

Price Makes First Visit to NIH As HHS Secretary

Dr. Thomas E. Price was sworn in as the 23rd Secretary of Health and Human Services on Feb. 10. He came calling at NIH on Feb. 21. An orthopedic surgeon when he practiced medicine, Price most recently served as U.S. representative of Georgia's 6th congressional district.

While on campus, the new Secretary met with several NIH leaders including NIH director Dr. Francis Collins, principal deputy director Dr. Lawrence Tabak and several institute and center directors. He also took a brief tour of the Clinical Research Center and discussed a clinical case with NCI Surgery Branch chief Dr. Steven Rosenberg.

SEE **SECRETARY**, PAGE 3



NIH director Dr. Francis Collins welcomes Dr. Thomas E. Price, the new HHS Secretary, on Feb. 21. Below, NCI's Dr. Steven Rosenberg discusses his research with Price.



WHY REMISSION FAILS

'Great Teacher' Sawyers Describes Cancer Drug Resistance

BY CARLA GARNETT

Dr. Charles Sawyers has spent much of the last two decades trying to outsmart relentlessly clever and resilient tumor biology. Over the years, he's used a simple formula with great success: Serendipity plus collaboration mixed with persistence equals remarkable results.

An HHMI investigator since 2002 who currently chairs the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering Cancer Center, he shared other lessons he's learned recently at a talk in NIH's Lipsett Amphitheater.

Sawyers delivered "The Changing Landscape of Cancer Drug Resistance," the Clinical Center's 2017 Distinguished Clinical

SEE **SAWYERS**, PAGE 6



Trailer will house GMP manufacturing at CRC. See story at right.

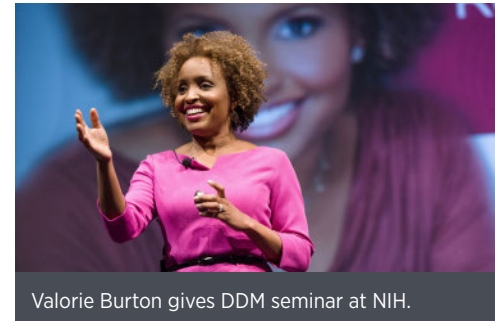
Temporary Manufacturing Facility Parked at CRC

BY DANA TALESNIK

It's not the site of a film crew and nobody's living in it. But NCI investigators soon will spend long hours in a 53-foot trailer parked by the ambulance entrance on the west side of the Clinical Research Center. And more trailers are on order or in the design phase.

From the outside, the white trailer bearing NIH's logo looks plain, but this is no ordinary rig. The aseptic, state-of-the-art module is a mini version of a large, sterile product manufacturing facility, explained Kurt Last, executive vice president of WorkingBuildings Group. His team supported NIH's Office of Research Facilities by designing the module and worked with NCI to specify the manufacturing equipment in it. They're now busy testing the controls, support systems and software so Trailer 1 is ready to spring into service in April.

SEE **TRAILERS**, PAGE 8



Valorie Burton gives DDM seminar at NIH.

Resiliency Needed in Times of Stress, Change, Burton Says

BY ERIC BOCK

Resilient people share common characteristics. They tend to see the big picture, learn from their failures, reach out to others and give back to their community, said Valorie Burton, founder of the Coaching and Positive Psychology Institute.

"Resilience is not just our ability to bounce back from setbacks," she said at a recent Deputy Director for Management

SEE **BURTON**, PAGE 4

ALSO THIS ISSUE

Briefs	2
Wagers To Give Mahoney Lecture; High School Student Shadows NIH Engineers	5
Digest	7
Milestones	10
Volunteers	11
Researchers Connect at 3rd BRAIN Investigators' Meeting	12

NINR To Hold Symptom Science Research Symposium

On Apr. 25, the National Institute of Nursing Research will convene a scientific symposium—Symptom Science Research: A Path to Precision Health—highlighting the NINR Intramural Research Program’s scientific advances and collaborations across NIH and other organizations. The symposium will take place in Masur Auditorium, Bldg. 10, from 8 a.m. to 2:30 p.m.

The NINR Intramural Research Program is dedicated to conducting basic and clinical research on the biological, genetic and behavioral mechanisms underlying symptoms of chronic conditions. The ultimate scientific goal is to enhance patient outcomes for individuals with conditions such as digestive disorders, cancer-related fatigue and traumatic brain injury.

The symposium will include scientific panels on: The Role of the Gut-Liver-Brain Axis on Inflammation, Addiction and Infection; The Role of Inflammatory and Glutamatergic Pathways on Fatigue; and Identifying Biomarkers to Improve Clinical Care of Patients with Brain Injury.

There will also be a poster session to highlight research conducted by NINR intramural fellows and trainees along with collaborating scientists from the NIH community and other Institutions.

For more information and to register for the event, visit <https://www.ninr.nih.gov/newsandinformation/events/symptom-science-event>.

Webinar on Mixed Methods in Disease Prevention, Health Promotion

The latest Medicine: Mind the Gap webinar will explore how quantitative research methods have the most power to appeal to collaborators in funding and policy, while qualitative studies can enhance the validity or trustworthiness of inferences and assertions by providing mutual confirmation of findings.

It will be held Monday, Mar. 27 from noon to 1 p.m. and registration is required. Speaker is Dr. Leonard A. Jason, professor of psychology at DePaul University and director of the Center for Community Research.

Jason is a former president of the division of community psychology of the American Psychological Association. He has served as vice president of the International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and as chair of the research subcommittee of the U.S. chronic fatigue syndrome advisory committee.

Jason will accept questions before and during his presentation via email at prevention@mail.nih.gov and on Twitter with #NIHMTG. Register for the webinar at <https://nih.webex.com/nih/onstage/g.php?MTID=e13cfa0afb1a68cfd13887e2462f27beb>.

