RESISTING ZIKA | POETIC RESPONSE | YOUNG SCIENTIST PROGRAM

Outlook

Washington University in St. Louis
School of Medicine

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WINTER 2016-17

Pathways to Autism

Producing neurons, tracking behaviors to fight the disorder

ROBERT BOSTON

COVER Populations of neurons derived from the cells of patients and their families may provide clues to autism's genetic roots. Story on page 10.

FEATURES

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Researchers are using three major approaches to understand the disorder's physical and psychological basis.

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For 25 years, the Young Scientist Program has increased participation of underrepresented groups and brought resources directly to K-12 schools.

22 **Resisting Zika**
Working quickly and collaboratively, School of Medicine scientists are on the leading edge of this growing public health crisis.

Shondra Miller, PhD (standing), and her team in the Genome Engineering and iPSC Center isolate epithelial cells in urine samples and convert them to stem cells. Another lab coaxes the stem cells into neurons. These scientists are playing a critical role in autism research at the School of Medicine. See story, page 10.

ROBERT BOSTON

Outlook

Washington University School of Medicine

OUTLOOK.WUSTL.EDU WINTER 2016-17

Not a spectator sport: The Young Scientist Program brings hands-on fun and serious insights to K-12 students. Story on page 17.

TIM PARKER

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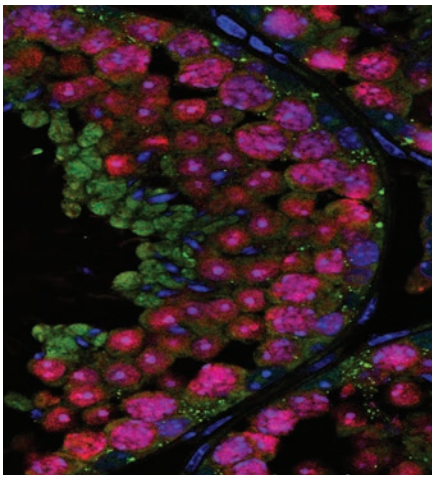

PRABAGARAN ESAKKY

In a healthy mouse, sperm (represented in pink) are abundant and flourishing. A recent study in mice revealed that the Zika virus breaks down the internal structure of the testes and lowers fertility. The finding could have implications for men. See story, page 22.

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ROBERT BOSTON

Biomedical engineering PhD student Ali Ross and Farshid Guilak, PhD, show a container with a prototype of a living hip replacement.

Stem cells engineered to grow cartilage

Technique uses 3-D weaving to grow a living hip replacement

With a goal of treating worn, arthritic hips without joint-replacement surgery, scientists have programmed stem cells to grow new cartilage on a 3-D template shaped like the ball of a hip joint. What's more, using gene therapy, they have activated the new cartilage to release anti-inflammatory molecules to fend off a return of arthritis.

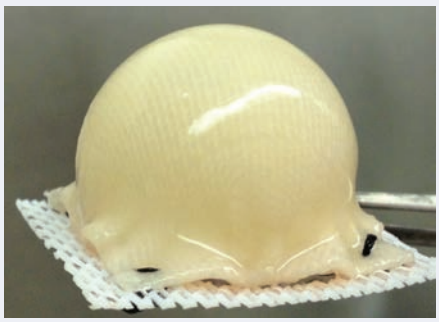
The technique, a collaborative effort between the School of Medicine and Cytex Therapeutics Inc. in Durham, North Carolina, is described in Proceedings of the National Academy of Sciences.

The scientists have tested various aspects of the tissue engineering in cell culture, and customized implants already are being tested in laboratory animals. Such devices could be ready for safety testing in humans in three to five years.

The discovery one day may provide an alternative to hip-replacement surgery, particularly in younger patients. Doctors are reluctant to perform such operations in patients under age 50 because prosthetic joints typically wear out after about 20 years. A second joint-replacement surgery to remove a worn prosthetic can destroy bone and put patients at risk for infection.

"Our hope is to prevent, or at least delay, a standard metal and plastic prosthetic joint replacement," said Farshid Guilak, PhD, professor of orthopedic surgery, of developmental biology and of biomedical engineering. Guilak also is the director of research at Shriners Hospitals for Children-St. Louis and co-director of the Washington University Center of Regenerative Medicine.

The technique uses a biodegradable, synthetic scaffold that Guilak and his team developed. The scaffold, molded into the precise shape of a hip joint, is covered with cartilage taken from a patient's stem cells. The stem cells are converted from fat cells and reprogrammed into cartilage. The scaffold then can be implanted.



GUILAK LABORATORY

A 3-D, biodegradable, synthetic scaffold has been molded into the precise shape of a hip joint.

Resurfacing the hip joint with living tissue is designed to ease arthritis pain.

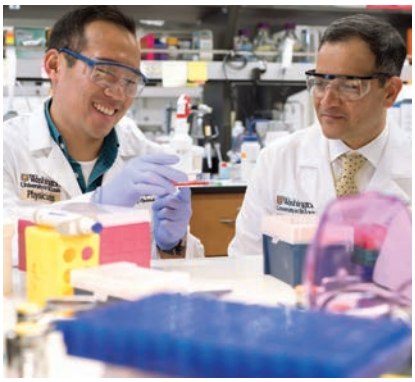
By inserting a gene into the newly grown cartilage and activating it with a drug, the implant also can orchestrate the release of anti-inflammatory molecules to fight a return of arthritis, which often triggers joint problems.

See weaving technique, back cover.

Culprit identified as major cause of vision loss

The eye's retina works like film in a camera. The retina's rods sense dim light, while cone cells detect colors, contrasts and sharp images seen during daylight. A wide range of disorders can damage those rods and cones and lead to vision loss. School of Medicine researchers have identified a pathway involved in harming rods and cones and have found a way to halt that damage.

Targeting the pathway with therapies could preserve sight in patients with many types of retinal disorders, including those for which there are no treatments, such as retinitis pigmentosa and advanced dry age-related macular degeneration.



ROBERT BOSTON

MD/PhD student Jonathan B. Lin (left) and Rajendra S. Apte, MD, PhD

The findings are published in the journal Cell Reports.

"We believe we have uncovered a unifying pathway involved in inflicting severe damage to and even causing the death of rods and cones," said Jonathan B. Lin, an MD/PhD student and co-first author with Shunsuke Kubota, MD, PhD, a former postdoctoral fellow. "These findings should help us develop treatments for retinal disorders, regardless of what's causing them."

Lin works in the lab of senior investigator Rajendra S. Apte, MD, PhD, the Paul A. Cibis Distinguished Professor of Ophthalmology and Visual Sciences. In a series of experiments first in mice and later in retinal cells, they identified a key molecule — NAD (nicotinamide adenine dinucleotide) — in the cascade that leads to the death of the retina's rods and cones.

Photoreceptor cells such as rods and cones are among the biggest energy users in the body. The researchers identified problems in the cells' mitochondria — where energy is produced — as a culprit in vision loss. The NAD molecule is known for its important role in energy production.

When the researchers treated damaged photoreceptor cells in mice with NMN (nicotinamide mononucleotide) — a precursor molecule that boosts NAD levels— the cells' degeneration ceased and vision was restored. NMN is of particular interest to scientists who study problems related to aging.

Apte expects human clinical trials could begin soon.

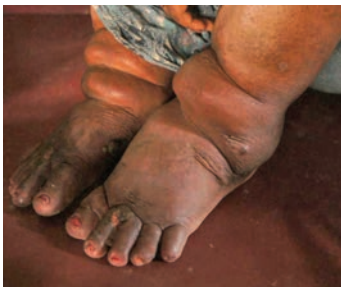
ROBERT BOSTON

ALAN L. SCHWARTZ, PHD, MD, the Harriet B. Spoehrer Professor, who until earlier this year had served as head of the Department of Pediatrics for 21 years, was celebrated at a symposium. Schwartz will devote more time to national leadership commitments, mentoring faculty and trainees, and to his research.

$8 million grant supports drug studies to eliminate lymphatic filariasis

The Bill & Melinda Gates Foundation has awarded the School of Medicine a two-year, $8 million grant to evaluate an investigational treatment for a neglected tropical disease.

More than 1 billion people in 73 countries live at risk of lymphatic filariasis. Without effective treatment, the infection can lead to massive swelling and deformity of the legs, known as elephantiasis.



CAITLIN WORRELL/CDC

A woman in India suffers severe swelling in her legs due to elephantiasis.

The grant supports a team led by Gary J. Weil, MD, professor of medicine and of molecular microbiology. Weil has studied lymphatic filariasis — which is caused by parasitic worms and spread by mosquitoes — for decades. His earlier research led to a new diagnostic test for the disease.

The grant will fund multicenter studies of an investigational triple-drug treatment – ivermectin, diethylcarbamazine and albendazole, also known as IDA. The community-based studies will enroll more than 30,000 people.

Recent clinical trials have shown that the three-drug regimen is more effective than the currently used two-drug regimens of diethycarbamazine plus albendazole, or ivermectin plus albendazole. In addition, it may only need to be given once while the two-drug treatment needs to be repeated for many years.

"If our studies confirm the safety and effectiveness of the triple-drug regimen, the treatment could be a game changer in accelerating the global program to eliminate lymphatic filariasis in the developing world," Weil said.

OTTAWA CITIZEN

UPDATE TO SUMMER 2016 OUTLOOK STORY

Man's paralyzed hand moves again

OTTAWA CITIZEN

In 2015, quadriplegic Tim Raglin became the first person in Canada to undergo a nerve transfer surgery to restore some movement to his hand. Raglin had been unable to move his hands or legs since shattering a vertebra in a diving accident nine years earlier. School of Medicine surgeons Susan E. Mackinnon, MD, who pioneered the technique, and Ida K. Fox, MD, traveled to Canada to supervise as Kirsty Usher Boyd, MD, formerly a surgical fellow at Washington University, performed the delicate operation. The surgeons took a still-functioning nerve that controlled Raglin's elbow and sutured it onto a pathway toward his right hand. For a year after surgery, Raglin felt nothing at all; damaged nerves regrow very slowly. Then, in February 2016, his index finger twitched. Now he can unfold his fingers and grip implements such as a fork, shaver and toothbrush. The process has been exhilarating for Boyd and Raglin. "It's all about independence," Raglin said.

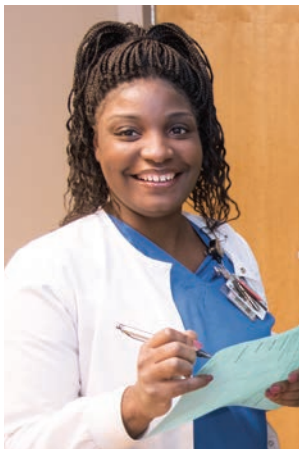
Response to Ferguson

Medical internship provides opportunities

When Adriana Isaac graduated from McCluer High School in Florissant, she didn't know what she wanted to do with her life. Although she had worked at Pizza Hut through high school and was promoted to manager after graduation, remaining in that job would mean working nights and earning less than $10 an hour.

"I knew the pay wasn't going to provide for my family, and the hours weren't working well with raising children," she said.

In July, Isaac began working as a medical assistant after participating in a new internship program. The program was created for adults with an interest in health sciences through a partnership involving the School of Medicine, the University of Missouri-St. Louis and St. Louis Community College.



ROBERT BOSTON

Adriana Isaac

Medical assistants — normally trained through area trade schools — bring patients into exam rooms, assess vital signs and document the primary reasons for their visits to doctors' offices and clinics.

The positions are difficult to fill and recently have become more so because students now have to pass a national certification exam. Training program enrollment also is low because students find it challenging to attend school for an average of 20 weeks without income. The internship provides students with an income during training. Interns are asked to make a two-year employee commitment after completion.

"This program was a life-changer for me and my family," said Isaac, who now works as a registered medical assistant in pediatric surgery for the medical school.

The idea grew out of the university's interest in supporting recommendations outlined by the Ferguson Commission. Missouri Gov. Jay Nixon appointed the 16-member board in November 2014 in the wake of unrest following the death of Michael Brown. The commission issued a report titled "Forward Through Ferguson: A Path Toward Racial Equity."

Higher education leaders zeroed in on a need for more economic mobility for residents of north St. Louis County and north St. Louis. Leaders on the Medical and Danforth campuses reached out to partner institutions, helped establish the curriculum, recruited the first class of trainees and placed them in clinical departments. Participating departments include medicine, orthopedics, surgery, neurology and neurosurgery.

ROBERT BOSTON

Building connections

Move-in has begun at Mid Campus Center (MCC), left, a 12-story building at 4590 Children's Place, just north of the Central West End MetroLink Station. The MCC further consolidates operations by housing collaborative and administrative space for Barnes-Jewish and St. Louis Children's hospitals and the School of Medicine, including the dean's office, as well as a joint emergency command center. This move provides more space for medical school faculty and clinics in other locations, such as at the Center for Outpatient Health. The MCC features a cafe, bookstore and extensions to the elevated walkway system, improving campus connectivity. Except for shelled space, the MCC will be fully occupied by April.

