

## PREVENTING DEADLY OVERDOSES

### Prescribers, Rethink Those Opioid Scripts

BY CARLA GARNETT

A dad clutches his daughter’s senior photo. She’ll never make it to graduation. After suffering a sports-related injury, the teen was prescribed an opioid for pain relief. She became addicted and joined a growing U.S. epidemic: People who died from an overdose of prescription opioids.

Images of grief-stricken families haunt Dr. Debra Houry, director of the National Center for Injury Prevention and Control at the Centers for Disease Control and Prevention. A practicing emergency room doctor for more than 15 years, she gave



Dr. Debra Houry of the CDC presents at NIH.

a lecture, “America’s Opioid Overdose Epidemic: What We Know and How Health Practitioners Can Help,” at NIDCR Clinical Research Grand Rounds recently.

“For me, the opioid epidemic has been

personal,” Houry explained. “I still see my patients’ faces and remember their stories. I’ve seen [the epidemic] evolve over the past 15 years. I’ve seen patients come in with really intractable pain—you want to take care of their pain. I’ve seen patients struggling with addiction and I’ve helped them navigate the system. I’ve also seen patients after they’ve overdosed and I’ve reversed them with naloxone. I’ve also not been successful at times and had to tell family members they’ve lost a loved one.”

### Dawn of an Epidemic

The first signs of trouble, according to CDC data, began around the mid-1990s, when opioids/heroin started dramatically rising as the cause for unintentional drug poisoning mortality. Drug overdoses became the second leading cause of death from injury in the late 1990s. [Death after motor vehicle injury was number one.]

SEE OPIOIDS, PAGE 6

## ‘ROME TO ROCKVILLE PIKE’

### Stimulating the Brain from Without: Therapy and Science

BY RICH MCMANUS

Renowned television host Dick Cavett once had this to say about electronic convulsive therapy (ECT), which he underwent for depression: “In my case, ECT was miraculous. It was like a magic wand.”

It is shock therapy’s stubborn efficacy that has kept it alive, despite the alarming image it typically conjures.

The procedure began in Rome in 1938, when Drs. Ugo Cerletti and Lucio Bini



NIMH’s Dr. Matthew Rudorfer

It is shock therapy’s stubborn efficacy that has kept it alive, despite the alarming image it typically conjures.

SEE NEUROMOD, PAGE 4

### Reducing Medical Errors Requires Leadership, Culture Of Learning

BY ERIC BOCK

How do you create a caregiving culture where employees are free to speak up if they see a problem and know what to do if there’s an issue? Two physicians addressed this topic at Clinical Center Grand Rounds on Mar. 22.

First, Clinical Center CEO Dr. James Gilman described how a military hospital responded to a large-scale adverse event that affected more than 2,000



Dr. James Gilman, CC CEO



Last time around for circus and kids. See p. 12.

### ALSO THIS ISSUE

Briefs .....	2
Three-Minute Talk Challenge at NIEHS .....	3
Manipulated Cells Can Rebuild Damaged Tissues, Says Duke’s West .....	7
Digest .....	9
Milestones .....	10

SEE SAFETY, PAGE 8

## ODP Early-Stage Investigator Awardees To Speak, May 3

Winners of the Office of Disease Prevention's inaugural Early-Stage Investigator Awards—Dr. Justin D. Brown and Dr. Katherine Keyes—will present on Wednesday, May 3 at 2 p.m. in Masur Auditorium, Bldg. 10. The talks will precede the Robert S. Gordon, Jr. Lecture in Epidemiology.

The award recognizes early-career prevention scientists who have not competed successfully for a substantial NIH-supported research project before the award nomination submission deadline, but who have already made significant, outstanding research contributions to their respective fields and are poised to become future leaders in prevention research.

Brown is a research fellow in population sciences at Dana-Farber Cancer Institute and Harvard Medical School. His presentation is titled “A Phase II Randomized Clinical Trial to Evaluate the Dose-Response Effects of Exercise on Prognostic Biomarkers among Colon Cancer Survivors.”

Brown has published more than 45 peer-reviewed papers in journals such as the *Journal of Clinical Oncology* and the *Journal of the National Cancer Institute* and is an editorial board member of *BMC Cancer*.

Keyes is an associate professor of epidemiology at Columbia University. Her presentation is titled “Alcohol Use and Morbidity Across Historical Time: What Does Variation Tell Us About Environmental Determinants of Alcohol-Related Outcomes?” Her research focuses on life course epidemiology with particular attention to psychiatric disorders, including examination of fetal origins of child and adult health, long-term outcomes of adverse childhood environments and cross-generational cohort effects on substance use, mental health and chronic disease.

Registration for the event is not required. The presentations will also be available via NIH Videocast. For more information, contact Dr. Stephanie M. George, [stephanie.george@nih.gov](mailto:stephanie.george@nih.gov).

## ‘Milestones in NINR History’ Released

The National Institute of Nursing Research has released an interactive timeline that highlights significant accomplishments, discoveries and initiatives over NINR's 30-year history. The new web feature at <https://www.ninr.nih.gov/milestones> includes dates, images and links to learn more about each milestone.

“We are pleased to share a visual representation of some of the most important advances in nursing research over the past 30 years,” said NINR director Dr. Patricia Grady. “As we look toward the future of nursing science, these milestones can inform and inspire the work that we have ahead of us.”

To learn more about NINR's 30th anniversary, visit <https://www.ninr.nih.gov/newsandinformation/30years>.



## Jazz Quintet Entertains at CRC

The University of Maryland Jazz Quintet returned to NIH on Mar. 23 for a noontime performance in the atrium of the Clinical Research Center. The group performed classical jazz favorites as well as original tunes. Members include (top, from l) Gerry Kunkel, guitar; Joey Antico, drums; Griffith Kazmierczak, trumpet; John Previti, acoustic bass; and Chris Vadala, saxophones and flute. The Clinical Center and the Foundation for Advanced Education in the Sciences presented the concert.

PHOTOS: BILL BRANSON



## Virologist Corey Gives Hill Lecture, May 9

Virologist and vaccine expert Dr. Lawrence Corey will deliver the 2017 James C. Hill Memorial Lecture on Tuesday, May 9, at 3 p.m. in Lipsett Amphitheater, Bldg. 10. His talk, titled “Getting to an

Effective HIV Vaccine: Perspectives on Progress,” will review the state of HIV vaccine development and describe current strategies to advance the field. The talk was originally scheduled for Mar. 14 but was postponed due to the weather. For more details, visit [https://nihrecord.nih.gov/newsletters/2017/02\\_24\\_2017/story5.htm](https://nihrecord.nih.gov/newsletters/2017/02_24_2017/story5.htm).