NIH’s D.C. Presence Deemed Historic

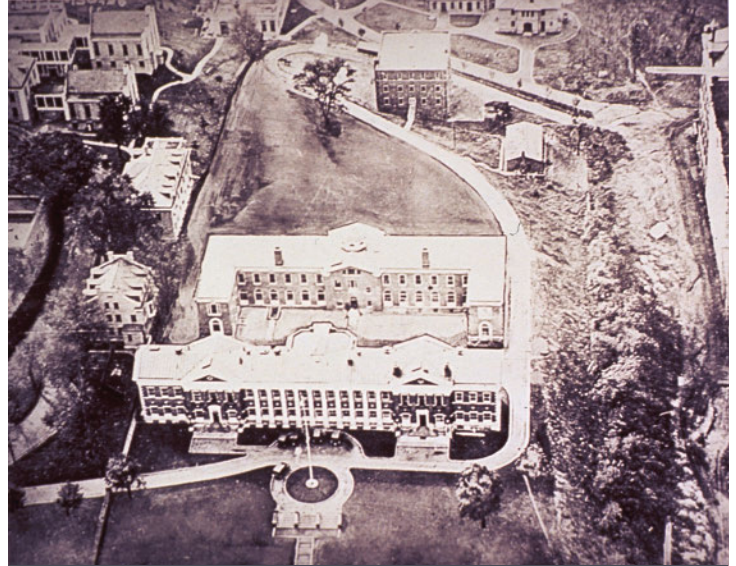
In January, a small cluster of buildings at Observatory Hill in Foggy Bottom were added to the National Park Service’s Historic Register through the efforts of former employees of the Office of Strategic Services (OSS), which later became the Central Intelligence Agency. What does this have to do with NIH? The buildings were constructed for and first occupied by NIH—which this year marks its 130th anniversary—before it moved to its current Bethesda campus.

In 1901, when NIH was still the Hygienic Laboratory, Congress authorized construction at the 25th and E Street site of a new building. Responsibility for studying and tracking infectious diseases had just been given to the Hygienic Laboratory—there would be no CDC for decades. The next year, the regulation and licensing of commercially produced serums and vaccines also became the Hygienic Laboratory’s responsibility (now FDA’s). In 1919, another building was added to the site. In 1930, the Hygienic Laboratory became the National Institute of Health—singular—with the responsibility for anything to do with disease, and more buildings were added to the Observatory Hill site.

But there was a limit to the site’s capacity. With its increased duties, personnel and animals, NIH needed more room and cutting-edge laboratories. Luke and Helen Wilson donated land in Bethesda in the mid-1930s for a campus for NIH, and most of the laboratories had moved to Bethesda by 1939. The campus was formally dedicated by President Franklin Roosevelt on Oct. 31, 1940.

The story of how NIH moved to Bethesda can be found in *70 Acres of Science* at <https://history.nih.gov/research/downloads/70acresofscience.pdf>.

During World War II, the buildings that NIH left behind at 25th and E Streets NW were turned over to the OSS, which was created in 1942. Perhaps William “Wild Bill” Donovan, head of OSS, and his staff were a little nervous about occupying buildings associated with medical research. But it is fortunate that their colleagues saved these historically important buildings for posterity.—**Michele Lyons**



Recently added to the National Park Service’s Historic Register were buildings in Washington, D.C., that originally housed NIH, but later became headquarters for a spy agency.



NIAMS Hosts Fellows for Symposium

NIAMS recently hosted a symposium in conjunction with the American College of Rheumatology-European League Against Rheumatism Exchange Program. The program promotes the international exchange of clinical and research skills, expertise and knowledge within rheumatology. It recognizes outstanding health professionals in both laboratory- and clinic-based research and provides exposure to the work being done by colleagues overseas. The all-day event, organized by NIAMS clinical director and program host Dr. Richard Siegel (standing, seventh from l), featured research presentations from exchange fellows as well as NIAMS faculty and Scholars in Translational Research. The meeting also offered networking opportunities for NIH staff and exchange program participants. Keynote sessions by Dr. Daniel Kastner (standing, l), NHGRI scientific director, and Dr. Constantino Pitzalis (not shown), program host at Queen Mary University of London, highlighted the day.

PHOTO: REAYA REUSS



At the Clinical Center model, CC CEO Dr. James Gilman (r) provides the new HHS secretary (c) with an overview of the research hospital complex as Collins looks on.



Price (l) meets CC patient Judy Anderson, who experienced a complete cancer regression under the care of NCI Surgery Branch chief Rosenberg (c). Following his Feb. 21 visit, Price took to social media to acknowledge NIH's work and to thank Collins and company for a warm welcome. He also promised to return for a longer tour.

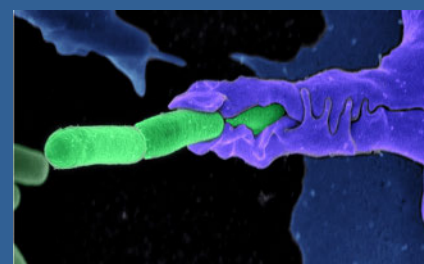
Secretary

CONTINUED FROM PAGE 1

Price also met a patient, Judy Anderson, a 51-year-old Florida resident “who had a complete cancer regression of metastatic breast cancer in the lungs and liver due to our new immunotherapy approach targeting

the unique mutations in her cancer,” explained Rosenberg.

Following the visit and promising to return for longer briefings, Price tweeted, “The @NIH is doing incredible work to improve lives, turning discovery into health. Thank you @NIHDirector and team for the warm welcome.”



ON THE COVER: Multiple anthrax bacteria (green) being enveloped by an immune system cell

IMAGE: CAMENZIND G. ROBINSON, SARAH GUILMAN & ARTHUR FRIEDLANDER, U.S. ARMY MEDICAL RESEARCH INSTITUTE OF INFECTIOUS DISEASES



Above, getting acquainted with Price (r) are NIH senior leaders (from l) Collins, NIAID director Dr. Anthony Fauci, Gilman, acting NCI director Dr. Douglas Lowy and NHLBI director Dr. Gary Gibbons. Below, in the Clinical Center's Medical Board Rm. for a meeting with NIH's senior leadership are (from l) Price, NIAMS director Dr. Stephen Katz, NIBIB director Dr. Roderic Pettigrew, NIDA director Dr. Nora Volkow, NIH principal deputy director Dr. Lawrence Tabak, Collins and Fauci.

PHOTOS: CHRIS SMITH



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Burton engages with an audience member.

Burton

CONTINUED FROM PAGE 1

Seminar Series talk in Masur Auditorium. “It’s also the ability to thrive, grow and be effective in the face of adversity, challenge and change.”

When faced with a challenge, resilient people think differently. They exhibit mental toughness and constructively talk to themselves when under pressure.

“That doesn’t mean when stress first hits them that they don’t necessarily fall apart,” Burton explained. “Resilience can look pretty messy. Resilience can start out with a whole lot of yelling and crying and feeling like you’re not going to make it. That’s absolutely okay.”

She argued that resiliency is most needed when people must do more with less, adapt to big changes quickly and meet tight deadlines and high expectations.

“In order to be resilient, it’s critical to understand why you are here,” she said. “If you understand why you’re here, it helps you to answer other questions about what you should be doing—especially when you’re in the midst of a challenge.”

There are several ways to augment resilience. First, you must be able to “picture the possibilities.” To do that, people must understand their purpose, which she likened to a compass—both guide you where you need to go. Everyone, she said, has a unique purpose. Some, for example, bring joy to others or explain complicated information.

