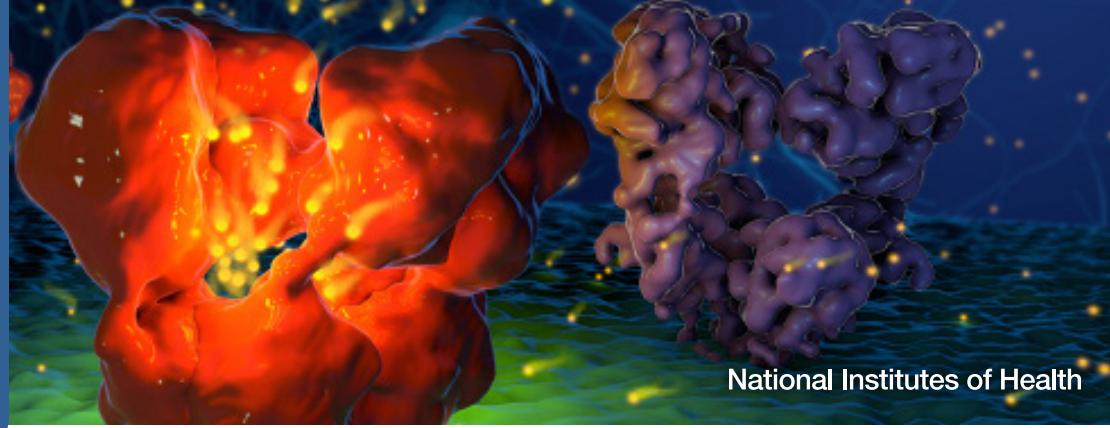


April 5, 2019
Vol. LXXI, No. 7



EVERY BREATH YOU TAKE Exposome Tells Where You've Been, and When

BY CARLA GARNETT

Every day, you encounter dozens of largely invisible microorganisms that are just hanging out in the atmosphere. You breathe them in. Your skin absorbs them. Most are harmless or exist in amounts so small they're unlikely to hurt you. Some could make you sick. Imagine that there's a way to identify and measure every substance you're exposed to on a daily basis. That's what visiting NIH Stadtman investigator Dr. Chao Jiang and his colleagues did a few years ago; they devised a method to capture and map



an individual's "exposome"—a person's total environmental exposures.

"Human health can be basically viewed as an interplaying product of genetics, lifestyle and environmental exposures," Jiang explained in "Exposing the Human Exposome," an NHGRI Faculty Search Seminar held recently in Bldg. 49. "Decades of research we have so far has given us a lot of information on genetics, genomics...[and even insights on aspects of lifestyle, such as stress and diet]. However, comparatively speaking, we know very little about environmental exposures...the exposome is not well understood and poorly studied...so we wanted to know, could we track and quantify personal environmental exposures?"

Studies of what's blowing in the wind have been conducted before, of course, especially in regions known to harbor harmful toxins—Ground Zero in NYC after 9/11

SEE EXPOSOME, PAGE 6



Safety upgrades set for popular byway. See p. 12.

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NIH Marks 9th Rare Disease Day in New Locale

BY RICH McMANUS



If you ever find yourself questioning your vocation as an NIH employee, take in a Rare Disease Day celebration. Like a good Willie Nelson song, NIH's 9th observance of RDD (it has been marked internationally for 12 years) on Feb. 28 was a mixture of

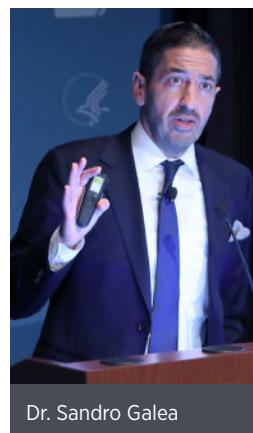
teardrops and laughter as the research community, the patient advocacy community and industry scientists gathered in Natcher Conference Center to inspire one another.

"This is a really, really big day for us," said

SEE RARE DISEASE, PAGE 4

HEALTH AS A HUMAN RIGHT Galea Seeks to Widen the Dialogue

BY DANA TALESNIK



A sturdy building needs a strong foundation with numerous pillars to support it. The whole structure could be compromised if builders overlook proper materials and design.

The same can be said for health, which can thrive from a supportive infrastructure. Strengthening our health requires addressing societal symptoms that weaken it, argued Dr. Sandro Galea, epidemiologist, dean

SEE GALEA, PAGE 8



Arizona State University's Dr. Melissa A. Wilson and the chromosomes she studies.

PHOTOS: MELISSA A. WILSON



Sex, Disease, Chromosome Size To Feature in Early-Career Investigator Lecture, Apr. 10

For decades, scientists have sought to understand genomic differences between men and women by studying the sex chromosomes (X and Y). In general, women carry two X chromosomes and men have one X and one Y. But the story is much more complicated. For example, about a million people in the United States have an atypical number of sex chromosomes—and many don't even know it.

At the 4th annual NIGMS Director's Early-Career Investigator Lecture, Dr. Melissa A. Wilson, a computational biologist at Arizona State University, will explain what she and other researchers are learning about sex chromosomes. She will share her team's findings about the divergent evolution of X and Y, and will describe how new techniques can help scientists better understand sex-linked diseases.

The lecture, "Sex-Biased Genome Evolution," takes place Wednesday, Apr. 10 at 10 a.m. in Lister Hill Auditorium, Bldg. 38A. After a 30-minute lecture, Wilson will answer questions from the audience about her research and career path.

Open to everyone in the scientific community, the early-career investigator lectures are designed to introduce undergraduate students and others to cutting-edge research and inspire them to pursue careers in the biomedical sciences.

NIH trainees are encouraged to attend in person or by NIH videocast (live or later). For more details, see www.nigms.nih.gov/ECI/2019.

NHLBI's Geller Awarded for Mentoring

Dr. Herbert Geller, director, Office of Education and chief, developmental neurobiology section at the National Heart, Lung, and Blood Institute, was recently selected as one of two recipients of the 2018 Bernice Grafstein Award for Outstanding Accomplishments in Mentoring given by the Society for Neuroscience (SfN). The award recognizes an individual or individuals who have shown dedication to mentoring female neuroscientists and to facilitating their entry into or retention in the field. Established in 2009, the award is supported by Dr. Bernice Grafstein, who was the first female president of SfN.

"Since the early 1980s, Geller has mentored dozens of students and fellows, including 30 female neuroscientists. He has mentored countless others through SfN programs and as program director for NIH training programs," according to the SfN web announcement. "Even in the earliest stages of his career, Geller focused on promoting the training and retention of female neuroscientists. He is well-regarded throughout the field for tailoring his guidance to individuals to cultivate their unique talents and assets as well as for remaining in touch with and available to former trainees and colleagues."