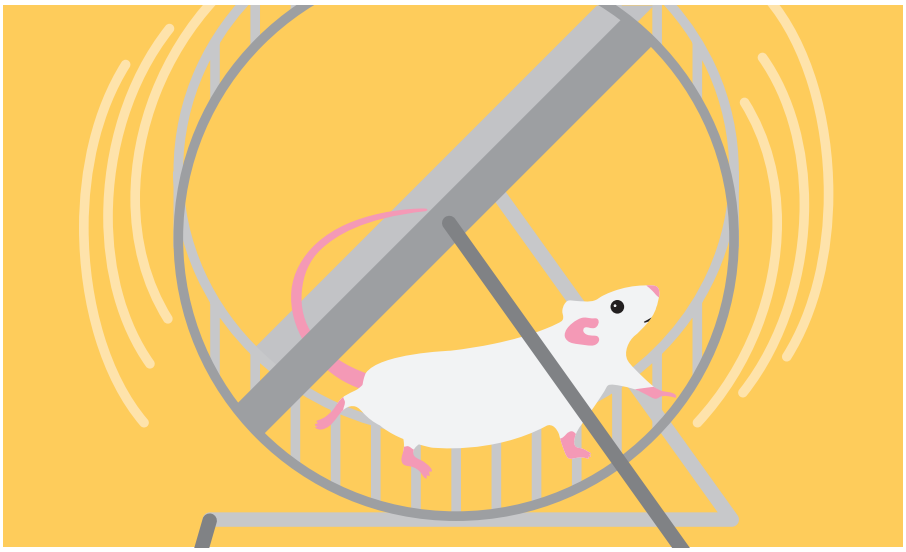
Compound reduces signs of aging in mice

Supplementing healthy mice with a natural compound called NMN can compensate for loss of cellular energy production, reducing typical signs of aging. The study is published in the journal Cell Metabolism.

"We have shown a way to slow the physiologic decline that we see in aging mice," said Shin-ichiro Imai, MD, PhD, professor of developmental biology and of medicine. "This means older mice have metabolism and energy levels resembling that of younger mice. Since human cells rely on this same energy production process, we are hopeful this will translate into a method to help people remain healthier as they age."

Imai is working with researchers conducting a clinical trial to test the safety of NMN in healthy people. The phase 1 trial began earlier this year at Keio University School of Medicine in Tokyo.

With age, the body loses its capacity to make a key element of energy production called NAD (nicotinamide adenine dinucleotide). Past work by Imai and co-senior author Jun Yoshino, MD, PhD, an assistant professor of medicine, has shown that NAD levels decrease in multiple tissues as mice age. Research also has shown that NAD is not effective when given directly to mice so the researchers sought an indirect method to boost its levels. To do so, they only had to look one step earlier in the NAD supply chain to a compound called NMN (nicotinamide mononucleotide).



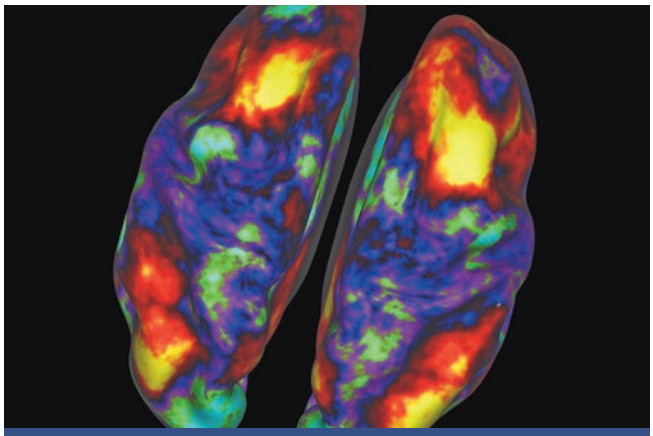
MICHAEL WORFUL

Older mice drinking water supplemented with NMN resembled younger mice in measures of metabolism and energy production.

NMN can be given safely to mice and is found naturally in a number of foods, including broccoli, cabbage, cucumber, edamame and avocado.

The new study shows that when NMN is dissolved in drinking water and given to mice, it appears in the bloodstream in less than three minutes. Importantly, the researchers also found that NMN in the blood is quickly converted to NAD in multiple tissues.

The researchers found a variety of beneficial effects, including in skeletal muscle, liver function, bone density, eye function, insulin sensitivity, immune function, body weight and physical activity levels.



M.F. GLASSER AND S.M. SMITH

THE AGING BRAIN A research team led by Washington University scientists will scan the brains of kindergartners to centenarians to capture the changes that occur as brains develop, mature and age over the lifespan. The endeavor, a followup to the Human Connectome Project, is funded by two grants totaling $34 million from the National Institutes of Health (NIH). The above composite image shows healthy adult brains at rest, as captured by MRI.

Macones elected to National Academy

Obstetrician/gynecologist George Macones, MD, has been elected to the National Academy of Medicine. Membership in the organization is one of the highest honors in the fields of health and medicine in the U.S.

Macones is the Mitchell and Elaine Yanow Professor and chair of the Department of Obstetrics and Gynecology.

He is among 70 regular members and 9 international members whose election to the National Academy of Medicine was announced in October. Current members of the organization elect new members based on their contributions advancing public health, health care and medical science. All members volunteer time to serve on committees examining a broad range of health policy issues.

Macones, also chief of obstetrics and gynecology at Barnes-Jewish Hospital, is a specialist in maternal-fetal medicine. He has expertise in caring for pregnant women with complicated pregnancies and those at risk for preterm birth.

The author or co-author of more than 300 scientific articles, he is internationally renowned for his research on the safety of vaginal birth after cesarean sections and developing new guidelines on monitoring fetuses during labor. He directs the March of Dimes Prematurity Research Center at Washington University.

Sets of DNA variants: a cheaper, faster solution

Some 10 million points of genetic variation are scattered across a molecule of DNA, and those variations make us who we are as individuals. But in some cases, those variants contribute to diseases, and it's a major challenge for scientists to distinguish between harmless variants and those that are potentially hazardous.

Now, School of Medicine researchers have developed a technique to cheaply and rapidly create myriad sets of DNA fragments that detail all possible genetic variants in a particular stretch of DNA. By studying such DNA fragments, scientists can more easily distinguish between genetic variants linked to disease and those that are innocuous.

The findings, published in Nature Methods, allow researchers to create sets of DNA variants in a single day for a few hundred dollars. Current methods take up to a week and cost tens of thousands of dollars.

"As a pediatric neurologist who does a lot of genetic studies of kids with developmental disabilities, I frequently will scan a patient's whole genome for genetic variants," said Christina Gurnett, MD, PhD, the study's senior author and an associate professor of neurology and of pediatrics. "Sometimes I'll find a known variant that causes a particular disease, but more often than not I find genetic variants that no one's ever seen before, and those results are very hard to interpret."

Postdoctoral researcher Gabriel Haller, PhD, who was working in Gurnett's lab, realized that he could harness common laboratory techniques and tools to create sets of DNA variants without the expensive equipment and reagents that drove up the price.

Haller copied a DNA sequence using the four standard DNA letters and a nonstandard letter known as inosine. Each copy of the sequence was identical except for one inosine, which was located at a random spot and served as a placeholder. Then, he replaced the inosine with one of the standard DNA letters, creating a single mutation in each copy of the sequence.

Gurnett envisions the creation of a catalog listing the effects of every possible variant.

Innovative light therapy able to reach deep tissues

ROBERT BOSTON

Samuel Achilefu, PhD

Samuel Achilefu, PhD, the Michel M. Ter-Pogossian Professor of Radiology, is the first recipient of the Breast Cancer Research Program Distinguished Investigator Award from the U.S. Department of Defense.

The $4.5 million award will support his efforts to develop a safer, more effective way to treat breast cancer than currently available chemotherapy drugs.

Using a mouse model of cancer, scientists led by Achilefu devised a way to apply light-based therapy, known as phototherapy, to deep tissues never before accessible with this method. They delivered light directly to tumor cells via an imaging agent frequently used in positron emission tomography (PET) scans. This light source, along with a novel cancer-targeting product and a chemotherapy drug, selectively kills cancer cells.

Long used in cancer treatment, phototherapy is effective only as far as light can penetrate. This has limited usage to skin cancers and areas of the body accessible with an endoscope.

Co-investigators are Katherine N. Weilbaecher, MD, professor of medicine, and Robert D. Schreiber, PhD, the Alumni Endowed Professor of Pathology and Immunology.

Immunotherapy for leukemia shows promise

A new type of immunotherapy shows promise against acute myeloid leukemia (AML) cases that recur or never respond to treatment.

A small clinical trial at the School of Medicine provides evidence that the immune system's "natural killer" cells can be dialed up in the lab and trained to destroy cancer cells in some patients. The findings are published in Science Translational Medicine.

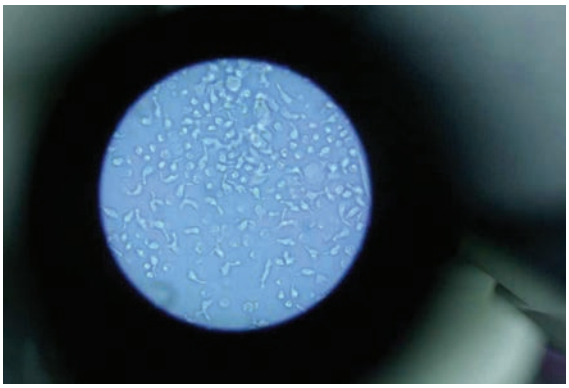
In the trial of nine patients, four achieved complete remission; there was no evidence of leukemia for at least one month after treatment. One patient achieved a partial remission, with some abnormal cells reappearing at the one-month mark. The remaining four patients did not respond to the therapy.

The longest complete remission lasted about six months. The average life expectancy for patients with active AML that does not respond to therapy is about three months.

"This is a small study, but a 50 percent response rate is promising since these are patients with very poor prognoses and very few options," said Todd A. Fehniger, MD, PhD, co-principal investigator of the study and an associate professor of medicine.

Natural killer (NK) cells are immune cells that can attack tumor cells and cells infected by viruses. For this therapy, the NK cells are taken from a closely related donor, separated from the rest of the blood, and incubated overnight in a mixture of interleukins 12, 15 and 18. These chemical signals activate and train the NK cells to attack leukemia cells more effectively in the patient following infusion.

Rizwan Romee, MD, co-principal investigator of the study and an assistant professor of medicine, refers to the process as "boot camp." "When the NK cells see the real cancer for the first time, they remember their training and respond more effectively than cells that don't have this exposure."

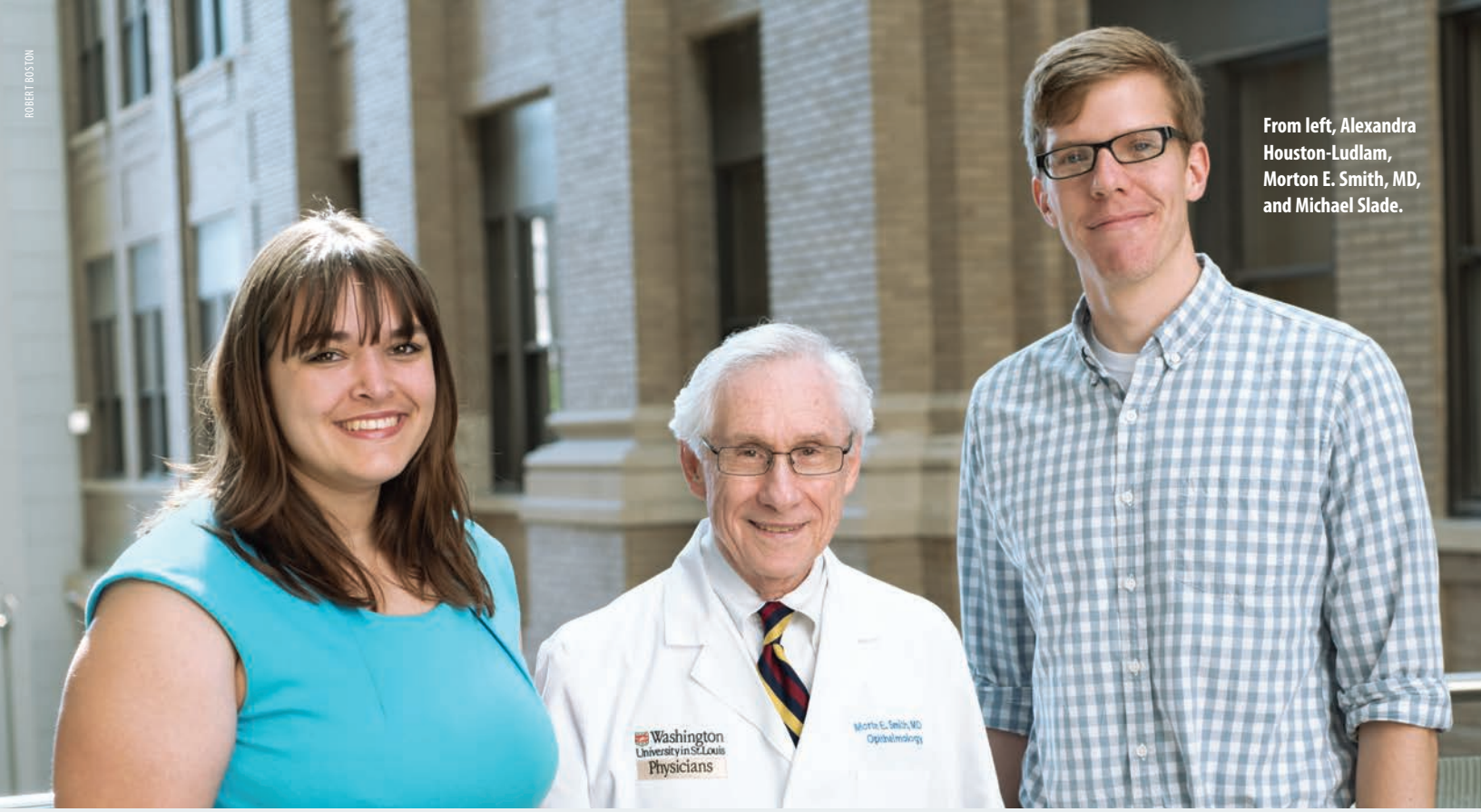


HUY MACH

Viewed through a microscope, NK cells incubate in a chemical cocktail.

This phase 1 trial primarily was designed to test the safety of the new therapy. "We saw remissions at each dose level, even the lowest one," Fehniger said. "Now that we have established the safety of this immune therapy, we would like to find out how consistently the patients respond when we treat a large number at the highest dose level, which is what we're in the process of doing now."

MICHAEL WORFUL



ROBERT BOSTON

From left, Alexandra Houston-Ludlam, Morton E. Smith, MD, and Michael Slade.