Fear, however, can prevent people from moving forward even if they know what they need to do. We need to recognize it’s there and talk through it. “Fear is normal, but it’s not a stop sign,” Burton said.

Resilient people also learn from their failures, which can nudge a person in a new direction. Failure, she noted, doesn’t define anyone’s intelligence, capability or talents. Rather, it’s an opportunity to learn about oneself and do better in the future.

★ ★ ★

“Have something you do. Not because it’s something you perform well at, but simply because it brings you joy.”

-VALORIE BURTON

★ ★ ★

After she graduated from high school, Burton enrolled in the U.S. Air Force Academy. Her first year didn’t go as planned and she was placed on academic probation. She left after one year. Although she failed, “It pushed me in a new direction.” She learned a lot about herself that she wouldn’t have otherwise known.

Resilient people also know when to reach out to others for help. Optimistic people should make an effort to seek out pessimistic people, while pessimistic people should seek out optimistic folks.

Burton said these groups put things in perspective. Optimists don’t worry about events outside of their control; they focus on what they can control and do what they can. Resilient people avoid what she calls “catastrophizing.”

“Catastrophizing is when you go from zero to dead in 10 seconds after you’ve discovered something stressful,” she explained. “If you’re a catastrophizer, you typically don’t stop at the first thought.”

An example of catastrophizing is when

a boss asks an employee to stop by his or her office in 5 minutes. Some people will irrationally think they are getting fired. From there, thoughts spiral downward—they will lose their house and their children because they have no salary.

Burton advised catastrophizers to be aware of this tendency.

“If we become aware of what we are saying to ourselves, we can be very intentional about shifting our thoughts,” she explained.

The most resilient people think accurately, “which means they acknowledge when there is a problem.” Although they recognize problems, they are optimistic about navigating through. For leaders, “optimism is essential,” Burton added.

Additionally, those who are resilient think about how they can give during tough times. “When we’re feeling hopeless, one of the best things we can do is help someone,” she said. Serving others puts things in perspective.

Finally, Burton said resilient folks do things that make them happy, to “cultivate



Audience members interact at the recent Deputy Director for Management Seminar. Many of the talks in the series include participation by attendees.

PHOTOS: ANDREW PROPP

APRIL 5

Wagers To Give Mahoney Lecture

Dr. Amy Wagers, the Forst family professor of stem cell and regenerative biology at Harvard University, will discuss “Stem cells, aging and aging stem cells” Apr. 5 at 3 p.m. in Masur Auditorium, Bldg. 10. Her presentation is the annual Florence S. Mahoney Lecture on Aging, sponsored by NIA and part of the NIH Director’s Wednesday Afternoon Lecture Series.

Wagers is a leader in the field of stem cell biology. Her groundbreaking research has uncovered new migratory pathways and signaling networks that regulate the function of hematopoietic stem cells. Understanding how these cells work could lead to better treatments for a range of diseases including cancer, anemia and diabetes. Wagers will discuss the fundamental principles that govern tissue aging and determine stem cell function in organ regeneration and degenerative disease.

Wagers received her Ph.D. in immunology and microbial pathogenesis from Northwestern University and completed postdoctoral training in stem cell biology at Stanford University. She has received numerous awards for her work in stem cell biology, including the Vincent Cristofalo “Rising Star” Award from the American Federation of Aging Research (2015), NIA’s Nathan Shock Award (2014), the New York Stem Cell Foundation-Robertson Stem Cell Prize for Significant Achievement in Translational Research (2013), Presidential Early Career Award for Scientists and Engineers (PECASE, 2010), Glenn Foundation Award for Research in Aging (2010), Howard Hughes Medical Institute Early Career Award (2009) and NIH Director’s New Innovator Award (2008). She is a recipient of multiple NIH grants from several institutes.

The annual Mahoney Lecture is named in honor of Florence Stephenson Mahoney (1899–2002). She devoted the last half of her life to successfully advocating for the creation of NIA and increased support for NIH.

There will be a reception and an opportunity to talk with the speaker in the NIH Library immediately following the lecture.

D.C. High Schooler Shadows NIH Engineers in Lab

In observance of National Engineers Week, Feb. 19-25, National Institute of Biomedical Imaging and Bioengineering intramural researchers provided a District of Columbia high school student with a unique professional shadow day experience.

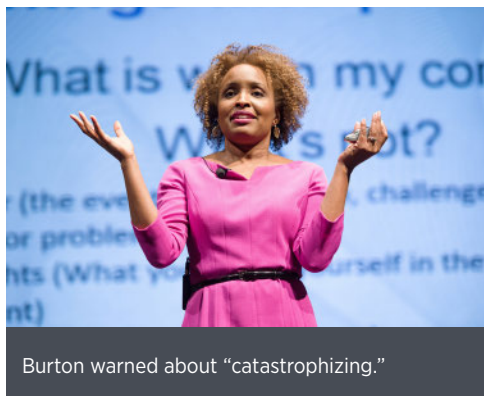
Ahmed Elvis is in the 11th grade at Phelps Architecture Construction and Engineering (ACE) High School and participates in the Academy of Engineering program there. His professional shadowing opportunity on Feb. 17 was arranged with Dr. Hank Eden, deputy scientific director, NIBIB, who provided Elvis with an overview of biomedical imaging and bioengineering, and with Dr. Nicole Morgan, NIBIB staff scientist and chief of the microfabrication and microfluidics unit, trans-NIH shared resource on biomedical engineering and physical science, who introduced Elvis to activities in the unit’s lab.

This is the third year that Phelps has held an Engineering Shadow Day for students to observe engineers at work. It is the second year that Eden and Morgan have participated as mentors. Phelps provides students preparing to pursue a career in an engineering field with access to intellectually challenging studies in engineering, mathematics, science and technology. An integral goal included in the ACE mission is to encourage more women and underrepresented minorities to pursue STEM fields.



NIBIB’s Dr. Hank Eden (l) and Dr. Nicole Morgan (r) introduce Ahmed Elvis, a student at Phelps ACE High School, to the work of a professional engineer.

PHOTO: REA RAVIN



Burton warned about “catastrophizing.”

positive emotion.” They plan events to look forward to—whether that’s a long nap or a vacation—and take breaks to recuperate after accomplishing a goal.

“Have something you do. Not because it’s something you perform well at, but simply because it brings you joy,” Burton concluded. **R**

Hopp, Chen Have New Roles at NCCIH

Dr. Craig Hopp and Dr. Wen Chen of the NCCIH Division of Extramural Research recently assumed new roles within the division.

