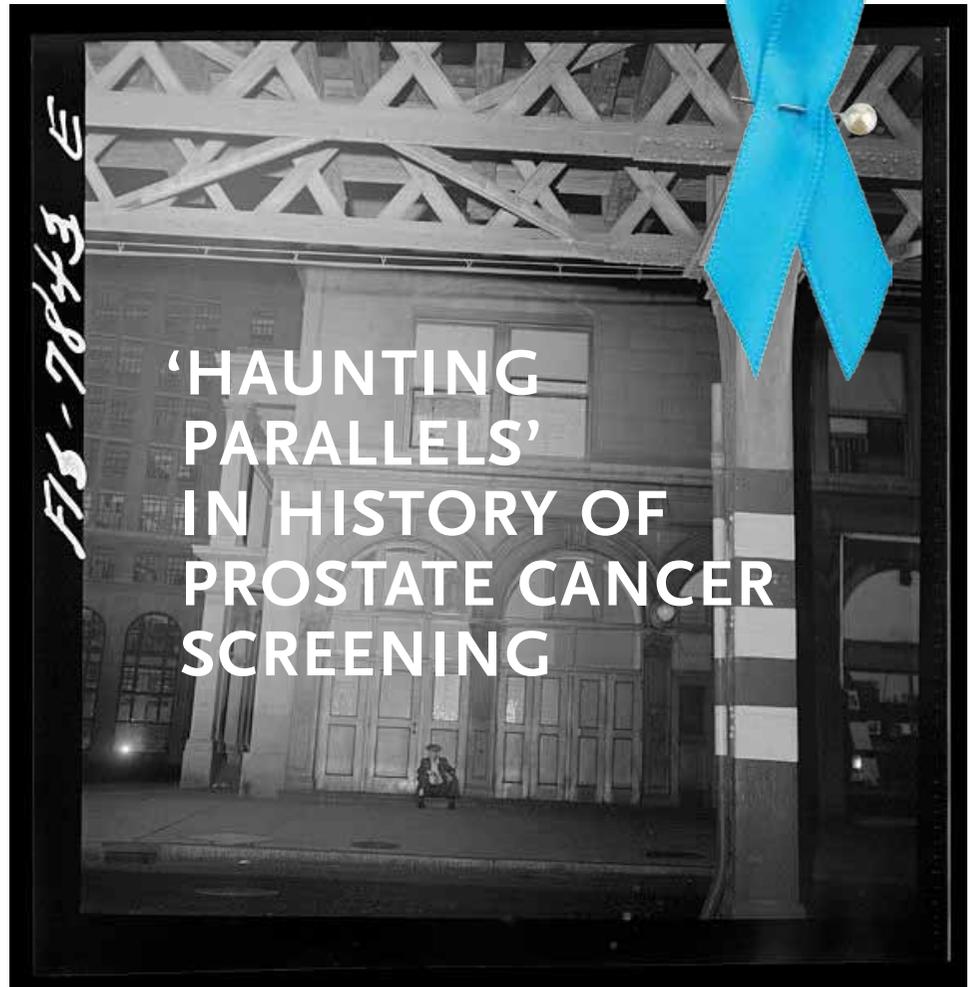
In two articles published in the *American Journal of Public Health* and the *Bulletin of the History of Medicine*, Aronowitz reconstitutes the history of the Bowery series, providing the medical and social context for why and how these practices were initiated, persisted, and eventually discontinued.

Aronowitz says the ethics of taking alcoholics from homeless shelters in the Bowery and subjecting them to invasive biopsies and radical surgery is "very troubling," but there are "many haunting parallels" to present-day prostate cancer treatment practices, such as the widely used prostate-specific antigen (PSA) test.

"Instead of 1,200 asymptomatic men over the course of a decade and a half, more than 1 million men are biopsied each year today," he says. "And yet, until very recently, long after our modern screening paradigm was well established, we had no results from clinical trials about this program's safety and efficacy. And when the results started appearing, they cast doubt on the wisdom of past and present practices."

Aronowitz—who says he has some sympathy for what Hudson was trying to do—says the Bowery series and subsequent developments are part of one continuous story of how medical and lay people came to believe in the efficacy of population screening followed by aggressive treatment without solid supporting scientific evidence.