Students win national poetry contest

Alpha Omega Alpha Honor Medical Society publishes their work

Life on the brink of death inspired the poetry of two School of Medicine students who won first and second place in an annual competition sponsored by the Alpha Omega Alpha Honor Medical Society (AOA).

Michael Slade's first-place poem, "Requiem," and Alexandra Houston-Ludlam's second-place piece, "My First Patient," were published in AOA's literary journal The Pharos.

"Winning the top two spots is unprecedented," said Morton E. Smith, MD, professor emeritus of ophthalmology and visual sciences, associate dean emeritus and councilor for the school's Alpha Omega Alpha chapter. "It speaks to the compassion and talent of Michael and Alexandra."

Altogether, AOA received 123 poetry submissions from chapters across the country.

"For two students from the same institution to rise to the top is an extraordinary feat," said Dee Martinez, managing editor of The Pharos.

Slade, a fourth-year medical student, said the patient he wrote about came from a blend of experiences and conversations he has had with attending physicians, residents and other medical students. "He's a product of frustrations I've had with friends and relatives," Slade said. "He is also, more than a little bit, me.

"When you start working in the hospital in your third year of medical school, absolutely everything is overwhelming," Slade continued. "You're trying to keep track of a million tasks and impress a seemingly endless parade of people evaluating you. It's easy to lose track of the fact that, as future physicians, we're a part of seminal events in people's lives.

"Writing is a chance to stop and reflect, to synthesize the stress and the chaos and the heartbreak we see and participate in on a daily basis. It's a chance to find something meaningful in what often feels completely random."

Inspired by first-semester anatomy lab, Houston-Ludlam wrote about her expectations compared with her realities of medical school. "Before I came here, I saw the science of medicine being distinct from the interpersonal intimacy of physician-patient contact," she said.

"The people who donate their bodies to Wash U for the purpose of furthering medical education have had a significant impact on me," said Houston-Ludlam, who is enrolled in the Medical Scientist Training Program.

"In my case, this person not only taught me about human anatomy, using the physical self as an example. This person also helped me practice how to put aside my own reservations and anxieties to focus on the patient-centered task at hand, and serves as a metaphor for my transition to medical student. This poem is first and foremost an expression of my gratitude to this person."

Requiem

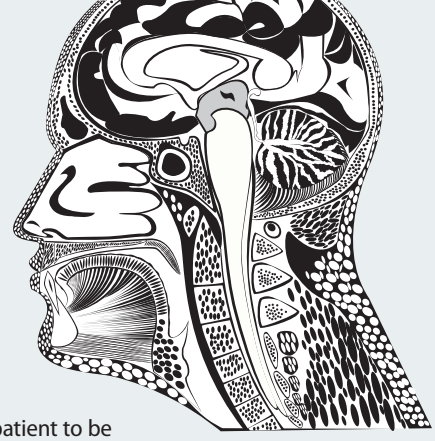
I find you outside, smoking
oxygen tank placed carefully to the side
basking in the last colors of the fall
I would've covered you in nicotine patches
gone back in time and snuffed your cigarette
when you first stole one from Dad's pack
and lit it out behind the shed
trying to hide the scent with Febreze
and orange-scented hand sanitizer

With each drag, your cells shivered
swelling until some poor intern
sat down on the edge of your bed
and stuttered out a death sentence
"We've found something"
as if it could be treasure or puppies
and isn't always something ugly and slimy
slithering forth from an organ system
you'd long stopped considering

I sit down on the bench beside you
and watch the ambulances go by
You smile crooked and ask if I want one
I laugh, knowing my wife will kill me
just for having the smoke on my jacket
and that bitter look in the back of my eyes
A moment of silence slides past us
joining the bustling exodus
of newly christened and sacred old

Finally, you turn and ask me how long
I'm sure your world will never be green again
but will end in brown or red or gold
Instead I tell you it's hard to know
and you pull deeply on your cigarette
Each of us charts our course
and waits for the last leaf to fall.

Michael Slade



My first patient

I always pictured my first patient to be
wrapped in a dressing gown
frail and thin
laying in a hospital bed
kindly, quietly answering the many questions I would ask as a beginning medical student.

My first patient is
wrapped in muslin
cold and swollen
laying on a metal table
kindly, silently answering the questions I never knew I would ask as a beginning medical student.

I always expected my most intimate patient moments to be
dealing with the devastation of personal illness and loss
described in words and punctuated with tears
like the most intimate moments I've shared with family and friends.

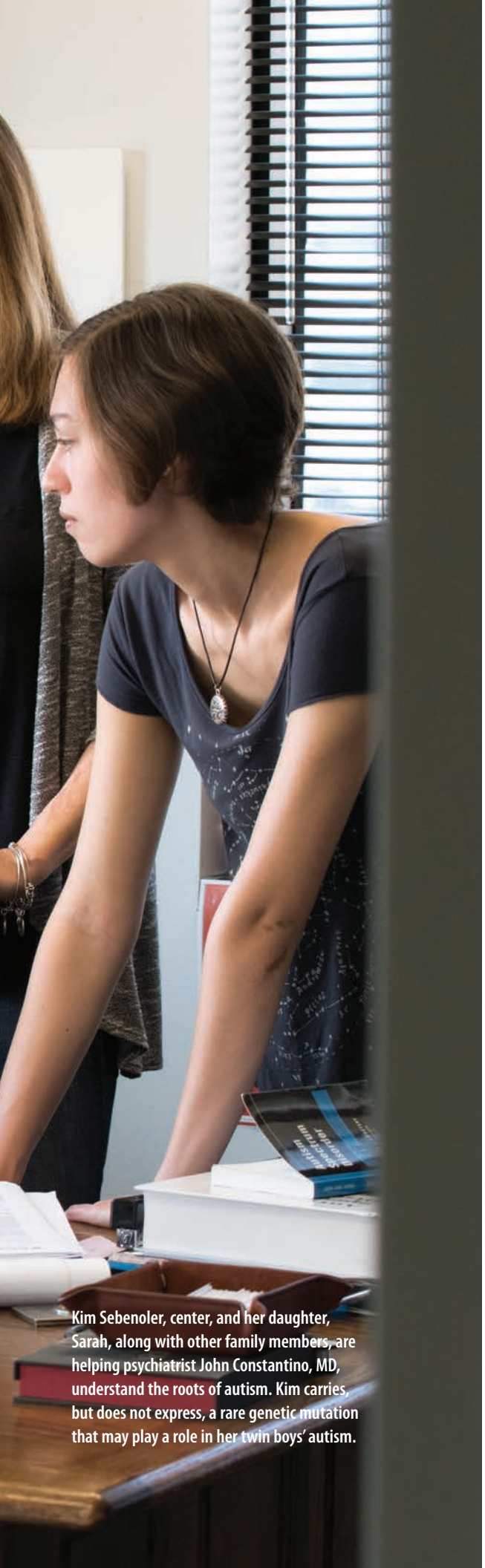
My most intimate patient moment is
peeling away layers of skin and flesh and bone to discover what lies beneath
holding the nerve that controlled the hand that touched family and friends with warmth and love
unlike anything I have ever experienced with another human being.

I always expected my first patient to teach me
the clinical presentation of some disease process I recently learned in class
the human side of disease and illness
how to be a good doctor
with words and stories and mannerisms.

I never expected my first patient to teach me
that a cancerous lymph node looks like a black and white marble with the texture of a dried bean
the specific sound of separating fibrous cobwebs of collagen encapsulating arm and leg compartments
how to be a good human
without ever speaking a word.

Alexandra Houston-Ludlam


John Nicholas Constantino M.D.
Child & Adolescent Psychiatry
John Nicholas Constantino, M.D.
John N. Constantino, MD 1988
search for compensatory factors
SOX2
OCT4
DAPI
Merge
Sox2 and Oct4 are pluripotency markers
DELL



ROBERT BOSTON PHOTOS

Kim Sebenoler, center, and her daughter, Sarah, along with other family members, are helping psychiatrist John Constantino, MD, understand the roots of autism. Kim carries, but does not express, a rare genetic mutation that may play a role in her twin boys' autism.

Unraveling autism

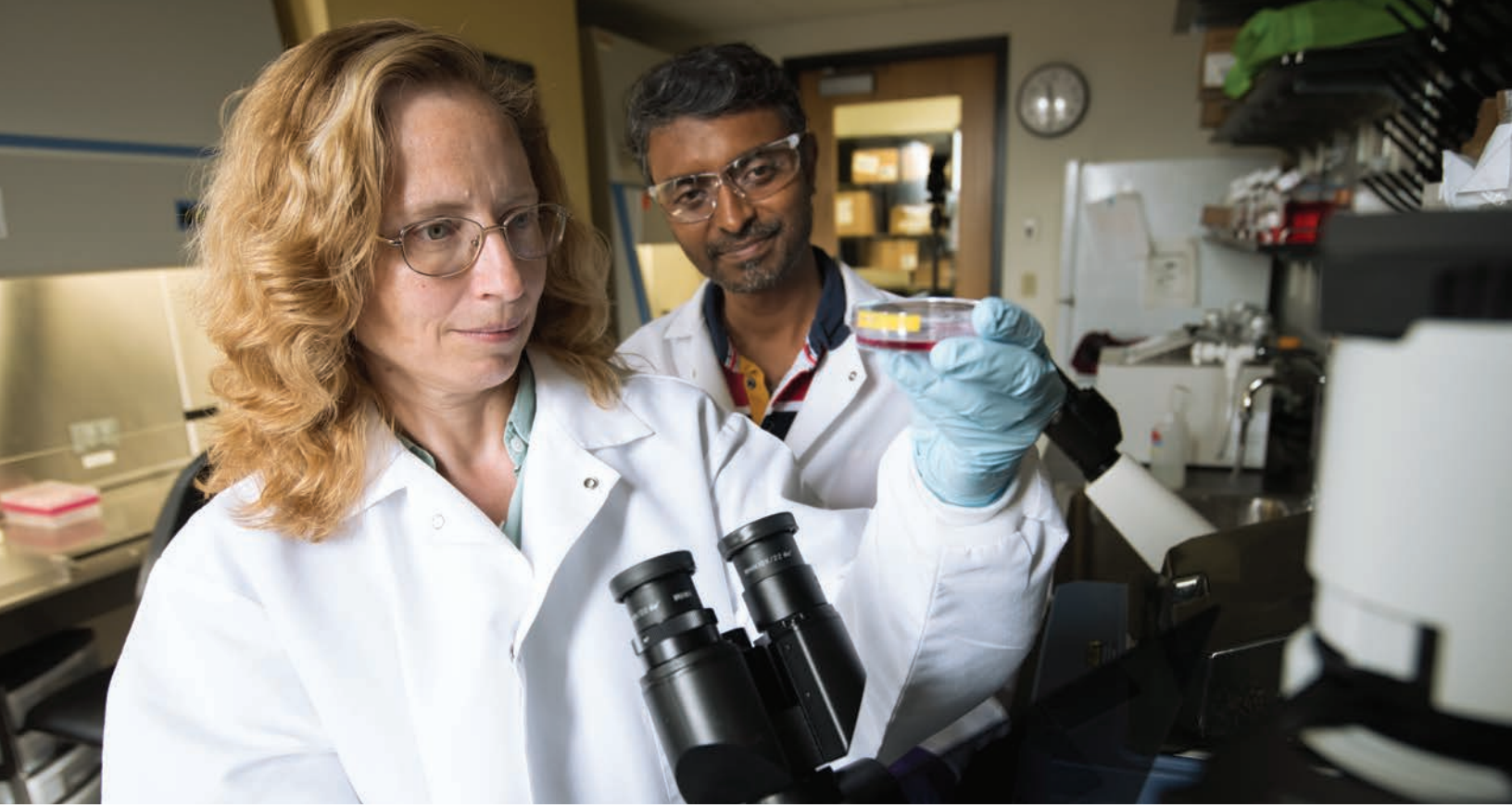
Multifaceted approach aims to detect, treat and even reverse the disorder.

BY REBECCA BOYLE

Like many patients visiting a doctor's office, Kim Sebenoler started out her appointment by heading to the nearest restroom to give a urine sample. But her visit to the lab of John Constantino, MD, director of the William Greenleaf Eliot Division of Child Psychiatry, was not a typical exam. The goal was not to measure proteins in her urine or check her overall wellness.

Instead, researchers took her urine cells to replicate human brain cell function in a Petri dish. The study is one of three major approaches School of Medicine researchers are using to unravel the physical and psychological underpinnings of autism. The unique, multifaceted effort — studying genes, brain activity patterns and behavior — is giving researchers and practitioners a better understanding of the disorder, which today affects one in every 100 Americans.

The cells are helping co-investigators Constantino and neuroscientist Azad Bonni, MD, PhD, explore how brain function changes in people with autism spectrum disorder (ASD). Both researchers are international leaders — Constantino in clinical autism studies and Bonni in advancing understanding of the underlying mechanisms of brain development.



How are neurons created?

Researchers isolate epithelial cells found in urine.

The cells are regressed into nimble stem cells.

Stem cells are converted into neurons.

Researchers observe neuron function in Petri dish.

Autism is most commonly characterized by repetitive behaviors and difficulty with communication and social interaction. It has a multitude of forms, and psychologists recognize a wide spectrum of skills, symptoms and disability.

"We are engaging people across disciplines — geneticists, molecular biologists, child psychologists, neuropsychologists and human brain imaging researchers," said Bonni, the Edison Professor of Neuroscience and chair of the Department of Neuroscience. "There is no single pathway toward treatment or discovery. It's absolutely the case that we need multifaceted approaches. Washington University is uniquely positioned to address these challenges."

Researchers collected urine samples from several members of the Sebenoler family, including daughter Sarah, 18, and 16-year-old identical twin boys, Mark and Jack. Kim Sebenoler is not on the autism spectrum, and Sarah has not been formally diagnosed, but the twins were diagnosed at age 3.