Hopp has been appointed deputy director of the division. Previously, he was acting chief of NCCIH’s Basic and Mechanistic Research in Complementary and Integrative Health Branch and a program director. In addition to his duties as deputy director, he will continue to oversee administration of the NCCIH Product Integrity Policy, serve as NCCIH lead on large-scale projects such as the NIH Centers for Advancing Research on Botanical and Other Natural Products Program and help shape the center’s research priorities. Hopp holds a Ph.D. in pharmacognosy from Purdue University.



Chen is new acting branch chief of basic and mechanistic research, overseeing NCCIH’s portfolio on the neurobiology and integrative physiology of mind and body programs and of natural products. She is also the center’s lead on various NIH-wide activities, including the NIH Common Fund’s SPARC program and the BRAIN Initiative. Chen received her Ph.D. in biological chemistry and molecular pharmacology from Harvard University.



PHOTOS: LISA HELFERT



At left, Dr. Charles Sawyers lectures at NIH. CC CEO Dr. James Gilman (l) and NCI scientific director for clinical research Dr. William Dahut (r) congratulate Sawyers as 2017 Distinguished Clinical Research Scholar.

PHOTOS: ERNIE BRANSON

Sawyers

CONTINUED FROM PAGE 1

Research Scholar and Educator-in-Residence Lecture, a segment in the Contemporary Clinical Medicine Great Teachers series.

Part traditional Grand Rounds, part pep talk for young investigators early in their research careers, the presentation concluded Sawyers' 2-day visit to NIH, where he met with clinical and lab fellows, medical students and other trainees as well as various senior investigators for state-of-the-science conversations.

"I'll try to give a lecture that appeals to everybody in the audience, including a lot of prostate cancer experts, who I've also met with," Sawyers said, acknowledging the challenge of tackling in 1 hour a complex topic for attendees at various points along the career spectrum from entry level to advanced. "I'm going to give you a bit of a whirlwind tour, with a little bit of history to go with it."

Outlining his lecture's general premise, Sawyers said resistance to targeted therapies can occur by different mechanisms.

He began by tracing his group's current theories on prostate cancer drug resistance back to 2001 research involving patients experiencing a similar effect using the drug Gleevec (imatinib) to combat chronic myeloid leukemia.

That year, he showed that 95 percent of first-phase CML patients treated with Gleevec experienced a long-lasting remission. About 70 percent of patients with late-stage CML (also called blast crisis CML) went into remission on Gleevec, but the remission lasted only a few months, the 2001 data showed.

Why didn't remission hold? Sawyers wanted to know. The reason was in the genes—a single mutation in the kinase domain.

Some 15 years ago, his team included a then-grad student in his lab, Mercedes Gorre, and then-clinical fellows Neil Shah and Mike Burgess. Ultimately they revealed

"the first explanation for why patients with CML develop resistance to Gleevec," Sawyers said, pointing out career parallels between his group back then and NIH trainees he recently met—"physicians in medical school who took time out to do research."

Many of his former trainees now have positions as independent investigators, he reported.

That research team went on to discover that the kinase mutation could occur at not just one site, but several. During the year that followed, Sawyers said, he and his colleagues became dismayed. They were stumped about how to solve the problem.

"Then," he said, "we serendipitously learned about crystallography work from John Kuryian's group and formed a collaboration with his team. A eureka moment came as we modeled these [mutation] structures." Turns out, the mutation interfered with kinase's ability to form into an optimal shape to bind with Gleevec.

Further proving the organic and synergic nature of medical research, a scientist at the pharmaceutical firm Bristol-Myers Squibb happened to hear a talk Sawyers gave about the crystal models. The pharma investigator contacted Sawyers. A BMS team had a compound—dasatinib—that Sawyers might want to test against the kinase mutations.

In 2009, Sawyers shared the Lasker-DeBakey Clinical Medical Research Award for the work developing imatinib—and later dasatinib, the drug that combats imatinib resistance—as CML therapies.



Sawyers and NIH director Dr. Francis Collins chat before the lecture.

Fast forward to 2017. Sawyers and his current team are studying prostate cancer treatments. He said he's often asked: How did you jump from CML to prostate cancer?

"The theme is resistance," Sawyers answered, "and in this case resistance to hormone therapy."

Advanced prostate cancer cells feed on androgen hormones, he explained. Treatments to combat the cancer suppress that food source. He and his group co-discovered enzalutamide, an anti-androgen drug approved by the FDA in 2012 to treat metastatic prostate cancer.

But Sawyers' team also identified several ways tumor cells can adapt to lack of androgen, with determined cells even going so far as to change their biological identities.

The team documented what they called "identity fraud" or "lineage plasticity" after years of collaboration with several other research groups, including the Prostate Cancer Foundation, cBioPortal for Cancer Genomics and a 7-lab consortium affiliated with Stand Up to Cancer's Dream Team studying prostate cancer. Sawyers' group published the work in *Science* in January.

Concluding his lecture, he said he and colleagues now have several questions they're pursuing: What genotypes are predisposed to reprogram themselves? Does drug treatment speed up the plasticity? What molecular events drive the reprogramming and are there ways to intervene?

Sawyers closed by observing that the cell identity changes his group found in advanced prostate cancer can also translate to other malignancies.

"You could draw a similar analogy with lung cancer treated with EGFR drugs and with BRAF-mutant melanoma," he said.

Sawyers ended with a public service announcement: Scientists, step up your data-sharing efforts. His and 7 other cancer centers formed a partnership with the American Association for Cancer Research called GENIE, he noted.

"We released data from 19,000 patients sequenced in routine clinical practice, with the idea that we have much to learn and we need large numbers," he said. "The model by which we convened the 8 centers was a lesson in how to play in the sandbox and how to get institutions and legal departments to work together." **R**

Study Finds Effective Interventions to Prevent Alcohol Use Among Youth

Community-based and individual-level prevention strategies are effective ways to reduce alcohol use among American Indian and other youth living in rural communities, according to a new study supported by NIAAA; NIDA also provided support for the work.

"This important study underscores our commitment to finding evidence-based solutions for alcohol problems in American Indian and other underserved populations," said NIAAA director Dr. George Koob. "This study is one of the largest alcohol prevention trials ever conducted with an American Indian population and the first to demonstrate the effectiveness of screening and brief counseling intervention in significantly reducing youth alcohol use at a community level."

Although American Indian teens drink at rates similar to other U.S. teens, they have a higher rate of early onset alcohol use compared to other groups and higher rates of alcohol problems. Rural youths, including those who are a racial minority relative to their community, are also at increased risk for alcohol misuse. Early prevention is critical in these populations, but both American Indians and rural communities have been underrepresented in studies aimed at finding effective solutions for underage drinking.

To address this gap, researchers worked with the Cherokee Nation, the second largest American Indian tribe in the United States, to implement a rigorous research trial of two strategies to reduce underage drinking and its consequences. Communities Mobilizing for Change on Alcohol is a community-organizing intervention designed to reduce alcohol access, use and health and social consequences among underage youths. The second strategy, called CONNECT, is an individually delivered screening and brief intervention presented in schools.