"Patients today are often not fully informed about risks and benefits of PSA screening," he says. "More important, and like the Bowery men, many men today, and certainly men in the era before results from good clinical trials were available, have not been informed in the sense of knowing whether the test, and all that it may trigger, is worth it or not." ■



*Aronowitz says the Bowery series is part of one continuous story of how people came to believe in the efficacy of population screening and aggressive treatment without solid evidence.*

with  
Marybeth  
Gasman

**Marybeth Gasman, a professor of higher education in the Graduate School of Education, says she has every reason to believe that anything is possible.**

It wasn't long ago that Gasman, 46, was growing up alongside her large family on the upper peninsula of Michigan. Her parents had little more than an eighth-grade education, together making less than \$10,000 per year. She speaks frankly about her father's racism and openly about her mother's job scrubbing toilets to put her through college.

"I grew up in dire poverty, and that shaped my career in many ways," Gasman says. "When you're poor, people don't want to give you opportunities."

So with the help of a teacher, Gasman learned how to create them for herself. She enrolled in an undergraduate program on a Pell Grant and learned to question the status quo—especially when it came to her father, who she says spewed gross inaccuracies about African Americans.

"I wanted to find a truer history of this country, and of African Americans," Gasman says.

Today, Gasman is considered one of the country's most eminent scholars of higher education, historically black colleges and universities (HBCUs), and minority-serving institutions (MSIs). She's written and edited 21 books and is a regular contributor to national publications such as the *Chronicle of Higher Education* and *The New York Times*.

In 2014, she founded the Penn Center for MSIs, a national hub for resources and research surrounding these schools.

"I can't completely relate to students of color because I have white skin, but I can relate to a lot of things that some low-income students of color go through—not having a financial fallback and being told that you're not going to amount to anything in school," says Gasman, who also holds courtesy appointments in the School of Arts & Sciences and the School of Social Policy & Practice. "I went through all of that. [MSIs] serve those students. For me, my whole research agenda is about creating opportunities for others."

**Q: What are MSIs, and what is their role in the higher education landscape?**

There are four major types of MSIs: historically black colleges and universities, tribal colleges, Hispanic-serving institutions, and Asian American and Native American Pacific Islander-Serving Institutions [AANAPISIs.]

Right now, there are about 600 MSIs in the country, and they educate roughly 20 percent of all college students. If you think about President Obama's My Brother's Keeper initiative, of four-year institutions, MSIs educate 28 percent of men of color, and 48 percent in two-year institutions. That's actually a lot, and I think that people don't realize what a profound impact these institutions are having. Not a lot of other institutions are educating low-income students of color at this level because they're not willing to take risks and put forth the effort.

**Q: What are some of the other types of risks that MSIs assume in admitting low-income students of color?**

The more selective [a college is], the more likely they are to have a high graduation rate. If you're more selective, your students are more likely to be more affluent. So they're going to give more, and it all builds upon itself. With many, but not all MSIs, you have large numbers of students with lower test scores and lower GPAs.

Many MSI students come from low-income homes. On average in the U.S., 38 percent of the students are on Pell Grants. But, for instance, at HBCUs, 84 percent of students are on Pell Grants. At tribal colleges, 74 percent are on Pell Grants. So the MSIs are really the ones taking students who are low-income.

**Q: In 2013, you opened the doors to the Penn Center for MSIs. What are some of your goals for the Center?**

Two of the Center's goals are to elevate the knowledge about MSIs through rigorous research and innovative programs, and to provide them with free resources. We provide lots of tools, data, programs, and services.

Another one of our goals is to provide opportunities for emerging scholars. We have 45 emerging affiliates of the Center, and we promote their careers, put them in touch with people, introduce them to funders, the media, and often ask them to join our research projects.

**Q: You're currently a co-principal investigator for several of the Center's research projects. What are some of the top items on your research agenda?**

One of our projects, funded by a \$1.5 million grant from the Helmsley Charitable Trust, is focused on looking at education that's taking place in the STEM gateway courses at black colleges. One of the things we do with the grant money we get is give capacity-building grants. So we're funding 10 HBCUs at \$50,000 each while researching STEM education at those institutions.