Geller is a fellow of the American Association for the Advancement of Science. His contributions to teaching and mentoring have been recognized with an NHLBI Director's Award for Promoting Diversity.

Dr. Elaine Del Bel, professor and leader of the Laboratory of Cellular Neurobiology at the University of São Paulo at Ribeirão Preto Dental School, also received the 2018 Grafstein prize.



Dr. Herbert Geller (r), director of NHLBI's Office of Education, receives Bernice Grafstein Award from the Society for Neuroscience. The award's namesake, Dr. Bernice Grafstein (l), served as the first female president of SfN.

PHOTO: SOCIETY FOR NEUROSCIENCE

June 19-20

ODP To Host Workshop on Preventive Services

The NIH Office of Disease Prevention will hold a Pathways to Prevention Workshop: Achieving Health Equity in Preventive Services June 19-20 at Natcher Conference Center. It will assess the scientific evidence on achieving health equity in the use of clinical preventive services in a health-care setting.

The workshop will focus on three leading causes of death in the United States: cancer, heart disease and diabetes. These diseases are responsible for 7 of every 10 deaths among Americans each year and account for 75 percent of the nation's health spending.

The workshop is designed for researchers, practitioners and other professionals who are interested in clinical preventive services and issues of health equity. Cosponsors include NCI, NHLBI, NIDDK and NIMHD.

The workshop is free and open to the public. Register at <https://www.eventbrite.com/e/nih-p2p-workshop-on-achieving-health-equity-in-preventive-services-registration-54002740651>. Attendees can join either in person or via NIH videocast.

NIH Community Drives ‘Optimize NIH’ Improvements

BY ERIC BOCK

Twenty-seven institutes and centers make up NIH, giving the agency the ability to conduct and support a variety of promising avenues of scientific research. Still, there may be room for improvement, explained NIH principal deputy director Dr. Lawrence Tabak.

“What ReImagine HHS and, in turn, Optimize NIH have been about is identifying areas that we can enhance and improve by working together,” he said at a Mar. 4 town hall meeting on Optimize NIH in Masur Auditorium.

Optimize NIH is part of ReImagine HHS, an effort to improve efficiency and effectiveness within the department, said Charles Keckler, an associate deputy secretary at HHS. ReImagine HHS includes 6 strategic shifts with 10 initiatives. Each one focuses on improving programs and rethinking how HHS serves the American people.

“Optimize NIH is special in a number of ways,” Keckler said. “It represents a pilot model for how ReImagine principles can cascade down to the [operating] division level.”

Tabak noted that the Optimize NIH team first focused on committee management, ethics and Freedom of Information Act functions. Subject matter experts identified what could be improved, studied best practices and made recommendations.



Charles Keckler, HHS associate deputy secretary, speaks at the Optimize meeting.



Dr. Alfred Johnson, NIH deputy director for management, was among the panelists presenting a town hall meeting on Optimize NIH.

PHOTOS: MARLEEN VAN DEN NESTE

They designed strategic plan templates and developed metrics and standards that can be used NIH-wide.

• • •

“What ReImagine HHS and, in turn, Optimize NIH have been about is identifying areas that we can enhance and improve by working together.”

-DR. LAWRENCE TABAK

• • •

Staff have made “extraordinary” progress since the start, he said. The FOIA group built a platform called FOIAxpress, which allows users to share documents and track the progress and timelines of requests. The committee management group reduced the cost and time it takes to process nomination slates and committee appointments and improved the onboarding process for members. The ethics group decreased the number of steps employees must take and forms they must fill out across all ICs.

For the next phase, staff worked with leaders of Optimize NIH to develop criteria for identifying other areas that could be improved, said Dr. Alfred Johnson, NIH deputy director for management. They used what they learned from the first phase.

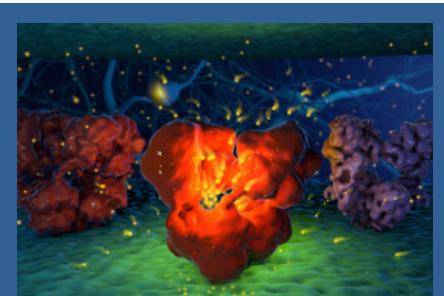
Together, they came up with five new areas to examine. These include acquisitions, IT security, processes for attracting and retaining senior staff with outstanding

scientific, technical and clinical skills under a flexible mechanism called Title 42, travel and property.

The first three areas must be harmonized “across the entire agency,” Tabak said. The remaining two areas, travel and property, “lend themselves to doing experiments” to figure out the best practices and develop tools.

Tabak thanked the many staffers who have volunteered time from their busy schedules and their expertise.

NIH’ers can watch the whole town hall online at <https://videocast.nih.gov/summary.asp?Live=31562&bhcp=1>. Also, an intranet site devoted to the effort is updated regularly at <http://employees.nih.gov/pages/optimize-nih.aspx>. 



ON THE COVER: Illustration of the ionotropic glutamate receptor (iGluR) gating cycle using high-resolution cryo-electron microscopy data from the research of Dr. Joel Meyerson of NCI. iGluRs mediate excitatory synaptic transmission in the brain.

IMAGE: VERONICA FALCONIERI & SRIRAM SUBRAMANIAM, NCI

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National Institutes of Health
Turning Discovery Into Health

Rare Disease

CONTINUED FROM PAGE 1

NCATS director Dr. Christopher Austin, whose center has housed the Office of Rare Disease Research for the past 5 years. "Rare diseases research is like music—a universal language that transcends disciplines and national boundaries." A musician himself, Austin announced the theme for the day, which coincides with a new, multi-faceted NIH initiative: "Rare Diseases Are Not Rare!"

The event, traditionally held in the Clinical Center—a major partner in addressing rare diseases, with 552 rare disease research protocols currently underway—moved to Natcher this year to accommodate more than 650 attendees. It opened with video salutations from EURODIS, a rare disease patient advocacy group in Europe, the National Organization for Rare Disorders based in the U.S., as well as from rare disease organizations in Hong Kong, Japan, China, Taiwan, Malaysia, India, Iran, Malta, Spain, Kenya, South Africa, Argentina, Mexico and Canada.

"The medical truth is that rare diseases [of which there are some 7,000], though individually rare, cumulatively affect about 8 percent of the population—about the same as type 2 diabetes," Austin said, "but with a greater morbidity and mortality, especially among young people. The economic costs, both for direct health care and in lost productivity, are enormous. We need to redefine, in the public's mind, the importance and impact of rare diseases."