The study was conducted within the 14 counties of northeastern Oklahoma that comprise the Cherokee Nation jurisdictional area, which is home to about 40 percent of the tribe. While Cherokee citizens constitute a significant proportion of the population, whites and other racial/ethnic minorities also live within this area. Results of the trial are reported in the March 2017 issue of the *American Journal of Public Health*.

"Community organizing has been used effectively in multiple other health intervention trials and appeared to be an optimal strategy to engage diverse citizens in these multicultural communities," explained research leader Dr. Kelli Komro of the Rollins School of Public Health at Emory University.

Key Step Discovered in DNA Damage from Oxidative Stress

Humans need energy to function and yet a naturally occurring process that generates power for the body can also harm its cells. Cellular mitochondria produce energy, as well as molecules known as reactive oxygen species (ROS). Through a process called oxidative stress, ROS harm cellular DNA by producing frayed ends that cannot be properly fixed during DNA repair processes. The presence of broken DNA will trigger the cell to self-destruct. This is one way the body preserves DNA integrity.

Based on work done by research fellow Dr. Melike Caglayan, a team led by Dr. Sam Wilson reported in *Nature Communications* how the damage from oxidative stress leads to DNA strand breaks, and ultimately, cell death. Using biochemical and cell biology methods, along with X-ray



crystallography, the scientists demonstrated a subtle way that cells can accommodate the damage inflicted by ROS.

The killing power of ROS is important for the process known as innate immunity, or the natural immunity a person is born with. When a bacterium enters the body, a white blood cell activates an immune cell called a macrophage, which douses the bacterium with ROS. Just as ROS causes breaks in human cellular and mitochondrial DNA, it also breaks the bacterium's DNA, thus killing it. The scheme is a resourceful way to kill living things that could make a person sick, but the ROS response is also triggered when the invaders are particles, such as those in cigarette smoke or smog. In human lung cells, the process may eventually lead to fibrosis, or the thickening or scarring of tissue. Oxidative stress is also linked to chronic lung disease, cataracts, cardiovascular disease and some neurodegenerative disorders. The scientists hope the new findings will lead to better understanding of the origins of these diseases.

Youth with Type 2 Diabetes Develop Complications More Often Than Type 1 Peers

Teens and young adults with type 2 diabetes develop kidney, nerve and eye diseases—as well as some risk factors for heart disease—more often than their peers with type 1 diabetes in the years shortly after diagnosis. The results are the latest findings of the SEARCH for Diabetes in Youth study, published Feb. 28 in the *Journal of the American Medical Association*.

Funded by NIH and the Centers for Disease Control and Prevention, SEARCH researchers examined how quickly and often youth developed signs of kidney, nerve and eye diseases, among the most common complications of diabetes. They also measured several risk factors for heart disease. Participants had diabetes an average of under 8 years at the end of the study.

The study is the largest of its kind in the United States. Key findings are:

- For youth with type 2 diabetes, nearly 20 percent developed a sign of kidney disease by the end of the study, compared to about 6 percent of youth with type 1 diabetes.
- For youth with type 2, about 18 percent developed nerve disease, versus about 9 percent with type 1.
- For youth with type 2, about 9 percent developed eye disease, compared to about 6 percent of youth with type 1.
- Measures for two risk factors for heart disease (hypertension and arterial stiffness) were greater for youth with type 2 but close to equal for a third risk factor (cardiovascular autonomic neuropathy).
- Though youth with type 2 diabetes showed signs of complications more often in nearly every measure than their peers with type 1, many youth in both groups developed complications.

"There's often the assumption that young people don't develop complications from diabetes, but that's just not true. We saw that young people with diabetes are developing signs of major complications in the prime of their lives," said Dr. Barbara Linder, a study author and senior advisor for childhood diabetes research at NIDDK. "Particularly for youth with type 2, this research demonstrates the clear need to learn how to reduce or delay the debilitating complications of diabetes, itself a huge challenge for young people to manage."



Trailers

CONTINUED FROM PAGE 1

Trailer 1, officially labeled CC TR 10B, will be used by NCI's Surgery Branch to engineer immune cells for cancer therapy. At least three more modules are planned to help fulfill NIH's sterile product and cell-processing needs.

"The future trailers are intended to supplement part of the department of transfusion medicine, called the cell-processing section, which generates engineered cells for different studies," said Dr. Andrew Griffith, deputy director of intramural clinical research.

The trailers provide a space-saving, compliant environment for investigators to develop and manufacture sterile products used in their studies. And, these modules offer a way to meet good manufacturing practice (GMP) standards.

"In [scientists'] laboratories, from a compliance standpoint, air purity, air flow and pressurization were fighting against [investigators] all the time and that increases the risk of product failure," said Last. "When a facility works with you and provides the pristine environment and the equipment is working...that dramatically reduces the

risk of product contamination and failure. It increases throughput...and it's better for patient safety."

Trailer 1, the viral vector unit, will be devoted to NCI's immunotherapy research. The Surgery Branch will be developing retroviruses that enable them to introduce genes into cells to create new immunotherapies.

"The trailer is going to enable us to resume what I think is very high-priority research developing these new gene therapy approaches for cancer," said Dr. Steven Rosenberg, chief of the branch. "We can now vigorously resume our studies in developing gene therapies for common epithelial



The new trailer is located at the ambulance entry to the Clinical Research Center on the west side of the hospital. Several other trailers are on order.

PHOTOS: ERNIE BRANSON

cancers that kill over 90 percent of everyone who dies of cancer. So this trailer is going to be a major asset for us."

Trailer 2, on order, will also support NCI research and serve as a backup to the CC pharmacy department. "We understand these trailers are unlikely to adequately support clinical research in these areas by

"Patients in the hospital need doses immediately," said Last, "and the only place on campus to do that, other than the Clinical Center's pharmacy, would be these trailers."

At least two additional trailers are planned for cell-processing activities that will support the research of multiple ICs. "It's about creating more qualified space to



"The trailer is going to enable us to resume what I think is very high-priority research developing new gene therapy approaches for cancer. We can now vigorously resume our studies in developing gene therapies for common epithelial cancers that kill over 90 percent of everyone who dies of cancer. So this trailer is going to be a major asset for us."

-DR. STEVEN ROSENBERG



themselves," said Dr. Bill Dahut, NCI's scientific director for clinical research. "There are planned renovations in the CC to help [which likely will take years to complete] so right now we're looking to these trailers to support these activities on a grander scale."