We have another project funded by the Kellogg Foundation for \$750,000, focusing on teacher education in MSIs. We're going to work with four exemplary MSIs, one of each type, and we're going to invest in their teacher education program by giving them capacity-building grants. We're also going to study what they do and see if we can replicate the good work they're doing elsewhere.

We're also working on a project funded by the Mellon Foundation that focuses on increasing Latino faculty. We are considering the feasibility of pipelines between Hispanic-serving institutions and highly selective institutions such as Penn, Berkeley, and Michigan, and we're hoping that if we give support to both types of institutions and create a partnership, that we can make a dent in increasing Latino faculty.

**Q: What types of challenges present themselves in this realm of research?**

These institutions don't have a lot of resources, so to participate in a study with us takes time away from them; it takes people away from their own work. Many MSIs don't have a lot of infrastructure, and that can be really frustrating. It is often difficult work. But it's a little easier now—and it becomes easier when you're giving out capacity grants, as these grants offset the work that MSIs have to do.

**Q: What's the overarching value in studying MSIs?**

I think that this research is important because it focuses on low-income and students of color. For me, it's a moral issue—a social justice issue. However, if we want the United States to be globally competitive, if we're worried about social issues such as the economy, our future, and our livelihood, all we have to do is look at the demographics of the country to see where we should be focusing.

And for me, these are institutions that say, 'We're going to take care of everyone.' I believe in giving people opportunity. I believe in looking deeply for all the talent that people have, and giving people a chance to embrace equity. For me, that is what my research is all about. ■



**C**oastal planners' efforts to design protective barriers between cities and the rising sea have been met with limited success. But two professors at Penn's School of Design have come up with an entirely different solution for the vulnerable coast of the Chesapeake Bay—a solution that promises to be highly adaptable to coastal communities across the globe.

Anuradha Mathur and Dilip da Cunha, professor and adjunct professor of landscape architecture, respectively, are part of the Structures of Coastal Resilience project aimed at generating resilient designs for cities along America's North Atlantic coast. Supported by a grant from the Rockefeller Foundation, Princeton University invited researchers at Penn, Harvard, and the City College of New York to

participate in the project, asking each team to focus on a specific urban environment along the coast.

Mathur and da Cunha were asked to devise design strategies that would build resilience in the face of rising sea levels for the Norfolk/Hampton Roads area of the Chesapeake Bay. Early in their research, they noted how the land was "fractured toward the sea" in narrow sloping ridges that naturally accommodated changing water levels.

With the help of their team, which included recent PennDesign graduates Caitlin Squier-Roper, Jamee Kominsky, and Graham Laird Prentice, and graduate student Matthew Wiener, they did extensive field work, as well as developed a range of drawings that highlighted the diverse nature of the Virginia coast.

They concluded that the most effective design solution would be to engineer what they called Fingers of High Ground, which enhance natural as well as built landforms.

This highly unconventional idea required them to "change the design vocabulary from 'coastline' to 'gradients'" not only for

CONTINUED ON PAGE 33



OPPOSITE: Researchers compiled photos of the Chesapeake Bay region, including some beachfront horizons, in order to understand the nuances of the land.

ABOVE: The team looked at oyster beds as part of their on-site research.

## The Transformation of Paris

The French capital of Paris is a world-class city often used as the benchmark for other bustling metropolises across the globe: Beirut was once known as the Paris of the Middle East, Shanghai has been called the Paris of the East, and Buenos Aires has been described as the Paris of South America.

It was not until the 17th century, however, that Paris began to transform into the cosmopolitan megalopolis that exists today. In her book "How Paris Became Paris: The Invention of the Modern City," Joan DeJean, a professor of romance languages in Penn's School of Arts & Sciences, traces the growth of the city from the 1600s to its "uniquely prominent" present.

At the beginning of the 17th century, DeJean says that Paris was known for isolated monuments, but the city had not yet put its brand on urban space. Rome, with its rich history dating back to antiquity, was far more celebrated than Paris.