## Credit Union Announces ‘Student Choice’ Loan Programs

The NIH Federal Credit Union has introduced its new Student Choice education loan programs. As a not-for-profit lender, NIHFCU can now help

borrowers fund an undergraduate education. It also now has the ability to refinance existing student loan debt and potentially save borrowers thousands of dollars. Undergraduate lines of credit are available up to \$75,000. Refinance loans go up to \$250,000 for practicing physicians and \$125,000 for all other professions.

“As the cost of an education and the level of student loan debt continue to rise, we know that many individuals are challenged by this burden and potentially delay other important life decisions,” said Steve Levin, NIHFCU vice president of marketing. “We are thrilled to now offer new solutions to help our members take more control of their student loan debt and simplify their lives.”

Rick Wiecek, NIHFCU president and CEO adds, “The NIHFCU looks forward to proudly helping our current and future members navigate through the financial demands of funding and paying for an education. The Student Choice program is one of many new products we are developing to support the financial needs of the NIH workforce and the local health care community at large.”

To learn more about Student Choice, visit [nihfcu.org/education](http://nihfcu.org/education) or stop by any NIHFCU branch.

## NIEHS Trainees Excel in 3-Minute Talk Challenge

For the second year in a row, 15 NIEHS and National Toxicology Program trainees accepted the challenge to distill their biomedical research into a 3-minute talk, using language that a general audience would understand. In keeping with that theme, the participants were judged by a panel of five volunteers from across the institute that included only one scientist.

The audience cheered the high-energy and often fascinating presentations, which provided glimpses into a range of biomedical research topics, cutting-edge techniques and effects on public health.

Three winners were chosen; each will receive a travel award to attend the conference of her or his choice. They are Lee Langer, chromatin and gene expression group, Epigenetics and Stem Cell Biology Laboratory; Priya Jayaraman, immunogenetics group, Immunity, Inflammation, and Disease Laboratory (IIDL); and David Scoville, cell biology group, IIDL.

“It was great to see so many take advantage of this opportunity to polish an important skill that doesn’t always get the attention it should,” said Tammy Collins, director of the NIEHS Office of Fellows Career Development. “By that, I mean explaining to a lay audience the nature and importance of their research. In an age of social media, there are lots of ways to spread the word about environmental health research and it is critical to give people information they can understand.”

The challenge was framed as a simple question that might be asked by a relative, neighbor or new acquaintance: “So, what type of research do you work on?” Combine that with two more topics competitors were asked to address—the broader impact on society and what the presenter has gained personally from the experience—and the challenge might well seem impossible.

“At only 3 minutes in length, these talks challenged the speakers to tackle the meat of why their research matters, while at the same time pressing them to explain that in a way that doesn’t require a Ph.D. to



From left, Tammy Collins congratulated winners Lee Langer, David Scoville and Priya Jayaraman on their presentations. “They were outstanding,” she said.

understand,” said Ian Thomas of the NIEHS Office of Communications and Public Liaison, who served as a judge.

Some contenders spoke without notes and many opened with an attention-grabbing hook. Thomas praised the level of competition. “Picking three winners out of the 15 who presented was a real challenge,” he said. “All of the talks were wonderful, and in the end, the three we chose were separated from the rest by a points margin that was barely in the single digits. That’s how tight these folks were. They were really, really impressive.”—**Kelly Lenox**



Timer Dr. Gary Bird kept the event running efficiently by raising warning cards as the minutes wound down.

PHOTOS: STEVE MCCAWE

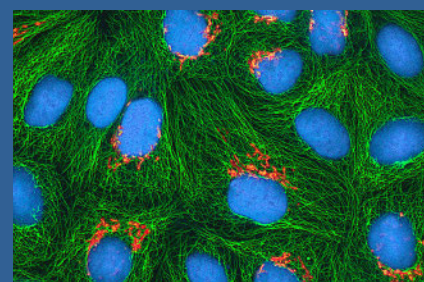
## Postbac Poster Day Set, May 4

Postbac Poster Day, set for Thursday, May 4, will be held at the Natcher Conference Center from 10 a.m. to 3:30 p.m.

The keynote address will begin at noon, followed by presentation of mentoring awards. Poster session I will take place from 10 a.m. to noon; poster session II goes from 1:30 to 3:30 p.m.

Postbacs share research they have been conducting at NIH and develop their scientific communication and networking skills. Investigators, staff scientists and scientific administrators contribute by visiting posters and engaging authors in discussion.

For more information, visit [https://www.training.nih.gov/postbac\\_poster\\_day](https://www.training.nih.gov/postbac_poster_day).



ON THE COVER: *Multiphoton fluorescence image of cultured HeLa cells with a fluorescent protein targeted to the Golgi apparatus (orange), microtubules (green) and counterstained for DNA (cyan)*

IMAGE: TOM DEERINCK

### The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email editor or phone (301) 496-2125.

**Editor:** Rich McManus  
[Rich.McManus@nih.gov](mailto:Rich.McManus@nih.gov)

**Associate Editor:** Carla Garnett  
[Carla.Garnett@nih.gov](mailto:Carla.Garnett@nih.gov)

**Staff Writers:**  
Eric Bock • [Eric.Bock@nih.gov](mailto:Eric.Bock@nih.gov)  
Dana Talesnik • [Dana.Talesnik@nih.gov](mailto:Dana.Talesnik@nih.gov)

Subscribe via email: [listserv@list.nih.gov](mailto:listserv@list.nih.gov) Follow: <http://nihrecord.nih.gov/>



The *NIH Record* is recyclable as mixed paper.

**NIH** National Institutes of Health  
*Turning Discovery Into Health*

## Neuromod

CONTINUED FROM PAGE 1

induced seizures in patients by shocking them with electricity. Two years later, at an American Psychiatric Association meeting in Cincinnati, shock therapy made its U.S. debut, said NIMH's Dr. Matthew Rudorfer. He was one of two speakers from that institute who walked a Lipsett Amphitheater Grands Rounds audience through the history and future prospects of "non-invasive neuromodulation" on Mar. 15.

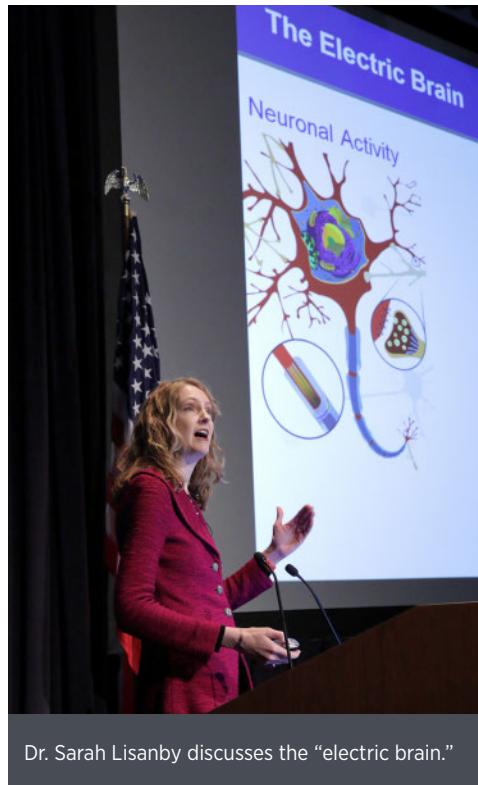
Over the years, ECT has come in and out of fashion, said Rudorfer, who came to NIH in 1985 and has been involved in protocols employing ECT in Clinical Center patients with depression, and more recently has worked with NIMH grantees around the country seeking to optimize the intervention. True, in its early days, shock therapy fractured bones and broke teeth, but it has also offered relief in the most intractable cases of depression. Its adherents, including Kitty Dukakis, wife of former presidential hopeful Michael Dukakis, swear by its efficacy. The ECT of the moment is kinder and gentler than its brutal predecessor.