Both trailers are to be equipped with the HVAC system and tools to meet an emergency need for compounding standards for sterile products and hazardous medications in the event of an unplanned downtime of the CC pharmacy department clean room. In the event of an emergency in the hospital, the trailers would also provide an environment for compounding patient medications.

continue the science," said Dondi Pulse-Earle, associate director for facilities, Office of Research Support and Compliance. "The plan is for strategic coordination of the work for all trailers to be fully operational and utilized."

The software and controls in each trailer are designed for multiple users and uses, offering the flexibility to change quickly between programs by the day to accommodate different or shorter research protocols. Keeping operations running smoothly in the trailers will require a campaign manager to acquire the proper materials and oversee regulatory



Interior of CC Trailer 10B

requirements, maintenance, cleaning and safety during and between protocols.

“Another fascinating challenge is trying to anticipate science that doesn’t exist yet using materials that don’t exist yet,” said Last.

His team is working with PIs, IC directors and NIH senior leadership to anticipate changing needs so they can stay in front of the research curve.

“Nobody knows what the NIH is going to be doing 5 years from now,” he said. “These systems need to be available for these scientists to prove a concept if they come up

they’re going to develop.”

The additional trailers will be located next to the CC, though their exact location has not yet been determined. Another facility, the vacant Bldg. 53 (an old power substation) adjacent to Bldg. 13, is being retrofitted for NCI’s use.

“[The trailers provide] a short-term solution to close gaps,” said Last, “but also a long-term solution given their long life expectancy—of 10-12 years—to stand by as new, emerging manufacturing processes are developed.” **R**

with something new... so we can rapidly move researchers into these units and configure them for specialty use.”

And, the fact that the trailers are self-contained units prevents possible cross-contamination.

“Whatever PIs do in these modules, it can’t spread to the next clean room,” said Last. “This is a good idea for the long term for NIH because we don’t know what kind of science



Dr. Namandjé N. Bumpus of Johns Hopkins will give NIGMS’s annual lecture for undergraduate students.

PHOTO: KEITH WELLER/JOHNS HOPKINS MEDICINE

2nd NIGMS Early Career Investigator Lecture Set, Apr. 5

Dr. Namandjé N. Bumpus, a molecular pharmacologist at Johns Hopkins University School of Medicine, will give the NIGMS Director’s Early Career Investigator Lecture on Wednesday, Apr. 5 at 2 p.m. in the Natcher Conference Center, balcony A.

During her talk, titled “Drug Metabolism, Pharmacogenetics and the Quest to Personalize HIV Treatment and Prevention,” Bumpus will describe her studies on how the body breaks down and distributes antiretroviral drugs. She hopes that through a clearer understanding of these processes in cells and tissues, we will move toward predicting drug responses in a given person.

After a 30-minute lecture, she’ll answer questions from students about her research and career path. Bumpus is an associate professor of medicine in the division of clinical pharmacology and an NIGMS-funded recipient of the Presidential Early Career Award for Scientists and Engineers.

Her talk is part of an annual series that highlights the achievements of NIGMS’s early career grantees.

Open to everyone in the scientific community, the lectures are designed to introduce undergraduate students to cutting-edge science while inspiring them to pursue biomedical research careers. NIH trainees are encouraged to attend the lecture and submit questions in advance via info@nigms.nih.gov or #ecilecture on Twitter.

For details, see <https://www.nigms.nih.gov/News/meetings/ECI/Pages>.

1ST IN NEW SERIES

ULT Freezer Show Scheduled for Apr. 26

The NIH Division of Scientific Equipment and Instrumentation Services will host NIH DSEIS Presents: The ULT Freezer Show from 10 a.m. to 1:30 p.m. on Wednesday, Apr. 26 in the Bldg. 10 south lobby.

Intramural principal investigators, lab managers and other interested researchers are invited to inspect ultra low temperature (ULT) freezers that meet new energy-efficient requirements. (See <https://nems.nih.gov/programs/Pages/NIH-Ultra-Low-Temperature-Freezer-Policy.aspx> for details.)

DSEIS staff will also be on hand to answer questions about options for obtaining and maintaining ULT freezers and other scientific equipment.

According to Tammie Edwards, DSEIS acting director, “This event is just one way DSEIS is fulfilling its mission to help members of the NIH intramural community acquire and maintain scientific equipment and laboratory instrumentation.”

The ULT Freezer Show is the first in the NIH DSEIS Presents series of on-campus events for the intramural research community. Each event will feature a different type of equipment or instrumentation so that intramural researchers can get “up close and personal” with the tools they need to conduct their important work.

For more information about DSEIS, visit <http://dseis.od.nih.gov>.

For equipment sales and rental, contact Anju Verghese at (301) 496-9748 or email rental@ors.od.nih.gov. For equipment maintenance, repairs and fabrication, contact Jerry Tyus, (301) 496-4131 or email DSEIS_repairs@nih.gov.

Khalsa Named Director of NCCIH Extramural Activities Division

Dr. Partap Khalsa has been named director of the Division of Extramural Activities at NCCIH.

He began his NIH career in 2006 as a program director in NCCIH's Division of Extramural Research, in which he administered the center's portfolio related to manual (hands-on) therapies. Topics ranged from massage, soft-tissue



Dr. Partap Khalsa

PHOTO: LISA HELFERT

therapies and manipulation/mobilization to mechanisms, translational tools and clinical trials, with a particular emphasis on musculoskeletal pain.

In 2014, Khalsa became deputy director of the extramural research division. Among his other accomplishments have been serving as the NIH co-chair of the task force on chronic low-back pain, a

group of external scientific experts convened by NIH, and administering NCCIH's Centers of Excellence program in complementary and integrative therapies.

Khalsa received a doctor of chiropractic degree from Southern California University of Health Sciences and led a successful private practice for a decade. He then decided to pursue additional scientific training, obtaining an M.S. in biomedical engineering from Boston University and a Ph.D. in biomedical sciences from Worcester Polytechnic Institute and the University of Massachusetts Medical School.

He was a postdoctoral fellow in neurophysiology at Yale University School of Medicine. Khalsa came to NCCIH from the State University of New York at Stony Brook, where he was a tenured associate professor and vice chairman in the department of biomedical engineering.

"I am delighted to announce this appointment, which followed a rigorous nationwide search," said Dr. Josephine Briggs, NCCIH director. "Dr. Khalsa has a sustained history of exceptional accomplishment, recognition and leadership in the field of complementary and integrative health. He has brought the center unique expertise; has developed a strong program in complementary therapies with a particular focus on biomechanics, manual therapies and back pain; and is an exceptional manager of clinical and basic research as well as an expert in NIH administrative operations."