Clinical Center CEO Dr. James Gilman noted that rare disease studies make up a little over half of the total of patient protocols underway in the CC. "Fifty-seven percent of all Clinical Center patients, or 13,113 people, are enrolled in rare disease research protocols."

Most are in clinical trials, but some are in so-called natural history studies, known euphemistically, Gilman disclosed, as "admiring the disease." These protocols involve discovery of the usual course of development of a disease or condition.

The daylong event also included four scientific sessions, poster sessions, award presentations and a display of awareness-raising art.

"Rare Disease Day gets bigger every year," said NIH director Dr. Francis Collins. "This

year is just absolutely amazing. Awareness is steadily growing, certainly at NIH. Most institutes and centers are involved...But we still need to find treatments for most [rare diseases]."

A few days earlier, Collins and a cadre of IC directors had attended a Capitol Hill reception in support of the Children's Inn at NIH, where many young patients with rare diseases stay with their loved ones during treatment at the Clinical Center.

"The Congress of the United States is increasingly aware of, and sympathetic to, the need for more resources [for rare disease research]," Collins said. Some 30 members from both parties attended the inn event. "There is a unanimous sense that medical research is important—nobody



Geoff Spencer (shown on background image), who served in NCATS's Communications Branch before passing away from a rare disease, was remembered on RDD. Austin stands with Geoff's family along with a photo signed by his NIH colleagues. Family members include (from l) Jennifer Krafchik, Ellie Krafchik, Amy Spencer, Patricia Spencer, Greg Brock, Nicole Brock and Sarah Brock.

disagrees—and worthy of support."

Collins said that when he meets with members of Congress nowadays, he often talks about sickle cell disease, a rare disease affecting some 100,000 people in the U.S. Advances in gene therapy offer fresh promise of not only treating, but perhaps also curing sickle cell disease, he said. [News magazine *60 Minutes* featured the work on Mar. 10.]

"This approach could fit other diseases as



Beyond the Diagnosis CEO and founder Patricia Weltin (l) presents the newest painting to the rare patient art collection. The painting by artist Jota Leal features 9-year-old Amber (second from r) who is part of a gene therapy trial at the Clinical Center and a resident of the Children's Inn at NIH. The portrait was unveiled at Rare Disease Day. Amber's parents, Miguel and Leticia, stand on either side of the portrait with Stephanie Feinberg of the inn.

PHOTOS: DANIEL SOÑÉ

well,” Collins added. “The excitement of that kind of outcome cannot be overstated.”

The Common Fund—NIH’s “venture capital space”—is becoming involved in *in vivo* gene editing, Collins continued. “It seems like we’re at a real juncture of opportunity, to go right to the heart of genetic disorders using the CRISPR-Cas system.” Muscular dystrophy might be a good candidate for this type of therapy, he said.

Collins announced that a consortium of 17 academic research institutions receiving \$190 million over the next 6 years from NIH has been formed to develop safeguards and standards around therapeutic genome editing. “We’ll be hearing more about that in the next year or two,” he said, noting that the work “does not involve embryos—let’s be clear on that...The work will start in animal models, then hopefully move to patients soon.”

Collins himself has spent 15 years working on Hutchinson-Gilford progeria syndrome, a research interest that began in the 1980s, when he took care of a patient, Meg Casey, with the disease.

“She was about 3 feet tall and could curse like a sailor,” said Collins. “I remember thinking, ‘I hope someday, some scientist would figure out a way to help her.’”

Later in his career, Collins met another memorable progeria patient, Sam Berns, who was 3 when Collins first saw him. During a span of 14 years before Berns died, researchers learned that progeria, which affects about 200 children in the world, arises when “a simple letter in the DNA code is misspelled—there should be a C instead of a T—in a nuclear structure protein,” Collins said.

Working with the Progeria Research Foundation and Sarepta Therapeutics, Collins and his team think they may be nearing a way to treat progeria successfully. “It’s not out of reach at this point,” he said. “I want this same story of progress to happen for all the conditions you represent,” he told the audience. “You have powerful stories to tell...This is the time, scientifically, to take advantage.”

He left the crowd with the four tenets of Sam Berns’ philosophy: Be okay with what you can’t do, surround yourself with people you like, keep moving forward and never miss a party.

“This is your party today,” Collins concluded. **R**

NIMH Symposium Tackles Mind-Wandering, Mindfulness

A SEESAW

The human mind can at one moment wander miles away and at the next be acutely conscious of the present. At one moment, it can be intensely aware of one’s surroundings, while at another look deep within. This continual seesaw between external and internal events is supported by two tightly linked cognitive functions—attention and awareness. How we attend and what we are aware of affect how we feel, how we evaluate choices, how we make decisions, how we interact with others, how we learn, etc.

Recently, a symposium was held at NIH to tie together the basic science research topics of attention and awareness and highlight their relevance in mental health and daily life. “From Mind-Wandering to Mindfulness: The Role of Attention and Awareness,” the meeting held Mar. 5-6, was organized by staff scientist Dr. Shruti Japee and research fellow Dr. Marine Vernet of the section on neurocircuitry in NIMH’s Laboratory of Brain and Cognition.

Attention and awareness are fundamental to many aspects of cognitive neuroscience, including visual perception, decision-making, goal-directed actions, memory, learning and emotion processing. In addition, mind-wandering and mindfulness are important current research topics in cognitive psychology and neuroscience. For example, mind-wandering has been shown to reduce reading performance and negatively affect mood.

On the other hand, there is growing evidence of the positive impact of mindfulness on the brain and several researchers are exploring meditation as a treatment strategy for mental disorders.

The symposium invited experts in each of these fields to present work and promote dialogue among basic and clinical research scientists on topics of mutual interest.

On the first morning, speakers discussed neural states, dynamics and pathways underlying conscious and unconscious visual processing and how humans automatically and implicitly model other people’s attention.

In the afternoon, invitees discussed the neural correlates of consciousness and how this can be leveraged in patients with disorders of consciousness. Dr. Hakwan Lau (University of Hong Kong/University of California, Los Angeles) proposed the use of neurofeedback to investigate the content of awareness during mind-wandering and mindfulness. Dr. Amishi Jha (University of Miami) wrapped up the day with a presentation on the use of mindfulness-based training to promote cognitive resilience in elite military cohorts.

Day 2 began with Dr. Naotsugu Tsuchiya (Monash University, Australia) proposing that the content of consciousness is richer than typically assumed. Dr. Marvin Chun (Yale University) showed ways in which resting state fMRI network connectivity could be leveraged to reconstruct the focus of attention and quantify sustained attention. The symposium was rounded out by speakers who summarized the use of mindfulness to reduce anxiety, stress and mind-wandering, enhance cognitive performance and modify functional connectivity in the brain.