The notion that causing a seizure might be helpful in patients with mental problems began not with electricity, but with camphor oil, Rudorfer explained. In 1934, Hungarian physician Ladislav Meduna induced an epileptic seizure in a 33-year-old man with catatonic schizophrenia who had been suffering for 4 years in that state. After 5 injections of camphor, the patient came to in his right mind and asked how long he had been hospitalized. When told, he was incredulous.

This speaks to two of convulsive therapy's enduring virtues—rapidity of response and efficacy, Rudorfer noted. Given that depression is the largest cause of disability worldwide, and increased by 18 percent in the years 2005-2015, shock therapy is not yet ready for retirement.

Multiple studies pitting ECT versus anti-depressant medications over the years have shown that ECT has the upper hand in cases of severe depression, acute psychosis and some cases of schizophrenia, said Rudorfer. "We have a lot of options today, but still not enough."

These days, ECT is administered to a sleeping, anesthetized patient pre-treated



Dr. Sarah Lisanby discusses the "electric brain."

with muscle relaxants. There is no thrashing about, small currents are applied in ultra-brief pulses, and electrode placement is more judicious—putting both leads on the right side of the scalp has proven more beneficial than the original scheme of attaching electrodes on both sides. Patients wake up less confused, have fewer memory problems and tend to do well.

However, "Even when it works well, ECT doesn't prevent relapse," said Rudorfer. One study showed that, over 6 months, 84 percent of ECT patients relapse when the therapy is not accompanied by some kind of antidepressant drug.

A recent NIMH cooperative agreement study dubbed Prolonging Remission in Depressed Elderly (PRIDE), conducted at 12 sites and enrolling 240 acutely depressed patients, demonstrated an impressive remission rate greater than 60 percent. Among those whose depression had remitted, patients who received a personalized schedule of maintenance ECT sessions in addition to medication (an antidepressant plus lithium) exhibited "a significantly lower incidence of relapse," Rudorfer said, compared to those randomized to maintenance medications only.

It is still not clear how ECT works, but it is thought to involve dopaminergic circuits

in the brain, he said. "Brain imaging and circuitry studies are ongoing."

Rudorfer said ECT is still not universally available in the U.S. "There is still lots of prejudice and stigma, and there are legislative restrictions in some states." He anticipates further minimization of cognitive adverse effects in ECT and the development of more focal, localized brain stimulation techniques.

The second speaker, Dr. Sarah Lisanby, director of NIMH's Division of Translational Research and director of the noninvasive neuromodulation unit in the Experimental Therapeutics and Pathophysiology Branch, dialed the voltage down dramatically. Her specialty is brain stimulation technologies including transcranial magnetic stimulation (TMS), a therapy born abroad in 1985 but pioneered in this country at the Clinical Center. She said TMS has been transformative as a tool to test causal relationships between brain and behavior and to measure and modulate plasticity in the brain.

The normal human brain generates a weak electric field as it goes about its business. TMS induces small currents in the brain and is considerably more "non-invasive" than ECT (although its

★ ★ ★

*"We acknowledge that the brain is much smarter than we are...I think we can teach the old dog of ECT some new tricks."*

-DR. SARAH LISANBY

★ ★ ★

cousin, magnetic seizure therapy, or MST, induces focal seizures that, like ECT, exert an anti-depressive effect). TMS induces weak fields on the surface of the cortex and stimulates selected brain circuitry.

Lisanby and her colleagues are exploiting the targeted use of TMS to measure plasticity, or the ability of the brain to change before and after treatment.

"We can modulate plasticity in a lasting way, with therapeutic value," she said, "either as a stand-alone treatment or in combination with other modalities."

Cortical reactivity can be measured with standard tools such as EEG and EMG,



Rudorfer and Lisanby entertain questions after their presentation in Lipsett Amphitheater.

PHOTOS: ERNIE BRANSON

which have helped establish that deficient plasticity is a hallmark of schizophrenia and depression. Anything that can stimulate plasticity—such as repetitive TMS (rTMS)—can potentially remediate disease.

Lisanby said that 1.5 months of daily rTMS has been shown to exert a significant anti-depressant effect in depressed patients.

In 2008, the first TMS devices were cleared by the FDA. They normally induce no seizures in patients, have a remission rate of only 15-30 percent (three times less effective than ECT), have no known risk of memory loss and only a small risk of seizure, dependent on the dose.

“ECT is already highly effective, but we need to improve its neurocognitive safety,” said Lisanby. “In the case of TMS, it’s already very safe, but we need to enhance its efficacy.” Her vision of next-gen neuro-mod includes optimized, personalized TMS with improved precision in the spatial, temporal and contextual aspects of dosing.

At her most optimistic, she believes that sculpting of brain plasticity for therapeutic ends may be possible. One way to target the plastic changes is to engage the brain in a specific action while it is being stimulated, to target the effects of the stimulation to specific task-related networks. Lisanby has used this approach to improve working memory by having subjects perform a working memory task while receiving stimulation.

“We acknowledge that the brain is much smarter than we are,” she concluded.

“This is an exciting time...New tools are helping us discover more than we ever could a few decades ago. I think we can teach the old dog of ECT some new tricks.” **R**

## NEI Lecture Features Stanford’s Huberman

Figuring out how to get neurons to regenerate and re-integrate in the brain is one of the biggest unsolved challenges in neuroscience, said Dr. Andrew Huberman, professor of neurobiology at Stanford School of Medicine. NEI featured Huberman at a recent Audacious Goals Initiative seminar in neuroregeneration. His success in regrowing retinal ganglion cells—neurons that carry visual signals from the eye to the brain—suggests neural activity is key.

During development, retinal ganglion cells extend their long telephone wire-like axons from the retina in the back of the eye to visual centers all over the brain. Diseases such as glaucoma initially damage axons at the optic nerve, where the axons leave the eye, eventually causing cell death and potentially vision loss.