Mandler Retires from CSR

BY PAULA WHITACRE

"The first child of the first child"—that's how Dr. Raya Mandler describes her childhood on Ramat Rachel, a 95-year-old kibbutz near Jerusalem, Israel. Mandler transferred her love of farming and closeness to animals and plants on the kibbutz to a biological scientific career that led her to NIH. She recently retired from the Center for Scientific Review as a scientific review officer.



Dr. Raya Mandler

Mandler's grandparents were early pioneers in Israel. Her mother was the first child born on the kibbutz, a momentous event for the new community; her father came to Israel from Nazi Germany as a young man in the 1930s. In turn, Mandler was the oldest child in a family with another sister and a brother.

"I grew up immersed in nature, so looking back, it was natural that I studied biology," she said. Mandler remembers creating a make-believe cancer research lab as a child, complete with beakers, flasks and colored water as "chemicals," a harbinger of her career to come.

She attended Haifa University and taught life sciences in high school for 2 years. During a summer program at the Weizmann Institute, a professor encouraged her to apply as a graduate student. "The Weizmann Institute exposed me to the fact that science flourishes on international collaborations," she said. She studied at Case Western University and the Uniformed Services University of the Health Sciences, earning her Ph.D. in physiology.

Mandler spent 8 years as a postdoc and staff associate at NCI. She was part of a team that focused on studies of membrane receptors that could be targeted for highly specific oncological therapy. The work culminated in an international patent for the development of immunoconjugates as novel reagents in breast cancer treatment.

Her switch to extramural research came when, she said, "I wanted to impact science in a different, broader way." An exhibit about CSR, which she happened upon in Bldg. 31, intrigued her, and she applied for an internship in the center.

Dr. Noni Byrnes, director of CSR's Division of Basic and Integrative Biology, coordinated the intern program. Mandler then became an SRO supporting cell biology study sections under Byrnes. Byrnes said she appreciated Mandler's candor, professionalism and drive to keep learning. "She also has

tremendous scientific breadth," Byrnes noted. She said these qualities enabled Mandler to handle the variety of scientific areas covered by her study sections and to recruit leading scientists as reviewers.

In 2007, Mandler was appointed to launch the molecular and integrative signal transduction (MIST) study section. "The mind power in the room [during study section meetings] was incredible," Mandler said. She worked with several Nobel laureates and, she predicted, "probably several others who will be in years to come."

"She kept us on track and focused on the big picture," said Dr. Richard A. Kahn, a former MIST chair from Emory University. "Those of us in the field will miss her voice in the conversations."

Mandler will continue conversations, but for a different purpose. A principal goal during retirement is to write a book about the kibbutz, including interviewing present and past members. As the "first child of the first child," she has an important story to share.

NCCIH's Goldrosen Bids Farewell

Dr. Martin Goldrosen, director of the Division of Extramural Activities at NCCIH, recently retired. For many years, he planned and led the activities of scientific reviewers and other NCCIH staff to ensure



Dr. Martin Goldrosen

PHOTO: LISA HELFERT

the highest quality, objectivity and accountability in the center's peer review process.

"Dr. Goldrosen's contributions to NCCIH and to the NIH have been immeasurable," said NCCIH director Dr. Josephine Briggs. "He joined NCCIH (then known as NCCAM) when it had just been established and for 16 years helped

shape the center and its direction in crucial ways. All of us will truly miss his thoughtful advice, good judgment and caring relationships with everyone with whom he worked."

Goldrosen began his NIH career in 1991 as a health scientist administrator in the Grants Review Branch of NCI's Division of Extramural Activities. In 2001, he moved to NCCIH to direct its Office of Scientific Review, a position that he held for 7 years before being appointed acting director and then director of the center's extramural activities division.

Prior to joining NIH, Goldrosen was a cancer researcher at Roswell Park Cancer Institute, focusing on tumor immunobiology. He performed the first orthotopic transplant procedure in mice, which ultimately became the standard for animal models simulating human cancer, and oversaw

several clinical immunology research programs. Concurrently, he was a research professor of experimental pathology at the State University of New York at Buffalo, where he trained dozens of doctoral and postdoctoral students who went on to become successful clinicians and scientists in oncology. His interest in mentorship continued throughout his career at NCCIH.

Goldrosen received his Ph.D. in immunology from McMaster University. His many awards and honors included the NIH Director's Award and three NCCIH Director's Awards.

Nursing Icon Abdellah Mourned

Dr. Faye Glenn Abdellah, 97, founding dean of the Uniformed Services University of the Health Sciences Daniel K. Inouye Graduate School of Nursing and retired rear admiral of the Public Health Service, died Feb. 24 after a long struggle with Alzheimer's disease. In the mid-1960s, she worked in NIH's Division of Nursing, part of the old Bureau of Health Manpower Education.

In 1937, 18-year-old Abdellah witnessed the explosion of the German passenger airship Hindenburg in Lakehurst, N.J., which became a turning point in her life. In an interview years later she said, "I could see people jumping from the zeppelin and didn't know how I would take care of them, so I vowed that I would learn nursing."



Dr. Faye Glenn Abdellah

Abdellah earned a nursing diploma from Ann May School of Nursing in Neptune, N.J., undergraduate, masters and doctoral degrees from Columbia University and did graduate work in the sciences at Rutgers University. She wrote more than 153 publications, including her seminal works *Better Nursing Care Through Nursing Research* and *Patient-Centered Approaches to Nursing*, which changed the focus of nursing theory from disease-centered to patient-centered.

She received 12 honorary degrees and numerous awards, including the Allied Signal Award in 1989 and the Institute of Medicine's Gustav O. Lienhard Award in 1992, all recognizing her innovative work in nursing research and health care.

Abdellah was the first nurse and the first woman to serve as deputy surgeon general (with Dr. C. Everett Koop) and was first nurse to hold the rank of rear admiral. Her leadership resulted in many accomplishments, including development of the first tested coronary care unit, saving thousands of lives.

Abdellah was renowned as an expert in health policies related to long-term care, the developmentally disabled, aging, hospice and AIDS.

In 1989, she retired from the PHS and went on to serve as founding dean of the Graduate School of Nursing at USUHS. In 2002, she retired with almost 50 years of government service.

Abdellah was a charter fellow in the American Academy of Nursing, later serving as its president. In 1994, she was one of the first fellows to receive the academy's highest honor, the Living Legends Award.

In 1999, she was elected to the Hall of Fame for Distinguished Graduates and Scholars at Columbia University and the following year was inducted into the National Women's Hall of Fame.

"This is an incredible loss to the nation and nursing," said Rear Adm. Susan Orsega, PHS chief nurse officer, who works at NIAID. "Her intellect,

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"We will remember [Abdellah] as a true leader whose combination of dedication, intellect and approach brought experts from many different fields together. Her prominent presence in nursing will be greatly missed."