More than 100 researchers from NIH and local institutions including Georgetown University, George Washington University, George Mason University, Johns Hopkins University and the University of Virginia attended the meeting.



Symposium speakers and organizers include (from l) Shruti Japee, Michael Graziano, Claire Sergent, Marvin Chun, Amishi Jha, Diane Beck, Melanie Boly, Jonathan Schooler, Naotsugu Tsuchiya, David Leopold, Elizabeth Hoge and Marine Vernet. Not shown are Hakwan Lau and Martin Monti.

Exposome

CONTINUED FROM PAGE 1

or Three Mile Island and Chernobyl after nuclear power plant disasters. However, the monitors in those investigations were stationary, installed in designated locations and not meant to be mobile. Jiang's method is different, more personalized. It can travel with you.

A Stanford University postdoc in Dr. Michael Snyder's lab and an inventor who has published extensively on bacterial genomics, Jiang and his labmates spent several years inventing a portable, battery-powered device—"smaller than an iPhone 6," he noted wryly—that individuals can wear like an armband, or set up on their desks.

The mechanism includes sensors, a collection container with filter and a pump that simulates human breathing. The sensors can detect both biologicals (biotics) and chemicals (abiotics). So airborne substances from plants and pets as well as such common emissions as tobacco smoke and automobile fumes are all fair game for collection.

Jiang's device also continuously measures atmospheric temperature, humidity and particle concentration.

For its longitudinal study, the research team recruited more than a dozen folks to use the device as they went about their daily lives—for several weeks or months and up to 890 days, in the case of one wearer. All 15 volunteers were San Francisco Bay-area residents, males and females ages 28–61. Some traveled—across North America, Europe and parts of Asia; others stayed primarily in their own geographical comfort zone.

Results, which the team analyzed and categorized using DNA and RNA sequencing samples, were fascinating and informative. The study also contains broad implications for public health.

"So there were all sorts of different particles," Jiang said, showing slides from analysis of the data sample. "We saw plant pollens from the different plant species and contact spores...There were also brochosomes, which I would never have known about without doing this project. They look like viral particles, in a sense, but it's actually some sort of hydrophobic proteins/lipids mixture made by insects as a waterproof mechanism on their body."

The researchers identified more than 2,500 species, including bacteria, fungi, plants, Metazoa and more than 200 viruses.

"We know that the exposome is highly diverse, but also highly dynamic," Jiang said.

His team was able to determine not only where volunteers had been, but also approximately when they'd traveled.

"The seasons were pretty much a major driving factor, with all of the changes in temperature, humidity and other things," he explained.

For example, he noted, pine pollen in northern California is heaviest in late spring or early summer. Jiang's analysis of samples clearly showed times that wearers had spent in that region, when dense concentrations of pine pollen were detected. Other geographic regions revealed similar unique characteristics.

"This can really be a validation of our approach," Jiang said. "We were actually following people around, but of course the people are exposed to everything floating around them, so even environmental species with seasonal patterns we were able to detect. [However], instead of just one or two species we were able to do hundreds at the same time...With so many seasonal



In his talk, Jiang describes the portable, battery-powered device—about the size of a cell phone—that can be worn like an armband or set on your desktop. The mechanism includes sensors, a collection container with filter and a pump that simulates human breathing.

IMAGE: ALLISON ZHANG

signatures in our data we were able to construct a seasonal prediction model."

The study enabled chemical profiling as well, Jiang pointed out. "Chemicals are influenced by locations," he noted. "Chemicals are correlated with biologicals."

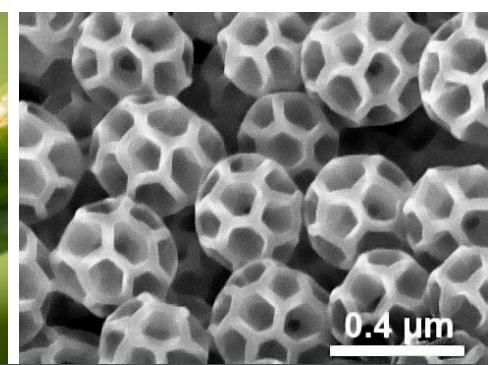
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"We know that the exposome is highly diverse, but also highly dynamic."

-DR. CHAO JIANG

★ ★ ★

All told, Jiang tracked 66 locations from across the U.S.—California, Montana, Texas, Michigan as well as Boston and Bethesda—to as far away as Indonesia and Australia. Participant 1 (P1) provided the most data,



In the air, up close: At left, see the white dots on the wings of a glassy-winged sharpshooter, a large leafhopper insect. The dots are a liquid containing a great number of microscopic structures called brochosomes. IMAGE: ALEX WILD, UNIVERSITY OF TEXAS-AUSTIN/WIKICOMMONS At right, brochosomes of a leafhopper, via scanning electron micrograph IMAGE: ROMAN RAKITOV/WIKICOMMONS



Jiang and colleagues plan to fine-tune the device filter so it can better detect and identify disease microbes.

LECTURE PHOTOS: CHIA-CHI CHARLIE CHANG

carrying around the device for nearly 2½ years. A 66-year-old university professor, P1 also traveled frequently, so the portability of the device and data collection methods were thoroughly tested.

The study, published in *Cell* in September 2018, also found that “people can have distinct personalized exposomes, even when geographically close.”

And, if knowing about all of the hitch-hikers you inadvertently pick up everyday creeps you out a bit, Jiang’s group also concluded that the overwhelming majority of microscopic riders are safe. In addition, air pollution isn’t nearly as much of a health problem in the U.S. as it is in India and China.

As for next steps in the research, Jiang and colleagues plan to fine-tune the device filter so it can better detect and identify disease microbes.

In an interesting future personal exposome study, Jiang is launching an investigation of mysterious colic. Using criteria dating back to the 1950s, doctors diagnose babies with colic when they cry for 3 hours a day for at least 3 days a week over the course of 3 weeks. Once physical and medical causes are ruled out, pediatricians deem the upset “mysterious.”

What leads infants to develop colic and why it clears are also unknown in many cases. Jiang hopes analyzing babies’ personal exposomes will penetrate the cloud surrounding the condition.

“The idea is to try to establish a longitudinal comprehensive exposure profile and long-term tracking,” Jiang concluded, “so maybe we can see what is changing before the onset of colic as well as what happens before its regression. Then we may be able to provide some therapeutic targets.” **R**

Im To Present NINR Director's Lecture, Apr. 25

On Thursday, Apr. 25, Dr. Eun-Ok Im will present “Midlife Women’s Health: Using Technology to Enhance Research and Eliminate Disparities,” from 1 to 2 p.m. She will discuss her program of research, which uses computer and mobile technologies to eliminate gender and ethnic disparities. The lecture will take place in Lipsett Amphitheater, Bldg. 10 and will also be broadcast live and archived at <http://videocast.nih.gov>.