DeJean says some of the "big ideas" that led to the transformation of Paris were the construction of new kinds of streets, bridges, and residential architecture.

Paris was also one of the first cities to demolish its fortifications and focus on urban planning.

"In terms of urban planning, I think tearing down the fortifications and putting the first boulevard ever made around the city's edge was the biggest thing that they did," DeJean says.

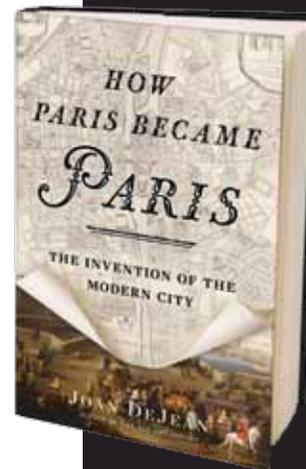
In the 1660s, Paris had a public transportation system consisting of horse-drawn carriages. By 1700, central Paris had become the capital that would revolutionize the public's conception of the city and urban life.

DeJean says she spent about six years conducting research for the book, using Parisian archives, libraries, museums, print rooms, and paintings of Paris in the 17th century.

After studying the city for many years, DeJean says she thought she knew 17th-century Paris well, but her research unearthed many unknowns.

"I didn't know the story of public transportation," she says. "I didn't realize that this boulevard that I walk on all the time began in 1669."

DeJean says she hopes the book gives the public a renewed appreciation of urban planning in Paris before the 19th century "and a realization that it wasn't just the 19th century that marked the city." ■



**T**he taxation of U.S. multinational corporations is one of the most important policy issues on the desks of elected officials. Proponents of a reduced tax rate argue that the current tax code puts American companies at a competitive disadvantage internationally and leads corporations to shift profitable aspects of their companies to foreign countries offering tax relief.

Chris William Sanchirico, a professor of law, business, and public policy at Penn Law School and co-director of Penn

LAW

## Are U.S. Companies Really American-Owned?



BUSINESS

Law's Center for Tax Law and Policy, says U.S. multinationals make two principal arguments supporting tax-friendly policies: a competitive argument—keep taxes low to help American businesses—and a call for a repatriation tax holiday that would allow companies to bring their foreign assets to the United States at a reduced tax rate.

Sanchirico says both arguments are based on the presumption that these companies are largely U.S.-owned.

“The truth is, we actually don’t know very much about who owns these companies,” he says.

In his paper “As American as Apple Inc.: International Tax and Ownership Nationality,” Sanchirico investigates the role of ownership nationality in the taxation debate and to what extent these ostensible “U.S.” companies are owned by foreign investors. The article was published in *Tax Law Review*.

The U.S. Department of the Treasury collects information on foreign holdings of U.S. stocks, but Sanchirico says existing reports “reveal almost nothing about the foreign ownership share of large U.S. multinationals.” He says establishing national ownership is nearly impossible.

Advocates of the repatriation tax day holiday contend that

if U.S. multinationals were able to bring the reported \$2 trillion that they are legally holding in foreign subsidiaries back to America at a reduced tax rate, the money will flow through shareholders into the American economy.

“Once again you see a premise, which is that the shareholders of the parent are largely U.S. persons,” Sanchirico says. “If the shareholders are sitting in Iowa, they’re more likely to plow that money back into the U.S. economy. If those shareholders are located in China or in France, you would imagine a lot more of it would go outside of the U.S. economy.”

Foreign investment is advantageous for U.S. multinationals, but Sanchirico says the companies should not be allowed to take advantage of the assumption that they are owned by U.S. shareholders.

“We need to think harder about who actually owns these companies in evaluating the tax benefits that we offer them,” he says. “There might be very good economic arguments for helping these companies, there might be arguments that go to global welfare. But until we sort out their ownership nationality, we should be wary of patriotic arguments.” ■



## The Benefits and Hazards of 401(k) Loans

**At any given time, 20 percent of American workers have an outstanding loan from their own 401(k) plan. Looking at a five-year period, that number jumps to 40 percent.**

The practice is common—but is it a sound financial decision?

For some people, it is, says Olivia S. Mitchell, professor of business economics and public policy at the Wharton School and co-author of the study “Borrowing from the Future: 401(k) Plan Loans and Loan Defaults.”