—SURGEON GENERAL VIVEK MURTHY

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compassion and passion for excellence will be deeply missed. As a former student at USUHS, I feel personally blessed to have learned from her leadership."

"We will remember [Abdellah] as a true leader whose combination of dedication, intellect and approach brought experts from many different fields together," said Surgeon General Vivek Murthy. "Her prominent presence in nursing will be greatly missed."

The Graduate School of Nursing at USUHS, in collaboration with PHS, plans a memorial tribute to honor Abdellah and the nearly half-century of her contributions to the nation. **R**

NCI Study Seeks Brain Tumor Survivors

A study is open at the Pediatric Oncology Branch of the National Cancer Institute for children, ages 8 through 18 years, who have had a brain tumor that was treated with radiation at least 1 year ago. The study is evaluating whether a novel home physical activity program improves cognitive late effects, which may include difficulties with attention, memory and processing speed. For more information, call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read more at <http://go.usa.gov/x8MDY>. Refer to study 14-C-0116.

Patients with Epilepsy Needed

Is epilepsy taking over your life? Join the NIH Epilepsy Research Program's research study. All study-related tests, procedures and medications are provided at no cost. For more information, contact the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read about the study at <http://go.usa.gov/x9fHp>. Refer to NIH study 01-N-0139.

Study Seeks Healthy Older Adults

Healthy older adults, ages 55-70, are invited to participate in an outpatient research study investigating the benefits of tart cherry and aroniaberry supplementation on vascular health. The goal of the study is to determine whether the supplements improve blood flow and blood vessel function that can affect your heart. Eligible participants must be medication-free and in good general health. The study will be carried out in an outpatient clinic and includes 7 visits over 3-4 months. Compensation for the study is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 15-NR-0085 or visit www.clinicaltrials.gov.

People with Dry Mouth Needed

NIDCR is seeking people with dry mouth due to radiation therapy for head and neck cancer. Researchers are testing whether an investigational gene therapy using "AAV2hAQP1" increases saliva in patients who have received radiation therapy for head and neck cancer. Travel to and from the Clinical Center (within the U.S.) will be provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more online at <https://go.usa.gov/x8yXE>. Refer to study 15-D-0129.

Researchers Connect at 3rd BRAIN Investigators' Meeting

BY CHRISTOPHER G. THOMAS

The Bethesda North Marriott Hotel was invaded recently by a bunch of brainiacs—literally. For 3 days, engineers, mathematicians, neuroscientists, chemists and physicists met in workgroups to discuss the latest topics such as ultrasound neuro-modulation, embedded ensemble encoding theory of brain circuits and genetically encoded voltage indicators.

In hallways, researchers discussed plans to collaborate and share resources. And in one large room, the aisles—formed by rows of poster boards—were crowded with scientists presenting their latest work. It was the third annual BRAIN Initiative Investigator's meeting and, with more than 750 attendees, it was the biggest one yet.

Launched in 2013, the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is a large-scale effort funded by NIH, other government agencies and private organizations to equip researchers with new tools to interrogate and modulate brain activity. The hope is that these technologies will



Researchers discuss latest results at recent BRAIN Initiative investigators' meeting.

PHOTO: VIVIAN YANG

partners and advocacy groups. In addition to presenting their latest scientific results, attendees discussed how researchers can work together and share data, techniques and technologies.

"We want to bring new people with fresh ideas into neuroscience research," said Dr. Joshua Gordon, director of the National Institute of Mental Health. "There are as many engineers as neuroscientists working on BRAIN Initiative projects."

Each morning of the meeting, attendees gathered in the main hall for plenary addresses from leading scientists. Immediately after, researchers met in a

by NPR's Joe Palca; and presentations by several of the initiative's early stage researchers.

On the final day, NIH director Dr. Francis Collins announced that the recently passed 21st Century Cures Act assigned \$1.51 billion over 10 years for the BRAIN Initiative and discussed the importance of making the public more aware of the initiative.

"I'm a huge fan of this program," he said. "To see how far we have come has been truly gratifying...The BRAIN project will be successful if it changes the way in which everybody working in neuroscience approaches problems. Decades from now, I believe historians will write that by working together in novel ways, BRAIN Initiative researchers transformed the foundations of brain science and changed the course of medicine." **B**

"Our mission is to do nothing less than revolutionize our understanding of brain function."

-DR. WALTER KOROSHETZ

open a window onto the brain that will transform the diagnosis and treatment of brain disorders including schizophrenia, autism, epilepsy, chronic pain and traumatic brain injury.

"Our mission is to do nothing less than revolutionize our understanding of brain function," said Dr. Walter Koroshetz, director of the National Institute of Neurological Disorders and Stroke. "BRAIN Initiative researchers are turning science fiction into reality."

A major goal of BRAIN is to encourage researchers and organizations from diverse disciplines to work together. The annual meetings reflect this effort. Researchers and engineers from around the world were joined by staff from public and private

ballroom to discuss their latest results presented on posters. In the afternoons, attendees had a choice between small sessions where researchers made short presentations of their work, or large panel discussions on a range of topics including Global Efforts in Neurotechnology Development, Clinical Implications for BRAIN, NeuroEthics and Synergy of BRAIN Initiative Efforts.

Highlights included a brief history of the BRAIN Initiative by Thomas Kalil, formerly of the White House Office of Science Technology and Policy; a plenary talk on Brains, Behavior and Evolution by Dr. Cori Bargmann of the Chan Zuckerberg Initiative; a special evening panel on Exciting New Technologies from BRAIN co-moderated

'PROMOTING RESILIENCE'

Gewirtz Gives Next Lecture in NCCIH Series

The National Center for Complementary and Integrative Health will present the next talk in its Integrative Medicine Research Lecture Series, "Promoting Resilience in Military Families: After Deployment, Adaptive Parenting Tools," by Dr. Abigail Gewirtz on Monday, Mar. 27 at 10 a.m. in Lipsett Amphitheater, Bldg. 10. In addition, at 2 p.m., Gewirtz will be available via a Facebook Live Q&A session, www.facebook.com/nih.nccih/.

The After Deployment, Adaptive Parenting Tools (ADAPT) program is the first of its kind focused on post-deployment parenting practices in military families. Developed in response to the effects of a parent's deployment on children, the ADAPT program incorporates emotion socialization techniques including yoga, mindfulness meditation and emotion coaching.

Gewirtz will share the rationale for incorporating mindfulness approaches into a parenting program, walk through the goals and content of the ADAPT program's different formats and discuss two NIH-funded randomized trials evaluating program outcomes.

Gewirtz is director of the Institute for Translational Research in Children's Mental Health and the John and Nancy Lindahl leadership professor in the department of family social science and Institute of Child Development at the University of Minnesota.