To see if he could recapitulate the developmental process in adult mice, Huberman injured the optic nerve from one eye and then tested a variety of known axonal guidance factors, including mammalian target of rapamycin (mTOR). He saw modest regrowth of axons with mTOR, but more robust growth when he combined it with exposure to high-contrast visual stimulation, achieved by placing the mice in a chamber displaying changing patterns of black lines for several hours each day. Growth was further enhanced by forcing the animal to use the injured eye.

“Regenerating retinal ganglion cell axons not only regrew from the site of injury, they preferentially re-innervated correct visual targets in the brain,” said Huberman. Three weeks after optic nerve crush, mice that received combination therapy experienced axonal growth at a rate 500 times greater than untreated animals.

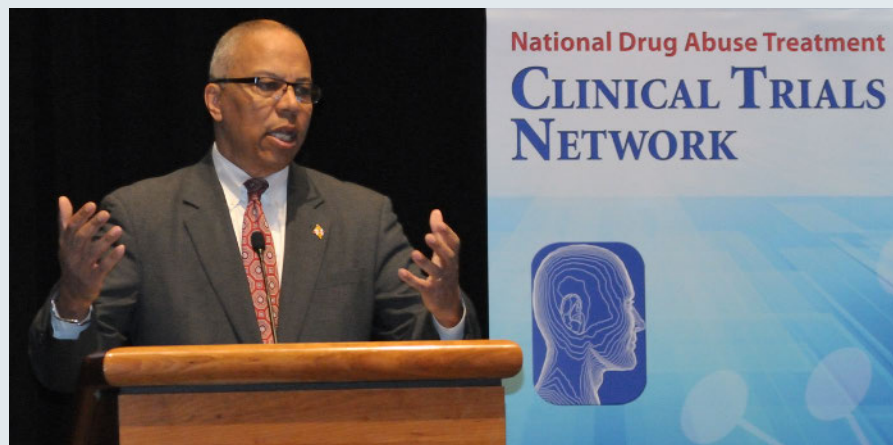
Huberman cautioned that the treatment restored only a small fraction of axons. “It’s very few axons—probably less than a hundred—that reach the brain.” Nonetheless, mice regained some visual function, suggesting the approach holds promise for treating disease and injury in people.

For more information about the AGI, including information about upcoming seminars, visit [www.nei.nih.gov/audacious](http://www.nei.nih.gov/audacious).

## Lieutenant Governor Opens NIDA Meeting

Maryland Lt. Gov. Boyd Rutherford presents opening remarks at the National Institute on Drug Abuse’s annual Drug Abuse Treatment Clinical Trials Network scientific meeting held Mar. 23-24 at Bethesda North Marriott Hotel & Conference Center. The gathering provides the CTN and its collaborators an opportunity to review and discuss the latest findings in substance abuse treatment research and their implications for substance use disorder researchers. Rutherford chairs the Maryland heroin and opioid task force.

PHOTO: ANTHONY DEPANISE



'AUDACIOUS  
GOALS'



At NIDCR Clinical Research Grand Rounds are (from l) NIDCR acting deputy director Dr. John Kusiak, NIDCR director Dr. Martha Somerman, Houry and NIDCR clinical director Dr. Janice Lee. Rounds occur four times a year to inspire clinical research trainees. Leading scientists and clinicians address advances in clinical, translational and basic research in areas related to the dental, oral and craniofacial complex and bone metabolism.

PHOTOS: ERNIE BRANSON

## Opioids

CONTINUED FROM PAGE 1

By the early 2000s, medical examiners and health departments in states such as Maine and North Carolina began to report growing prescription drug abuse and an increase in drug deaths due to prescription narcotics. In a decade and a half, the epidemic spread across the U.S.

What was driving these increases? CDC wanted to know.

After launching an investigation in 2004 with data from the Drug Enforcement Administration, the Substance Abuse and Mental Health Services Administration and other agencies, CDC published findings in 2006 in *Pharmacoepidemiology and Drug Safety*.

“We started seeing that it was linked to opioid sales,” Houry said. “There was a really close association between opioid analgesic deaths and opioid analgesic prescribing.”

### More Prescriptions, More Deadly

Data show that the amount of opioid prescriptions dispensed has quadrupled since 1999, Houry said. The pain Americans report, however, has not changed.

“About 250 million [opioid] prescriptions are written each year in the U.S.—enough for every single adult in the U.S. to have his or her own bottle of pills,” she noted. Americans account for more than 80 percent

of the world’s opioid consumption.

Prescription opioids can be blamed for 165,000 deaths since 1999, Houry continued. Factor in illicit opioids such as heroin and fentanyl, and 78 people die each day in the U.S. from an opioid.

In addition, data show that misusing a pain prescription puts people at risk of using heroin. Three out of 4 people who used heroin in the past year misused opioids first.

“A lot of the changes are thought to be due to the widespread availability of illicit drugs,” Houry said. Another reason for the increase in overdose deaths is that today’s drugs are so deadly, she

pointed out. Fentanyl is a hundred times more potent than a regular prescription pain reliever such as Vicodin. As a result, emergency medical service providers now need higher doses of anti-opioids to reverse overdoses.

“One of the ways we can change this [deadly cycle] is by focusing on not having people get addicted to prescription opioids in the first place,” Houry said. “Then they wouldn’t be going on to use heroin and fentanyl.”

### Prescribers Play a Part

The National Institute of Dental and Craniofacial Research, a founding institute of NIH’s Pain Consortium, invited Houry’s opioid conversation.

“Opioids are an important topic for us because dentists are one of the major prescribers of immediate-release opioids,” said NIDCR acting deputy director Dr. John Kusiak, who introduced the lecture. “Oral-facial pain is one of the important common pain conditions that afflicts people in the United States.”

Overall, dentists prescribed more than 6 percent of all opioids in 2012, Houry reported. For patients ages 10 to 19, 30 percent of prescription opioids come from dentists. Youngsters often are initiated to

opioid use following tooth extractions or athletic injuries.

Practitioners need to think about alternatives to opioids and perhaps to prescribing drugs in general, Houry said. Non-steroidal medications to manage pain and non-drug options such as exercise therapy should be considered more often.

“We need to manage pain, but we need to manage pain appropriately and safely,” she emphasized.

### Awareness Important, Prevention Paramount

Last year, CDC released its *Guideline for Prescribing Opioids for Chronic Pain*. The document targets primary care providers for adults ages 18 and older in outpatient settings. People who have active cancer diagnoses or who need palliative or end-of-life care were specifically excluded.

In general, CDC recommends that opioids not be routine therapy for chronic pain, that they be prescribed at the lowest effective dosage and that all patients be monitored closely.

“As practitioners, we have to realize that everything we do has a long-term impact—for better or worse,” Houry said.

She noted that CDC prevention efforts have three pillars: improve data quality, timeliness and track trends; strengthen state initiatives by scaling up effective public health interventions; and equip health care providers with information and tools for evidence-based decision-making.