In research with colleagues from Peking University and the Vanguard Center for Retirement Research, Mitchell found that those with liquidity constraints are more likely to borrow, yet those who have accumulated more in their pensions borrow the most. The profile of borrowing is hump-shaped, with people ages 35 to 45 borrowing both more frequently and in larger amounts.

The researchers also discovered that an employer’s loan policy has a significant effect on whether people borrow in the first place. If the plan sponsor allows multiple loans, people are more likely to borrow from their 401(k)s.

While people do pay an interest rate when they use 401(k) funds, this is usually below rates charged by credit cards or

### WEB EXTRA



[goo.gl/Y5BT9u](http://goo.gl/Y5BT9u)

Olivia Mitchell discusses 401(k) loans with [Knowledge@Wharton](mailto:Knowledge@Wharton).

other lending sources, Mitchell says, making a 401(k) plan loan an attractive way to gain access to funds.

The majority of people do pay back their 401(k) loans—about 90 percent, according to Mitchell’s study. Nevertheless, when people leave their jobs, they must repay their loans in full or else they are deemed to have defaulted. That is expensive, since the borrower must pay income tax, plus a penalty on the full amount not yet repaid. Of those who terminate their jobs with a loan, 86 percent default. Yet this does not affect the borrower’s credit score.

“If you take a loan and remain with the employer, you have to repay yourself the company-specified interest rate. If you lose your job, then you must repay it—that’s tax law,” Mitchell explains. “Many people don’t know they’re going to face this hit.”

She concludes that it’s inappropriate to restrict loans completely, especially since they provide a valuable line of credit for lower paid workers. At the same time, however, employers should consider how they allow access to their plans: Instead of offering multiple loans—which implicitly encourages people to borrow more—they can offer only one loan at a time.

Mitchell, who also directs Wharton’s Pension Research Council, says people must become better educated about the benefits and consequences of 401(k) loans.

“I would keep the loan policy in place, but I’d warn employees of the taxes and penalties when borrowers leave their jobs,” Mitchell says. “Everyone with a defined-contribution pension plan faces the tradeoff of consuming today or waiting until retirement.” ■

About **90%**

of defined contribution plan participants have access to plan loans.

**1 OUT OF 5** defined contribution plan participants have an outstanding loan at any point in time.

**42**

The average age of borrowers

Slightly more than

**\$7,800**

The average individual loan amount borrowed (in 2010 dollars) with a median of nearly \$4,600.

**9 out of 10**

loans are repaid, yet when workers with an outstanding loan balance terminate employment, 86 percent of them default on their loans.



## Culture of ‘Companionate Love’ Integral to a Healthy Workplace

**“Love” might not be the first word that comes to mind when thinking of professional relationships built on conference-room banter and watercooler small talk.**

But according to Wharton Management Professor Sigal Barsade, a specific type of love known as companionate love not only exists in the workplace but is crucial to employee morale, teamwork, and customer satisfaction.

“Companionate love is different than romantic love,” Barsade says. “It is the degree to which you express caring, compassion, affection, and tenderness. And research has shown it’s the type of love that is actually felt the most.”

In research published in *Administrative Science Quarterly*, Barsade makes the argument that the more coworkers see each other expressing companionate love, the more likely that these emotions become contagious.

Set in a long-term health-care facility, the 16-month longitudinal study involved participants composed of 185 employees, 108 patients, and 42 family members of patients. The work was funded by the Wharton Center for Leadership and Change Management and the Wharton Center for Human Resources.

To measure the effect of a culture of companionate love on emotional and behavioral outcomes of employees, health outcomes of patients, and satisfaction of patients’ family members, Barsade and her colleagues constructed a scale designed to measure the cornerstones of a culture of companionate love: affection, caring, compassion, and tenderness.

Participants were asked to rate the level at which they witnessed colleagues expressing these emotions. An independent rating group also observed the work environment and rated these factors among employees on the unit.

The researchers found that when a culture of companionate love was strong on the unit, there were also greater levels of employee engagement and less absenteeism. The patients in highly rated companionate love units also noted better moods, fewer trips to the emergency room, and an overall higher quality of life.