Im is associate dean for research development and regulatory affairs and Mary T. Champagne professor at Duke University School of Nursing. She has gained national and international recognition as a methodologist, researcher and theorist in international, cross-cultural women’s health.

Im’s most outstanding contribution to nursing research is a program that adopts computer and mobile technologies to eliminate gender and ethnic disparities. She has taken the lead in this new field and her current studies are among the first of their kind to use these technologies to build nursing knowledge. Im has integrated this line of work with research projects on breast cancer survivorship, cancer pain, menopausal symptoms and physical activity. She has numerous national and international awards, including the 2014 International Nurse Researcher Hall of Fame Award from Sigma Theta Tau International.

The event is free and open to the public. For more information and to register, visit <http://ow.ly/nuNQ30o1ct>.



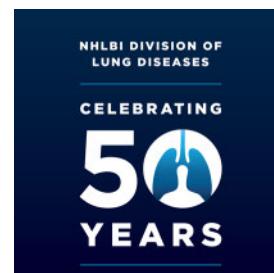
Division of Lung Diseases Celebrates 50th Anniversary, Apr. 9 at NLM

For 50 years, the National Heart, Lung, and Blood Institute’s Division of Lung Diseases (DLD) has advanced research on the causes, diagnosis, prevention and treatment of lung diseases and sleep disorders, as well as supported the researchers of the future.

This research will take center stage at an NIH symposium: “50 Years of Progress in Pulmonary Science Innovation in Lung Imaging for Diagnosis, Treatment and Management of Lung Diseases” on Tuesday, Apr. 9. All staff are welcome to attend the event, to be held from 1 to 4 p.m. at Lister Hill Auditorium, Bldg. 38A.

Experts in pulmonary science will discuss the progress and promise of lung disease research, including lung imaging and clinical applications. Among the event’s speakers are NHLBI intramural researchers Dr. Marcus Chen and Dr. Adrienne Campbell-Washburn. Campbell-Washburn received an Orloff Award this year for her leadership in developing cutting-edge, low-field MRI technologies that are more accessible to underserved communities.

NHLBI-funded extramural researchers will also join to discuss the progress and promise of lung imaging in epidemiological, technological and clinical applications. DLD director Dr. Jim Kiley and NHLBI director Dr. Gary Gibbons will moderate the



symposium and lead the audience in a Q&A session following presentations.

Those who cannot attend in person can join online through the live NIH videocast. Watch for upcoming DLD 50th anniversary events in Outlook or follow along on social media using #Lung50. **R**

Walk, Run to Celebrate National Minority Health Month

The 3rd Minority Health 5K Walk/Run is scheduled for Wednesday, Apr. 24 at 11:30 a.m. Lace up your sneakers and grab a colleague to walk or run in recognition of National Minority Health Month. There will be music, food trucks and opening remarks by newly appointed deputy assistant secretary for minority health Capt. Felicia Collins.



The event will take place on the main campus in front of Bldg. 1. Don’t forget your NIH ID (the course goes outside the perimeter fence). Register today at <https://nimhd.nih.gov/contactform/registration-form02.html>.

The event is jointly sponsored by the National Institute on Minority Health and Health Disparities, the Office of Research Services and the Recreation and Welfare Association’s Fitness and Wellbeing Program.



"Science has to be accompanied by a value set that promotes health," said Galea.

PHOTOS: CHIA-CHI CHARLIE CHANG

Galea

CONTINUED FROM PAGE 1

and professor, Boston University School of Public Health. He delivered an impassioned talk at a recent NIMHD Director's Series seminar in Lipsett Amphitheater.

"Ultimately, we cannot generate health without paying attention to the other forces that generate health outside the health care system," said Galea.

These forces, he said, are encapsulated in the story of blues legend Blind Willie Johnson, who lived a century ago. Johnson, who grew up poor and black in the south, was blinded as a child in a domestic violence incident. In his 40s, he contracted malaria; the hospital refused to admit him and he died. The disease may have killed him, said Galea, but so did poverty, domestic violence, racism and poor access to health care.

The problem, Galea said, stems from "a mismatch between our spending on health and our health indicators." U.S. health spending is much higher than in other developed nations, yet America fares worse on noncommunicable disease mortality and other health indicators across every age group.

Investing in measures to counter the forces that threaten health may seem utopian and unattainable, but the situation wasn't always so dire, said Galea, and doesn't have to be. Until the early 1980s, the United States ranked high among its peers in annual life expectancy. Today, the U.S. sits toward the bottom of that list, in its third consecutive year of declining life expectancy.

not intended to diminish the importance of investing in health care and scientific research. He considers both pieces of a larger puzzle.

We might dismiss a disease outbreak across the world, for example, until that disease arrives in the U.S. Vaccine skepticism matters because it can create pockets of infection that spread, such as the recent measles outbreak in southwest Washington state.

"Our health is collectively intertwined," said Galea. "We will not be able to do anything to improve our health if we do not deal with the health of all."

When health isn't considered a public good, said Galea, we wind up with such incidents as polluted drinking water in Flint, Mich. Clean water should be a public good, he said, and health is something we all should own.

Politics sometimes drives health, said Galea, and it also presents opportunities to expand the national dialogue while pushing

"It's hard to think of any other sector where we are consistently outspending all our competitors, but getting less out of it," Galea said.

The outspending is on medicine and health care, not on other health determinants such as socioeconomic conditions and access to care. Galea underscored that his views are

a healthy agenda. For example, since 1968, more Americans have been killed by firearms than all U.S. service men and women killed in all foreign wars combined. Traditionally, though, the gun rights lobby spends much more than the gun control lobby. The current national dialogue on gun violence, he said, was almost unimaginable a few years ago.

"It's important to have humility to recognize that our lens with which we look at the world is fixed to a particular point in time," said Galea. "Be part of the vanguard shifting these [ideas] forward."

While the leading causes of death include heart disease, cancer, respiratory disease and stroke, the underlying causes may include tobacco, poor diet and microbial agents. Digging further, one can argue that underlying social causes such as poverty, low education and racial segregation also heighten morbidity and mortality, said Galea.

Furthermore, health should be a means, not an end. The goal should not just be treating people's conditions, Galea said, but also keeping them healthier, longer.

Precision medicine is important, he said. "It's [also] distracting us with it being an ever-targeted genetic molecular approach to fix [disease, while ignoring societal determinants]." Advances in discovery science are exciting and promising, he added, but let's not get distracted from the larger picture. Rather than chase perpetuity, he said, let's celebrate living.