CDC also urges more practitioners to use state PDMPs, or prescription drug monitoring programs. Such tools help prescribers keep track of critical clinical data that could warn of possible drug interactions or signal a patient’s potential risk for overdose.

Still, ER physician Houry concluded, tools and knowledge of trends cannot replace actual conversations between individual patients and their health care providers about prescription use—and abuse.

“At CDC, I was able to take a step back and look at the big picture view, look at data and what we could do with state health departments,” she said, “but I think it’s important to keep that grasp of reality on the ground and remember those faces and those stories, because that’s really what should drive what we do—the patients and the public.” **R**

## Manipulated Cells Can Rebuild Damaged Tissue, Says West

BY RAYMOND MACDOUGALL

Biomaterials expert Dr. Jennifer West is a leader in her cutting-edge field, a field inventor at two companies, holder of 20 biotechnology patents and the Fitzpatrick family university professor of engineering and associate dean for Ph.D. education at Duke University's Pratt School of Engineering. She spoke Mar. 22 at the NIH Director's Wednesday Afternoon Lecture Series.

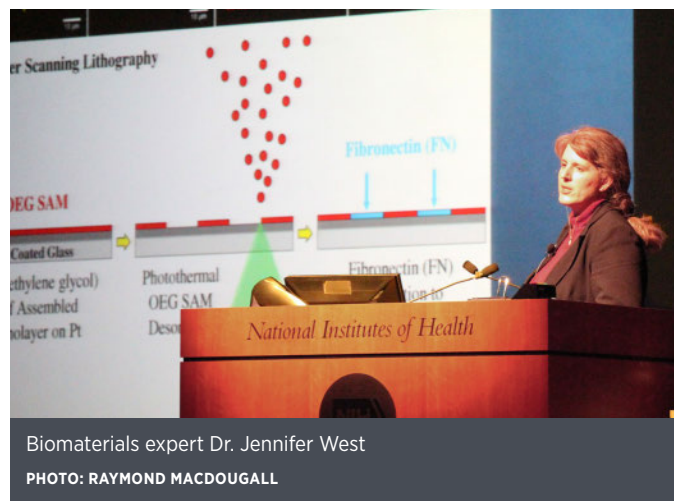
West's talk focused on work in her lab to design biomaterials for regenerative medicine, a field that includes tissue engineering and research on self-healing, where the body uses its own systems, sometimes with help from foreign biological material, to recreate cells and rebuild tissues and organs. She described several projects that use regenerative medicine principles to create controlled environments for cells where researchers can manipulate cell behaviors.

From 2006 to 2009, West was part of a team that received the first Quantum Grant from NIH's National Institute of Biomedical Imaging and Bioengineering. Quantum Grants support research projects that target solutions to a major medical or public health challenge through technological innovation. The project investigated ways to regenerate damaged brain cells and blood vessels for the treatment of stroke.

Since that time, West has been a principal or co-investigator on a range of NIH-funded projects that continue to push the envelope with ever more sophisticated techniques, moving into the realm of bioprinting—first in 2-D and then with 3-D printing. Of her current work with cell regeneration, West said, "It's not just a cell's identity, but how it is spatially localized and organized, which controls the signals for cell differentiation, proliferation and other behaviors."

Among the technologies featured in her lecture, West described bioprinting in hydrogel layers with strategically positioned, nano-scale chemical switches, some that are turned on with laser optics. The switches send cellular signals at times and at locations that are critical in forming cell material. The approach uses cues from nature that can mimic some of the functions and spatial relationships of the extracellular matrix—the structural and biochemical support to the surrounding cells.


"You can take images from vasculature of lots of different tissues that give us different geometries and chemo-dynamics—and then generate those same patterns in hydrogels," West explained. The



Biomaterials expert Dr. Jennifer West

PHOTO: RAYMOND MACDOUGALL

patterns resemble the capillaries on the underside of a leaf, but each is distinct, to mimic the vasculature of such tissues as heart, brain and the retina.

"This is an exciting time, where cell biology is advancing, providing a lot more information about how to design systems to get the best possible tissue engineering and medicine outcomes," West said. "But where engineering is advancing we can really contribute a lot to tools that help us develop a better understanding of cell biology. Hopefully, as we move forward we'll see the iterative interactions between those two fields and reap the benefits that can come from engineering and biology working together." 

## Roberts Series To Feature NICHD's Storz, May 16

NICHD associate scientific director Dr. Gisela Storz will give the 2017 lecture in the Anita B. Roberts Lecture Series: Distinguished Women Scientists at NIH, sponsored by the NIH women scientist advisors committee. Her talk, "The hidden



secrets of small genes," will be held Tuesday, May 16 at 1 p.m. in Lipsett Amphitheater, Bldg. 10. This series highlights outstanding research achievements of women scientists in the Intramural Research Program at NIH.

Storz's research focuses on identification and characterization of small and often overlooked classes of biological molecules. This includes identification and characterization of regulatory RNAs in *E. coli* and proteins of less than 50 amino acids.

Storz is a fellow of the American Academy of Microbiology, American Academy of Arts and Sciences and National Academy of Sciences, and received the American Society for Microbiology Eli Lilly Award in 2000. Mentoring is important to Storz; she has received both the Distinguished Mentor Award presented by postbaccalaureate trainees and the Outstanding Mentor Award from the graduate student trainees.

The seminar series is dedicated to the memory of Dr. Anita B. Roberts, former chief of NCI's Laboratory of Cell Regulation and Carcinogenesis from 1995 to 2006. Prior to her death in May 2006, she spent 30 years at NIH as a research leader.

The lecture is open to all and will be followed by a reception to talk with Storz about career issues for women in science. Individuals with disabilities who need reasonable accommodation to participate should contact Margaret McBurney at (301) 496-1921 and/or the Federal Relay, 1-800-877-8339, 5 days before the lecture.

## Belkaid To Give Dyer Lecture

APR. 26

Dr. Yasmine Belkaid, director of the NIAID Microbiome Program and chief of the mucosal immunology section, will present the annual Rolla E. Dyer Lecture at 3 p.m. on Wednesday, Apr. 26 in Masur Auditorium, Bldg. 10. Her talk is titled "The primary shield: role of our microbes in health and diseases."



Belkaid's work explores the field of immune regulation and has defined fundamental mechanisms that regulate tissue homeostasis and host immune responses. Her work uncovered key roles for the commensal microbiota and dietary factors in the maintenance of tissue immunity and protection against pathogens.

Established in 1950, the lecture series honors former NIH director Dr. Rolla E. Dyer, a noted authority on infectious diseases.

## Safety

CONTINUED FROM PAGE 1

patients. Then, Dr. Peter Pronovost, senior vice president for patient safety and quality at Johns Hopkins Medicine and director of Johns Hopkins' Armstrong Institute for Patient Safety and Quality, chronicled efforts to improve patient safety using principles of high-reliability organizations.