Barsade says these findings are valuable, not only because it helps us to better understand the importance of companionate love at work, but also because it is one of the first studies that focuses on emotional culture (values and norms about emotions employees should show at work) rather than cognitive culture (values and norms about how employees should think at work).

“We see this research as the first building block to better understanding the whole concept of emotional culture at work,” Barsade says. “We are going to be doing future studies looking at emotional cultures other than love, like joy and fear, as well as how they all interact with cognitive culture.” ■

## Probing RNA

CONTINUED FROM PAGE 21

all the cells of a tissue sample, but only activate those in the specific cell they wanted to study.

“By shining blue light,” says Ivan Dmochowski, associate professor of chemistry, “the molecule falls apart in such a way that it can start binding to RNA.”

After using the blue laser, the researchers extracted the tissue and destroyed its cells, releasing and collecting the tags with captured RNA. Because only the tags inside the target cell were activated, the isolated RNA identified which proteins were in the process of being made at that specific place and time. ■

## Tomb of an Unknown Pharaoh

CONTINUED FROM PAGE 23

with paintings of the goddesses Isis, Nephthys, Nut, and Neith.

Although it appears that ancient tomb raiders had once ripped apart Senebkay’s mummy and stripped the pharaoh’s tomb contents of its gilded surfaces, the team was able to recover the remains of Senebkay amid debris of his fragmentary coffin, funerary mask, and canopic chest. Preliminary work on the pharaoh’s skeleton indicates Senebkay was a man of approximately 5 feet 10 inches who died in his mid- to late 40s.

The discovery of Pharaoh Senebkay also has broader implications in understanding the political and social history of Egypt’s Second Intermediate Period. Wegner says it proves the existence of the Abydos dynasty and identifies the location of their royal necropolis at South Abydos in an area anciently called Anubis-Mountain.

“The standard picture was that dynasties from the north and south were divided and at war with one another off and on,” Wegner says. “Now we know there is, in fact, a third kingdom—the Abydos dynasty—which is in between the two, so the political picture of this period becomes much more interesting.” ■

## Coastal Planning

CONTINUED FROM PAGE 29

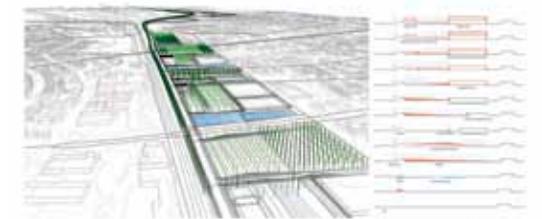
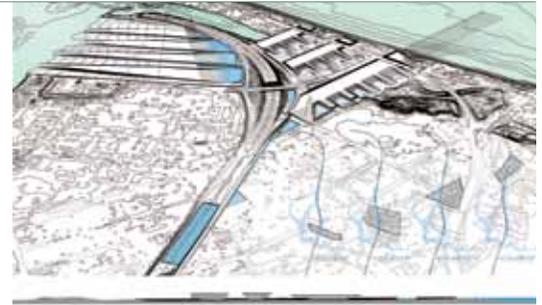
themselves, but for the initially skeptical engineers and scientists at the Army Corps of Engineers, the Virginia Institute of Marine Science, and Old Dominion University, da Cunha says.

Mathur says it was the power of the visual material they developed to document their investigations that ultimately convinced these scientists and coastal planners of the design’s potential.

The next step, they say, is to convince the affected residents of its efficacy by showing them the drawings and models that will help them revisualize the coast they call home.

The team has developed two specific design proposals on test sites that will demonstrate how Fingers of High Ground can be integrated incrementally into the existing city fabric. When realized, the unprecedented landscape designs would offer residents an immediately functional emergency evacuation system, and also provide much-needed long-term benefits such as flood-safe residential, commercial, and ecologically preserved areas.