The challenges are vast. With an open mind, we can change the lens and expand the conversation. Demand the conditions that generate better health for all, urged Galea. "Science is seldom enough," he said. "Science has to be accompanied by a value set that promotes health."

In a soccer game, concluded Galea, the net is huge, so the goalkeeper relies on the whole team to play good defense and keep the ball away from the net.

The goalkeeper, he said, is medicine, that cures us when we get sick. But we should invest in the other players so that we "promote health for everybody, making sure we have compassion to change the structures that generate health," said Galea. "We need to make sure we pay attention to where we live, how we live, the air we breathe, the cities around us—that's how we're going to reverse the problem." ▶



Galea engages with the audience after his talk.



IMAGE: ALEKSANDARNAKIC/GETTY

First-Ever Drug Specifically for Postpartum Depression Approved

Approximately 1 in 9 women in the United States experiences symptoms of postpartum depression, according to the Centers for Disease Control and Prevention. Now, the Food and Drug Administration has approved brexanolone, an analog of the endogenous human hormone allopregnanolone and the first drug specifically designed to treat postpartum depression.

Some psychiatric drugs owe their discovery to chance—serendipitous observations of clinical benefit—or a process of incremental improvement based on drugs previously discovered by chance. Not so with brexanolone, which has a truly novel mechanism of action and was developed by design, thanks to a series of basic and translational neuroscience studies. FDA approval represents the final phase of a bench-to-bedside journey for this drug—a journey that began in NIMH's Intramural Research Program.

In the 1980s, NIMH researchers discovered that metabolites (products formed when the body breaks down or “metabolizes” other substances) of the steroid hormones progesterone and deoxycorticosterone bound to and acted upon receptors for gamma-aminobutyric acid (GABA)—a major inhibitory neurotransmitter in the brain. These steroids were found to amplify GABA-activated chloride ion currents, thereby affecting the excitability of neurons.

This finding led to a series of studies, completed by researchers at or funded by NIMH, that clarified how these metabolites fluctuate during times of stress and during the estrous cycle in rats and the menstrual cycle in humans. Research indicated that the concentration of one of these metabolites (allopregnanolone) increases during pregnancy, but then drops after birth. In some women, this drop triggers the development of depression and anxiety.

A biopharmaceutical company utilized these basic research findings to develop brexanolone, a drug that can be used to treat postpartum depression by restoring levels of this metabolite. Successful clinical trials led to FDA approval of an injectable version of this drug.

New Approach Shows Promise for Cystic Fibrosis

Researchers say a widely used antifungal drug may hold promise for treating people with cystic fibrosis, a life-threatening genetic disorder that causes serious damage to the lungs. In studies using human cells and animal models, the researchers found that the medication, called amphotericin, helps lung cells function in a way that could make it easier for patients to fight chronic bacterial lung infections that are a hallmark of the disease. The findings from the study, which was supported in part by NHLBI, will appear in the journal *Nature*.

If human studies validate the findings, the use of the drug could be good news to the more than 30,000 people in the United States and 70,000 worldwide who live with cystic fibrosis, a disease with no cure and few treatment options. It holds special promise for a subset of patients, about 10 percent of the people with cystic fibrosis, who do not respond to any treatment.

“The really exciting news is that amphotericin is a medicine that’s already approved and available on the market,” said Dr. Martin D. Burke, leader of the study and professor of chemistry at the University of Illinois in Champaign. “We think it’s a good candidate.”

Cystic fibrosis is caused by a defect in a gene called CFTR (cystic fibrosis transmembrane conductance regulator). This gene normally makes a protein that controls or channels the movement in and out of cells of such materials as salt, bicarbonate and water—all of which are important to normal lung function. In people with cystic fibrosis, however, the defective gene makes a protein that is itself defective, causing the accumulation of acidic and sticky mucus that not only clogs the lungs and makes it hard to breathe, but also makes the lungs vulnerable to bacterial infection.

While some treatments are currently available, they are limited because different people have different types of mutated proteins, and because 10 percent of people with cystic fibrosis make no protein at all. But amphotericin, Burke said, has the potential to work regardless of the kind of mutation, and even when the protein is missing.

Our Brains May Ripple Before Remembering, Study Suggests

A sound, a smell, a word can all flood our minds with memories of past experiences. In a study of epilepsy patients, researchers at NIH found that, split seconds before we recall these events, tiny electrical waves called ripples may flow through key parts of our brains that help store our memories, setting the stage for successful retrieval.

“We showed for the first time that ripples may be the neural substrates through which the human brain successfully recalls memories,” said Dr. Kareem Zaghloul, NINDS neurosurgeon-researcher and senior author

of the study published in *Science*. “These results help us understand how the brain processes the details of our past waking experiences or episodic memories.”

The study was led by Alex Vaz, an M.D.-Ph.D. student at Duke University who was completing his dissertation work with Zaghloul. For years, Zaghloul’s team has been using grids of surgically implanted electrodes to record the electrical brain activity of drug-resistant

epilepsy patients enrolled in a trial at the Clinical Center. The recordings have helped identify the source of a patient’s epileptic seizures as well as provide an opportunity to study how the brain encodes memories.

As many labs have established, Zaghloul’s team knew that our episodic memories are controlled by neurons in at least two different parts of the brain, but they did not know exactly how the cells worked together to retrieve memories. Based on a growing body of evidence, they suspected that the short, high-frequency electrical waves seen in ripples may somehow be involved. For instance, two earlier patient studies suggested that ripples may be important for solidifying memories during sleep.



IMAGE: SCYTHER5/ISTOCK

NHLBI's Engelgau Retires After 33 Years

BY MARK SAMPSON

Dr. Michael Engelgau, who helped establish and guide NHLBI's Center for Translation Research and Implementation Science (CTRIS) in his role as its first deputy director, has retired. His 5-year stint at NIH topped off a 33-year career with the Department of Health and Human Services that took him around the world and garnered international recognition for his efforts to improve the prevention and treatment of noncommunicable diseases.

"My life has been filled with opportunities," Engelgau said. "You never know where you'll end up, but you've got to be prepared."

Engelgau was ready in 2014, when Dr. George Mensah, then newly appointed CTRIS director, recruited him to help create something new—a center that would study sustainable delivery strategies for the many highly effective treatments and therapies that had emerged from NHLBI's biomedical research investments in heart, lung, blood and sleep-related diseases. A major goal of the new center: to help reduce persistent health disparities among people with these conditions.