In 2009, Gilman had oversight responsibility of a military hospital. Back then, a young nurse alerted the hospital's chief nurse to the improper use of insulin pens. The pens are intended for single patient use because of the risk of transmitting blood-borne diseases.

Although nurses changed the needle for every patient, they used the same pen on multiple patients.

The chief nurse alerted hospital leadership. They determined 2,114 patients with diabetes received treatment at the hospital. There was no way to find out who received insulin from a pen used in another patient.

"There is really no way to keep this quiet with 2,114 patients," said Gilman. "There was a lot of interest in the media."

The hospital alerted the Food and Drug Administration, let the public know what happened and set up a call center to answer questions from patients. The hospital also contacted affected patients and offered HIV and hepatitis A, B and C testing and treatment.

Once the incident went public, local press and elected officials called for someone to be held accountable. The hospital commander suggested reprimanding the chief nurse. Gilman advised this approach wouldn't help. It would discourage other nurses from speaking up when they saw a problem. Although many nurses were involved, they didn't realize they violated safety protocols. The commander never reprimanded anyone.

"This was clearly a systems error," Gilman said. The hospital did everything it needed to do—from building a culture where young nurses can speak up without fear to offering free treatment. Scapegoating a nurse wouldn't have helped the situation.

Next, Pronovost recounted his efforts to reduce the frequency of medical errors at Johns Hopkins Hospital and Health System, which consists of 6 hospitals, 10 surgery

centers, 90 primary care sites and 3 home care companies.

In 2001, a young girl named Josie came into the Hopkins pediatric intensive care unit with burn wounds. Although she was treated, she contracted a catheter-related bloodstream infection and died. At the time, Pronovost thought, "When you care for sick people, sometimes little girls like Josie are going to die."

On the anniversary of Josie's death, her mother asked Pronovost if things [at the hospital] were better. He couldn't say yes, but promised improvements.

He introduced a 5-item checklist for preventing bloodstream infections. Soon after, the infections disappeared at Hopkins. "We took this program and spread it state by state across the U.S. and, now, to 15 countries," he said. These types of infections are now down by 80 percent across the country.

The hospitals most successful at fighting infections create an "infrastructure to improve." Pronovost said these organizations did several things. They declared a goal of zero infections, organized training programs, gave clinicians relevant data and helped with project management. Doctors regularly met with leadership. The organizations also transparently reported results.

Pronovost said clinicians at the hospitals believed a kind of mantra: "Infections are preventable and I am capable of doing something about it." They thought this because their bosses trusted them and, in turn, clinicians talked among themselves about how to improve. There was a culture of learning, not judging.

"We felt pretty good about that story until I had to look into the eyes of another mother who lost a child," he said. "Nothing humbles you more than looking into the eyes of a parent who had a child die needlessly from medical errors."

The girl succumbed to cardiac arrest after undergoing elective orthopedic surgery. She had been given pain medication that stopped her breathing. In the operating room, a drug infusion pump didn't communicate with the monitor that measures breathing. No one knew what happened until it was too late.

That prompted Pronovost to study highly reliable systems or organizations that regularly perform complex, dangerous actions without catastrophe.



Dr. Peter Pronovost, director of Johns Hopkins' Armstrong Institute for Patient Safety and Quality, chronicled efforts to improve patient safety using principles of high-reliability organizations.

PHOTOS: BILL BRANSON

He discovered that such organizations standardized wherever they could and fostered resiliency. They also respected every employee, each of whom was taught that he or she has two jobs—the one they are hired to do and the job to make the workplace better.

"These organizations don't see quality as this whack-a-mole game," Pronovost explained. "Rather, it's an integrated structure of governance, leadership and management, capacity-building and informatics, all aimed towards zero harm."

At Hopkins, a computer program keeps track of 1,300 measures across the entire system. The analytics focus on safety, patient experience, best practices and health care equality.

"Too often, accountability means 'I shame you by starving you of resources,'" Pronovost concluded. "What we created in this shared accountability system is a very simple model that says 'Any higher level in the organization is only allowed to hold a lower level accountable if they hold themselves accountable to maximally set those under them up to succeed.'" **R**





Data showed that young people with a new psychosis diagnosis had surprisingly low rates of medical oversight and only modest involvement with psychosocial treatment providers.

## Higher Death Rate Among Youth With First Psychosis

A new study shows that young people experiencing first episode psychosis have a much higher death rate than previously thought. Researchers analyzed data on approximately 5,000 individuals ages 16-30 with commercial health insurance who had received a new psychosis diagnosis and followed them for the next 12 months. They found that the group had a mortality rate at least 24 times greater than the same age group in the general population in the 12 months after the initial psychosis diagnosis.

The study, funded by NIMH, underscores that young people experiencing psychosis warrant intensive and proactive treatments, services and support.

The research, led by Dr. Michael Schoenbaum, senior advisor for mental health services, epidemiology and economics at NIMH, was published online Apr. 6 by *Schizophrenia Bulletin*.

The research team used insurance claims data to identify young people ages 16-30 who had been diagnosed with a first episode of psychosis in 2008-2009. They used data from the Social Security Administration to identify deaths in this population within 12 months of the initial psychosis diagnosis. Data on cause or manner of death were not available for this research.

The 12-month mortality rate for these young people—from any cause—was at least 24 times higher than their peers in the general population. In the general United States population, only individuals over age 70 come close to a similar 12-month mortality rate.

“These findings show the importance of tracking mortality in individuals with mental illness,” said Schoenbaum. “Health systems do this in other areas of medicine, such as cancer and cardiology,

but not for mental illness. Of course, we also need to learn how these young people are losing their lives.”

In addition to mortality, the study examined the health care individuals received in the 12 months after the initial psychosis diagnosis. Those data showed that young people with a new psychosis diagnosis had surprisingly low rates of medical oversight and only modest involvement with psychosocial treatment providers.

## Monoclonal Antibody Cures Marburg Infection in Monkeys

Scientists funded by NIH have found that an experimental treatment cured 100 percent of guinea pigs and rhesus monkeys in late stages of infection with lethal levels of Marburg and Ravn viruses, relatives of the Ebola virus. Although the Marburg and Ravn viruses are less familiar than Ebola virus, both can resemble Ebola in symptoms and outcomes in people and both lack preventive and therapeutic countermeasures.

The research was published Apr. 5 in *Science Translational Medicine*.

The study involved giving the animals a therapeutic candidate, MR191-N, which is a monoclonal antibody derived from a person who survived Marburg disease. Monoclonal antibodies are immune system fighters designed to bind to a specific part of an invading virus or bacterium to treat disease.