The researchers took the samples and separated solid material from liquid material. They isolated epithelial cells, a type of cell found in the lining of the kidneys that the body sheds all the time. From these, they produced induced pluripotent stem cells, which can become any type of cell in the body. Then, they reprogrammed the stem cells into neurons. This yielded a population of brain cells that could be studied, enabling side-by-side comparisions. Researchers are continuing to watch for variations in neuron viability and activity.

Later, the Sebenolers returned to the lab for brain imaging studies, so researchers can study activity in their entire brains, not just cells in a Petri dish.

The family has participated in studies on autism prevalence in twins, and Kim's son Nicholas, 9, is part of a study examining the younger siblings of children with autism. Nicholas has participated since he was a baby, and is helping researchers study the earliest possible evidence for autism-related symptoms, which may be visible as soon as 2 months of age.

Ultimately, the researchers are trying to diagnose and treat autism as early as possible, aiming to develop treatments and possibly drugs that can halt or even reverse autism-related symptoms.

"Identifying genetic susceptibilities — and how they relate to the development of a human brain, and how genetic liabilities early in development could take a child off track — those are all of very high interest to us," said Constantino, the Blanche F. Ittleson Professor of Psychiatry and Pediatrics and psychiatrist-in-chief at St. Louis Children's Hospital.

He and Bonni say with early diagnosis and a suite of treatment options, doctors may be able to re-route children toward a developmentally typical track — rewiring their neurological trajectories, and eliminating or preventing autism-like behaviors.

The Kroll lab has figured out not only how to create neurons, but also to create neuron types that perform specific functions. These types — cortical excitatory neurons and inhibitory neurons — often are abnormal in patients with autism. This process includes a specific chemical treatment to generate these types of neurons in a Petri dish. In this case, populations of neurons are derived from the cells of the Sebenoler family. From left, Kristen Kroll, PhD, associate professor of developmental biology, and postdoctoral fellow Kesavan Meganathan, PhD.

Rates of autism diagnosis have skyrocketed in recent years, but scientists say this is due to improved diagnostic techniques, not necessarily an increase in people with the disorder.

Autism is highly heritable; a person with an autistic sibling is 20 times more likely than a person in the general population to also develop autism. Among identical twins, like Mark and Jack Sebenoler, if one twin has autism there is a 95 percent likelihood that the other twin will develop autism — evidence that suggests a strong genetic link. Most commonly, autism results from an accumulation of subtle genetic changes.

Female protective effect

With help from the Sebenolers and funding from the National Institutes of Health (NIH), Constantino and Bonni are trying to tease out genetic markers that might offer a protective effect against autism. Earlier, the researchers showed that autism is four times more likely to develop in boys than girls not because autism favors the male sex, but because most girls seem to be relatively protected. Capturing this protective effect — the effect of the extra X chromosome — could be a way to treat or reverse autism symptoms.

"Females carry the same genetic factors, but they don't express them, which is a huge clue. We think that's going on all the time in autism transmission," Constantino said. "If we understood the biology of that, we could harness biology to treat the children who succumb to the genetic liability."

In the Sebenolers, the research team has located a rare genetic mutation that is likely to have a significant role in causing the boys' autism, and is carried (but not expressed) by their mother.

"We wanted to know, is there a way that we could identify, at the level of an individual cell, whether the neuron of a female carrying a mutation is behaving differently than a neuron of a male carrying this mutation?" he said. "If the difference is traceable to a cell, there is a better chance that pharmaceutical targets might be identified."

In one study published last year, Constantino and colleagues at the University of California-San Francisco were unable to isolate a single gene that conferred protection to females. He is still looking, but noted that whatever biological defense is protecting females might not be obvious at the behavioral level. It might be more obvious at a cell- or tissue-based level, which is why the researchers have elected to differentiate populations of neurons derived from the cells of the family members themselves.

Alternatively, that protective effect might play out in a particular pattern of brain activity, which researchers can study using functional magnetic resonance imaging (fMRI). The Sebenolers, and many other patients, are taking part in studies that will look at all these factors.

Bonni said researchers are still trying to understand whether people on the spectrum share common traits. "It will be easier to develop therapies if we identify common mechanisms. On the other hand, assuming there are multiple different mechanisms, we will have to address those, and the approach that we're taking with this family is the way to do it. That's an example of laying the foundations for precision or personalized medicine. We have to consider both approaches as we move forward."

Potential clues?

Autism is four times more likely to develop in boys than girls not because autism favors the male sex, but because most girls seem to be relatively protected. Girls carry the same genetic factors, but don't always express them. Capturing this protective effect could be a way to treat or reverse autism symptoms.

Advancing three frontiers against Autism

The developmental disorder, which today affects one in every 100 Americans, manifests in a multitude of forms, with a wide spectrum of symptoms and disabilities. Because of this, School of Medicine researchers are using three major approaches to understand the disorder's physical and psychological basis. Researchers say there is no single pathway toward treatment.

Brain mapping

Do structural differences play a role?

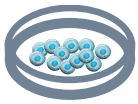
Preliminary evidence suggests there are unique features of early brain structure and function among patients with autism. By comparing brain scans, scientists may be able to find physical evidence of autism and use that data pre-symptomatically to determine which child will develop the disorder.

Behavior

What do children with autism see?

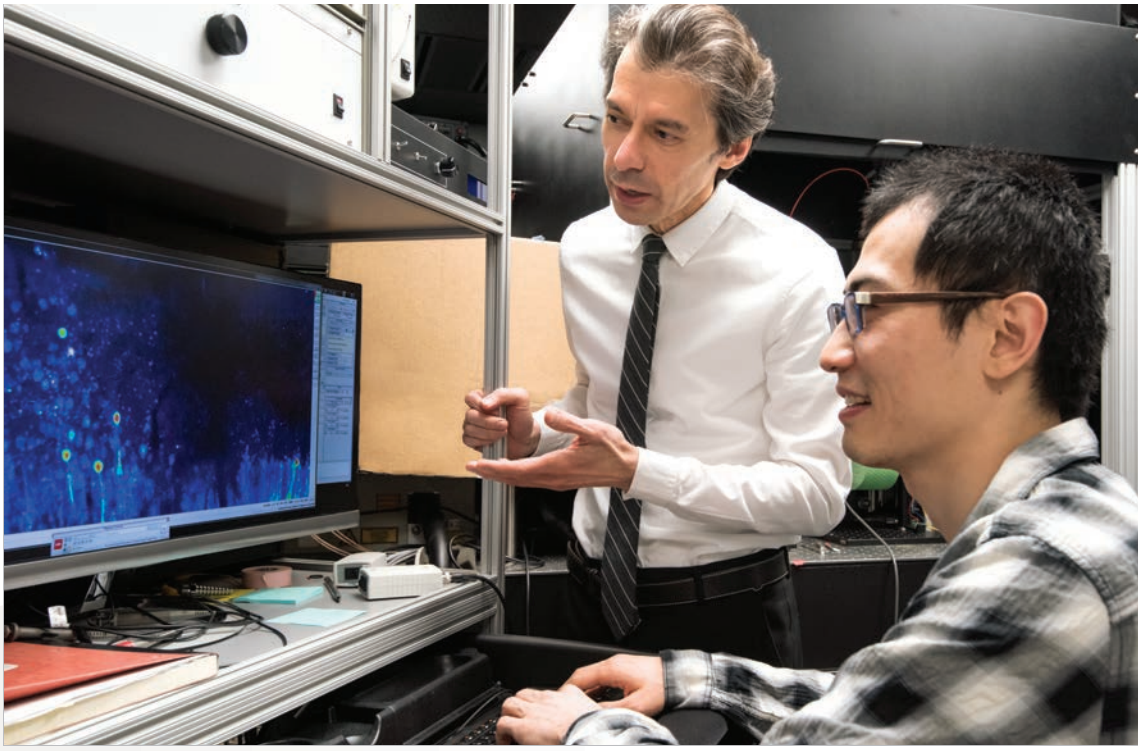
Young children with autism avoid eye contact, and are captivated by inanimate objects. Such tendencies are visible at 2 months of age. Eye-tracking technology may detect these warning signs, and early therapeutic intervention could prevent autism-like behaviors.

Biology



Can autism be traced to a cellular level?

Because autism involves higher orders of thinking, animal models often are insufficient to test theories. And brain cells cannot be safely removed from patients. By taking human urine cells and converting them to neurons, researchers can explore genome-regulated function and development in a Petri dish.



Over the past decade, Azad Bonni, MD, PhD, has contributed insights on how the brain is hardwired, and how neurons take shape and connect to each other. He also is determining how mutations in proteins implicated in autism cause problems. Here, Bonni (standing) confers with staff scientist Yue Yang, PhD.

Scientists have spent decades studying gene mutations that can lead to problems or disorders. Now they are increasingly focusing on genetic and environmental factors that might provide resilience to disorders, said Bradley Schlaggar, MD, PhD, the A. Ernest and Jane G. Stein Professor of Developmental Neurology, head of the Division of Pediatric Neurology, and neurologist-in-chief at St. Louis Children's Hospital.

Schlaggar and Constantino co-direct Washington University's 6-year-old Intellectual and Developmental Disabilities Research Center (IDDRC). This signature research effort seeks to find better prevention and treatment strategies for childhood developmental disabilities, including autism and the neurodevelopmental consequences of preterm birth.

The so-called "resistome" is more difficult to study, Schlaggar said, especially in formal clinical research, because there are so many competing and confounding factors; it's difficult to control for every possible thing that could make someone more or less susceptible to autism.

"The pathway to treat the disease may not come from turning off or on the gene that is a problem, but recapitulating what the organism is doing to provide protection," he said. "It's not gratifying, though. It's a strategy that doesn't really lend itself to the usual scientific methods. It requires a big data approach. All the fundamental parameters of investigation are challenged by this strategy."

Predicting outcomes

Just as genomics-based medicine is enabling personalized treatments, brain imaging is increasingly used not only to observe behavior and diagnose disorders, but to make predictions about a person's possible outcomes.

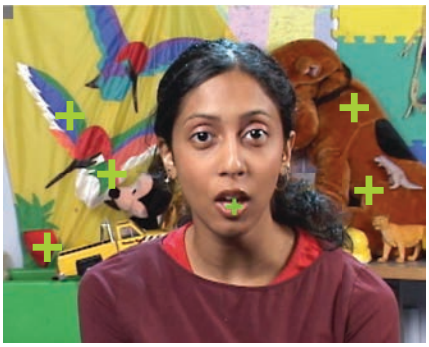
Constantino, Schlaggar and their colleagues are using functional MRI and functional connectivity MRI to study brain architecture and understand how the brain's physical attributes can affect a person's psychological attributes. Schlaggar said studies on the brain's organizational principles may help scientists understand what happens in atypical development.

He said most imaging studies look at the central tendencies of either patients and controls, or adults and children, and focus on the differences between them.

"That's interesting, but it doesn't get at the characteristics of individual patients. What you want to be able to do is use the data to make predictions about people," he said. "We want to use data pre-symptomatically. Can we identify information from imaging that would allow us to predict which child is going on to that diagnosis?"

The research is still in early stages, but preliminary results suggest there are some types of brain activity scientists may be able to use to make predictions, Schlaggar said.

ROBERT BOSTON



PHOTOS COURTESY OF EMORY UNIVERSITY

NORMAL

AUTISM SPECTRUM DISORDER

Eye tracking

The way young children explore the world with their eyes is under strict genetic control. When comparing the viewing habits of kids, patterns emerge. Bottom left, as illustrated by the crosshairs, normally developing children typically focus on people's faces, particularly eyes and mouths. In atypical development, children fixate on inanimate objects. Identifying this lack of social engagement is a useful tool in early diagnosis.

This level of analysis requires sophisticated software to crunch each person's data. Network approaches are becoming increasingly useful tools for brain imaging research, and Schlaggar said he relies on Washington University's multidisciplinary collaborations, such as those enabled by the IDDRC.

"It used to be that you needed supercomputers to do this, but not now. The computational power we have just by linking our desktops here is amazing," he said. "It's been a really cool experience to see how these methods merge, and how they provide the kinds of insights we didn't anticipate we would have access to when we started."

Along with MRI imaging, Constantino is using eye tracking to catch autism-related behavior abnormalities in early development. Lack of eye contact is a distinguishing feature of autism. Several years ago, Constantino's collaborators at Emory University in Atlanta published research demonstrating that infants with autism spend less time focusing on people's eyes and faces, and more time focusing on objects. The eye-tracking differences were traceable to just 2 months of age.

Constantino wanted to look deeper to determine whether this difference was driven by the kind of genetic influences that characterize autism. He launched a study examining identical and non-identical infant twins and found that the way babies explore the world with their eyes is under stringent genetic control. He and his team also observed that some normal infants had as low a level of eye- and mouth-looking as the children with autism in the prior study.

"There has to be some other factor that combines with visual disengagement, to produce the autistic syndrome," he said. "This gives us another opportunity to learn how susceptibilities to autism (like low levels of eye-looking) might be weathered and overcome. These are windows of observation on how various components of early human development collide, interact with or compensate for one another."

Currently, the earliest possible diagnosis for autism is around 1 year old. Intervention programs, including behavior analysis, speech and language instruction, and occupational therapy, typically don't start until age 2. Scientists suspect that very early interventions might improve the chances of redirecting a child's development.

"These three frontiers — gene discovery, brain imaging, and development — all feed each other," Constantino said. "We need to get our arms around as many factors as we can. We are thinking about all possible places where disparate genetic pathways to autism converge."

Kim Sebenoler said she hopes her family can help researchers find those convergences. Along with participating in several studies, her children are in behavioral therapy programs and visit Constantino for psychiatric appointments on a regular basis.

"I like the spin that Dr. Constantino puts on it, which is, 'Let's see how far you can get.' He sees the potential that's in every child — that there's not limitations," she said. "These studies hopefully will end up in good results. So I'm very hopeful."