Mensah recalled that as inaugural deputy director, Engelgau quickly got to work. He helped launch translation studies as a new science direction for NHLBI, developed a research portfolio targeting this science and established a research unit within NHLBI to foster and administer it. He gave a host of presentations across the institute, NIH and the broad research community, communicating the importance of translation research both domestically and globally. Engelgau also contributed to many scholarly publications promoting the research. And he played a major role in vetting and hiring key leadership staff and helping existing staff develop new skill sets.

"Dr. Engelgau has been invaluable at the NHLBI as a seasoned clinician-scientist and an empathetic and compassionate leader," Mensah said. "His efforts have resulted in a substantial NIH investment for translation research that has resulted in healthier and longer lives, both in the United States and globally. I am definitely going to miss him."

NHLBI director Dr. Gary Gibbons echoed those sentiments at a recent advisory council meeting, where he called Engelgau "an exemplar of a commitment to excellence in public service." Engelgau "was always insightful, collegial, collaborative and constructive." Gibbons expressed appreciation



Dr. Michael Engelgau

"for his contributions to the NHLBI, for standing up CTRIS as a new unit and just being a fabulous leader and colleague."

Engelgau grew up in Coquille, Ore., a small, rural town that once had a population of only about 4,000 people. He would later earn a medical degree from Oregon Health Sciences University and specialize in internal medicine.

From 1986 to 1990, Engelgau served as a medical officer with the National Health Service Corps, part of HHS, in Palau, Micronesia, a group of small islands in the western Pacific Ocean. At the time, he recalled, the region was extremely isolated by today's standards, with no phones and virtually no televisions. But what the tropical region did have was disease, and plenty of it.

"When I first arrived, the hospital and clinics had very little routine primary and preventive care," Engelgau said. "I saw high rates of heart disease, diabetes, obesity and hypertension."

While there, he also witnessed an outbreak of dengue fever, a mosquito-borne illness that can cause pain and sometimes a deadly hemorrhagic fever. But after 4 years, his medical team had made a big impact, increasing primary care activities that reduced avoidable illness with better treatments for hypertension and diabetes to the point that the doctors were seeing fewer sick patients, particularly in emergency rooms and hospitals.

"That was highly rewarding," he said. "That experience helped launch me on my public health career."

Engelgau went on to hold many positions within the Public Health Service, where he earned the rank of captain. He worked as a medical epidemiologist and in various leadership positions at the Centers for Disease Control and Prevention, including as director of noncommunicable disease activities at its office in Beijing, China. He also worked as senior public health specialist at the World Bank in Washington, D.C.

Widely recognized for his wealth of experience in medical prevention, Engelgau contributed to more than 200 peer-reviewed research articles. He also wrote dozens of published reports and contributed to numerous books and monographs. He held several teaching positions throughout the country (he is currently on the faculty at Georgetown University) and served as a peer reviewer for more than a dozen scientific journals.

Now that he has brought his official career to an end, Engelgau said it hardly means he will abandon his longtime research and public health interests. He plans to stay active in the community by teaching a class in global health and collaborating with public health colleagues on special projects from time to time. He has even considered seeing patients again.

Engelgau said he is also looking forward to having some old-fashioned fun. He loves the outdoors and plans to move eventually to Florida with his wife Terry, to whom he has been married for 40 years.

"I want to express my deepest thanks for all the support that CTRIS received over these years—from throughout the entire organization and throughout NIH," Engelgau concluded. "NHLBI is a great organization and its biggest strength is from its people and their unwavering commitment to serving the country and the world with excellence in science. Finally, I want to give a huge heartfelt thanks to George Mensah, who took a chance and hired me—from thousands of miles away when I was in China. I could not have a better supervisor, colleague and friend."

NINR Mourns Loss of Fourie

Dr. Nicolaas (Nic) Fourie, a longtime member of NINR's Intramural Research Program, died suddenly on Feb. 23. He came to the program as a visiting fellow in 2012, worked as a research fellow from 2013–2017, and remained a special volunteer until his unexpected passing.

Fourie received his Ph.D. in hominid paleobiology from George Washington University in 2012. His novel research included morphometric analysis, stable isotope techniques and work in stress physiology, as well as substantial field research experience with wild primates in Africa prior to joining NINR.



Dr. Nicolaas Fourie

Fourie was a founding inventor on two patents during his time in NINR's digestive disorders unit. During his research tenure, he discovered miRNA signatures in digestive and liver disorders and significantly contributed to a novel "nucleic acid detection on paper" method for detecting pathogens in resource-limited settings with the potential to save many lives around the world. Fourie was also featured in a LabTV video discussing his research (<https://www.youtube.com/watch?v=gEZsf8thHLM>).

"Over the past 7 years, Dr. Fourie actively and immeasurably contributed to NINR's research," said Dr. Wendy Henderson, who, as chief of the digestive disorders unit, worked closely with Fourie. "He was a sought-after mentor, winning several mentoring awards for his selfless attitude toward science and approachable human nature. He was energetic and enthusiastic in his life and in his work, yet always sensitive, accommodating and patient."

"Nic was a great person. His caring attitude and sense of fun will be remembered by many," noted Dr. Ann Cashion, acting director of NINR. "He set a strong example for research excellence and human kindness."

Fourie is survived by his wife Angela and young son Jannie, as well as his sister, mother and father.



Former CC deputy director and acting director Dr. Saul Rosen rarely was seen without a smile on his face. Shown below in his beloved white lab coat, he will also be remembered for his love of opera.

Former CC Leader Rosen Mourned

Dr. Saul Rosen, whose 35-year career was spent entirely at NIH, died peacefully at home on Feb. 28 at age 90. Named deputy director of the Clinical Center in 1984, he became acting CC director in 1990 and remained there until his retirement in 1994.

Rosen earned undergraduate and medical degrees from Harvard and got his Ph.D. in biochemistry at Northwestern University. He came to NIH in 1958 after a residency in internal medicine at the University of California, San Francisco.

He spent 2 years as a clinical associate in what was



then the National Institute of Arthritis, Metabolism and Digestive Diseases, then studied for a year on sabbatical in London. He returned to NIH in 1961, becoming a senior investigator in the Clinical Endocrinology Branch, where he worked on Bldg. 10's 8 West before being named CC deputy director in 1984. His research during those years involved the inappropriate production of hormones by tumors and the body's production of placental proteins in general.

Rosen was known for his love of opera, chocolate and the Clinical Center, a building in which he spent virtually his entire career. "The CC stands for more than the Clinical Center to me," he said in a retirement interview. "It also represents competency and collegiality. And I hope that's what we have been."

Rosen was proud of his clinical white coat, which was festooned with patches from different CC departments. He presided with pleasure over Clinical Center Grand Rounds for years, taking as much delight in introducing a new investigator as he did in presenting what he called "a heavy-hitter" to the crowd.