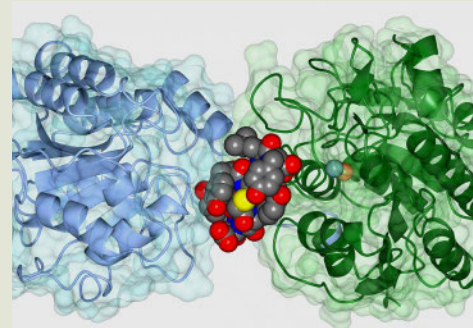
The authors report that two doses of MR191-N were able to confer protection of up to 100 percent when treatment was started up to 5 days post infection. Prior studies of different experimental Marburg treatments involved daily dosing for 7 and 14 days, respectively, with treatment beginning closer to the time of infection.

The study was led by scientists at the University of Texas Medical Branch Galveston National Laboratory and Mapp Biopharmaceutical, Inc., and included collaborators from Vanderbilt University Medical Center, the University of Natural Resources and Life Sciences in Austria and the Scripps Research Institute. NIAID provided project funding.

The researchers are now working with NIAID's preclinical services group to perform the additional safety testing necessary to advance the monoclonal antibody treatment to initial human clinical studies.

## International Scientific Teams Find Potential Approach Against Parasites

Research teams from NIH and abroad have identified the first inhibitor of an enzyme long thought to be a potential drug target for fighting



The cyclic peptide ipglycermide binds to an iPGM enzyme, blocking its activity.

disease-causing parasites and bacteria. The teams, led by NCATS and University of Tokyo scientists, sorted through more than 1 trillion small protein fragments called cyclic peptides to uncover two that could shut down the enzyme.

The finding, reported Apr. 3 in *Nature Communications*, could set the stage for the potential development of new types of antimicrobial drugs.

NCATS' expertise in early-stage, pre-clinical molecule discovery helped the teams find potential drug candidates that could have implications for millions of people worldwide.

“The work is an excellent demonstration of how NCATS delivers on its mission to provide improvements in translational processes,” said Dr. Anton Simeonov, scientific director, NCATS Division of Pre-Clinical Innovation. “Scientists have shown that a therapeutic target, previously considered undruggable by pharmaceutical companies, is actually druggable through a non-traditional therapeutic agent.”

The target enzyme, cofactor-independent phosphoglycerate mutase (iPGM), is found in both parasites and bacteria.

Several types of parasitic roundworms have iPGM, including *Brugia malayi* and *Onchocerca volvulus*, which infect roughly 150 million people living mostly in tropical regions. These parasites can cause devastating infectious diseases such as river blindness.

The enzyme also is found in bacteria, including *Staphylococcus aureus*, which can cause the hospital-borne infection MRSA (methicillin-resistant *Staphylococcus aureus*), and *Bacillus anthracis*, which causes anthrax.

## Caspi Named Chief of NEI Laboratory of Immunology

Dr. Rachel Caspi has been named chief of the NEI Laboratory of Immunology.

A longtime member of the NIH intramural community, Caspi is among the

foremost authorities on uveitis—an autoimmune disease of the eye that accounts for up to 15 percent of blindness in developed nations. Her uveitis mouse model has been adopted worldwide, enabling significant contributions to understanding of the disease. Her studies of basic mechanisms driving uveitis have informed the design of clinical trials for uveitis.

In 2015, she showed that intestinal bacteria are capable of triggering uveitis by a mechanism involving recognition of a surrogate bacterial antigen, a finding with implications for other autoimmune disorders.

“Dr. Caspi has repeatedly introduced new concepts, challenged established dogmas and shifted paradigms—driving the uveitis field forward and creating new lines of inquiry,” said NEI scientific director Dr. Sheldon Miller.

Caspi holds a Ph.D. from Bar Ilan University, Israel. She joined NEI in 1984 as a visiting fellow in the Laboratory of Immunology. Since 1990, she has served as chief of the lab’s section on immunoregulation. She is also an adjunct professor at the University of Pennsylvania. She served as deputy chief of the Laboratory of Immunology from 1999 until she became acting chief in 2016.

“Throughout her career, Dr. Caspi has been devoted to training, earning a reputation as one of the NEI’s most outstanding and effective mentors,” said Miller. She has mentored more than 60 trainees.

Caspi has authored or coauthored more than 230 publications. She is the recipient of the 2010 Friedenwald award and the 2012 Alcon Research Institute award.



Dr. Rachel Caspi

## NIGMS Gains Science Education Coordinator, Program

Dr. L. Tony Beck recently joined NIGMS as a program director in the Center for Research Capacity Building. In that role, he will continue to direct the Science Education Partnership Award program and other educational and diversity pipeline efforts that target pre-K to grade 12 students.

Prior to joining NIGMS, Beck managed science education projects in the Office of Research Infrastructure Programs and in the former National Center for Research Resources. During his 11 years at NCRR, he also managed Clinical and Translational Science Awards and human embryonic stem cell infrastructure programs. He started his NIH career in 2000 as a scientific review officer at NIAAA. For the decade before that, he worked for three different biotechnology companies in Maryland.

Beck earned B.A. and M.S. degrees in biological sciences at the University of California, Riverside, and a Ph.D. in cell and molecular biology from the University of California, Irvine. He conducted postdoctoral research in Denver at the University of Colorado Health Sciences Center and the Eleanor Roosevelt Institute for Cancer Research in Denver.



Dr. L. Tony Beck

## ORF Project ‘Big Gun’ Kutlak Retires

BY RICH MCMANUS

If the many major research buildings he honchoed to completion on the NIH campus and Ft. Detrick are as fun to work in as he had making them, then Frank Kutlak can consider his 25 years as an architect and project manager at the Office of Research Facilities a rousing success.

The string of big buildings came to an end recently when Kutlak retired. No more will he rise before dawn to oversee the pouring of concrete at 4 a.m., as he did when his favorite project, the Louis Stokes Laboratories, was under construction in the late 1990s. On that job, he gleefully inspected every detail from the sand at the bottom of the caissons dug to support the structure to the last beam topping the roof, where he was instrumental in having an extra story built atop what was originally a 5-story building.

At a sendoff Mar. 30 in the Cloister, ORF Director Dan Wheeland credited Kutlak with delivering “exceptional projects, nothing ever boring or routine...I can’t imagine NIH functioning without those facilities. The campus would look much different.”

Kutlak’s projects, in addition to the Stokes Labs, included the occupancy phase of the Silvio O. Conte Bldg.; the NIAID Integrated Research Facility at Ft. Detrick; the John Edward Porter Neuroscience Research Center II; the ARC, a study for a future animal center on the south side of campus; and the design phase of the renovation of Bldg. 10’s E-wing, which was Kutlak’s last official duty.