Sparking Curiosity

Youth outreach program shares the wonder — and career prospects — of science

BY KRISTIN BAIRD RATTINI

As part of a Young Scientist Program field trip to the Medical Campus, middle schoolers held animal brains.

TIM PARKER

TIM PARKER

Teaching Teams from the Young Scientist Program (YSP) lead hands-on demonstrations in area classrooms. Above, Vashon High School students build a Winogradsky column — a soil layer cake — during a presentation on ecology and evolution.

The decibel and excitement levels were considerably higher than usual as students huddled over preserved human hearts during biology class at Vashon High School in St. Louis. A visiting Teaching Team — made up of graduate and medical students from Washington University's Young Scientist Program (YSP) — led the hands-on demonstration.

Vashon biology teacher Samantha Lurie stepped back as the YSP team took charge, explaining how to measure blood pressure, use a stethoscope and identify parts of the heart. The team also showed the hearts of a smoker and nonsmoker, and discussed the related health risks.

"The Teaching Team sparked the students' curiosity," she said. "It was great to see my students asking a lot of questions, and then later bragging about the experience to others."

Participation is the cornerstone of the YSP. For 25 years, the YSP has increased the participation of underrepresented groups in science by bringing resources directly to St. Louis-area public schools.

"When I first came to the School of Medicine, there wasn't much going on in terms of science education outreach to the surrounding community," said James McCarter, MD, PhD, who co-founded the YSP in 1991 during medical school. McCarter now is head of research at Virta Health and an adjunct professor of genetics at the medical school.

"I was struck by the differing demographics between the urban communities we were serving and the people who were doing the research on campus," he said. "I wanted to open the doors of opportunity to a broader group of people."

To kick things off, an inaugural class of two high school students completed on-campus summer internships through the YSP. Now known as "Summer Focus," it is a unique program that annually brings up to 16 outstanding high school students into university research labs for eight-week intensive biomedical internships, and provides a stipend. To honor the YSP's 25th anniversary, McCarter, his wife Rosalie Truong, MD, PhD, and his parents, John and Judith McCarter, made a $100,000 gift commitment to the Summer Focus Program.

The YSP creates "experiments-in-a-bag" available online to K-12 schools.

The YSP since has expanded significantly beyond its flagship summer initiative. Teaching Teams regularly ignite the interests of K-12 students in subjects ranging from robotics to forensics to genetics. And YSP Teaching Kits (experiments-in-a-bag that include instructions and materials) help enable any adult, regardless of background, to lead inquiry-based science experiments with students. Kit topics cover nine subjects — such as DNA extraction and natural selection — to enhance a school's science curriculum, and can be requested through the YSP's website, ysp.wustl.edu.

Additionally, the YSP hosts field trips to the Medical Campus and presents "Family Medical School," a series of annual public workshops at the Saint Louis Science Center. There, children and their parents learn about human anatomy and physiology, as well as diseases and ways to stay healthy. Through these and other efforts, the YSP has connected with more than 10,000 students.

Students leading students

Throughout its growth and evolution, YSP has remained a volunteer-led effort. Graduate and medical students coordinate the program, solicit funding, and generously share their time and talents to cultivate greater diversity in the next generation of scientists.

"The Young Scientist Program played a big part in my decision to attend Washington University," said Reyka Jayasinghe, YSP co-director and a doctoral candidate in molecular genetics and genomics. "Many schools have great research and great faculty. But Washington University was the only school I could find with an opportunity for graduate students to mentor and work directly with students of all ages."

Volunteerism both distinguishes and enriches YSP tremendously. "First, the motivation of our leadership is entirely mission-driven, as opposed to a financial or professional obligation," McCarter said. "Second, it allows for change. The Washington University students come into a leadership role for a year or two and move on. The program continually reinvents itself. Over the past 25 years, I have seen the program improve and iterate with each new generation of student leadership."

Boahemaa Adu-Oppong, a YSP co-director and doctoral candidate in evolution, ecology and population biology, helped launch the newest outreach effort: Continuing Mentoring.

In its 25 years of existence, the YSP has connected with more than 10,000 students, encouraging many to consider STEM (science, technology, engineering, math) careers.

ROBERT BOSTON

ROBERT BOSTON

Mentor Jeffrey Gamble (center), a doctoral candidate in biomedical engineering, interacts with students at Soldan International Studies High School. YSP Continuing Mentor volunteers meet regularly with students during all four years of high school.

Continuing Mentoring provides a steady source of mentorship for science-interested students from Soldan International Studies High School and the Collegiate School of Medicine and Bioscience, a public magnet school.

"There was no curriculum when we started," Adu-Oppong said. "We had to build it from scratch."

In the program, mentoring PhD or MD students meet twice monthly with the local students during all four years of high school and facilitate job shadowing opportunities with STEM (science, technology, engineering and math) professionals. Mentors also assist with ACT preparation, résumé making and the college application process.

For Jeffrey Gamble, a doctoral candidate in biomedical engineering, volunteering as a Continuing Mentor for students at Soldan was an easy decision. "As a young black man from this area, I thought it was important for the students to see someone striving to do his best in a field that traditionally has few black people participating," he said.

Gamble said some of his best mentoring memories are the unscripted ones, when he simply shared his own struggles with students. "I was having problems with my PhD research," he explained. "I was able to show them that things are going to be hard, but you can push through it."

The first cohort that participated for all four years graduated this past May. Out of the dozen Soldan graduates, half are now pursuing STEM fields in college.

Thinking in new ways

An overarching message runs through all of the YSP's efforts: Consider science in the broadest context. "There are a lot of ways you can pursue a scientific career," said Elizabeth Danka, PhD, who volunteered with YSP in several roles during her doctoral studies in molecular cell biology. Danka is now a postdoctoral scholar at the University of North Carolina at Chapel Hill.

"If a student is smart, people tell them, 'You should be a doctor.' Well, maybe. But not everyone is good at interacting with people at their sickest and unhappiest.

"We help students think about the many ways — biomedical sciences, engineering, physics, and so forth — they can use their brain and incorporate their scientific interests and make an impact," she said.

Two years ago, Danka was paired as a Summer Focus mentor with India Bradley, a Cardinal Ritter College Prep High School student, who was interested in science but hadn't chosen a specific focus. "I just knew I wanted to gain hands-on experience that summer," Bradley said. She and her 15 fellow Summer Focus interns spent 40 hours a week, for eight weeks, on the Washington University campus. As part of the internship, Bradley worked alongside Danka, researching *E. coli* strains that cause urinary tract infections.

"Elizabeth was a wonderful role model," Bradley said. "She broke everything down for me in a way I could understand." Before long, Bradley was working independently at the lab bench, preparing protein gels and observing mice infected with *E. coli* strains. "It became my favorite part of my work, to see how the bacteria affected the mice and made them act," she said.

The program also taught Bradley to read scientific literature and write about her work. Summer Focus participants present their research at a concluding forum, which is proudly attended by family members. "It's exciting when people from the community see their children succeed in a world-class environment," said John Russell, PhD, the YSP's faculty adviser and associate dean for graduate education at the School of Medicine.

Bradley earned her first academic publishing credential when her Summer Focus research paper was accepted to the Journal for Emerging Investigators.

"Now that I'm in college, I realize how much YSP has helped and prepared me," said Bradley, who is now a sophomore majoring in biology and pre-medicine at Howard University on a full-tuition scholarship. "My professors were impressed that I was already published and have told me that this makes me more competitive for medical school.

"The Summer Focus writing course put me ahead of my class, in terms of scientific writing. When I started working in the lab at Howard, I already knew the equipment and procedures."

Later, she was invited to a national conference to present her freshman research on bacterial phages. "It was a breeze," she said, "because of my Summer Focus experience."

TIM PARKER

Wearing prism goggles and throwing balls at a target, students learned about visual-motor adaptation. At first, the students missed the target by as much as 10 feet. As their brains adapted to the distorted vision, the students began hitting the mark.

The legacy continues

Bradley is hardly alone among the 300-plus Summer Focus alumni in carrying YSP's lessons with them into their academic and professional careers. In 1995, Bart Bartlett had none other than YSP founder Jim McCarter as his Summer Focus mentor. Two decades later, Bartlett, PhD, an associate professor of chemistry at the University of Michigan, still draws on his formative experiences.

"Even though Summer Focus started out with me doing some simple lab work, Jim made certain I could see the connection between what I was doing and the goals of what the lab was doing," Bartlett explained.

"Now that I have undergraduates working in my lab, I try to emulate that mentorship by providing young people the opportunity to do something with their own hands in the lab, to contribute intellectually and to develop those connections," he said. "What started at Summer Focus continues on."

Resisting Zika

Undeterred, researchers tackle a global crisis from multiple directions

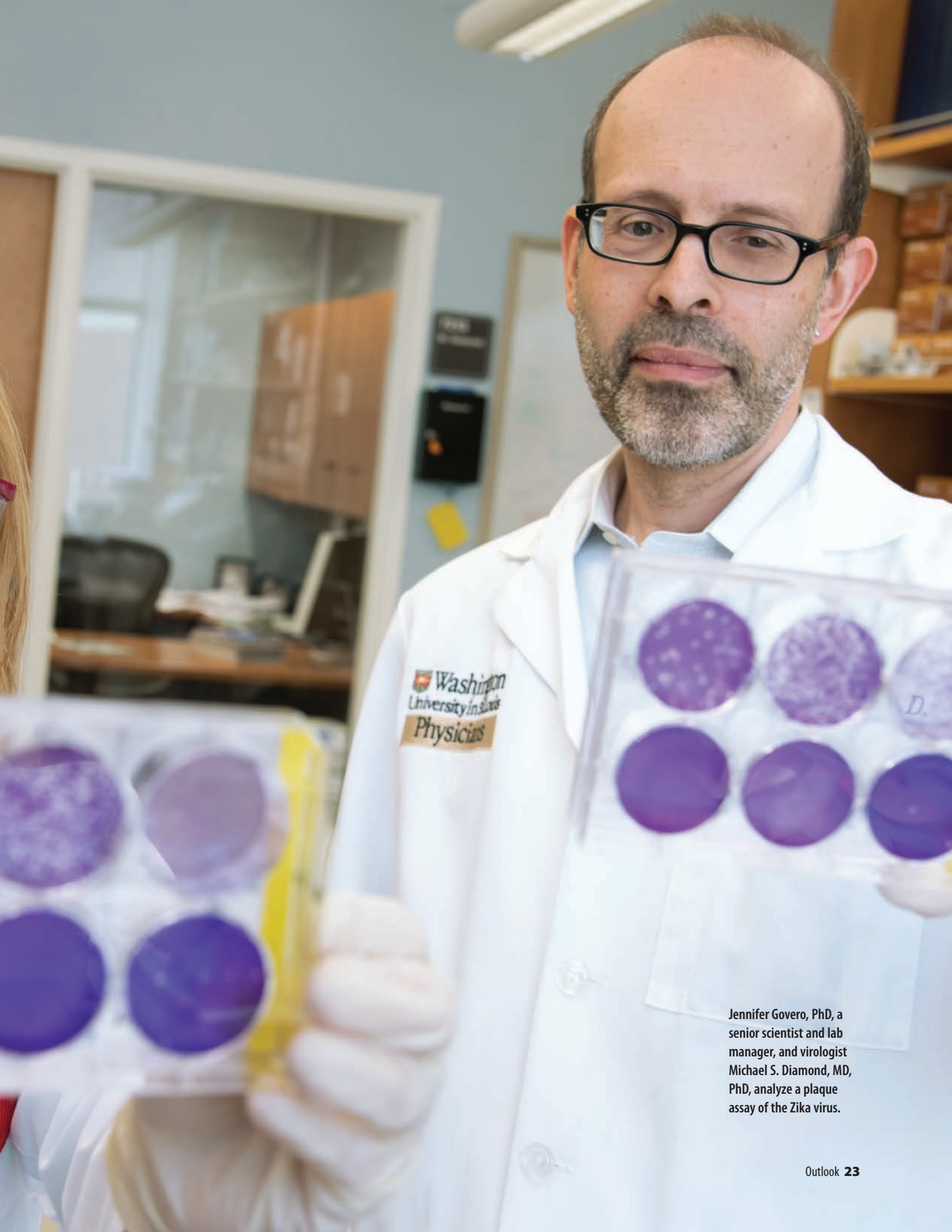
BY TAMARA BHANDARI

Throughout 2015, increasingly worrisome reports trickled out of Brazil about an obscure virus called Zika. A member of the flavivirus family, which includes dengue and West Nile, Zika was a new arrival in the Americas. Identified almost 70 years earlier in Africa, the virus was thought to cause only mild disease. In Brazil, however, it became associated with birth defects and a progressive form of paralysis known as Guillain-Barré syndrome.

As the Zika epidemic took hold, leaders at the National Institutes of Health (NIH) realized they needed to learn about the virus quickly. They started phoning select scientists, and offered funding for Zika research.

One of those researchers, Michael S. Diamond, MD, PhD, the Herbert S. Gasser Professor of Internal Medicine and Infectious Diseases, is known for his studies on flaviviruses. When the NIH called, the virologist already had been working on Zika for six months, collaborating with experts across the School of Medicine — in neurobiology, reproductive biology, structural biology, immunology and other fields — to determine what damage the virus could do and what could be done to stop it.

ROBERT BOSTON



Jennifer Govero, PhD, a senior scientist and lab manager, and virologist Michael S. Diamond, MD, PhD, analyze a plaque assay of the Zika virus.

Less than a year later, the School of Medicine is one of the hotspots of Zika research. Researchers have developed two highly useful mouse models of Zika infection; identified potential drug targets to block the spread of the virus; showed that Zika can persist in the eye and testis; and identified specific anti-Zika antibodies that could be the basis for vaccines, diagnosis or treatment.

These accomplishments are impressive, but not reassuring. The more researchers learn about the virus, the more dangerous it looks.