“It’s about constructing a community,” says da Cunha, “one that can thrive by accommodating the rising sea rather than building barriers in futile attempts to fight it.” ■



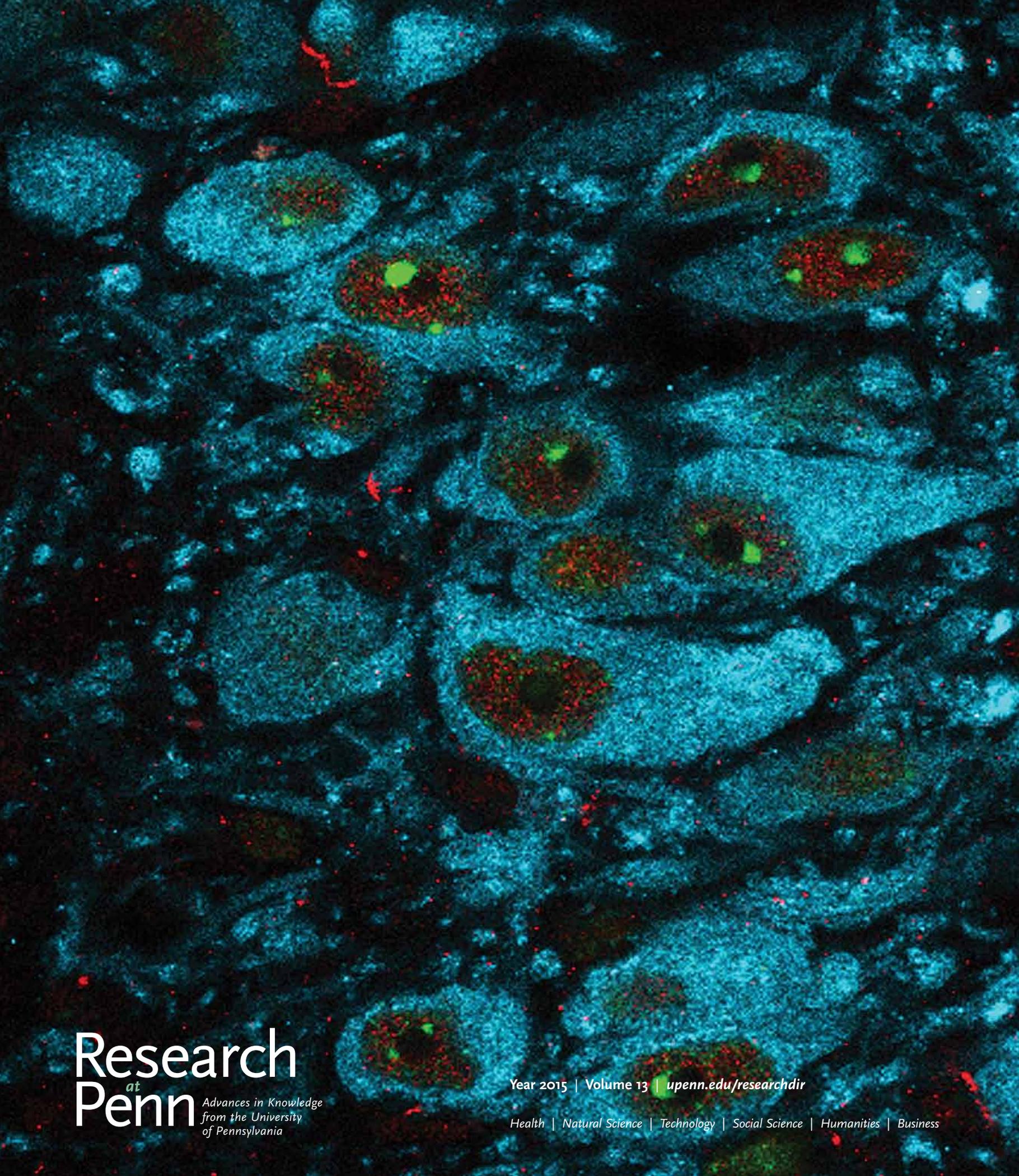
TOP: A rendering of Willoughby Spit, a peninsula of land in Norfolk, Va.

SECOND FROM TOP: Development of Lamberts Point Ridge, near Norfolk, Va.

ABOVE: PennDesign grad Caitlin Squier-Roper takes photos at Virginia’s Eastern Shore.

BELOW: Norfolk, Va. and surrounding areas from above.





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