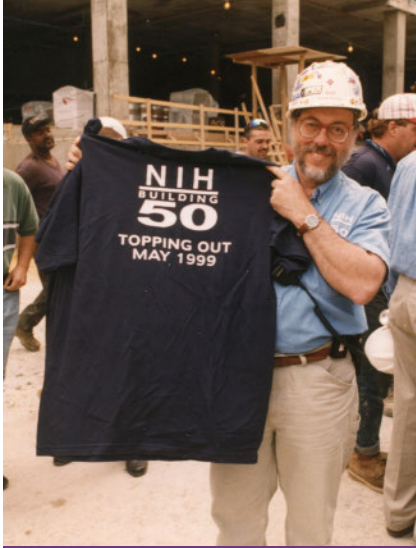
“Frank earned the status of being a big

## Kester Heads NCCIH Policy Office

Mary Beth Kester is the new director of the Office of Policy, Planning and Evaluation at NCCIH. She came to NCCIH from NIAMS, where she was a health policy analyst whose duties included overseeing the Science Policy and Planning Branch staff. Prior to working at NIAMS, she was a health policy analyst at NIBIB and NIDDK. Kester holds a master of science degree in toxicology from the University of Maryland.

PHOTO: BRYAN EWSICHEK





At left, Frank Kutlak proudly displays commemorative T-shirt marking the “topping out” of Bldg. 50 (Stokes Laboratories) on May 13, 1999. “I’m having fun,” he said that day. “I feel sort of like the father of the bride.” PHOTO: RICH MCMANUS At right, Kutlak (l) with Rep. Louis Stokes at the dedication ceremony for the official Stokes portrait in March 2013 PHOTO: ERNIE BRANSON

gun,” said Wheeland. “He never let us down. He is an authentic person who always lets you know what he thinks. We always counted on him to tell us what he thought and we appreciated his expert advice...Frank gave it all he had. He has been instrumental in making NIH such a great institution.”

“I have been very fortunate that I got to do all of these big projects,” said Kutlak. “It’s

Kutlak took a job with Marriott Hotels in Bethesda that lasted 6 years. “I managed the design and construction of 75 of the 200 Marriott Courtyards,” he recalls. “I came to NIH 6 months after the bottom fell out of the hotel market.”

His first assignment at NIH was organizing occupancy of then-new Bldg. 49, the Conte Bldg. At one point, ORF had to



*“Frank earned the status of being a big gun. He never let us down....[He] gave it all he had. He has been instrumental in making NIH such a great institution.”*

-DAN WHEELAND



never one person [who should be credited]...I’ve just been driving the bus. There were hundreds of hardworking ORS/ORF service providers, consultants, IC staff and scientists on the bus.”

Kutlak, a native of Buffalo, arrived on campus in June 1991. He had begun his career in the desert of Saudi Arabia, where for 6 years he worked for ARAMCO. Returning to the United States in 1983, he took a job with HOK Architects in Manhattan, which is where he met his wife, Barbara Thompson, a Clinical Center nurse for the past 31 years.

They spent two years in New York, then

inform two floors of IC scientists that they would not be moving into 49 as planned because then-NIH director Dr. Bernadine Healy had decided a highly regarded new recruit from the University of Michigan would get their space in the new building—it was Dr. Francis Collins.

Kutlak’s next job was the one that made him proudest.

“Lou Stokes was very nice to me,” said Kutlak, “very generous.” Kutlak took pleasure in touring Bldg. 50 as it was under construction with Stokes and his wife Jay.

Their relationship did not end when the building was complete.

“We kept in touch,” said Kutlak. “He invited me to various luncheons and to the opening of the Howard University Health Sciences Library, which is also named in his honor.”

A resident of Laytonsville, Md., Kutlak says he won’t miss the early morning drives down 270. He and Barbara enjoy their three Dobermans and a 7-acre property on which Kutlak grew 95 tomato plants of various kinds last summer, in addition to lettuce, spinach and other vegetables. He has high hopes for this year’s crop, having built a seedling incubator, with special heating and lighting, over the winter to raise his own plants from seed.

“I’ve been getting into it,” he said. “It’s kind of fun.”

He had grown up in the city of Buffalo, but his family owned 13 acres outside of town, near the site of what is now the University of Buffalo. “I basically sat on my father’s lap” as he worked the property with an old Farmall tractor, Kutlak remembers.

Five years ago he found, on the Internet, a 1947 Farmall tractor on sale in Virginia. He bought it and now mows his own 4-acre field with the bush-hog attachment on the tractor’s rear. He belongs to and manages Facebook pages for two antique tractor clubs, which he joined in order to learn more about maintaining his rig.

“It’s a beast, it’s a bear,” he said of the 70-year-old tractor, “but it runs wonderfully.”

“Frank is leaving us because his exotic tomatoes await him,” concluded Wheeland. “How could that be more interesting than NIH projects?...We thank you for an amazing journey.”

A Kutlak anecdote about his experience in Saudi Arabia could serve as the defining metaphor for the projects that occupied him at NIH: “Every time they drilled for water, they hit oil.”

He hopes to keep in touch with people he worked with over the years and can be reached at [kutlakf@verizon.net](mailto:kutlakf@verizon.net). **B**



As in years past, clowns from the circus visited NIH prior to the evening performance, stopping at both pediatric units in the CC as well as at the inn. Above, Jahmir Glenn (l) smiles at the comical antics.

## Last Time Around for Circus, Clown Visits

PHOTOS: ERNIE BRANSON, MICHAEL SPENCER

NIH patients, employees and their families were able to attend a special evening with the 146th and final edition of Ringling Brothers and Barnum & Bailey Circus. The event Mar. 30 at Verizon Center adopted a theme of intergalactic adventure.

For 20 years, the NIH R&W has partnered with Easter Seals to offer local children the chance to see circus performances in Washington, D.C. Both organizations bring many guests who normally would not be able to attend.

The evening begins with a pizza party for patient families from the Clinical Center, the Children's Inn

at NIH and families from Special Love Inc., which sponsors Camp Fantastic. This year, R&W was also able to host families from Montgomery County social service agencies, Operation Second Chance with military families from Walter Reed, along with many clients of Easter Seals. Total attendance for the evening was close to 9,000.

"Our gratitude [to R&W] is unbounded," said Sue Kirk, executive director of Bethesda Cares. Added Holly Parker of the CC, "The children had a magical time and will always remember the evening. I have many fond memories of all the lives touched by R&W and its efforts."

As in years past, clowns from the circus paid a call to NIH prior to the evening performance, stopping at both pediatric units in the CC as well as at the inn.



Sophia Trujillo takes a selfie in a CC corridor. This is the 20th year that Ringling Brothers has dispatched its comic emissaries to NIH, toting cheer for children, families and staff.



Kristen Wells (r) enjoys visit from circus clowns making their annual pilgrimage to NIH.



ABOVE: **Last Grand Rounds.** In a final visit to Clinical Center patient units by Ringling Brothers and Barnum & Bailey clowns, kids and families alike engage with the pranksters. At left, Avery Ponzar is treated to an impromptu concert. At right, kids at Verizon Center clown around before the evening show begins.



Young driver Ellasyn Berry offers a lift to visiting circus clowns as well as Rylan Michael Pederson.