"Zika hits us where it hurts. It interferes with our ability to have healthy babies. It damages our babies' brains. It persists in people long after the initial infection, so it affects our reproductive options in the future," said Indira Mysorekar, PhD, an associate professor of obstetrics and gynecology, who evaluated a pregnant mouse model of Zika infection. "These are all things that affect our humanity at a very fundamental level."

A chance conversation

It was a chance conversation at an international scientific meeting devoted to another virus that set Diamond on a path to studying Zika.

"The meeting was focused on chikungunya, but at the breaks, people get together and talk about all kinds of things. A colleague from Brazil mentioned that they were seeing unusual cases associated with another RNA virus, called Zika," recalled Diamond. "So when I got back, members of my laboratory started some pilot projects."

"These are all things that affect our humanity at a very fundamental level."

At the time, in June 2015, very little was known about Zika.

"There was a non-human primate experiment done when they isolated the virus in 1947, and one or two other mouse experiments done in the '70s, and that was about it," Diamond said. "It seemed to be associated with Guillain-Barré syndrome and congenital defects, but causality had not been established."

Over the next few months, as the Zika outbreak escalated thousands of miles away, Diamond acquired samples of the viruses, learned how to grow them and, along with Helen Lazear, PhD, now an assistant professor at University of North Carolina, and Jonathan J. Miner, MD, PhD, an instructor in medicine, started injecting them into mice, in the hopes of creating an animal model of Zika infection.

The project hit a bump right away: Unlike humans, the mice were able to resist Zika infection. Diamond, Lazear and Miner learned that they had to knock out or block a part of the animals' immune systems before the virus could gain a foothold.

With this realization, they were able to create a mouse model of Zika infection, showing that the virus multiplied in the brain, spinal cord and testes, and developed a model of in utero transmission of Zika virus to fetuses.

Meanwhile, Diamond teamed up with Mysorekar to evaluate the sequence of events that enable Zika virus to be transmitted during pregnancy.

"We showed that Zika kills placental progenitor cells that are important for maintaining the health of the fetus while it's in utero," Mysorekar said, referring to a kind of cell that is capable of dividing and reproducing into one or more kinds of cells. "It also infects the fetal brain directly. This provides strong evidence that Zika is causing the brain damage we see in human newborns."

The virus seemed to have an affinity, or tropism, for not just placental progenitor cells but other progenitor cells as well. Kevin K. Noguchi, PhD, an assistant professor of psychiatry, thinks that Zika has a tropism for neural progenitor cells, which may explain the neurological damage that occurs when fetuses are infected.

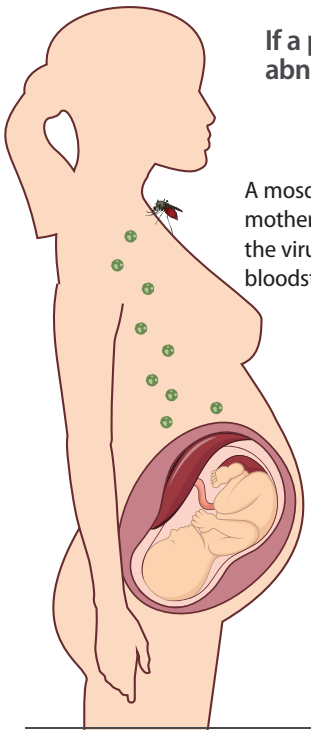
"If you kill off a neuron, you have a net loss of one cell. But if you kill off a neural progenitor cell, you kill off every cell that it would have produced in the future, which can be thousands or even millions of neurons," said Noguchi, who studies the effect of toxic exposures on the fetal brain, and recently began collaborating with Diamond and Miner to study Zika. "You can see how a virus that kills off neural progenitor cells could cause microcephaly."

The kind of damage done by Zika would be difficult — maybe impossible — to treat.

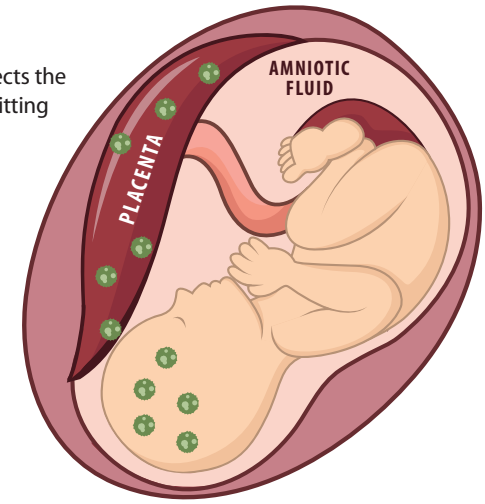
"It's really hard to reverse something that disrupts neurodevelopment because you can't go back and reinitiate that development again," Noguchi said. "Other parts of the brain may be able to compensate for some of the defects, but you can't reverse the brain damage that's already there."

How Zika affects fetal development

If a pregnant woman is infected with Zika, the fetus may develop abnormalities, including one of the most striking results — microcephaly.



A mosquito infects the mother, transmitting the virus to her bloodstream.



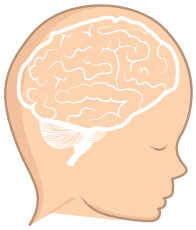
Zika breaches fetal circulation, causing potential placental insufficiency and damaging neurons.

Potential adverse outcomes

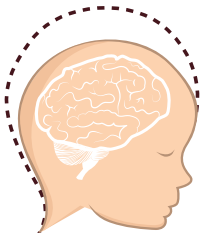
- Microcephaly
- Intrauterine growth restriction
- Ocular abnormalities
- Fetal death

Other long-term effects are unknown.

Typical head size



Microcephaly



Dodging a bullet

The Centers for Disease Control and Prevention estimates that lifetime costs to care for one child with severe microcephaly could total $10 million, not to mention the emotional toll on families. The risks in Central/South America and in the Caribbean are particularly high: infections in women who are pregnant or become pregnant in the near future, or in male sex partners, potentially could result in severe birth defects. Despite this very large global health problem, the overall risk in the U.S. is much lower. Even in Florida's Miami-Dade County, the heart of the U.S. epidemic, fewer than 1 out of every 20,000 people has contracted the disease locally.

"It hasn't had much impact in the continental U.S. compared to developing countries, and I don't expect it to," said Steven Lawrence, MD, an infectious disease specialist and associate professor of medicine. "The most problematic mosquito vector — *Aedes aegypti* — isn't found frequently anywhere in the U.S. other than along the Gulf Coast and in parts of the Southwest. We have relatively few people living without window screens or access to bug spray, so there just aren't as many opportunities for people to come in contact with infected mosquitoes."

The same cannot be said of tropical, developing countries such as Haiti. Only a few dozen cases of Zika in pregnant women have been reported in Haiti, but experts agree that the number vastly underestimates the problem. The Dominican Republic, which shares an island with Haiti and has better public health surveillance, has reported more than 1,000 cases in pregnant women.

"The WHO-approved test for Zika is based on amplifying the RNA from a blood sample, and very few clinical labs in Haiti are set up to do that," said Sarah Brown Riley, PhD, an assistant professor of pediatrics and of pathology and immunology. "It's not that the virus isn't there; it's just that we can't detect it."

Brown Riley, who travels to Haiti four times a year, is part of a team of Haitian and American medical professionals, public health experts and scientists designing a strategy to identify possible cases of Zika throughout the country.

"Right now, I am trying to figure out whether we can diagnose Zika from dried blood spots," Brown Riley said. "Then we could just take a drop of blood, dry it onto a card, and then send it by motorcycle, without refrigeration, from anywhere in the country to one of the government labs that is set up to do Zika testing."

The Haitian government is focusing on low-tech prevention measures, encouraging residents to eliminate potential breeding grounds for mosquitoes by draining standing water near their homes.

Local governments in the parts of the U.S. with *Aedes aegypti* mosquitoes are exhorting their

ROBERT BOSTON

Kelle H. Moley, MD, Andrea Drury, research technician, and Prabagaran Esakky, PhD, the study's first author and instructor in obstetrics and gynecology, meet to discuss the latest Zika findings.

PRABAGARAN ESAKKY

The testicles of male mice showed cellular damage and shrinkage three weeks after Zika infection. On the left is a healthy mouse testicle; on the right, a testicle following Zika infection.

Zika reduces fertility in male mice

Studies needed to determine whether men are similarly affected

Most Zika research focuses on how the virus affects pregnant women and causes severe birth defects.

A study in mice indicates that the virus also targets the male reproductive system, suggesting that Zika may have consequences for men. The study was published last October in Nature.

"While our study was in mice – and with the caveat that we don't yet know whether Zika has the same effect in men – it does suggest that men might face low testosterone levels and low sperm counts after Zika infection, affecting their fertility," said Michael Diamond, MD, PhD, a co-senior author on the study and the Herbert S. Gasser Professor of Medicine.

To find out how the Zika virus affects males, Diamond, co-senior author Kelle H. Moley, MD, the James P. Crane Professor of Obstetrics and Gynecology, and colleagues injected male mice with the Zika virus.

After one week, the virus had migrated to the testes, which bore microscopic signs of inflammation. In three weeks, their testicles had shrunk to one-tenth of their normal size and the internal structure was completely destroyed. Sex hormone levels had dropped and fertility was reduced. These mice were less likely to impregnate female mice.

The mice were monitored until six weeks, and in that time their testicles did not heal, even after the mice had cleared the virus from their bloodstreams.

"We don't know for certain if the damage is irreversible, but I expect so, because the cells that hold the internal structure in place have been infected and destroyed," Diamond said.

"This is the only virus I know of that causes such severe symptoms of infertility," said Moley, a fertility specialist and director of the university's Center for Reproductive Health Sciences.

Diamond and Moley said human studies in areas with high rates of Zika infection are needed to determine the impact of the virus on men's reproductive health.

residents to do the same, and in addition, some also are spraying insecticides. But the best hope for a permanent solution is a vaccine.

Daved H. Fremont, PhD, a professor of pathology and immunology, has been working on developing a Zika vaccine. A vaccine made from a live but weakened virus would be relatively simple to create, but it could not be used in pregnant women because the virus, although weakened, could still be strong enough to infect the fetus and cause disease.

Earlier this year, Fremont identified a portion of a Zika protein that elicits a strong, protective antibody response. He plans to collaborate with a primate research facility in Oregon to test whether the engineered vaccines protect non-human primates against Zika infection.

Diamond, in collaboration with Fremont, Mysorekar and researchers at Vanderbilt University, recently has shown that human antibodies can protect developing fetuses from Zika infection and adults from Zika disease, at least in mice. The discovery suggests that treating pregnant women with anti-Zika antibodies may prevent the worst outcomes — microcephaly and other birth defects — and that a vaccine eliciting similar antibodies could do the same.

Where next?

Despite the enormous progress made by the ever-growing community of Zika researchers, there is much work left to be done, including:

- **Determining whether Zika can cause brain damage in children and adults.** Neural progenitor cells, which are abundant in fetuses, are still present, although at much lower numbers, after birth. Robyn S. Klein, MD, PhD, a professor of infectious diseases and neuroscience, studies the impact of the virus on neurodevelopment, with an emphasis on learning and memory.

- **Identifying other routes of transmission.** Haina Shin, PhD, an assistant professor of medicine, is studying protective immunity against sexually transmitted Zika, as well as risk factors that may make women more susceptible to this form of transmission. Mysorekar, an associate director of the Center for Reproductive Health Sciences, is researching how the virus crosses the placental barrier, which separates maternal and fetal bodily fluids. Rajendra S. Apte, MD, PhD, the Paul A. Cibis Distinguished Professor of Ophthalmology and Visual Science, co-led a team (with Diamond and Miner) that characterized Zika in the eye and demonstrated presence of virus in tears. He is now studying whether corneal transplants could transmit the virus. This is the most common transplantation surgery in the U.S., with about 40,000 performed yearly.

- **Determining the effect of Zika virus on fertility.** See story, previous page.

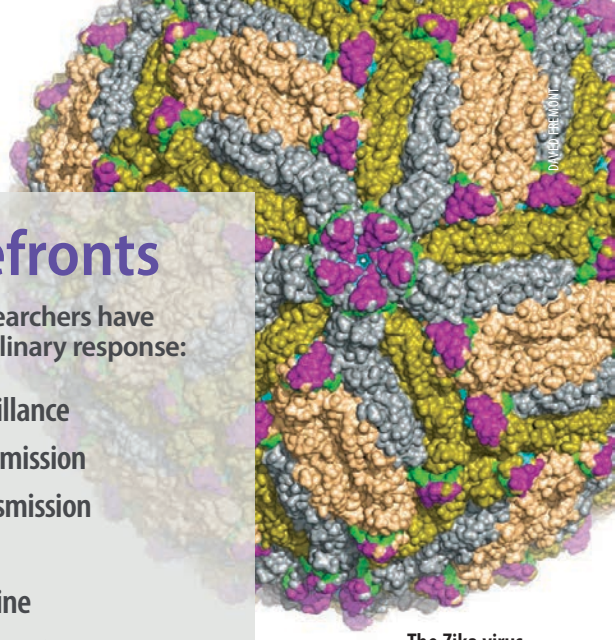
The list of unanswered questions is daunting, but Diamond is undeterred. The lesson of Zika is not that epidemics can spring up out of nowhere, although that is true, he said. The true lesson is that the scientific community has shown itself to be up to the task of responding to such epidemics.

"While it was true that few were studying Zika before last year, it's not true that we weren't prepared for this outbreak. Within a very short period of time we've generated vaccine candidates, therapeutic candidates, and animal models both in mice and non-human primates," Diamond said. "It shows that by studying basic properties of pathogens, whether it is bacteria, viruses, or otherwise, we'll learn enough so that if something does happen, we'll be prepared, poised and nimble enough to move into the field very quickly to make significant progress. And that's what's been done in Zika."