As an administrator, Rosen was fond of the sticky-note—handwritten messages that were both encouraging and frequent. He oversaw a period of growth and medical advances at the Clinical Center that included the AIDS epidemic, gene therapy, early immunotherapy and the initial planning for what would become the Mark O. Hatfield Clinical Research Center.

Rosen also spent more than 20 years working at Prince George's County General Hospital, where he attended rounds for a month each year.

In retirement, he pursued his favorite pastimes of listening to opera and sending citations of new word usage to the Oxford English Dictionary.

Rosen is survived by his wife of 30 years, Deborah Kieffer; his three children Craig Rosen, Dr. Laura Rosen and her husband Jonathan Zerkowski, and David Rosen and his wife Elisabeth Rosen-Arevalo; and three grandchildren, Jillian and Madelyn Zerkowski and Liam Rosen-Arevalo.

There will be a celebration of Rosen's life this spring.



Mary Bochanis, one of the longest-serving volunteers at the Children's Inn at NIH, passed away at age 94. A Greek immigrant, she went to medical appointments with inn families from Greece. NICHD's scientific director Dr. Constantine Stratakis (r) recently thanked her at the inn.

PHOTOS: CHILDREN'S INN AT NIH, MEREDITH DALY

Long-Time Children's Inn Volunteer Bochanis Mourned

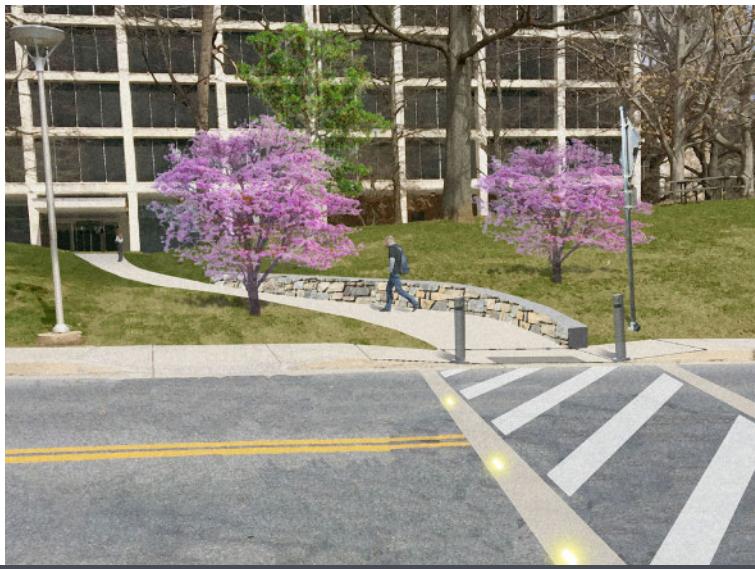
Mary Bochanis, who was one of the longest-serving volunteers at the Children's Inn at NIH, passed away Mar. 7 at age 94. She was a volunteer at the inn when it opened in 1990 and served there in weekly shifts for 28 years. She was also the longest-tenured volunteer with the American Red Cross, serving for more than 74 years at Walter Reed National Military Medical Center.

Bochanis met her late husband Charles "Gus" Bochanis at Walter Reed while he was recovering from losing a limb in World War II. She met him during her volunteer rounds, offering blankets and books.

A Greek immigrant, Bochanis went to medical appointments with inn families from Greece. NICHD's scientific director Dr. Constantine Stratakis had the opportunity recently to thank her at the inn.

"It is so important for our patients to have somebody who not only understands their language," Stratakis said, "but who also makes them feel so comforted and welcome."

Bochanis had a strong faith and belief in serving others, said Laura King, inn senior director of community engagement. "Her grace, sense of humor and ability to show love and compassion to everyone she met will be deeply missed at the Inn."—Meredith Daly



Within the next couple of months, the heavily used walkway in front of Bldg. 31A (shown as it currently is at left, with the new version on the right) will be replaced. A new accessible walkway has been designed to reduce the steepness of the walk while maintaining existing healthy trees. A retaining wall will be required to accommodate elevation changes and a new pedestrian-activated LED-lit crosswalk and flashing warning signs will be installed across Center Dr.

MORE CROSSWALKS COMING Safety Improvements for Campus Pedestrians Continue

NIH has made significant strides to create a safer Bethesda campus for pedestrians. Progress includes the addition of 20 LED-lit crosswalks under construction or already in operation. In 2019, new safety improvements are planned at several more intersections.

Currently under construction is a major improvement at the intersection of Memorial Dr. and Center Dr., near the northeast corner of the Clinical Research Center. The reconfigured intersection will improve vehicle, bicycle and pedestrian safety. (See the Nov. 2, 2018 *NIH Record* for a rendering of the new site.)

Within the next couple of months, the



heavily used walkway in front of Bldg. 31A will be replaced. A new accessible walkway has been designed to reduce the steepness of the walk while maintaining existing healthy trees. A retaining wall will be required to accommodate elevation changes and a new pedestrian-activated LED-lit crosswalk and flashing warning signs will be installed across Center Dr. During approximately 30 days of construction, pedestrians will need to follow a detoured path.

In addition to the new walkway, Center Dr. between Bldg. 31 and Bldg. 2 will receive new pavement and a speed hump. Several of the larger intersections throughout campus, including Wilson Dr. at Center Dr., will also be tightened to reduce the pedestrian crossing length.

The bulk of the construction is expected



At left is the current walkway at Wilson and Center Drives; at right is the improved version.

to be completed this year. No road closures are anticipated. Lane closures are limited to nights and weekends and one lane of traffic will be open at all times.

Michael Oppelt, the Office of Research Facilities project officer overseeing installation, can be reached at michael.oppelt@nih.gov or (301) 435-7827. [R](#)

Postbaccalaureate Poster Day Set

May 2

Postbac Poster Day is scheduled for Thursday, May 2. It will be held at Natcher Conference Center from 10 a.m. to 3:30 p.m. The keynote address will begin at noon, followed by presentation of Postbac Distinguished Mentoring Awards to NIH investigators selected by the postbacs. Poster session I will take place from 10 a.m. to noon and session II is from 1:30 to 3:30 p.m.

Poster Day is an opportunity for postbacs to share the research they have been conducting at NIH and at the same time develop their scientific communication and networking skills.

Posters will be reviewed by teams composed of graduate students, postdocs and staff scientists/clinicians. The authors of the top 20 percent will receive a letter acknowledging their accomplishments.

Investigators, staff scientists and scientific administrators can make an important contribution by visiting posters and engaging their authors in discussion.

For more information, visit www.training.nih.gov/postbac_poster_day.