Zika battlefronts

School of Medicine researchers have mounted a cross-disciplinary response:

- Diagnosis and surveillance
- Maternal-fetal transmission
- Other routes of transmission
- Animal models
- Reproductive medicine
- Fetal brain development
- Neurological effects on adults
- Ocular health
- Vaccine, drug development



The Zika virus

ROBERT BOSTON

New endowed professors in basic science, from left, Linda J. Pike, PhD, Phyllis I. Hanson, MD, PhD, and Tamara L. Doering, MD, PhD.

Key drivers

BY HILARY DAVIDSON

Investments in basic science fundamental to biomedical discovery

School of Medicine investigators are harnessing new technologies to create precision and personalized approaches to diseases — advances that could not occur without prior investments in basic research.

"Basic research is a key driver of biomedical discovery and an essential part of the robust research environment at the School of Medicine," said David H. Perlmutter, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

"Our university boasts a uniquely collaborative culture in which basic, clinical and translational scientists work together to explore some of the world's most challenging medical problems," he said.

In keeping with the medical school's commitment to basic research, three outstanding women scientists recently were awarded endowed professorships. The funding will enable them to initiate promising research projects, while teaching the next generation of scientists and medical professionals. "Endowed professorships reward and honor those who do extraordinary work," Perlmutter said.

The new endowed professors are:

Linda J. Pike, PhD, the Alumni Endowed Professor of Biochemistry and Molecular Biophysics

Phyllis I. Hanson, MD, PhD, the Gerty T. Cori Professor in the Department of Cell Biology and Physiology

Tamara L. Doering, MD, PhD, the Alumni Endowed Professor of Molecular Microbiology

The three awardees share a common passion for solving complex biological puzzles and are strong advocates for basic research.

"Essentially all of the progress made in the past 50 years in identifying new drugs has been a result of basic science research," Pike said.

"In my own field of cancer research, in the last 30 years I have seen medicine go from having absolutely no understanding of what drives cancer to now having dozens of drugs that specifically target the many different proteins that drive cancers," she added. "None of this would have been possible without the work of basic scientists."

Improving cancer outcomes

Pike is studying how cell-surface receptors in the tyrosine kinase family stimulate cell proliferation, a process that can result in breast, lung and other types of cancers. Tyrosine kinase-inhibiting drugs, which resulted from this type of work, are used by oncologists worldwide, and dramatically have improved outcomes for cancer patients. The insights provided by Pike's work also may lead to additional targeted therapies.

Hanson agrees. "Most, if not all, diseases and disorders originate in problems or defects at the cellular and molecular level," she said. "Understanding how cells and the molecules within them normally work is critical to understanding how diseases arise and how to treat these diseases."

Like Pike, Hanson focuses on cellular function, investigating how other proteins interact to regulate the structure and organization of cell membranes both inside and outside the cell.

Her work has clinical applications in cancer, neurodegenerative disease, including Alzheimer's disease, and the debilitating movement disorder dystonia. Hanson is a member of the Hope Center for Neurological Disorders, and collaborates with scientists in neurology and ophthalmology.

Halting deadly infections

While Doering shares her colleagues' fascination with the microscopic, her work focuses on one significant pathogen. She has devoted almost 20 years to studying the pathogenic yeast *Cryptococcus neoformans*. This microbe causes fungal meningitis, which has a devastating effect on immunocompromised individuals worldwide, and also causes disease in immunocompetent people. Doering is investigating a feature unique to the organism: its polysaccharide capsule, which plays a key role in the infection process. She has conducted biochemical and genetic studies to identify the cellular machinery involved in producing the capsule. Her work could lead to new medications to combat the deadly fungus, which are greatly needed, especially in resource-limited settings.

Women in leadership

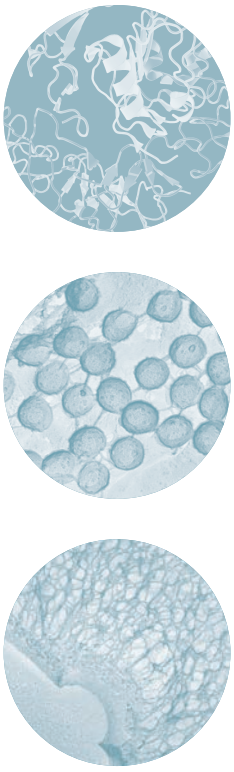
The women acknowledge that it is a great honor to be named endowed professors.

Hanson said she is thrilled and humbled to hold the professorship honoring the late Gerty T. Cori, a Washington University faculty member who, with husband and fellow faculty Carl Cori, also deceased, won the 1947 Nobel Prize for Physiology or Medicine for their work on cellular metabolism. "Gerty Cori exemplifies how a single-minded commitment to understanding a specific mechanism or set of mechanisms can have an extremely broad impact," she said. "Carl and Gerty Cori's accomplishments led to many applications downstream."

The presence of women in leadership positions sends a strong message to talented young women considering science careers, said Pike and Doering.

"It is really important for young women to see that women who do good science are rewarded in the same way that men are," said Pike, who co-founded the Academic Women's Network (AWN) at the School of Medicine.

"Such awards are important not only for career development of the scientist, but also for raising the visibility of women researchers, which, in turn, helps provide role models for women trainees," Doering added.



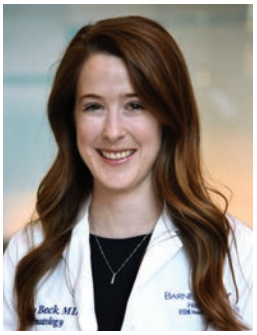
The three researchers focus on: (top to bottom) protein receptors, cell membrane pathways and pathogenic fungi.


ROBERT BOSTON

Generations

BY HILARY DAVIDSON

Deep appreciation for medical school spurs alumni support across decades



Robert Parsons, MD '54, began his career as a plastic surgeon over a half century ago. He is one of the medical school's longest continuous donors and has given annually for 61 years.

Emily Beck, MD '13, a fourth-year dermatology resident, is the new chair of the Annual Fund, which is supported by unrestricted gifts from alumni and former house staff. This fund benefits scholarships, educational initiatives and community outreach, among other activities.

Both view philanthropy as a way to ensure that Washington University remains at the forefront of medical education and research for years to come.

Beck and Parsons recently spoke about their dedication to Washington University, and how all gifts, large and small, make a difference.


WASHINGTON UNIVERSITY PHOTOGRAPHIC SERVICES


JERRY NAUNHEIM


ROBERT BOSTON

Why did you decide to support Washington University so soon after medical school?

Parsons
I've always felt it was my responsibility to give back to the school that provided my training. Even though we couldn't give a lot of money in 1957, my wife and I wanted to support the school that prepared me for my career. I was very lucky to get accepted into Washington University.

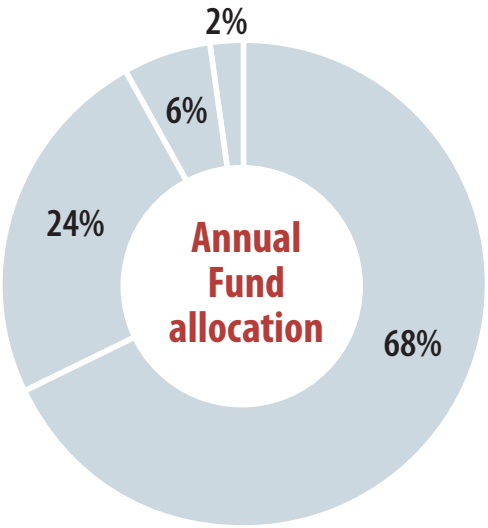
Beck
I feel strongly tied to the School of Medicine and am grateful for the opportunities I received, which motivated me to find ways to get involved and help support the school.

I was interested in chairing the Annual Fund because it provides so many opportunities to students, faculty and house staff. As a student, I realized that supporting it is one way to help our school remain one of the best medical schools in the country and help it continue to grow.

Have you directly experienced how philanthropy helps students?

Parsons
Alumni support makes an enormous difference in students' ability to finance their educations. I've been working with medical students for years, and the debt load is overwhelming for them. I was fortunate that it didn't cost as much when I went to medical school.

That's why, in addition to giving every year, I created the Robert W. and Elise Hampton Parsons Scholarship.



Annual Fund gifts support wide-ranging educational and service initiatives, including scholarships; simulation centers; the Saturday Neighborhood Health Clinic, providing health care to the uninsured; the Young Scientist Program, teaching hands-on science investigation to area youth; the Forum for International Health and Tropical Medicine (FIHTM), offering study abroad opportunities; and the Geriatrics Outreach Group, hosting intergenerational events and dialogue.

Scholarships: 68%

Student groups, educational initiatives and community outreach: 24%

Other student activities: 6%

Academic and honor societies: 2%


ROBERT BOSTON


JERRY NAUNHEIM

In 2013, Congress voted that you could make a one-time gift out of your IRA without tax consequences. I had made arrangements in my will for the scholarship, but I thought it could help more students if I did it now. That law has since become permanent.

I'm so glad I did. I met a couple of the scholarship students at the Scholarship Dinner last year. I was very impressed. I don't know if I could get into medical school nowadays!

Beck
Many of my friends received scholarships like the one Dr. Parsons created, and said that scholarship support made the difference between coming to Washington University and going somewhere else. Through Annual Fund support, others went on international trips where they learned about medicine in different environments, and lots of us received our first clinical experiences at the Saturday Neighborhood Health Clinic.

I don't think people realize how necessary philanthropy is to maintaining the caliber of this school. For one thing, it supports the amazing faculty here in teaching and research.

Tuition alone doesn't cover the cost of training the next generation of physicians and scientists. It's up to us to do that.

What would you say to alumni who cannot afford to make large contributions?

Parsons
Every contribution counts, whether it's a little bit or a lot. Many of us feel an obligation to those who have educated us, and alumni gifts support an outstanding medical education for students, residents and fellows.

Beck
As Annual Fund chair, one of my goals is to communicate how important it is to give. Young alumni especially need to know that small donations make a huge difference.

For example, last year the number of donations that were less than $100 actually added up to $1.8 million. So, smaller donations really add up to make a huge contribution.

Even young professionals not yet well-established in their careers can make a big impact with their gifts. Stable support of small amounts over time, like those from Dr. Parsons, not only demonstrates a commitment to the school, it provides meaningful resources to current students.

Loyalty Society

JOIN US TODAY!

The Washington University Loyalty Society was created to celebrate those who, like Parsons and Beck, have committed to Washington University School of Medicine and its mission of teaching, patient care and research. The society is open to students, alumni, residents and fellows who give consecutively for at least two fiscal years. Donors are automatically inducted and remain members each year a contribution is made. Membership benefits include gifts of appreciation, recognition in the annual Honor Roll of Donors, and invitations to special events.

For more information, contact Medical Alumni and Development at **314-935-9691** or **meddev@wustl.edu**.

classnotes

Find your friends.

Classnotes are organized first by year of degree/training completion and then in alphabetical order.

How about you?

Share your news via the online form at wumcnews.org/classnotes. Submissions will be printed in a subsequent issue of Outlook magazine as space allows. Photos are welcome.

1950s

William "Bill" A. Reynolds, MD 56, was awarded the Centennial Legacy Award from the Montana chapter of the American College of Physicians in 2015, and continues to serve on the Board of Directors for Intermountain Children's Home in Helena, Mont.

Akie Ruth Oshiro, NU 57, is still employed at age 81 by the Los Angeles Unified School District, checking middle school students' vision. She enjoys working with the students and other retired nurses. She is delighted to report that her granddaughter plans to go into nursing.

Shirley Martin, GN 58, reports that, after a long and successful career as a dean at several institutions, including Florida State University, Indiana State University and the University of Missouri-St. Louis, she is enjoying retirement.

1960s

Mordecai P. Blaustein, MD 61, served as an associate editor of the American Journal of Physiology — Heart and Circulatory Physiology and was elected as a fellow of the American Physiological Society in 2015.

Elissa Brown, NU 69, is a psychiatric/mental health clinical nurse specialist, and retired from the VA Greater Los Angeles Healthcare System two years ago. She is still very involved in nursing activities, serving on boards and committees for the American Nurses Association (ANA), the ANA-California, the National Association of Clinical Nurse Specialists, the California Association of Clinical Nurse Specialists, and the Ethics of Caring collaboration.

1970s

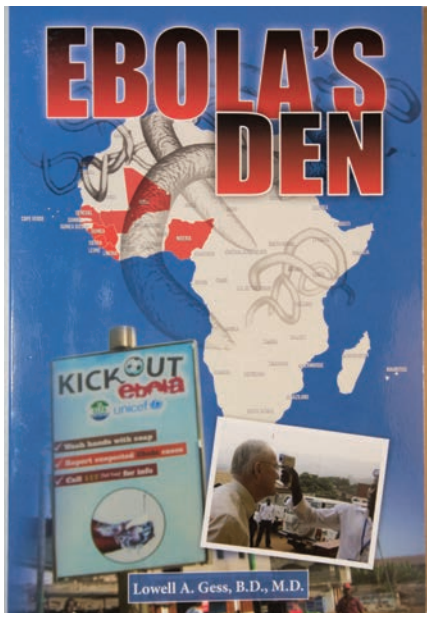
Ted Harrison, MD 75, has opened a practice in the new specialty of regenerative medicine in Port Angeles, Wash. His book, "Regenerative Medicine," was published in spring 2015.

1980s

Irwin Feuerstein, MD 82, began a new position as medical officer with the Office of Research on Women's Health at the National Institutes of Health (NIH) in Bethesda, Md.

Frontlines

When ophthalmologist Lowell Gess, MD '51, flew to Freetown, Sierra Leone, in January 2015, he knew he was entering a "lion's den." Just five months earlier, an Ebola epidemic had broken out, causing the World Health Organization to declare a state of emergency in West Africa. Conditioned to risk by his 50-plus years as a medical missionary, Gess brought $60,000 worth of donated medical supplies and monetary donations from his church. His latest book, "Ebola's Den," recounts his experiences. Gess has been volunteering in Africa for decades and in the 1980s helped found the Kissy UMC Eye Hospital in Freetown. "Ebola's Den" is his fourth book.



classnotes

Richard W. Gross, HS 82, received the Solomon A. Berson Medical Alumni Achievement Award in Basic Science from the New York University (NYU) School of Medicine in April 2016. It is awarded to a NYU School of Medicine graduate who has distinguished himself or herself by major accomplishments in fundamental scientific research.

Walter Peters, MD 82, was named chief of the Division of Colon and Rectal Surgery at Baylor University Medical Center in Dallas.

Alison Whelan, MD 86, was named the new chief medical education officer of the American Association of Medical Colleges (AAMC) following a nationwide search. She will lead initiatives to transform the current models of education and workforce preparation across the full continuum of medical education. She also will lead AAMC efforts that support medical education officers, regional campuses, education researchers, students and residents. Whelan served previously as associate dean for medical student education at WUSM.

1990s

Jeffrey Dale Grills, MD 90, was named vice president of medical affairs for Freeman Health System in Joplin, Mo.

Stephanie Bullard Lancaster, OT 91, is an assistant professor in the Department of Occupational Therapy at the University of Tennessee Health Science Center in Memphis. Lancaster lives with her husband and two daughters in Collierville, Tenn.

Marc Bernstein, MD 92, is serving as the 2016-2017 president of the Executive Council of the Washington University Medical Center Alumni Association.

2000s

Yi Wang, MD 13, recently completed a year abroad in Lesotho (Southern Africa) working at the Center of Excellence for HIV care and Queen Mamohato Memorial Hospital.

Teaming up

Alumni Lee M. Krug, MD '94, left, and Chris Boerner, LA '93, made a stop at Brookings Hall in September before continuing their cross-country ride to raise money for cancer research. The ride extended from the Oregon Coast to New Jersey. All participants in the annual Coast 2 Coast 4 Cancer Ride are cancer researchers with Bristol-Myers Squibb. Krug is Immuno-oncology Disease Head for Thoracic and GI Malignancies, and Boerner is president and head of U.S. commercial business. Both are based in New Jersey.

Small world

From left, Jennifer Gould, MD '97, HS '98, HS '02, John Stoffel, MD '97, and Rekha Rao, MD '97, got a great surprise when they ran into one another on a Mediterranean cruise. The three members of the Class of '97 planned vacations separately and found each other on the second day of their cruise. They are set to celebrate again, this time with all of their classmates, at their 20th Medical School Reunion April 27-30, 2017.

Pioneer Jessie Ternberg dies at 92

The first female surgical resident at Barnes Hospital, Ternberg served for decades at the School of Medicine and St. Louis Children's Hospital

Jessie L. Ternberg, PhD, MD

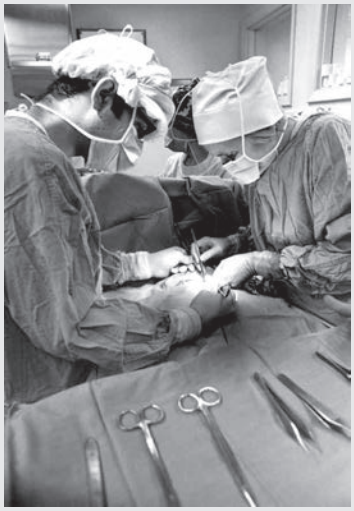
In 1954, when Jessie L. Ternberg, PhD, MD, became the first female surgical resident at Barnes Hospital in St. Louis, her male peers did not extend a warm welcome. Ternberg forged on, paving the way for women in medicine, and serving on the School of Medicine faculty for 37 years.

A professor emerita of surgery and of surgery in pediatrics, Ternberg died July 9, 2016, of natural causes while vacationing in Zermatt, Switzerland, one of her favorite places, according to longtime friend Mabel Purkerson, MD, also a School of Medicine professor emerita. Ternberg, of Creve Coeur, Missouri, was 92.

Ternberg earned a bachelor's degree from Grinnell College in 1946 and a doctorate in biochemistry from the University of Texas at Austin in 1950. There, she and Robert Eakin, PhD, reported their discovery of the mechanism by which Vitamin B-12 is absorbed in the intestine, helping to establish a cure for pernicious anemia. In 1953, she graduated from Washington University School of Medicine.

During an internship at Boston City Hospital, Ternberg decided she wanted to be a surgeon. When she couldn't find a surgical residency program that would consider a female applicant, she wrote to Carl Moyer, MD, the head of surgery at Washington University. "I told him I thought it was a bum rap they wouldn't take women," Ternberg once said. "He agreed — and he accepted me."

There were still many obstacles to overcome. "She had to be twice as good and twice as smart as everybody else to survive, and she was," said longtime friend Timothy J. Eberlein, MD, the Bixby Professor of Surgery and head of the Department of Surgery and director of Siteman Cancer Center. "She had a fierce determination, and that's probably how she overcame all those obstacles over the years. She was like that to the end."



Ternberg (right) in surgery.

In 1959, she became an instructor in surgery. Promoted to professor in 1971, she helped establish the Division of Pediatric Surgery and was named its director in 1972. She became the first woman to be elected head of the medical school's faculty council.

Ternberg routinely performed more than 500 operations a year, and led a surgical team in successfully separating two sets of conjoined twins, connected at the pelvis, a very rare condition.

In 1993, former pediatric surgical residents and colleagues established the Jessie L. Ternberg Award, to be given annually to a female medical graduate exemplifying Ternberg's "indomitable spirit of determination, perseverance and dedication to her patients."

In 2000, Ternberg was named a fellow of the American Association for the Advancement of Science. Her book, "A Handbook for Pediatric Surgery," became known as the bible of pediatric surgery and made her name familiar to a generation of pediatric surgeons.

In 2009, friends and admirers funded the Jessie L. Ternberg, MD, PhD, Distinguished Professorship in Pediatric Surgery. Ternberg is survived by a multitude of friends, and by her nieces and nephews.

In Memoriam

1940s

Rita J. Hustava, NU 47; April '16
Lindsay J. Kirkham Jr., MD 46; Aug. '16
Charles R. Park, GM, HS 49; May '16
Arthur Schmidt Jr., MD 46; Aug. '16
Gerry A. Smyth, MD 47; May '16
S. Ernest Torigoe, DE 44; Feb. '16
Glenn Turner, MD 42; Aug. '16

1950s

Richard H. Fallon, HS 57, GR 74; June '16
Ashby Grantham, LA 52, MD 55; Sept. '16
Adolphe Kiczales, HS; Aug. '16
James Nelson, HS; Sept. '16
Richard Royer, HS 51; Aug. '16
Robert Rubin, LA 50, MD 54; Jan. '16
Roger Schuessler, MD 55; July '16
Anwar A. Shah, HS 57; April '16
Marcia L. Shouse, NU 54; Jan. '16
Ljubinka "Lili" Vojcanin, NU 50; March '14
Patricia Waterfield, PT 56; Sept. '16
Joseph R. Williamson, MD 58; June '16

1960s

Alan L. Brodsky, MD 67; Sept. '16
Robin Lowy, NU 69, LA 69; May '16
David Sirota, MD 60; April '16
John C. Soucy Jr., HS 63; May '16
Jerrold Vesper, DE 65; Aug. '16
Newton B. White, HS 66; April '16

1970s

Thomas Black Jr., GB 75, DE 75; Aug. '16
Wendy Eider, MD 76; March '16
Christopher Maret, MD 79; June '16
Julian Mosley, MD 72; Sept. '16
Susan Nelson, MD 78; May '16
M.S. Rao, HS 71; May '16
Joseph Swope, HS; June '16

1980s

Kevin Kowaleski, MD 80; Sept. '16

For full obituaries, visit:
wumcnews.org/obits

Advancing Health, *Transforming Lives*

Great news! The law allowing tax-free charitable IRA gifts is now permanent. If you are age 70½ or older, you can reduce your taxable income by making tax-free gifts up to $100,000 each calendar year directly from your IRA to Washington University School of Medicine. Best of all, your gift will be used as you wish to support scholarships, professorships, research or another purpose you choose!

Make a tax-free charitable IRA gift and:

- Reduce your taxable income
- Satisfy your required minimum distribution
- Support the School of Medicine

To qualify:

- You must be 70½ years of age or older when the distribution is made.
- The transfer must go directly from your IRA to Washington University.
- Your gift must be outright. Tax-free charitable IRA gifts cannot be used to fund a gift annuity, charitable trust, donor-advised fund or private foundation.

To learn more or notify us of your gift, contact Medical Alumni and Development at **314-935-9691 or meddev@wustl.edu.**

For help in planning a gift in your estate, contact Planned Giving at **800-835-3503 or plannedgiving@wustl.edu.**

Consult with your legal or tax adviser before making a charitable gift.

LEADING *Together*

The Campaign for Washington University

ROBERT BOSTON

Prized collection

Cori medals on permanent display

See video at outlook.wustl.edu

The two Nobel Prize medals awarded to Carl and Gerty Cori in 1947 for their work on sugar metabolism are on permanent display at the Center for the History of Medicine in Becker Medical Library. Their son, Thomas Cori, PhD, donated the medals to the School of Medicine. Carl Cori and Gerty Radnitz met in 1914 as first-year medical students at the University of Prague, married in 1920, and immigrated to the U.S. In 1931, Washington University offered Carl and Gerty positions, but the offers weren't equal. Carl was named head of the Department of Pharmacology, and Gerty became a research associate, reportedly at one-tenth of Carl's salary. Fifteen years later, Gerty finally was promoted to professor. She became the first American woman to win the Nobel Prize in physiology or medicine. Remarkably, six people who trained in the Cori lab went on to win Nobel Prizes.

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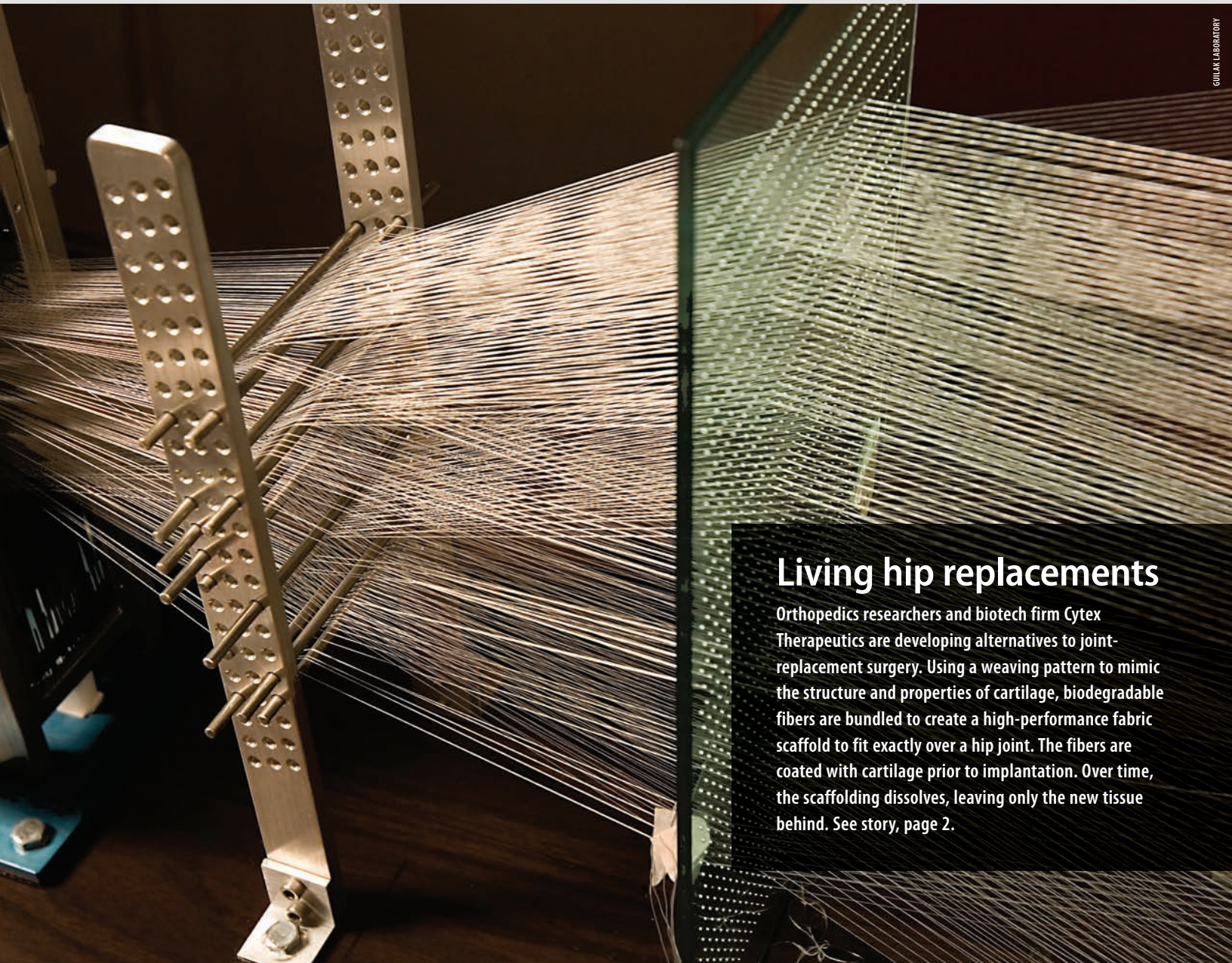

GUILAK LABORATORY

Living hip replacements

Orthopedics researchers and biotech firm Cytex Therapeutics are developing alternatives to joint-replacement surgery. Using a weaving pattern to mimic the structure and properties of cartilage, biodegradable fibers are bundled to create a high-performance fabric scaffold to fit exactly over a hip joint. The fibers are coated with cartilage prior to implantation. Over time, the scaffolding dissolves, leaving only the new tissue behind. See story, page 2.